EPA Policy on Consultation and Coordination with Indian Tribes: Draft Guidance for Discussing Tribal Treaty Rights

Summary
EPA recognizes the importance of honoring tribal treaty rights. This draft Guidance is designed to enhance EPA's consultation efforts in situations where tribal treaty rights are most likely to be relevant to a proposed EPA action.

The draft Guidance provides assistance on implementing the *EPA Policy on Consultation and Coordination with Indian Tribes* when tribal treaty rights relating to natural resources may exist in a specific geographic area that is the focus of a proposed EPA decision or action. In these instances, during consultation with federally recognized tribes, EPA will seek to obtain tribal treaty rights information in accordance with this draft Guidance. EPA will subsequently consider treaty rights information obtained to help ensure that EPA's actions do not conflict with treaty rights, and to help ensure that EPA is fully informed when it seeks to implement its programs to further protect treaty rights and resources when it has discretion to do so.

Background
EPA Administrator McCarthy released a Memorandum commemorating the 30th Anniversary of EPA's Indian Policy on December 1, 2014. The Memorandum provided a clear statement on the need to honor and respect tribal treaty rights and their role in the context of EPA's actions. EPA is developing this draft Guidance to help implement the treaty rights objectives in the Administrator's memorandum.

What does this draft Guidance do?
It provides guidance on asking about tribal treaty rights as part of the consultation process when: an EPA action occurs in a specific geographic location, treaty rights related to a natural resource or an environmental condition necessary to support the natural resource are present, and EPA's action may affect the treaty rights. This draft Guidance does not create any new legal obligations for EPA, expand the authorities granted by EPA's underlying statutes, or alter or diminish any existing EPA treaty responsibilities.

What are the next steps?
The tribal consultation period will be open for 60 days: August 17 through October 16, 2015.

Where do I go for more information?
The draft Guidance, related documents, and the tribal leader notification letter can be found at http://tcots.epa.gov.

When is the deadline for submitting comments?
The deadline to submit comments is October 16, 2015.

Where do I submit my comments?
You may submit your written comments **electronically** at:
http://www.epa.gov/tribalportal/consultation/comments-ttr.htm.

You may also submit your written comments **by postal mail** to:
Mr. Jeff Besougloff
U.S. EPA American Indian Environmental Office (2690R)
1300 Pennsylvania Avenue, NW
Washington, DC 20460

EPA Policy on Consultation and Coordination with Indian Tribes: DRAFT Guidance for Discussing Tribal Treaty Rights

Introduction

EPA recognizes the importance of honoring tribal treaty rights.[1] The purpose of this Guidance is to enhance our consultation efforts in situations where tribal treaty rights are most likely to be relevant to a proposed EPA action. Specifically, this Guidance provides assistance on implementing the *EPA Policy on Consultation and Coordination with Indian Tribes* when tribal treaty rights relating to natural resources may exist in a specific geographic area that is the focus of a proposed EPA decision or action.[2] In these instances, during consultation with federally recognized tribes (tribes), EPA will seek to obtain tribal treaty rights information in accordance with this Guidance. EPA will subsequently consider treaty rights information obtained to help ensure that EPA's actions do not conflict with treaty rights, and to help ensure that EPA is fully informed when it seeks to implement its programs to further protect treaty rights and resources when it has discretion to do so.[3] This Guidance does not, however, create any new legal obligations for EPA or expand the authorities granted by EPA's underlying statutes nor does it alter or diminish any existing EPA treaty responsibilities.

Determining When to Ask About Treaty Rights During Tribal Consultation

EPA consultation with tribes provides the opportunity to ask whether a proposed EPA action that is focused on a specific geographic location may affect treaty-protected rights. Because treaty rights analyses are complex, staff are encouraged to inquire early about treaty rights.

Based on experience to date, certain types of EPA actions, which are focused on a specific geographic area, are more likely than others to have potential implications for treaty-protected natural resources. For example, EPA review of tribal or state water quality standards as a basis for National Pollutant Discharge Elimination System permits typically focuses on a specific water body. If a treaty reserves to tribes a right to fish in the water body, then EPA should consult with tribes on treaty rights since protecting fish may involve protection of water quality in the watershed.

Another example of an action in a specific geographic area is a site-specific decision made under the Comprehensive Environmental Response, Compensation, and Liability Act, such as a Record of Decision for a site, or the potential use of Applicable or Relevant and Appropriate Requirements for a cleanup. Other examples include a site-specific landfill exemption determination under the Resource Conservation and Recovery Act or other similar types of regulatory exemptions for specific geographic areas. In each case, employing the following

[1] EPA Administrator McCarthy's December 1, 2014 Memorandum, Commemorating the 30th Anniversary of EPA's Indian Policy (hereinafter *Administrator's December Memo*).

[2] This Guidance focuses on consultation in the context of tribal treaties. EPA recognizes, however, that there are similar tribal rights in other sources of law such as federal statutes (e.g., congressionally enacted Indian land claim settlements).

[3] *Administrator's December Memo*.

questions in this Guidance during consultation may inform EPA of when treaty rights are present in the defined area and may be affected by the proposed decision.

For purposes of this Guidance, the treaty rights most likely to be relevant to an EPA action are rights related to the protection or use of natural resources, or related to an environmental condition necessary to support the natural resource, that are found in treaties that are in effect. Other treaty provisions, for example those concerning tribal jurisdiction or reservation boundaries, are outside the scope of this Guidance.

EPA actions which are national in scope, and thus not within a focused geographic area, fall outside the scope of this Guidance. Examples of such activities outside the scope of this Guidance include the development of National Ambient Air Quality Standards under the Clean Air Act or the national registration of pesticides under the Federal Insecticide, Fungicide and Rodenticide Act.

In addition, EPA should be aware that treaty rights issues in the context of compliance monitoring and enforcement actions should be considered when consulting with tribes pursuant to the *Guidance on the Enforcement Principles of the 1984 Indian Policy* and the *Restrictions on Communications with Outside Parties Regarding Enforcement Actions*. EPA should also act consistent with the *EPA Policy on Environmental Justice for Working with Federally Recognized Tribes and Indigenous Peoples*.

Questions to Raise During Consultation

EPA should employ the following three questions during consultations when proposing an action within a specific geographic area and when EPA believes that treaty rights may be present. These questions may also be employed when tribes bring to EPA's attention treaty rights concerns in other contexts. Collaboration between program and legal staff before and during consultation is an important aspect of ensuring that these questions are both asked and the answers are understood.

(1) Do treaties exist within a specific geographic area?

This question is designed to help EPA determine when a treaty and its related resources exist within the specific geographic area of the proposed action. This question is important because tribes may possess treaty rights both inside and outside reservations. In some cases, EPA may already be aware of existing, relevant resource-based treaty rights in a specific geographic area, for example, when a tribe has treaty rights within the boundaries of its reservation or near its reservation. In other cases, EPA may not be aware of the full effects of the treaty rights or EPA may find it difficult to determine when a specific geographic area has an associated treaty right. For example, some tribes in the Great Lakes area retain hunting, fishing, and gathering rights in areas both within and outside their reservation

boundaries, commonly referred to as ceded territories. Similarly, some tribes in the Pacific Northwest retain the right to fish in their "usual and accustomed" fishing grounds and stations both within and outside their reservation boundaries.

(2)What treaty rights does the tribe believe it retains in the specific geographic area?

This question is designed to help EPA understand the type of treaty rights that a tribe may retain. By asking this question, EPA can better understand the complexities that are often involved in treaty rights. Some treaties explicitly state the protected rights and resources. For example, a treaty may reserve or protect the right to "hunt," "fish," or "gather" a particular animal or plant in specific areas. Treaties also may contain necessarily implied rights. For example, an explicit treaty right to fish in a specific area may include an implied right to sufficient water quantity or water quality to ensure that fishing is possible. Similarly, an explicit treaty right to hunt, fish or gather may include an implied right to a certain level of environmental quality to maintain the activity or a guarantee of access to the activity site.

(3) How are treaty rights potentially affected by the proposed action?

This question is designed to help EPA determine how a treaty right may be affected by the proposed action. EPA should explain the proposed action and solicit input about any resource-based treaty rights. It may also be appropriate to ask the tribe for any recommendations for EPA to consider to ensure a treaty right is protected.

Post-Consultation: EPA Actions That May Affect Treaty Rights

After consultation, EPA's next steps typically will involve conducting legal and policy analysis in order to determine how to protect the rights. These analyses are often complex and depend upon the context and circumstances of the particular situation. Issues that may arise often involve precedent-setting questions or warrant coordination with other federal agencies. It is expected that the EPA lead office or region that engaged in the tribal consultation about the potentially affected treaty rights will coordinate with the Office of International and Tribal Affairs (OITA), the Office General Counsel (OGC), and appropriate Offices of Regional Counsel (ORC) to conduct these analyses. Although the details of how to conduct such legal and policy analyses are not addressed by this Guidance, the process may warrant additional consultation with tribes.

Conclusion

EPA is committed to protecting treaty rights and improving our consultations with tribes on treaty rights. As experience on tribal treaty rights is gained, EPA may modify this Guidance to meet this commitment.

ATTACHMENT A

Analysis Supporting EPA's February 2, 2015 Decision to Approve, Disapprove, and Make No Decision on, Various Maine Water Quality Standards, Including Those Applied to Waters of Indian Lands in Maine

EXECUTIVE SUMMARY

Maine's Department of Environmental Protection (DEP) submitted numerous new or revised water quality standards (WQS) to EPA for review and approval under the Clean Water Act (CWA) between 2003 and 2014. In its decisions from 2004-2013 following review of such WQS, EPA limited its approvals of the new or revised WQS to state waters outside of Indian territories and lands in Maine ("Indian lands"), and explicitly refrained from taking any action on the WQS for waters in Indian lands. In its decision today, EPA is responding to the outstanding new and revised WQS from 2003-2014 as they relate to waters in Indian lands, and, in the case of some of the WQS, also as they relate to state waters outside of Indian lands.

As summarized below and explained in more detail in the body of this decision support document, Maine has the authority to establish WQS for waters in Indian lands, subject to EPA's authority under the CWA to review and approve or disapprove such standards. After evaluating the various new and revised WQS contained in DEP's submissions from 2003-2014, EPA is today approving all of the aquatic life criteria for toxic pollutants for waters in Indian lands except for ammonia, and all but one of the new aquatic life criteria submitted in 2013 for all waters, including in Indian lands.[1] EPA is also approving a number of other WQS provisions for waters in Indian lands, as well as Maine's classifications and designated uses for those waters. EPA is disapproving Maine's human health criteria as they apply to waters in Indian lands. Finally, EPA has identified a number of provisions on which it is taking no action because they are not WQS and therefore are not subject to EPA review.

The bases for two aspects of EPA's decision today are summarized below because of their complexity -- EPA's conclusion that Maine has the authority to establish WQS in waters in Indian lands, and EPA's conclusion that Maine's human health criteria do not protect the designated uses and therefore must be disapproved.

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[1] EPA is taking no action on the ammonia criteria and certain provisions related to bacteria and pesticides, based on our understanding from discussions with DEP staff that DEP will be revising these criteria and provisions in light of recent EPA criteria recommendations and to ensure the protection of designated uses, nor is EPA taking action on the reclassification of a non-tribal water (Long Creek), pending further discussion with DEP. See section 4.8 below. EPA is also taking no action on one of the new phenol criteria for all waters pending DEP's correction of a mathematical error, which DEP has agreed to correct. See section 4.3 below. Finally, EPA is taking no action on the cancer risk level for arsenic in light of EPA's disapproval of the arsenic criteria for waters in Indian lands. See section 4.2.4 below.

The Issue: The State of Maine submitted numerous new and revised water quality standards (WQS) for EPA to approve under the Clean Water Act in the territories and lands of the federally recognized Indian Tribes in Maine – the Penobscot Nation, Passamaquoddy Tribes, Houlton Band of Maliseet Indians, and Aroostook Band of Micmacs. Under well-established principles of federal Indian law, states generally do not have authority to regulate the environment in Indian country. Maine asserts that in the Maine Indian Claims Settlement Act (MICSA) Congress granted the State jurisdiction to regulate the environment in the Tribes' lands, including the authority to set WQS. The Tribes contest that assertion, noting especially that state WQS have the potential to determine how much fish they may safely eat in waters where the Tribes fish for their sustenance. The Tribes assert the State has not adequately accounted for their sustenance fishing practices in setting the WQS submitted to EPA.

Jurisdiction to set WQS: EPA analyzed the jurisdictional provisions of MICSA extensively, including a careful review of comments from the Tribes and Maine on the jurisdictional provisions of the statute. EPA concludes that under the unique jurisdictional formula Congress established in Maine, the State has jurisdiction to set WQS in the waters on the Tribes' lands. See *Maine v. Johnson*, 498 F.3d 37 (1st Cir. 2007). But the Agency also finds that this authority is not unconstrained. EPA is required under the Clean Water Act to review state WQS, and will approve them when they comply with the Act. In these circumstances, where Maine is authorized to set WQS in tribal waters, EPA is informed by the operation of the Indian settlement acts in Maine and will require that WQS in tribal waters protect the Tribes' sustenance fishing use of those waters.

Sustenance Fishing Use in Tribal Waters: The first step in establishing and reviewing WQS is to determine the uses of the waters. In tribal waters, EPA must harmonize the CWA requirement that WQS must protect uses with the fundamental purpose for which land was set aside for the Tribes under the Indian settlement acts in Maine. Those settlement acts, which include MICSA and other state and federal statutes that resolved Indian land claims in the State, provide for land to be set aside as a permanent land base for the Indian Tribes in Maine. One clear purpose of that set aside is to provide a land base on which these Tribes could continue their unique cultures. A critical element of tribal cultural survival is the ability to exercise sustenance living practices, including sustenance fishing. There are multiple provisions in the Indian settlement acts that specifically codify the Tribes' sustenance practices. Maine general law regulating fish take accommodates sustenance fishing, and in several regards also specifically codifies the Tribes' ability to sustenance fish. The legislative record supporting the Indian settlement acts in Maine makes it clear that the statutes intend to create a land base on which the Tribes in Maine may fish for their sustenance. Therefore, EPA interprets the State's "fishing" designated use, as applied in tribal waters, to mean "sustenance" fishing; and EPA is approving a specific sustenance fishing right reserved in one of the settlement acts as a designated use for certain tribal reservation waters.

Protecting the Sustenance Fishing Use: To adequately protect that sustenance fishing use, the State must revisit two aspects of its analysis supporting the human health criteria that determine how clean the waters must be to allow the Tribes to safely consume fish for their sustenance. First, the analysis must treat the tribal population exercising the sustenance fishing use as the target general population, not as a high-consuming subpopulation of the State. EPA guidance

calls for WQS that provide a high level of protection for the general population, while recognizing that small subpopulations may face greater levels of risk. However, the Tribes are not a subpopulation using the waters on their own lands; they are the population for which that land base was established and set aside. Second, the data used to determine the fish consumption rate for tribal sustenance consumers must reasonably represent tribal consumers taking fish from tribal waters and fishing practices unsuppressed by concerns about the safety of the fish available to them to consume. The data on which the State relied to develop fish consumption rates for these WQS did not include information about the sustenance practices of tribal members fishing in their own waters, nor did they represent consumption levels that were unsuppressed by concerns about pollution. EPA concludes that the best available data that represent the unsuppressed sustenance fishing practices of tribal members fishing in tribal waters are contained in the Wabanaki Lifeways study, which looked at the historic sustenance practices of the Tribes in Maine.

EPA has received a written legal opinion dated January 30, 2015 from the Solicitor of the Department of the Interior (DOI) addressing several of the issues involved in EPA's decision. EPA sought DOI's advice because the Department is the federal government's expert agency on matters of Indian law and is charged with administering the settlement acts in Maine. *Passamaquoddy Tribe v. State of Maine*, 75 F.3d 784, 794 (1st Cir. 1996) (DOI is the department that administers MICSA). DOI has provided EPA important insight into how the Indian settlement acts in Maine address the Tribes' right to fish and the critical relationship between those rights and water quality. In making our decision on Maine's WQS, EPA has carefully considered and relied upon the DOI Solicitor's analysis, which is reflected in DOI's written opinion and is included in the administrative record for this decision.

The Remedy: EPA is disapproving Maine's human health criteria because they are not protective of human health for the target population. They are based on a fish consumption rate of 32.4 grams per day, with the exception of arsenic which is based on 138 grams per day. However, the Wabanaki study indicates that consumption values between 286 and 514 grams per day represent the sustenance fishing use in tribal waters. EPA is approving Maine's regulation requiring that human health criteria, except for arsenic, be based on a cancer risk level of no more than one in a million (10^{-6}) as applied to the Tribe's waters, because that is a reasonable level of risk for a general target population. EPA is approving nearly all the State's aquatic life criteria, because they are consistent with the Clean Water Act and unlike the human health criteria, they do not implicate the safety of fish for human consumption. The Clean Water Act gives the State 90 days to address the bases for EPA's disapproval of the human health criteria, after which time, if the State does not do so, EPA will propose and promulgate appropriate human health criteria for waters in Indian lands in Maine.

1 Background

1.1 Overview

On January 14, 2013, the Maine Department of Environmental Protection (DEP) submitted a request to EPA to approve five new or revised water quality criteria (WQC) and specifically asked EPA to approve them in all waters located in the State of Maine, including waters in the territories and lands of the federally recognized Indian Tribes in Maine.

EPA's review of the State's submission determined that when the State provided public notice on its proposed WQS revisions, it was not clear on the record that the State had solicited comment on the question of the State's authority to set WQS in waters in the Tribes' territories and lands (as explained further below, hereinafter EPA will use the term Indian or tribal "lands" to refer to the entire tribal land base in Maine). Although EPA does not customarily provide public notice for state WQS submissions, the Agency exercised its discretion in the unique circumstances of this submittal to invite public comment on the issue of applying state WQS in waters in Indian lands in Maine. EPA identified two general areas for comment. First, has the State demonstrated adequate authority to set WQS in waters in Indian lands? Second, if so, are the WQC that the State submitted based on sound scientific rationale and adequate under the Clean Water Act (CWA) to protect uses in those waters?

This document contains the detailed explanation to accompany EPA's decision letter acting on the State's request that EPA approve these WQS for waters in Indian lands. In addition, from 2004 through 2010, in response to Maine's 2003 to 2009 submittals of new or revised WQS, EPA approved WQS for waters outside of Indian lands, but specifically stated that EPA was taking no action to approve or disapprove WQS within Indian lands. Today's decision addresses all of Maine's WQS submissions from 2003 through 2014 as they relate to waters in Indian lands, as well as certain submissions on which EPA has not yet acted for any waters in Maine.[2]

In summary, EPA finds that Maine has jurisdiction to set WQS for waters in Indian lands. Because EPA has not yet approved any of Maine's WQS for waters in Indian lands, EPA is first approving the State's classifications and associated designated uses for these waters. All of the relevant classifications include a designated use of "fishing," which the Agency interprets to include sustenance fishing consistent with these Tribes' sustenance practices in waters on their lands. EPA is also approving a specific sustenance fishing use for the inland waters of the reservations of the Penobscot Nation and Passamaquoddy Tribe. EPA is approving all but one of the State's aquatic life criteria. EPA has determined that Maine's human health criteria, however, do not adequately protect the designated use of sustenance fishing in the waters in tribal lands and, therefore, do not comply with the CWA's requirement that criteria protect the

[2] EPA is also approving today certain pre-2004 WQS for waters in Indian lands to the extent necessary to act on the submissions from 2003 through 2014. EPA intends to act on other pre-2004 WQS applicable to those waters as soon as possible. Before 2004, EPA's approvals or disapprovals of new or revised WQS in Maine did not address waters in Indian lands, or expressly consider the State's jurisdiction to establish WQS for such waters or the sufficiency of the State's WQS for such waters under the CWA. EPA thus takes the position that it has not previously approved any of the State's pre-2004 WQS for waters in Indian lands in Maine.

uses of the waters to which they apply. In a separate document EPA will respond to specific comments that interested parties submitted.

1.2 Indian Tribes in Maine

There are four federally recognized Indian Tribes in Maine represented by five governing bodies. The Penobscot Nation and the Passamaquoddy Tribe have reservations and trust land holdings in central and coastal Maine. The Passamaquoddy Tribe has two governing bodies, one on the Pleasant Point Reservation and another on the Indian Township Reservation. The Houlton Band of Maliseet Indians and the Aroostook Band of Micmacs have trust lands further north in the State. To simplify the discussion of the legal framework that applies to each Tribe's territory, EPA will refer to the Penobscot Nation and the Passamaquoddy Tribe together as the "Southern Tribes" and the Houlton Band of Maliseet Indians and Aroostook Band of Micmacs as the "Northern Tribes." EPA acknowledges that these are collective appellations the Tribes themselves have not adopted, and the Agency uses them solely to simplify drafting this decision.

1.3 Settlement Acts in Maine

1.3.1 MIA and MICSA

In 1980, Congress passed the Maine Indian Claims Settlement Act (MICSA), which resolved litigation in which the Southern Tribes asserted land claims to a large portion of the State of Maine. 25 U.S.C. §§ 1721, *et seq*. MICSA ratified a state statute passed in 1979, the Maine Implementing Act (MIA), which was designed to embody the agreement reached between the State and the Southern Tribes. 30 M.R.S. §§ 6201, *et seq*. In 1981, MIA was amended to include provisions for land to be taken into trust for the Houlton Band of Maliseet Indians, as provided for in MICSA. 30 M.R.S. § 6205-A, 25 U.S.C. § 1724(d)(1). Since it is Congress that has plenary authority as to federally recognized Indian Tribes, MIA's provisions concerning jurisdiction and the status of the Tribes are effective as a result of, and consistent with, the Congressional ratification in MICSA.

1.3.2 MSA and ABMSA

In 1989, the Maine legislature passed the Micmac Settlement Act (MSA) to embody an agreement as to the status of the Aroostook Band of Micmacs. 30 M.R.S. §§ 7201, *et seq*. In 1991, Congress passed the Aroostook Band of Micmacs Settlement Act (ABMSA), which ratified the MSA. 25 U.S.C. § 1721, Act Nov. 26, 1991, P.L. 102-171, 105 Stat. 1143. One principal purpose of both statutes was to give the Micmacs the same settlement that had been provided to the Maliseets in MICSA. See ABMSA § 2(a)(4) and (5). In 2007, the Federal Court of Appeals for the First Circuit confirmed that the Micmacs and Maliseets are subject to the same jurisdictional provisions in MICSA. *Aroostook Band of Micmacs v. Ryan*, 484 F.3d 41 (1st Cir. 2007).

Where appropriate, this document will refer to the combination of MICSA, MIA, ABMSA, and MSA as the "settlement acts."

1.4 Indian Territories and Lands in Maine

MICSA, MIA, MSA and ABMSA establish a unique framework for confirming and enhancing the Tribes' land base in Maine. For the Southern Tribes, MIA uses the term "Indian territory" to describe the combination of the Southern Tribes' reservations, as described in treaties with the States of Maine and Massachusetts, plus 150,000 acres of land for each Tribe to be held in trust for the Tribes by the United States. 30 M.R.S. § 6205(1) and (2). As such, the Southern Tribes' land base is made up of both the reservations continuously occupied by the Tribes, and subsequently acquired trust lands.

The land base for the Northern Tribes is made up entirely of trust lands. MIA provides for the Houlton Band of Maliseet Indians to acquire trust land, and Congress provided $900,000 in MICSA to fund that acquisition. 30 M.R.S. § 6205-A, 25 U.S.C. § 1724(d)(1). Similarly, the MSA provides for the Aroostook Band of Micmacs to acquire trust land, and Congress again provided $900,000 in ABMSA to fund that acquisition. 30 M.R.S. § 7204, ABMSA §§ 4(a) and 5(a).

In this document, where appropriate depending on the context, EPA will refer to the tribal land base relevant to this decision as follows: "territories" for the Southern Tribes' land base, which as described above includes both reservations and trust lands; "trust lands" for the Northern Tribes' land base; and "Indian" or "tribal" lands for the entirety of all the Tribes' land base in Maine.[3]

1.4.1 Identification of waters covered by this decision

The Penobscot Indian Nation and Passamaquoddy Tribe have reservation lands as defined in MIA. 30 M.R.S. § 6203(5) (defining Passamaquoddy Indian Reservation); § 6203(8) (defining Penobscot Indian Reservation). The trust lands acquired for the Maine tribes are the product of modern conveyances. Generally, based on the default Maine property rule under which owners of riparian land also own out to the thread, or middle, of most streams, *Wilson & Son v. Harrisburg*, 107 Me. 207, 212-213 (1910), Indian waters include waters adjacent to land held in trust by the Secretary of the Interior and lands in the Tribes' reservations as defined in the Settlement Acts.[4] In addition, Maine common law provides that owners of shore land above the mean high water mark presumptively hold title in fee to intertidal land. *Bell v. Town of Wells*, 557 A.2d 168 (Supreme Judicial Court of Maine, 1989). In *Bell* (often referred to as the "Moody Beach case"), the court explained that such title is subject only to the public's right to fish, fowl, and navigate, and that the rule of law governing titles to intertidal land has its origin in the

[3] In addition to their reservations and trust lands, the Tribes also hold certain lands in fee, which are not at issue in this matter. Any action EPA has taken to approve Maine WQS for waters outside Indian lands would apply to waters in these fee lands.

[4] See Report of the Joint Select Committee on Indian Land Claims, Maine Legislature (1980), par. 14. ("The boundaries of the Reservations are limited to those areas described in the bill, but include any riparian or littoral rights expressly reserved by the original treaties with Massachusetts or by operation of State law. Any lands acquired by purchase or trade may include riparian or littoral rights to the extent they are conveyed by the selling party or included by general principles of law. However, the Common Law of the State, including the Colonial Ordinances, shall apply to this ownership. The jurisdictional rights granted by this bill are coextensive and coterminous with land ownership.")

Colonial Ordinance of 1641-47 of the Massachusetts Bay Colony. As stated in an article written by the Marine Law Institute, University of Maine School of Law, "[t]he Moody Beach Case affirms that in Maine owners of beachfront property or property adjoining tidelands (also called littoral or riparian owners) have property rights to the low water mark or low tide area subject only to a public easement for fishing, fowling, and navigation." See Citizens' Guide to Ocean and Coastal Law, Public Shoreline Access and the Moody Beach Case, August, 1990. Therefore, the Passamaquoddy Tribe's reservation at Pleasant Point would include at least the waters present in the intertidal zone.

EPA acknowledges that there are remaining uncertainties over what waters are associated with Indian lands in Maine in a few locations. For instance, the boundaries of the Penobscot Nation's reservation are currently the subject of litigation in the United States District Court for the District of Maine. *Penobscot Nation v. Mills,* Case No. 1:12-cv-254-GZS. The United States has intervened in that case, and it is the Government's position that the reservation includes Penobscot River waters, while the State of Maine alleges it does not. Pending resolution of this dispute, EPA's decision to approve or disapprove Maine's WQS for Indian waters includes at least some portion of the Penobscot River in the main stem from Indian Island north surrounding the islands in the Nation's reservation.

In addition, this decision treats the Passamaquoddy Tribe's reservation as including the "15 islands in the St. Croix River in existence on September 19, 1794 and located between the head of the tide of that river and the falls below the forks of that river . . ." as specifically enumerated in MIA's definition of the reservation. 30 M.R.S. 6203(5).

It is not necessary or reasonable for EPA to suspend its decision on the State's WQS submissions to await an authoritative resolution of disputes over the boundaries of Indian waters. If any disputes over reservation boundaries result in an authoritative adjudication inconsistent with the assumptions made in this decision, EPA will revisit or clarify the scope of the Agency's determinations in this decision.

2 EPA's Determination that Maine has Authority to Set WQS in Indian Territories

EPA concludes that MICSA provides the State with jurisdiction to set WQS in the Northern Tribes' trust lands and that the federal statute ratifies provisions of MIA that provide the State with such authority in the Southern Tribes' territories. Although in both cases the settlement acts provide the State jurisdiction to establish WQS, EPA notes that MICSA provides a different jurisdictional framework for the Northern Tribes than that which applies to the Southern Tribes.

2.1 Northern Tribes

MICSA provides that the Northern Tribes are subject to state law:

> Except as provided in section 1727(e) and section 1724(d)(4) of this title, all Indians, Indian nations, or Tribes or bands of Indians in the State of Maine, other than the Passamaquoddy Tribe, the Penobscot Nation, and their members, and any lands or natural resources owned by any such Indian, Indian nation, Tribe or band of Indians and any

> lands or natural resources held in trust by the United States, or by any other person or entity, for any such Indian, Indian nation, Tribe, or band of Indians shall be subject to the civil and criminal jurisdiction of the State, the laws of the State, and the civil and criminal jurisdiction of the courts of the State, to the same extent as any other person or land therein.

25 U.S.C. 1725(a). In addition, MICSA ratified MIA, which also provides that all tribes in Maine, including the Northern Tribes are subject to state law:

> Except as otherwise provided in this Act, all Indians, Indian nations, and Tribes and bands of Indians in the State and any lands or other natural resources owned by them, held in trust for them by the United States or by any other person or entity shall be subject to the laws of the State and to the civil and criminal jurisdiction of the courts of the State to the same extent as any other person or lands or other natural resources therein.

30 M.R.S. § 6204. Both statutes make it clear that laws of the State include regulation and that lands and natural resources include water and water rights. 25 U.S.C. §§ 1722(b) and (d); 30 M.R.S. § 6203(3) and (4). The only exceptions to state jurisdiction provided in MIA apply to the Southern Tribes. There are no such exceptions for the Northern Tribes. Notably, the U.S. Court of Appeals for the First Circuit has expressly found that the State's jurisdictional reach in the Northern Tribes' lands is greater than in the Southern Tribes' territories. *Houlton Band of Maliseet Indians v. Ryan*, 484 F.3d 73, 74-75 (1st Cir. 2007). That same year the First Circuit ruled that, even as to the Southern Tribes, MICSA and MIA grant the State jurisdiction to regulate surface water discharge permitting. *Maine v. Johnson,* 498 F.3d 37 (1st Cir. 2007). As discussed below, EPA has concluded that the court's analysis controls our decision as to the State's authority to set WQS in the Southern Tribes' territories. Given that MICSA gives the State a broader scope of jurisdiction over the Northern Tribes than over the Southern Tribes, which are nevertheless subject to the State's authority to set WQS, it is clear that state law applies to the Northern Tribes, and the State has authority to set WQS for waters in these Tribes' trust lands.

The Aroostook Band of Micmacs has argued that the passage of ABMSA impliedly repealed the application of MICSA to the Tribe, and, therefore, that the Micmacs were not subject to the same jurisdictional framework as the Houlton Band of Maliseet Indians. The First Circuit, however, rejected that argument. *Aroostook Band of Micmacs v. Ryan*, 484 F.3d 41, 60-62 (1st Cir. 2007).

2.2 Southern Tribes

MICSA addresses the jurisdictional relationship between the Southern Tribes and the State by reference to MIA, which MICSA ratifies:

> The Passamaquoddy Tribe, the Penobscot Nation, and their members, and the land and natural resources owned by, or held in trust for the benefit of the Tribe, nation, or their members, shall be subject to the jurisdiction of the State of Maine to the extent and in the

> manner provided in the Maine Implementing Act and that Act is hereby approved, ratified, and confirmed.

25 U.S.C. § 1725(b)(1). As discussed above, MIA in turn provides generally that all Indian Tribes in the State are subject to state law:

> Except as otherwise provided in this Act, all Indians, Indian nations, and Tribes and bands of Indians in the State and any lands or other natural resources owned by them, held in trust for them by the United States or by any other person or entity shall be subject to the laws of the State and to the civil and criminal jurisdiction of the courts of the State to the same extent as any other person or lands or other natural resources therein.

30 M.R.S. § 6204. Importantly, MIA section 6204 refers to exceptions to the grant of state jurisdiction found elsewhere in the statute, and those exceptions are all applicable to the Southern Tribes. *See, e.g.*, §§ 6206 (internal tribal matters); 6207 (hunting and fishing in Indian territories); 6209-A & B (minor crimes, small claims, child custody, and domestic relations). EPA has carefully considered whether any of the exceptions provided in MIA operate to block the grant of jurisdiction to the State in the area of setting WQS in the Southern Tribes' waters. EPA concludes that they do not impede the State's jurisdiction to establish WQS under the CWA for the Southern Tribes' waters.

2.2.1 Maine v. Johnson Decision

The U.S. Court of Appeals for the First Circuit previously adjudicated the issue of Maine's authority to regulate water quality protection in the Southern Tribes' territories. In 2003, EPA approved the State to issue national pollutant discharge elimination system (NPDES) permits under the CWA generally in the Southern Tribes' territories, except for those dischargers where EPA concluded that permitting would qualify as an internal tribal matter. MIA section 6206 exempts the Southern Tribes' internal tribal matters from state regulation. EPA determined that two tribally owned and operated public treatment works, which served only tribal members on the Tribes' reservations and had minimal water quality impacts at the point of discharge, qualified as internal tribal matters, and thus excluded those two facilities from the State's approved permitting program. In *Maine v. Johnson,* 498 F.3d 37 (1st Cir. 2007), the First Circuit upheld EPA's approval of the State's program in the Southern Tribes' territories, but reversed EPA's decision to withhold approval of the State to issue the permits for the two tribal treatment works.

> In ordinary statutory construction, the [internal tribal matters] proviso thus reserves to the tribe matters pertaining to tribal membership and governance structure, expenditure of fund income and *other matters of the same kind . . .;* but it does not displace general Maine law on most substantive subjects, including environmental regulation. . . . [W]e readily uphold the position of the EPA and Maine that the nineteen non-Indian discharge sources draining into tribal waters can be regulated by the state. The only real question is the EPA's carve-out of the two source points that are on tribal lands and are owned by Tribe entities. . . .

> In our view, the Settlement Acts make ordinary Maine law apply, even if only tribal members and tribal lands are affected in the particular case, *unless* the internal affairs exemption applies; and the scope of that exemption is determined by the character of the subject matter. Discharging pollutants into navigable waters is not of the same character as tribal elections, tribal membership or other exemplars that relate to the structure of Indian government or the distribution of tribal property.

Id. at 44-46 (emphasis in original; citations omitted). EPA has concluded that the *Maine v. Johnson* decision makes it clear that the grant of jurisdiction to the State includes the area of environmental regulation, certainly as it applies to surface water discharge permitting. The Agency also finds no basis to distinguish the analysis in that case as applied to the State's authority to set WQS for surface waters in the Southern Tribes' territories.

2.2.2 Arguments Maine Tribes have Advanced for Exceptions to State Jurisdiction for Southern Tribes

EPA considered whether, given the jurisdictional provisions of the applicable statutes and the precedent set in *Maine v. Johnson*, there is any basis for concluding that the State's authority to administer the NPDES permitting program would not apply equally to the State's WQS program. EPA concludes there is no such basis.

2.2.2.1 Internal Tribal Matters

As a threshold matter, the court in *Maine v. Johnson* concluded that environmental regulation was part of the jurisdictional grant to the State in Indian lands:

> [T]he [internal tribal matters] proviso thus reserves to the tribe matters pertaining to tribal membership and governance structure, expenditure of fund income and *other matters of the same kind* . . .; but it does not displace general Maine law on most substantive subjects, including <u>environmental regulation</u>.

Id. at 45 (emphasis in original; underscore added). The WQS program is clearly a form of environmental regulation that would be covered by this characterization of the State's authority. Strictly speaking, the facts on which the court's holding rests only presented the question of the State's authority to issue waste water discharge permits. Nevertheless, the court's reasoning in that case makes it clear that this exception to State jurisdiction would not block the State from setting WQS.

When the Agency withheld approval from Maine to permit the two tribal treatment works, EPA conducted an analysis of the factors the First Circuit articulated in two prior cases examining whether a particular subject matter qualifies as an internal tribal matter not subject to state regulation. *Akins v. Penobscot Nation*, 130 F.3d 482, 486-490 (1st Cir. 1997); *Penobscot Nation v. Fellencer*, 164 F.3d 706, 710-713 (1st Cir. 1999). In its review of EPA's decision, the *Johnson* court found it unnecessary to apply the factors developed in the *Akins* and *Fellencer* cases; rather it concluded that this multi-factor assessment is relevant only when an area of regulation is

"arguably close to the (perhaps blurred) statutory borderline" of what might qualify as an internal tribal matter. 498 F.3d at 46. The court concluded that "discharging pollutants into navigable waters is not a borderline case in which balancing . . . or ambiguity canons . . . alter the result." *Id*. (citations omitted).

EPA evaluated whether the authority to set WQS is any closer to the statutory borderline the First Circuit has outlined and, therefore, might properly be analyzed using the *Akins/Fellencer* factors rather than the more categorical analysis in the *Johnson* decision. The Penobscot Nation commented to EPA that setting WQS directly affects the quality of fish the Tribe is able to consume for its sustenance, an area of concern at the core of the Nation's existence. The Penobscot Nation's view is that this effect on the Tribe's ability to safely consume fish makes setting WQS an internal tribal matter. EPA does not agree. Indeed, the Agency concludes that setting WQS is an exercise of jurisdiction even further from the "borderline" between state jurisdiction and internal tribal matters that the *Johnson* court posited.

The decision EPA is making is approval of WQS that are an integral part of a larger legal framework provided for in the CWA. Within that framework, the CWA and EPA's regulations provide that NPDES permits for upstream dischargers must include limits that assure compliance with downstream WQS. 40 C.F.R. § 122.44(d)(4) and CWA § 401(a)(2). In reviewing Maine's NPDES program, EPA found that permitting the two tribal treatment works involved only tribal members and would have minimal effect on water quality outside the Tribes' territories. See 498 F.3d at 45 n. 8. EPA cannot make a corresponding finding here that setting a WQS would not have the potential for an effect on non-members or on water quality outside the Tribes' territories. When it established the multi-factor internal tribal matters analysis, the *Akins* court noted that "*First, and foremost*, the [stumpage policy at issue] purports to regulate only members of the Tribe . . .." 130 F.3d at 486 (emphasis added). On this "foremost" factor, EPA concludes that the WQS program can have regulatory effects beyond the Tribe. Generally, downstream WQS determine what limits upstream dischargers must meet to assure protection of those WQS, which is a legal effect that could reach beyond the membership of the Tribes and the boundaries of their territories. These effects put the setting of WQS even further from the "(perhaps blurred) statutory borderline" of what qualifies as an internal tribal matter under the MIA and MICSA.

In *Maine v. Johnson* the court was prepared to accept EPA's finding that permitting the two tribal treatment works would not have a substantial effect outside the Tribes' territories, and it still refused to treat the category of waste water discharge permitting as an internal tribal matter. Here, EPA cannot find that setting WQS will have no potential for a substantial effect outside the Tribes' territories. Therefore, under the principles announced in *Maine v. Johnson*, EPA concludes that setting WQS does not qualify as an internal tribal matter.

2.2.2.2 The Southern Tribes' Sustenance Fishing Right

EPA has also considered whether the reservation in MIA of the Southern Tribes' right to take fish for their individual sustenance within their reservations provides an exception to the State's jurisdiction. That right is reserved to the Southern Tribes "[n]otwithstanding . . . any other law of the State." 30 M.R.S. § 6207(4). Arguably, if a state law interfered with the Southern Tribes' right to take fish for their individual sustenance, this provision would block that law's

application in the Southern Tribes' reservations. However, EPA concludes that the State's administration of WQS, subject to CWA requirements and EPA's oversight, does not have the potential to interfere with the Southern Tribes' sustenance fishing right.

MIA is clear that the basic grant of jurisdiction to the State includes the authority to apply laws of the State, which include regulations, to the Tribes' natural resources, which include "water and water rights and hunting and fishing rights." 30 M.R.S. §§ 6204, 6203(3) and (4). To conclude that the reserved fishing right precludes the operation of all state laws affecting environmental regulation that might indirectly affect the fishing right, one would have to conclude that the State's regulation of water quality is inherently and necessarily inimical to the Tribes' ability to take fish for their individual sustenance. EPA cannot reach that conclusion.

First, there are many state WQS that are reasonably adequate to support a fishery that could provide for an individual tribal member's sustenance. Indeed, as discussed below, EPA is approving many state WQS provisions that EPA has determined are sufficient to protect aquatic life. In *Maine v. Johnson* the court made it clear that decisions about the scope of the State's jurisdiction in the Southern Tribes' territories should be made on the basis of the category of the subject matter at issue – the court specifically rejected EPA's attempt to find or reject state jurisdiction based on the facts of any particular application of state jurisdiction within a subject matter category. "So we accept the EPA's factual premise as to the [limited] impact of the discharges but not the EPA's legal characterization. . . . [T]he scope of [the internal tribal matters] exemption is determined by the character of the subject matter." 498 F.3d at 45-46. The subject category at issue in *Maine v. Johnson* was environmental regulation of pollutants in surface waters, the same category at issue here. The impact of a specific state WQS regulation on the Tribes' sustenance fishing rights might provide the basis for a challenge to that specific regulation, but the bare potential for such a specific challenge at some point provides no basis for precluding all state regulation of that subject area. It is possible for the State to exercise jurisdiction to set WQS without necessarily or inevitably interfering with the Tribes' fishing rights.

Second, if the State does submit a new or revised WQS that would interfere with the Tribes' reserved fishing right, EPA has authority under the CWA to ensure that the Tribes' fishing right is protected. As described further below, EPA is approving the reserved sustenance fishing right as a designated use for the tribal waters to which the right applies. Where the State adopts a new or revised WQS, EPA has the authority and the obligation under the CWA to review and determine whether such new or revised WQS is consistent with the CWA. If EPA disapproves, the CWA directs EPA to propose and promulgate a new or revised WQS unless the State adopts an adequate revision to protect the use. The CWA thus provides the mechanism to protect the sustenance fishing use and prevent interference with the Southern Tribes' reserved fishing right. EPA's oversight of Maine's WQS is adequate to protect the Tribes' right while maintaining the basic statutory grant of jurisdiction to Maine, including the authority to set WQS, as provided under MICSA in the first instance.

2.3 The Relationship Among MISCA, Jurisdiction, and the Trust Responsibility

Several Tribes in Maine commented that it would be inconsistent with the federal government's trust relationship with the Tribes for EPA to approve the State to set WQS for waters in the Tribes' lands. On the other hand, the State argues that the trust relationship does not apply in the State because of MICSA.

EPA has consistently maintained that there is a trust relationship between the federal government and the Tribes in Maine in the general sense that the Tribes are federally recognized, they have sovereign governments that EPA interacts with on a government-to-government basis, and EPA has a responsibility to consult with the Tribes to understand and consider their interests when EPA is making a decision that affects the Tribes. This general trust relationship, however, does not alter the jurisdictional framework Congress ratified in MICSA. MICSA impacts the jurisdictional relationship among the Tribes and the State, within which EPA works to address the Tribes' interests as appropriate. It is consistent with the trust relationship for EPA to approve the State's authority to set WQS for waters in the Tribes' lands, because MICSA has dramatically revised the jurisdictional framework within which the trust operates in Maine as compared to the customary jurisdictional framework that applies in Indian country outside Maine. EPA intends to continue to act consistently with the trust relationship, to consult with the Tribes, and to consider their interests as we oversee the State's WQS under the CWA.

2.4 The Penobscot Nation's Application for Treatment in the Same Manner as a State

On October 8, 2014, the Penobscot Nation submitted to EPA an application "to administer water quality standards program and for federal approval of the standards" covering the Main Stem of the Penobscot River from Indian Island north to the confluence of the east and west branches of the river. EPA is not acting today on the Nation's application. EPA is only deciding today that the State of Maine has authority to set WQS for waters in Indian lands, and then acting on the State's WQS as applied to those waters. The Nation's application raises complicated issues that EPA will address in a separate decision.

3 EPA's Determination to Approve Classifications and Designated Uses for Waters in Indian Lands

In Section 2, above, EPA focused on the settlement acts and judicial interpretation of those statutes to analyze Maine's assertion of jurisdiction to set WQS in the waters in Indian lands. Having concluded that the State has jurisdiction to set those standards, EPA must now analyze whether the State's WQS as applied to waters in Indian lands are approvable under the CWA. So the balance of this document will focus primarily on the requirements of the CWA, as applied to the unique circumstances EPA must address here where a state is setting WQS for waters in lands that Congress has set aside for federally recognized Indian tribes.

The first step in developing and reviewing WQS under the CWA is to determine the uses of the waters to which the WQS apply. Here the State is not writing on a blank slate in the selection of uses for tribal waters. As described in detail in this section 3, EPA has concluded that the settlement acts operate to require Maine and the Agency to focus on the sustenance fishing use that federal and state law provide for the Tribes in Maine in waters in Indian lands. In light of

the sustenance fishing use, the CWA requires the State's water quality criteria to protect that use as explained in section 4, below.

3.1 Status of Previous State WQS as Applied to Waters in Indian Lands

3.1.1 EPA's Prior Decisions on Maine WQS

Maine has periodically submitted new or revised WQS to EPA for review and approval or disapproval. Before 2004, EPA acted on those WQS without expressly considering or approving the State's jurisdiction to establish WQS for waters in Indian lands or the sufficiency of the State's WQS for such waters under the CWA. Since 2004, EPA has expressly stated, in all decisions that it made to approve or disapprove new or revised WQS, that its decisions applied only to Maine waters outside of Indian lands.

3.1.2 EPA's Approach to State Programs in Indian Country

The State has commented to EPA that, prior to 2004, EPA approved state WQS submissions without reference to or exclusion of waters in tribal lands. From this the State infers that EPA approved the State's WQS for waters in tribal lands prior to 2004. EPA disagrees with this inference.

First, Maine did not obtain authority to regulate in tribal lands until Congress passed MICSA in 1980. While the State asserted the authority to govern the Tribes prior to MICSA, the First Circuit's decision in *Joint Tribal Council of the Passamaquoddy Tribe v. Morton*, 528 F.2d 370 (1st Cir. 1975), cast considerable doubt on that proposition, and the decision in *Bottomly v. Passamaquoddy Tribe*, 599 F.2d 1061 (1st Cir. 1979), effectively foreclosed this argument. So any WQS that Maine submitted prior to MICSA's passage could have no legal effect in tribal lands. At that point the State had no clear authority to set WQS in those waters.

But even as to WQS that Maine submitted following the passage of MICSA in 1980, EPA's position is that none of the State's WQS, whether submitted prior to or following enactment of MICSA, were approved under the CWA for waters in Indian lands. Prior to the Agency's decision today, EPA has never made a formal determination on the record expressly addressing either the State's jurisdictional authority or the sufficiency under the CWA of the State's WQS as applied to waters in Indian lands.

Today's decision demonstrates that in acting on new or revised state WQS for waters in Indian lands, EPA must consider the adequacy of such WQS to protect the uses in those specific waters. Where, as here, waters in Indian lands have a different designated use (*i.e.*, sustenance fishing) than waters outside of Indian lands, the analysis of the adequacy of criteria will necessarily be different. It would be arbitrary for EPA to assume, without analysis, that if criteria are protective for waters outside of Indian lands, they are also protective for waters in Indian lands.

In addition, under basic principles of federal Indian law, states generally lack civil regulatory jurisdiction within Indian country as defined in 18 U.S.C. § 1151. *Alaska v. Native Vill. Of Venetie Tribal Gov't*, 522 U.S. 520, 527 n.1. (1998) ("[g]enerally speaking, primary jurisdiction

over land that is Indian country rests with the Federal Government and the Indian Tribe inhabiting it, and not with the States."). See also *Okla. Tax Comm'n v. Sac and Fox Nation*, 508 U.S. 114, 128 (1993) ("[a]bsent explicit congressional direction to the contrary, we presume against a State's having the jurisdiction to tax within Indian Country . . . ."). Thus, EPA cannot presume a state has authority to establish WQS or otherwise regulate in Indian country. Instead, a state must demonstrate its jurisdiction, and EPA must determine that the state has made the requisite demonstration and expressly determine that the state has authority, before a state can implement a program in Indian country.[5] Such a demonstration and approval of Maine's authority to administer WQS in waters of Indian lands has not occurred prior to the decision EPA is making today. [6]

Maine cites to several actions by EPA employees that, in the State's view, indicate EPA's recognition that state WQS approved before 2004 apply in at least some tribal waters. EPA notes that some of those actions applied to stretches of rivers that either included both tribal and state waters or that were then and continue to be the subject of disputes over whether they included both tribal and state waters. As a result, those actions were inherently ambiguous as to their relevance to the tribal portions of the waters. But the Agency concedes that in some instances the Agency appeared to assume, without any express consideration or decision regarding the jurisdictional or CWA issues, that state WQS applied in certain tribal waters. For example, there are instances when the Region asked Maine DEP to certify under section 401 of the CWA that NPDES permits for tribal facilities discharging into tribal waters complied with state WQS. Simply put, those prior actions were mistakes that do not affect this decision. At the time, EPA had made no finding that Maine had jurisdiction to adopt WQS for tribal waters and had not approved the State's WQS for such waters. EPA notes that unexplained mistakes by mid-level Agency officials cannot unilaterally revise a considered Agency-wide policy. *Puerto Rican Cement Co. v. EPA*, 889 F.2d 292, 299 (1st Cir. 1989).

3.2 EPA Approval of Water Classifications and Associated Designated Uses

Many of the WQS revisions under review for approval or disapproval for waters in Indian lands are water quality criteria, and the CWA requires that criteria be protective of designated uses. In order to evaluate whether the submitted criteria are protective of designated uses, EPA must first approve designated uses for these waters. Accordingly, EPA also reviewed and is approving

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[5] Consistent with EPA's responsibility to consult with Indian tribes about decisions affecting their interests, as embodied in the Agency's 1984 Indian Policy and EPA's more recent Tribal Consultation Policy, EPA would offer to consult with any Indian tribe in the context of an Agency determination that a state has authority to set standards in that tribe's territory. Notably, no such consultations occurred in the context of EPA's prior decisions on the State's WQS submissions, further evidencing that the Agency's prior approvals were not intended to extend to waters in Indian lands.

[6] Indeed, as described above in the Agency's analysis of the State's jurisdictional authority to set WQS in Indian waters, EPA's review and assessment of how Maine's WQS affect tribal uses in Indian waters is an essential step in the argument that it is possible to reconcile the State setting WQS in Indian waters with the fishing rights that MICSA reserves to Tribes in Maine. Ignoring or side-stepping EPA's role in overseeing Maine's WQS submissions as they apply to Indian waters risks creating an irreconcilable conflict between the jurisdictional grant to the State in MICSA and the provision for Tribes in Maine to sustain themselves on the land base that the Maine settlement acts established for the Tribes. Respecting EPA's oversight role effectively harmonizes those elements of the settlement acts in Maine.

Maine's surface water classifications and corresponding designated uses, adopted and submitted to EPA for review to date[7], for waters in Indian lands.[8]

The general classifications and their corresponding uses consist of the following:

- 38 M.R.S. § 465(1.A) Class AA freshwater uses: drinking water after disinfection, fishing, agriculture, recreation in and on the water, navigation, and as habitat for fish and other aquatic life. The habitat must be characterized as free-flowing and natural.
- 38 M.R.S. § 465(2.A) Class A freshwater uses: drinking water after disinfection; fishing; agriculture; recreation in and on the water; industrial process and cooling water supply; hydroelectric power generation, except as prohibited under Title 12, section 403; navigation; and as habitat for fish and other aquatic life. The habitat must be characterized as natural.
- 38 M.R.S. § 465(3.A) Class B freshwater uses: drinking water supply after treatment; fishing; agriculture; recreation in and on the water; industrial process and cooling water supply; hydroelectric power generation, except as prohibited under Title 12, section 403; navigation; and as habitat for fish and other aquatic life. The habitat must be characterized as unimpaired.
- 38 M.R.S. § 465(4.A) Class C freshwater uses: drinking water supply after treatment; fishing; agriculture; recreation in and on the water; industrial process and cooling water supply; hydroelectric power generation, except as prohibited under Title 12, section 403; navigation; and as a habitat for fish and other aquatic life.
- 38 M.R.S. § 465-A(1.A) Class GPA lake and pond uses: drinking water after disinfection, recreation in and on the water, fishing, agriculture, industrial process and cooling water supply, hydroelectric power generation, navigation, and as habitat for fish and other aquatic life. The habitat must be characterized as natural. This section applies to great ponds (as defined in 38 M.R.S. § 480-B (5)), natural lakes and ponds less than 10 acres in size, and impoundments of rivers that are defined as great ponds pursuant to 38 M.R.S. § 480-B (5).
- 38 M.R.S. § 465-B (1.A) Class SA estuarine and marine water uses: recreation in and on the water, fishing, aquaculture, propagation and harvesting of shellfish, navigation, and as habitat for fish and other estuarine and marine life. The habitat must be characterized as free-flowing and natural.
- 38 M.R.S. § 465-B (2.A) Class SB estuarine and marine water uses: recreation in and on the water, fishing, aquaculture, propagation and harvesting of shellfish, industrial process and cooling water supply, hydroelectric power generation, navigation, and as habitat for fish and other estuarine and marine life. The habitat must be characterized as unimpaired.
- 38 M.R.S. § 465-B (3.A) Class SC estuarine and marine water uses: recreation in and on the water, fishing, aquaculture, propagation and restricted harvesting of shellfish,

[7] This includes the addition of "agriculture" as a designated use for freshwaters, submitted to EPA on August 26, 2003.

[8] There are other provisions of Maine's WQS that EPA is not approving or disapproving at this time because they are not directly related to the scope of this decision, which is responding to new and revised WQS submitted to EPA from 2003 to 2014. These remaining provisions include, for example, definitions, antidegradation policies, and WQS implementation policies in regulation and statute. EPA will review those elements in the coming months and make decisions accordingly.

industrial process and cooling water supply, hydroelectric power generation, navigation and as a habitat for fish and other estuarine and marine life.

Waters throughout Maine are identified by classification in 38 M.R.S. § 467 (classifications of major river basins), § 468 (classifications of minor drainages), and § 469 (classifications of estuarine and marine waters), which results in the assignment of designated uses for each waterbody.

Each of the classification categories identified above contains designated uses that are consistent with the requirements of Section 303(c)(2)(A) of the Clean Water Act and 40 C.F.R. § 131.6(a). In addition, EPA has concluded that the classifications as applied to specific waters in Indian lands are reasonable. Therefore, EPA is approving the general classifications and associated designated uses in 38 M.R.S. § 465(1.A), (2.A), (3.A), and (4.A); § 465-A(1.A) (and the definition of "great ponds" in 38 M.R.S. § 480-B (5)); and § 465-B(1.A), (2.A), and (3.A); as well as the classification of specific waters in 38 M.R.S. § 467, § 468, and § 468, as applied to waters in Indian lands, because they are consistent with Sections 101(a)(2) and 303(c)(2)(A) of the Clean Water Act and 40 C.F.R. §131.10(a). EPA is including in its approval of specific waterbody classifications the reclassifications, submitted to EPA on December 7, 2009, of Otter Creek, a tributary of Seboeis Stream, and Alder Stream from Class B to Class A; and of Grand Falls Flowage between Route 1(Princeton and Indian Township) and Black Cat Island from Class B to Class GPA.

3.3 EPA's Identification of the "Fishing" Designated Use as "Sustenance Fishing" in Waters in Indian Lands in Maine

3.3.1 The Purpose of the Tribal Land Base and Tribal Sustenance Fishing in Maine

The settlement acts in Maine include extensive provisions to confirm and expand the Tribes' land base, and the legislative record makes it clear that a key purpose behind that land base is to preserve the Tribes' culture and support their sustenance practices. MICSA section 1724 establishes a trust fund to allow the Southern Tribes and the Maliseets to acquire land to be put into trust. In addition, the Southern Tribes' reservations are confirmed as part of their land base. 30 M.R.S. § 6205(1)(A) and (2)(A). MICSA combines with MIA sections 6205 and 6205-A to establish a framework for taking land into trust for those three Tribes, and laying out clear ground rules governing any future alienation of that land and the Southern Tribes' reservations. Sections 4(a) and 5 of the ABMSA and 7204 of the state MSA accomplish essentially the same result for the Micmacs, consistent with the purpose of those statutes to put that Tribe in the same position as the Maliseets.

EPA has concluded that one of the over-arching purposes of the establishment of this land base for the Maine Tribes was to ensure their continued opportunity to engage in their unique cultural practices to maintain their existence as a traditional culture. An important part of the Maine Tribes' traditional culture is their sustenance life ways. The legislative history for MICSA makes it clear that one critical purpose for assembling the land base for the Tribes in Maine was to preserve their culture. The Historical Background in the Senate Report for MICSA opens with the observation that "All three Tribes [Penobscot, Passamaquoddy and Maliseet] are riverine in

their land-ownership orientation." Sen. Rep. No. 96-957, at 11. The Report's "Special Issues" section specifically refutes the concern that:

> *The Settlement will lead to acculturation of the Maine Indians*. – Nothing in the settlement provides for acculturation, nor is it the intent of Congress to disturb the cultural integrity of the Indian people of Maine. To the contrary, the Settlement offers protections against this result being imposed by outside entities by providing for tribal governments which are separate and apart from the towns and cities of the State of Maine and which control all such internal matters. The Settlement also clearly establishes that the Tribes in Maine will continue to be eligible for all federal Indian cultural programs.

Id. at 17. As the Tribes have extensively documented in their comments, their culture relies heavily on sustenance practices, including sustenance fishing. So if a purpose of MICSA is to avoid acculturation and protect the Tribes' continued political and cultural existence on their land base, then a key purpose of that land base is to support those sustenance practices.

As explained in more detail below, MICSA, MIA, ABMSA, and MSA include very different provisions governing sustenance practices, including fishing, depending on the type of Indian lands involved. But each set of provisions in its own way is designed to make a homeland for these Tribes where they may safely practice their sustenance life ways.

3.3.1.1 Southern Tribes' Sustenance Fishing Right Reserved in Their Reservations in MIA/MICSA

If there were any doubt that sustenance practices are central to tribal culture, MICSA ratifies the MIA's reservation of the Southern Tribes' right to take fish for their individual sustenance:

> SUSTENANCE FISHING WITHIN THE INDIAN RESERVATIONS. Notwithstanding any rule or regulation promulgated by the commission or any other law of the State, the members of the Passamaquoddy Tribe and the Penobscot Nation may take fish, within the boundaries of their respective Indian reservations, for their individual sustenance subject to the limitations of subsection 6.

30 M.R.S. § 6207(4). Under this section, "fish" is defined as "a cold blooded completely aquatic vertebrate animal having permanent fins, gills and an elongated streamlined body usually covered with scales and includes inland fish and anadromous and catadromous fish when in inland water." 30 M.R.S. § 6207(9).

The only limitation on the Southern Tribes' right to take fish for their individual sustenance on their reservations is the State's ability to limit the take based on a finding that the Tribes' fishing practices are threatening stocks outside the Tribes' reservations in a process in which the State carries the burden of proof. 30 M.R.S. § 6207(6). To date the State has made no such determination. So a plain language reading of this provision entitles the Southern Tribes to take as much fish as they deem necessary to sustain individual members.

The legislative history for MIA makes it clear that the Maine legislature intended to continue and ratify the State's practice of not regulating the Southern Tribes' sustenance fishing practices. See transcript of the public hearing held on March 28, 1980 by the Maine Legislature's Joint Select Committee on the Maine Indian Claims Settlement at 55-56. The special issues section of the Senate Report on MICSA confirms that the intent of this provision is to shield the Southern Tribes' right to take fish from the prospect that the State might someday interfere with it. By responding to a rhetorical assertion (in italics below), the report confirms that the Southern Tribes have a right to take fish that is subject to state regulation only under very limited circumstances:

> *Subsistence hunting and fishing rights will be lost since they will be controlled by the State of Maine under the Settlement*. – Prior to the settlement, Maine law recognized the Passamaquoddy Tribe's and Penobscot Nation's right to control Indian subsistence hunting and fishing within their reservations, but the State of Maine claimed the right to alter or terminate these rights at any time. Under Title 30, Sec. 6207 as established by the Maine Implementing Act, the Passamaquoddy Tribe and the Penobscot Nation have the permanent right to control hunting and fishing not only within their reservations, but insofar as hunting and fishing in certain ponds is concerned, in the newly-acquired Indian territory as well. The power of the State of Maine to alter such rights without the consent of the affected tribe or nation is ended by Sec. 6(e)(1) of S. 2829. The State has only a residual right to prevent the two tribes from exercising their hunting and fishing rights in a manner which has a substantially adverse effect on stocks in or on adjacent lands or waters. This residual power is not unlike that which other states have been found to have in connection with federal Indian treaty hunting and fishing rights. The Committee notes that because of the burden of proof and evidence requirements in Title 30, Sec. 6207(6) as established by the Maine Implementing Act, the State will only be able to make use of this residual power where it can be demonstrated by substantial [evidence] that the tribal hunting and fishing practices will or are likely to adversely affect wildlife stock outside tribal lands.

Sen. Rep. No. 96-957, pp. 16-17. Importantly, MIA section 6207 did not create a fishing right for the Southern Tribes. Rather it confirmed an aboriginal right the Tribes have continuously exercised, and shielded that right from state regulation absent a finding of depletion. DOI's legal opinion confirms that this statutorily reserved fishing right is rooted in treaty guarantees that were upheld through the settlement acts.

The Senate Committee's discussion of the similarity between MIA section 6207 and the structure of more traditional Indian treaty hunting and fishing rights is instructive. Essentially, the State of Maine has adopted into state law and Congress has ratified a reserved fishing right like the rights reserved to other Indian tribes by treaties, executive orders, or other statutes. It is axiomatic that the settlement acts in Maine significantly revised the customary formulae of federal Indian law that apply outside the State. *Akins*, 130 F.3d at 484. But it is equally important to recognize those elements of the settlement acts where both the state and federal governments made careful provision for tribal rights that mirror those more commonly seen elsewhere in Indian country. *See Washington v. Washington State Commercial Passenger Fishing Vessel Association*, 443 U.S. 658, 674 (1979) (Stevens Treaties explicitly reserved to the Pacific Northwest tribes "'[t]he

right of taking fish, at all usual and accustomed grounds and stations . . . in common with all citizens of the Territory'"). The Southern Tribes' reserved aboriginal right to take fish for their individual sustenance within their reservations is such a right.

3.3.1.2 Federal Law Framework for Sustenance Fishing in Trust Lands

Similarly, to understand how the Maine Tribes' sustenance fishing practices are provided for in their newly acquired trust lands, it is helpful to review the federal law background against which Congress and the State of Maine were legislating when they provided for land to be taken into trust for the benefit of the Maine Tribes. Courts have found that when Congress sets aside land for a fishing tribe, it implicitly grants to the tribe the right to carry out its traditional fishing practices on that land. See *Menominee v. U.S.*, 391 U.S. 404, 405-406 (1968) (holding that lands acquired for the Menominee Tribe included the implicit right to hunt and fish on those lands); *Parravano v. Babbitt*, 70 F.3d 539, 544 (9th Cir. 1995) (recognizing the doctrine "that the grant of hunting and fishing rights is implicit in the setting aside of a reservation 'for Indian purposes.'"); see also *Katie John v. U.S.,* 720 F.3d 1214, 1230 (9th Cir. 2013) (Reserved water rights "are created when the United States reserves land from the public domain for a particular purpose, and they exist to the extent that the waters are necessary to fulfill the primary purposes of the reservation.").

Courts have found an implicit fishing right based on legislative history indicating that, in setting aside land for a tribe, Congress intended to preserve a tribe's fishing culture/practices. See *Menominee*, 391 U.S. at 405 ("The essence of the Treaty of Wolf River was that the Indians were authorized to maintain on the new lands ceded to them as a reservation their way of life which included hunting and fishing."); *Parravano*, 70 F.3d at 542 (In enacting the Hoopa-Yurok Settlement Act, "[o]ne of the concerns of Congress at the time" was "to protect the Tribes' fisheries."); see also id. at 546 ("Although the 1988 Hoopa-Yurok Settlement Act did not explicitly set aside fishing rights, it did make clear that partitioning would not dispossess the Tribes of their assets. The legislative history of the 1988 Act indicates that Congress was aware that each Tribes' interests in their salmon fisheries was one of its principal assets."). As explained in greater detail below, there is such legislative history here.

There is an important distinction between the Southern Tribes' aboriginal fishing right, which Congress explicitly reserved on those Tribes' reservations, and tribal sustenance fishing on the trust lands, which Congress provided for based on its demonstrated intent to preserve the Tribes' riverine culture. EPA is not determining that the Tribes in Maine have an aboriginal fishing right in their trust lands. The Agency acknowledges there is dispute over the scope of the Tribes' aboriginal resource rights following enactment of MICSA. See 25 U.S.C. §§ 1722(b) and 1723(b) and Assessment of the Intergovernmental Saltwater Fisheries Conflict between Passamaquoddy and the State of Maine, Maine Indian Tribal-State Commission: Special Report 2014/1 (June 17, 2014) at 7.

But regardless of the status of aboriginal fishing rights outside the Southern Tribes' reservations, it is possible for Congress to make provision for tribal sustenance fishing on trust lands, not based on the reservation of aboriginal rights, but based on Congressional intent to establish a land base for a tribe in order to sustain its unique culture. As described in detail below, EPA has

determined that Congress did just that in the Maine settlement acts, and when Congress did so, it acted against the backdrop of the principles outlined in the cases above. The legislative record regarding the trust land provisions in MIA, MICSA, MSA and ABMSA demonstrate Congress's intent to provide the Tribes with the opportunity to exercise their traditional sustenance lifeways, including traditional sustenance fishing in waters of tribal trust lands.

3.3.1.2.1 Sustenance Fishing in the Trust Lands of the Southern Tribes

Both MICSA and MIA make it clear that the land acquisition fund for the benefit of the Passamaquoddy and Penobscot Tribes was established to ensure these Tribes not only had a land base to occupy, but also access to natural resources to sustain their continued existence as a unique culture, including their ability to exercise their fishing rights. "The Secretary is authorized and directed to expend . . . the land acquisition fund for the purpose of acquiring land or natural resources for the Passamaquoddy Tribe, [and] the Penobscot Nation . . . and for no other purpose." 25 U.S.C. § 1724(b) (emphasis added). "Land or natural resources" are defined to include "water and water rights, and hunting and fishing rights." 25 U.S.C. § 1722(b).[9]

As excerpted more fully above, MICSA's legislative history also makes it clear that the Southern Tribes would be engaged in sustenance fishing in the newly-acquired trust lands:

> Under Title 30, Sec. 6207 as established by the Maine Implementing Act, the Passamaquoddy Tribe and the Penobscot Nation have the permanent right to control hunting and fishing not only within their reservations, but insofar as hunting and fishing in certain ponds is concerned, in the newly-acquired Indian territory as well.

Sen. Rep. No. 96-957, pp. 16-17 (emphasis added). The legislative history of MIA also makes it clear that the Maine Legislature understood that MIA was designed to accommodate sustenance fishing practices in the Southern Tribes' trust lands. See transcript of the public hearing held on March 28, 1980 by the Maine Legislature's Joint Select Committee on the Maine Indian Claims Settlement at 151-152.[10] So it is clear that in creating the authority to take land into trust for the Southern Tribes, Congress understood that MIA made provision for the Tribes to engage in sustenance fishing in those trust lands and intended the trust lands to provide a base for the Tribes to engage in sustenance practices.

As recognized by Congress in MICSA's legislative history, the Southern Tribes' control of fishing in certain trust waters was specifically codified in MIA. Section 6207(1) provides that

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[9] Unlike MICSA, when MIA refers to Penobscot and Passamaquoddy trust lands, it uses the term "land acquired by the secretary [of Interior] for the benefit" of each tribe, without reference to natural resources. Compare 25 U.S.C. § 1724(d) with 30 M.R.S. § 6205(1)(B) and (2)(B). As explained in the section above, other provisions of MIA make it clear that the statute anticipated that those lands would include the attendant natural resources acquired with the land, especially fishing rights. Moreover, to the extent that this differing terminology suggests a conflict between MICSA and MIA in defining the scope of the tribes' interest in their trust lands and natural resources, the provisions of MICSA would control. 25 U.S.C.
§ 1735(a).

[10] "[The Tribes can adopt ordinances with respect to . . . fishing but only on ponds of less than ten acres in size. Those ordinances have to be equally applicable to Indians and non-Indians except that the Indians can make special provisions for sustenance hunting . . ." and fishing per MIA § 6207(1). Id. at 151.

the Southern Tribes have exclusive authority to enact ordinances regulating the taking of fish on ponds of less than ten acres in their trust lands. As with the Southern Tribes' fishing right in their reservations, this authority is subject only to the State's authority to limit the take after carrying the burden of proof that the Tribes are depleting fish stocks. MIA specifically anticipates that any tribal ordinances regulating fishing in these waters "may include special provisions for the sustenance of the individual members of the Passamaquoddy Tribe or the Penobscot Nation." *Id*.

As to greater ponds and rivers and streams in or along the Southern Tribes' trust lands, MIA also codifies the understanding that the Tribes would be engaged in sustenance fishing in those waters. MIA creates the Maine Indian Tribal-State Commission (defined as the "commission" 30 M.R.S. § 6203(1)), made up of representatives appointed by the State and the Southern Tribes. 30 M.R.S. § 6212. MIA provides that commission the exclusive authority to promulgate fishing rules in these waters. When it does so "the commission shall consider and balance" several factors, including "the needs or desires of the Tribes to establish fishery practices for the sustenance of the tribes or to contribute to the economic independence of the tribes, [and] the traditional fishing techniques employed by and ceremonial practices of Indians in Maine." 30 M.R.S. § 6207(3). Importantly, as analyzed in the record supporting this decision, none of the fishing regulations adopted by the commission would impinge on the ability of the Tribes to sustain themselves on fish taken from these waters.[11]

MICSA and MIA combine to authorize the establishment of trust lands for the Southern Tribes to provide a land base in which the Tribes can exercise their sustenance fishing practices. As compared with the sustenance fishing right reserved to the Southern Tribes within their reservations, MICSA and MIA allow for a greater, although still sharply limited, role for the State, through the commission, to participate in the development of fishing regulations on certain of the waters in the trust lands. But in exercising even that authority, the commission is charged with considering the Tribes' sustenance fishing practices. Therefore, it is clear that a critical purpose behind establishing the Southern Tribes' trust lands is to give the Tribes an opportunity to engage in sustenance fishing.

3.3.1.2.2 Sustenance Fishing in the Trust Lands of the Northern Tribes

Compared with the Southern Tribes' territories, the arrangement for the Northern Tribes' trust lands provides for more direct state regulation of fishing practices. Nevertheless, it appears Congress intended these trust lands to preserve the Northern Tribes' unique cultures as well. So the Northern Tribes' trust lands provide a land base in which the Tribes are able to exercise sustenance fishing practices to the extent consistent with the legal limits on their fishing. Again, similar to the situation for the Southern Tribes' trust lands, EPA is not concluding that there is an aboriginal fishing right reserved to the Northern Tribes on their trust lands. But the Agency does conclude that there is sufficient evidence in the legislative record to indicate that Congress intended the Northern Tribes to engage in sustenance practices on their trust lands to the extent they could.

[11] See memorandum from Ralph Abele to the file for this decision, regarding Effects of Maine Fishing Regulations on Sustenance Fishing by Maine Tribes, dated January 30, 2015.

Authority to establish the Northern Tribes' trust lands came in several rounds of legislation. The first involved the Maliseets, who came to the negotiations around MIA and MICSA late in the legislative process. In 1980, MICSA provided that "[t]he Secretary is authorized and directed to expend . . . the land acquisition fund for the purpose of acquiring land or natural resources for the . . . the Houlton Band of Maliseet Indians and for no other purpose." 25 U.S.C. § 1724(b) (emphasis added). "Land or natural resources" is defined to include "water and water rights, and hunting and fishing rights." 25 U.S.C. § 1722(b) (emphasis added).

At the time Congress authorized land to be taken into trust for the Maliseets, it specifically acknowledged that "[a]ll three tribes [Penobscot, Passamaquoddy and Maliseet] are riverine in their land-ownership orientation." Sen. Rep. No. 96-957, at 11. Congress also specifically noted that one purpose of MICSA was to avoid acculturation of the Maine Tribes:

> *The Settlement will lead to acculturation of the Maine Indians.* – Nothing in the settlement provides for acculturation, nor is it the intent of Congress to disturb the cultural integrity of the Indian people of Maine. To the contrary, the Settlement offers protections against this result being imposed by outside entities by providing for tribal governments which are separate and apart from the towns and cities of the State of Maine and which control all such internal matters. The Settlement also clearly establishes that the Tribes in Maine will continue to be eligible for all federal Indian cultural programs.

Id. at 17. Congress's purpose in providing for the establishment of the Maliseet trust lands was to provide a land base on which the Tribe could maintain its "cultural integrity." The Maliseets have submitted extensive comments documenting the sustenance fishing practices central to the Tribe's culture.

In 1981, the Maine Legislature added provisions to MIA to correspond to the action Congress took in MICSA to recognize the Maliseets and authorize trust lands to provide a resource base for the Tribe. In contrast to MIA's language describing the Southern Tribes' trust lands, the statute explicitly defines the Maliseet trust lands to include natural resources. 30 M.R.S.A §§ 6203(2-A) ("'Houlton Band Trust Land' means land or natural resources acquired by the secretary in trust for the Houlton Band of Maliseet Indians . . .."); see also § 6205-A ("Land or natural resources" may be taken into trust for the Maliseets). As in MICSA, MIA makes it clear that natural resources acquired for the Maliseets may include fishing rights. *Id*. at § 6203(3) ("'Land or other natural resources' means any real property or other natural resources . . . including, but without limitation, . . . water and water rights and hunting and fishing rights.")

It was not until 1989 that the Micmacs negotiated a settlement with Maine as codified in the MSA. Similar to the settlement with the Maliseets, MSA provides that the Micmacs' trust lands include natural resources. 30 M.R.S. § 7202(2) ("'Aroostook Band Trust Land' means land or natural resources acquired by the secretary in trust for the Aroostook Band of Micmacs . . .."). MSA further defines natural resources to include fishing rights. *Id*. at § 7202(3) ("'Land or other natural resources' means any real property or other natural resources . . . including, but without limitation . . . water and water rights and hunting and fishing rights.")

In 1991, Congress passed ABMSA, one key purpose of which was to ratify the MSA. ABMSA § 1(b)(4). Congress specifically found and declared that:

> It is now fair and just to afford the Aroostook Band of Micmacs the same settlement provided to the Houlton Band of Maliseet Indians for the settlement of that Band's claims, to the extent they would have benefited from inclusion in the Maine Indian Claims Settlement Act of 1980.

Id. at § 1(a)(5). To that end, Congress established the Aroostook Band of Micmacs Land Acquisition Fund, *id*. at § 4(a), and provided that:

> the Secretary is authorized and directed to expend, at the request of the Band, the principal of, and income accruing on, the Land Acquisition Fund for the purposes of acquiring land or natural resources for the Band and for no other purposes. Land or natural resources acquired within the State of Maine with funds expended under the authority of this subsection shall be held in trust by the United States for the benefit of the Band.

Id. at § 5(a). ABMSA defines "Band Trust Land" to mean "land or natural resources acquired by the Secretary of the Interior and held in trust by the United States for the benefit of the Band" and defines "land or natural resources" to mean "any real property or natural resources, or any interest in or right involving any real property or natural resources, including (but not limited to) . . . water and water rights, and hunting and fishing rights." *Id*. at § 3(3) and (4). As with the Maliseets, Congress clearly intended that the Micmacs' trust lands could encompass fishing rights.

The Senate conference report from the Select Committee on Indian Affairs on ABMSA indicates that Congress intended to remedy the plight of the Micmacs, who had been deprived of a land base on which to secure the Tribe's continuation as a unique culture. "As Maine's only Native American community without a tribal land base, the Aroostook Band of Micmacs faces major challenges in its quest for cultural survival." 102 S. Rpt 136 (1991). The report describes the cultural practices of the band, including its historic homeland range along the west bank of the St. John River. "The ancestors of the Aroostook Micmac made a living as migratory hunters, trappers, fishers and gatherers until the 19th century." It goes on to note that "[t]oday, without a tribal subsistence base of their own, most Micmacs in Northern Maine occupy a niche at the lowest level of the social order." The discussion of the Band's history ends by observing:

> It is remarkable that the Aroostook Band of Micmac Indians, as a long disenfranchised and landless native group, has not withered away over the centuries. To the contrary, this community in Northern Maine has demonstrated an undaunted collective will toward cultural survival.

As with the Maliseets, it is clear Congress intended to establish a land base for the Micmacs that would enable the Tribe to secure its "cultural survival" and avoid acculturation. Congress intended for the Northern Tribes' trust lands to provide a "subsistence base" on which the Tribes

could assure their continued existence as a unique culture. And Congress was aware that part of that subsistence base for the Northern Tribes was their sustenance fishing practices.

While Congress intended that the Indian lands in Maine provide a land base to support all the Tribes' sustenance practices, it ratified dramatically different regulatory frameworks within which the Southern and Northern Tribes could operate in exercising those practices. In their reservations and lesser ponds in their trust lands, the Southern Tribes are substantially free from state fishing regulations, and elsewhere in their trust lands any regulation of the Southern Tribes' fishing must consider their sustenance practices. As explained in the discussion of the State's jurisdictional authority above, the Northern Tribes and their trust lands are subject to the laws of the State, including the regulation of natural resources, which includes fishing rights. So unlike the Southern Tribes, the ability of the Northern Tribes to exercise their sustenance fishing practices is potentially subject to regulation directly under state law. As DOI's legal opinion explains, the Northern Tribes' trust lands include fishing rights appurtenant to those land acquisitions, which are subject to state regulation.

But this jurisdictional arrangement does not alter the fact that Congress established the Northern Tribes' trust lands for the purpose of providing these Tribes a land base on which to exercise their sustenance practices to the extent possible. Finding that state law applies to the Northern Tribes' fishing rights does not answer the question how those Tribes intend to use the waters on their trust lands consistent with the purpose of setting aside their land base. And the state law applicable to the Northern Tribes' fish take makes it clear that there are generous take limits that allow a catch sufficient to support sustenance fishing. As analyzed in the review of state fishing regulations supporting this decision, it appears state fishing regulations applicable to the Northern Tribes' trust lands do not impose limits that would prevent individual members of the Northern Tribes from taking fish sufficient to support a sustenance diet.[12] Further, under state law, the Department of Inland Fisheries and Wildlife has authority to set take limits on fisheries for the purposes of their preservation, protection, enhancement and use as well as the propagation of fish for the effective management of inland fisheries resources in public waters of the State. 12 M.R.S. § 10053.[13] While this regulatory process does not include the same kind of procedural and burden of proof protections MIA provides for the Southern Tribes' fishing rights, it still requires the State to have a legitimate, non-arbitrary reason for limiting the take in the Northern Tribes trust lands based on the need to preserve and protect state fisheries. So as provided under state law, there appears to be ample ability for the Northern Tribes to fish for their sustenance in tribal waters associated with their trust lands.

3.3.1.3 Passamaquoddy Marine Sustenance Fishing

The Passamaquoddy Tribe's Pleasant Point reservation is located on marine, not inland, waters. There is a dispute among the Tribe, the State, and the commission about whether the Tribe's aboriginal right to take fish in marine waters survived the passage of MICSA. See 25 U.S.C. §§ 1722(b) and 1723(b) and Assessment of the Intergovernmental Saltwater Fisheries Conflict between Passamaquoddy and the State of Maine, Maine Indian Tribal-State Commission: Special

[12] See memorandum from Ralph Abele to the file for this decision, regarding Effects of Maine Fishing Regulations on Sustenance Fishing by Maine Tribes, dated January 30, 2015.
[13] See memorandum from Greg Dain, re: Maine Fishing Regulation, December 23, 2014.

Report 2014/1 (June 17, 2014) at 7. EPA is taking no position at this time as to the Tribes' aboriginal rights to take fish in marine waters or the scope of the sustenance fishing right codified in MIA section 6207 in marine waters. Nonetheless, the marine waters that are part of the Pleasant Point reservation serve a function in supporting the sustenance of the Tribe identical to the inland waters in the Tribe's reservation and trust lands.

First, Congress understood that the Passamaquoddy Tribe exercised subsistence practices on its reservations, including the Pleasant Point Reservation. The Senate Report's discussion of Special Issues noted that "[p]rior to the settlement, Maine law recognized the Passamaquoddy Tribe's and Penobscot Nation's right to control Indian subsistence hunting and fishing within their reservations, but the State of Maine claimed the right to alter or terminate these rights at any time." As quoted more extensively above, the Senate Report then goes on to describe in detail MIA's provisions for the reserved sustenance fishing right of the Southern Tribes. Sen. Rep. No. 96-957 at 16-17. While some dispute whether the Southern Tribes' sustenance fishing extends into marine waters, at a minimum Congress understood that the Passamaquoddy Tribe fished for its sustenance on its reservation and that the State had accommodated that practice under state law.

Notably, Maine has continued its practice of recognizing and providing for the Passamaquoddy Tribe's sustenance marine fishing practices under state law. In 2013, the State codified a "tribal exemption" from otherwise applicable state fishing regulation of marine species for all four Indian Tribes in Maine to exercise a "sustenance use if the tribal member holds a valid sustenance fishing license issued by the tribe, nation or band . . .." That same subsection goes on to define "sustenance use" as:

> . . . all noncommercial consumption or noncommercial use by any person within Passamaquoddy Indian territory, as defined in Title 30, section 6205, subsection 1, Penobscot Indian territory, as defined in Title 30, section 6205, subsection 2, or Aroostook Band Trust Land, as defined in Title 30, section 7202, subsection 2, or Houlton Band Trust Land, as defined in Title 30, section 6203, subsection 2-A, or at any location within the State by a tribal member, by a tribal member's immediate family or within a tribal member's household.

12 M.S.A. § 6302-A(2)(emphasis added). This section imposes seasonal limits on the taking of sea urchins and limits on the number of lobster traps used to harvest lobsters for sustenance use. But it is a clear acknowledgement of and provision for the Passamaquoddy Tribe to take marine species for their sustenance "within Passamaquoddy Indian territory" as defined in MIA, which includes the Tribe's reservations.

Again, EPA acknowledges that there is a current dispute about the extent of the State's authority to regulate the Tribes' marine fishing practices. In citing section 6302-A, EPA does not take a position on the merits of that dispute. EPA is concluding, however, that even if EPA accepts the State's position on its ability to regulate the Passamaquoddy Tribe's marine fishing practices, state law makes ample provision for sustenance fishing on the Tribe's reservation. Therefore, as with the Northern Tribes' trust lands, even if the State has authority to regulate the Tribe's take of marine species, EPA concludes that one important purpose of the Tribe's reservation is to

serve as a land base for the Tribe's exercise of sustenance practices at least to the extent consistent with Maine law regulating the taking of fish. And consistent with that Maine law, the Tribe can consume sufficient marine species to sustain themselves under section 6302-A.

3.3.2 Purpose of MIA, MICSA, MSA, ABMSA and Water Quality

As explained above, all four settlement acts in Maine provide for the Tribes to exercise sustenance fishing practices on waters in Indian lands in Maine. The statutory mechanism supporting this conclusion is quite different depending on which element of Indian lands is involved. But the fundamental conclusion that Congress understood and intended that the Tribes be able to sustain their unique cultures and sustain themselves on Indian lands in Maine is clear.

EPA concludes that the purpose to which Congress dedicated these Indian lands has important implications for water quality regulation under the CWA. Some in Maine have argued that the fishing right reserved to the Southern Tribes in their reservations is simply an exception from otherwise applicable state creel limits, but has no bearing on whether the water supporting that fishing right must be clean enough to ensure that the fish that tribal members are consuming is safe to eat. EPA does not agree with this narrow approach to the relationship between the provisions for tribal sustenance practices on the one hand and water quality on the other. Fundamentally, the Tribes' ability to take fish for their sustenance under the Maine settlement acts would be rendered meaningless if it were not supported by water quality sufficient to ensure that tribal members can safely eat the fish for their own sustenance.

There are several examples of the courts finding that fishing rights for tribes encompass subsidiary rights that are not explicitly included in treaty or statutory language, but are nonetheless necessary to render those rights meaningful. One line of cases focuses on the tribes' ability to access fish. *See, e.g., United States v. Winans*, 198 U.S. 371, 384 (1905) (tribe must be allowed to cross private property to access traditional fishing ground); *Kittitas Reclamation District v. Sunnyside Valley Irrigation District*, 763 F.2d 1032, 1033-34 (9th Cir. 1985) (tribe's fishing right protected by enjoining water withdrawals that would destroy salmon eggs before they could hatch); *Grand Traverse Band of Ottawa and Chippewa Indians v. Director*, *Mich. Dept of Nat. Resources*, 141 F.3d 635 (6th Cir. 1989) (treaty right to fish commercially in the Great Lakes found to include a right to temporary mooring of treaty fishing vessels at municipal marinas because without such mooring the Indians could not fish commercially).

Another line of cases focuses on water quantity sufficient to support fish habitat. In *United States v. Adair*, the Ninth Circuit held that the tribe's fishing right implicitly reserved sufficient waters to "secure to the Tribe a continuation of its traditional . . . fishing lifestyle." 723 F .2d 1394, 1409-10 (9th Cir. 1983). *See also Colville Confederated Tribes v. Walton*, 647 F.2d 42, 47 -48 (9th Cir. 1981) (implying reservation of water to preserve tribe's replacement fishing grounds); *Winters v. United States*, 207 U.S. 564, 576 (1908) (express reservation of land for reservation impliedly reserved sufficient water from the river to fulfill the purposes of the reservation); *Arizona v. California*, 373 U.S. 546, 598-601 (1963) (creation of reservation implied intent to reserve sufficient water to satisfy present and future needs).

The preceding cases focus on fishing rights, and the attendant or implicit requirement that those fishing rights not be denied through collateral action impairing that right. Analogously, when diminished water quality has hindered tribal uses of water outside the fishing context, courts have held in favor of tribes and found that a right to put water to use for a particular purpose must include a subsidiary right to water quality sufficient to permit the protected water use to continue. This occurred in an Arizona case, *United States v. Gila Valley Irrigation District*, in which farmers whose properties were located upstream from an Indian reservation were required to take steps to decrease the salinity of the river reaching the tribe's reservation so that "the Tribe receives water sufficient for cultivating moderately salt-sensitive crops." 920 F. Supp. 1444, 1454-56 (D. Ariz. 1996), *aff'd*, 117 F. 3d 425 (9th Cir. 1997).

So there is precedent for the proposition that, when Congress identifies and provides for a particular purpose or use of specific Indian lands, an Agency should consider whether its actions have an impact on a tribe's exercise of that purpose or use and, to the extent possible, ensure that its actions protect that purpose or use. If a tribe could not survive on its land base without water, or water clean enough to farm, for example, courts have recognized that the purpose of that reservation or trust land would be entirely defeated. So too here, it would defeat the purpose of MIA, MICSA, MSA and ABMSA if the Maine Tribes cannot safely sustain themselves from the fish they can catch from their waters. DOI's legal opinion concludes that "fundamental, long-standing tenets of federal Indian law support the interpretation of tribal fishing rights to include the right to sufficient water quality to effectuate the fishing right." If EPA were to ignore the impact that water quality, and specifically water quality standards, could have on the Tribes' ability to safely engage in their sustenance fishing practices on their lands, the Agency would be contradicting the clear purpose for which Congress ratified the settlements in Maine and provided for the establishment of Indian lands in the State. Therefore, it is incumbent upon EPA when applying the requirements of the CWA to harmonize those requirements with this Congressional purpose.

3.3.3 Tribal Fishing Rights, the CWA, and the MICSA Savings Clauses

Accordingly, as explained in more detail below, EPA is identifying "sustenance fishing" to be a designated use in tribal waters, and is disapproving Maine's human health criteria because they are not stringent enough to protect the sustenance fishing use. EPA considered whether taking this action is prohibited by the so-called "savings clauses" in MICSA that are designed to block application of federal law in the State if it would both accord or relate to a special status or right for Indian tribes and affect or preempt the jurisdiction of the State. 25 U.S.C. §§ 1725(h) and 1735(b). EPA concludes that the savings clauses do not preclude EPA's actions under the CWA.

EPA is addressing the provisions of MICSA, which specifically provides for a land base for the Maine Tribes that is set aside for the purpose of preserving the Tribes' culture and sustenance practices, in the Agency's implementation of the CWA, which requires that water quality criteria protect designated uses and be based on sound scientific rationale. Unless EPA acts to ensure that the Tribes are able to safely exercise their sustenance practices, a key purpose behind the provisions in MICSA, MIA, ABMSA and MSA to assemble and preserve the Maine Tribes' land base and cultures would be largely defeated. When EPA identifies Maine's designated use of "fishing" to mean "sustenance fishing" in tribal waters, it is giving effect to MICSA within the

framework of Agency oversight of WQS provided for in the CWA. It certainly cannot be the case that the savings clauses in MICSA somehow operate to prevent the government from addressing MICSA itself.

In addition, the savings clauses cannot block operation of the CWA oversight authority EPA is exercising in this case. EPA's authority to review and approve or disapprove new or revised state WQS rests on the requirements of CWA section 303(c)(3), which provides general authority and a non-discretionary duty to review and approve or disapprove all new or revised WQS from states. Because this authority under the CWA neither "accords or relates to a special status or right of or to any Indian . . . tribe," nor "affects or preempts the … regulatory jurisdiction of the State of Maine…," it is not blocked by the operation of the applicable MICSA savings clause. See 25 U.S.C. § 1725(h)(note that section 1735(b) would not apply to CWA section 303, because section 303 was enacted in 1972, and section 1735(b) applies only to laws enacted in and after 1980.). Nothing about EPA's oversight of Maine's WQS limits the State's jurisdiction to set WQS for waters in Indian lands. As to the adequacy of the WQS, no state has authority under the CWA to set standards that are "not consistent with the applicable requirements of this chapter [of the CWA]." 33 U.S.C. § 303(c)(3). In determining whether Maine's new or revised criteria are protective of the sustenance fishing designated use in Indian waters, EPA is simply exercising the same oversight authority it would exercise inside or outside Indian country anywhere in the nation. So this action does not accord the Indian Tribes in Maine a "special status or right."

EPA also considered whether, in looking to the federal common law of reserved tribal fishing rights when interpreting MICSA and implementing the CWA, EPA has somehow applied federal law to affect the application of state law. As a threshold matter, the MICSA savings clauses appear to be drafted entirely with Congressional statutory enactments in mind, and do not appear to address federal common law. For example, MICSA section 1725(h) provides that "no law or regulation of the United States" in existence at the time MICSA passed will apply in Maine if the conditions of that section are met. The formulation of "law or regulation" suggests Congress had in mind statutes that are routinely implemented by regulation. And the example provided in the Senate Committee Report of the operation of that section is a description of how section 164 of the Clean Air Act, a statutory law, would not apply in Maine. Sen. Rep. No. 96-957, p. 31.[14]

Finally, the operation and effect of these savings clauses is irrelevant to the use that EPA is making of federal common law in this case. The savings clauses are designed to prevent the federal government from unintentionally re-writing the jurisdictional deal embodied in MICSA. Only Congress has the authority to do that. In referencing certain principles of federal common

[14] Section 1735(b) is the companion "savings" provision to section 1725(h), and it blocks the application of federal law enacted after 1980 if that law would benefit the Tribes and affect or preempt the application of state law. That section refers to "enacted Federal law" and includes the idea that a federal law may apply in Maine if it is made specifically applicable in Maine. This provision also appears aimed at statutes that Congress enacts where Congress has the opportunity to decide whether to call out Maine in particular. The Senate Report on MICSA confirms this reading: "*Subsection 16(b)* [codified as section 1735(b)] provides a rule of construction to govern interpretation of Federal *statutes* enacted after the date of enactment of this Act." Sen. Rep. No. 96-957, p. 35 (underscore added). Thus it appears that both of these savings provisions were designed to operate in combination to address congressional enactments and resulting regulations that might apply in Maine, not common law.

law noted above, EPA is merely acknowledging useful precedent that can inform how to interpret the purpose to which Congress dedicated the Tribes' lands under MICSA and the other settlement acts. Doing so does not revise MICSA or change its jurisdictional formula; rather EPA is ensuring that the tribal territories can continue to serve the purpose for which they were created under MICSA. This is precisely consistent with First Circuit precedent in which the court has looked to federal principles of Indian law to help interpret the meaning of MICSA. *Akins*, 130 F.3d at 489-490 and *Fellencer*, 164 F.3d at 711-712.

3.3.4 Designated Use of Sustenance Fishing

In section 3.2 above, EPA describes its approval of the designated uses contained in the various classifications of waters in Indian lands. Each classification includes the designated use of "fishing." As explained below, EPA is interpreting the designated fishing use for all waters in Indian lands to mean "sustenance fishing"; and for certain waters in the Southern Tribes reservations, EPA is also approving a sustenance fishing designated use specified in MIA.

3.3.4.1 EPA's Decision to Approve a Sustenance Fishing Use in the Southern Tribes' Inland Reservation Waters

As discussed above, MIA provides that: "Notwithstanding any rule or regulation promulgated by the commission or any other law of the State, the members of the Passamaquoddy Tribe and the Penobscot Nation may take fish, within the boundaries of their respective Indian reservations, for their individual sustenance subject to the limitations of subsection 6." 30 M.R.S. § 6207, sub-§ 4. "Fish" is defined to mean "a cold blooded completely aquatic vertebrate animal having permanent fins, gills and an elongated streamlined body usually covered with scales and includes inland fish and anadromous and catadromous fish when in inland water." 30 M.R.S. § 6207, sub-§ 9.

These provisions clearly codify a tribal right of sustenance fishing for inland, anadromous, and catadromous fish in the inland waters of the Penobscot Nation's and Passamaquoddy's reservations.[15] This right is subject only to 30 M.R.S. § 6207, sub-§ 6, which authorizes Maine's Commissioner of Inland Fisheries and Wildlife to, among other things, adopt remedial measures, including the rescission of any tribal ordinance or regulation by the Maine Indian Tribal-State Commission, to prevent substantial diminution of fish stocks in waters outside of the boundaries of lands or waters subject to regulation by the Passamaquoddy Tribe, the Penobscot Nation or the Commission.

EPA has evaluated whether 30 M.R.S. § 6207, sub-§§ 4 and 9, constitutes a new or revised water quality standard, in light of the Agency's recent guidance regarding how it determines what is or is not a new or revised WQS, summarized in EPA's 2012 Frequently Asked Questions (FAQ) publication on the subject.[16] As explained in the FAQ, EPA considers four questions in making this determination, and in this case, all four questions are answered in the affirmative. First,

[15] EPA is taking no position here on whether this codified right includes or excludes fish in marine waters. See section 3.3.1.3, above. EPA is approving these provisions for inland waters where there is no ambiguity.
[16] EPA, What is a New or Revised Water Quality Standard Under CWA 303(c)(3)? Frequently Asked Questions, October 2012.

these provisions are legally binding and were established as a matter of state law. Second, they include and address one of the three core components of a water quality standard (i.e., a designated use), since they articulate a specific fishing use for the specified waters. Third, they express or establish the desired condition of the waters, or level of protection afforded the waters, by specifically providing for *sustenance* fishing. (As discussed above, to protect sustenance fishing, the water quality must be both adequate to support healthy fish populations at levels that provide a sufficient quantity of fish to be taken for sustenance purposes, and adequate to ensure that such fish may be safely consumed at sustenance rates by tribal members.[17]) Lastly, these provisions establish a new water quality standard since they have not previously been approved by EPA.

Based on this evaluation, EPA has determined that 30 M.R.S. § 6207, sub-§§ 4 and 9, constitutes a new or revised water quality standard, specifically a designated use, subject to EPA review and approval or disapproval under section 303(c) of the CWA.[18] EPA further finds that the sustenance fishing designated use established by 30 M.R.S. § 6207, sub-§§ 4 and 9, is consistent with the provisions of sections 101(a) and 303(c)(2) of the CWA, as well as EPA's implementing regulations. Accordingly, EPA is today approving the designated use of sustenance fishing for inland, anadromous, and catadromous fish, applicable to all inland waters of the Southern Tribes' reservations in which populations of fish are or may be found.[19]

3.3.4.2 EPA's Decision to Interpret the State's Designated Use of "Fishing" to Mean Sustenance Fishing for Waters in the Northern and Southern Tribes' Trust Lands

As explained above, EPA is approving the State's designated use of "fishing" as it applies to waters in Indian lands. In inland waters of the Southern Tribes' reservations EPA is also approving a specific additional designated use of sustenance fishing, as explained immediately above. In the trust lands for all the Tribes in Maine and the marine waters of the Passamaquoddy Tribe's reservation, EPA must determine how to interpret the fishing use that EPA is approving for those waters. EPA concludes that to protect the function of these waters to preserve the Tribes' unique culture and to provide for the safe exercise of their sustenance practices, EPA must interpret the fishing use to include sustenance fishing.[20]

In reviewing Maine's WQS as they apply to waters in Indian lands, EPA must reconcile two statutory frameworks. On the one hand, the CWA generally assigns to a state the responsibility of determining the designated uses in its waters (subject to certain restrictions at 40 C.F.R. § 131.10). 33 U.S.C. §§ 1251(a)(2), 1313(c)(2)(A). On the other hand, as explained above, the

[17] As noted above, the sustenance fishing use is subject to the limitations of 30 M.R.S. § 6207, sub-§ 6, which authorizes Maine's Commissioner of Inland Fisheries and Wildlife to take steps to prevent substantial diminution of fish stocks. EPA considers this to be a fisheries management provision, and not a restriction on the *quality* of water needed to protect the sustenance fishing use.

[18] EPA's authority and duty to review and approve or disapprove new or revised WQS does not depend on whether such WQS have been submitted by the State to EPA for review, or on where in state law they are codified. *FAQ* at 2.

[19] EPA interprets this designated use of sustenance fishing as not applying to inland waters that are inherently incapable of sustaining fish populations, such as most ephemeral streams and vernal pools.

[20] EPA interprets the designated "fishing" use for the inland waters of the Southern Tribes' reservations in the same manner. However, because EPA is also approving a specific sustenance fishing use contained in 30 M.R.S. § 6207, sub-§§ 4 and 9 for those waters, the discussion in this section is focused on the waters in the Trust lands.

settlement acts in Maine recognize and create specific areas in the State to provide for the Tribes to use their waters in a way that is distinct from waters outside Indian lands. EPA is bound to attend to and comply with both statutory frameworks to the extent EPA is able to reconcile how they apply to the Agency's review of Maine's WQS in Indian waters.

It is possible to harmonize these two statutory frameworks by recognizing that the State's designated fishing use under the CWA must include the concept of sustenance fishing as provided for in the settlement acts. To do otherwise would run the risk that state WQS could be based on assumptions about fish consumption rates that could lead to criteria that fail to protect the Tribes' ability to safely consume fish for their sustenance. The settlement acts, adopted between 1980 and 1991, are designed to establish a land base on which the Tribes can sustain themselves as unique cultures going forward. Therefore, the Agency will interpret the designated fishing use to include the ability of tribal members to safely take fish for their individual sustenance.

The extent to which existing state law either codifies or at least accommodates tribal sustenance fishing supports this approach to harmonizing the settlement acts with the structure of the WQS program under the CWA. As described above, MIA codifies an express provision for sustenance fishing in the Southern Tribes' trust lands. The state fishing code as it applies to waters in the Northern Tribes' trust lands imposes take limits that appear to be consistent with those Tribes' ability to fish for their sustenance. And finally, in 2013, Maine explicitly provided for all the Tribes in Maine to take marine species for their sustenance. The role of tribal sustenance fishing is woven into the fabric of Maine law, so requiring that use to be protected in the State's WQS program as applied to tribal waters will not conflict with state law governing how the Tribes may use these waters.

As described above, EPA acknowledges that the Tribes' sustenance fishing practices are not free from state regulation. The State has varying degrees of authority to regulate the quantity of fish that can be taken depending on the type of Indian land involved. In the Southern Tribes' reservations, the State has very narrow authority to set limits in the reservations to prevent depletion of fish stock in waters outside the Southern Tribes' reservation waters. The commission can regulate fish take on certain waters on the Southern Tribes' trust lands based on factors enumerated in MIA. On the Northern Tribes' trust lands the State regulates take consistent with state law.[21] However, the State's authority to limit the taking of fish to manage fisheries for their protection and preservation is not inconsistent with the settlements acts' provision of sustenance fishing in tribal waters and EPA's identification of "sustenance fishing" as the designated use for these waters. Neither does the State's authority to limit take mean that state water quality criteria need not protect sustenance fishing in those waters. Water quality criteria must be sufficient to protect the designated uses, whether or not the uses are currently being achieved. CWA 303(c)(2)(A) and 40 C.F.R §§131.3(f) and 131.11.

[21] As noted earlier, EPA is not taking a position one way or the other on whether the State may regulate Passamaquoddy marine sustenance fishing where such fishing occurs within their reservation.

4 EPA's Decisions on Maine's New or Revised Water Quality Standards Submissions From 2003 through 2014

4.1 General Background

Section 303 of the CWA requires each state to adopt water quality standards to protect public health and welfare, enhance the quality of water, and otherwise serve the purposes of the CWA.[22] Any new or revised standard adopted by a state under section 303(c) must be submitted to EPA for review, to determine whether it meets the CWA's requirements, and approval or disapproval. 33 U.S.C. § 1313(c)(1) and (3); 40 C.F.R. §§ 131.5, 131.6 and 131.20.

WQS describe the desired condition of a waterbody and consist of three principle elements: (1) the "designated uses" of the state's waters, such as public water supply, recreation, propagation of fish, or navigation; (2) "criteria" specifying the amounts of various pollutants, in either numeric or narrative form, that may be present in those waters without impairing the designated uses; and (3) antidegradation requirements, providing for protection of existing water uses and limitations on degradation of high quality waters. EPA's regulations at 40 C.F.R. part 131describe the minimum requirements for each of these three elements of WQS.

In accordance with CWA § 303(c) and 40 C.F.R. §§ 131.5 and 131.11, EPA must ensure that new or revised criteria are based on sound scientific rationale and contain sufficient parameters or constituents to protect designated uses.

4.2 EPA's Decision to Disapprove Maine's Human Health Criteria for Waters in Indian Lands because They Do Not Protect the Designated Use of Sustenance Fishing in Waters in Indian Lands in Maine, and to Approve Maine's Cancer Risk Level of 10^{-6}

4.2.1 Maine's Human Health Criteria Submitted to EPA on May 14, 2004, January 11, 2006 and January 14, 2013

On May 14, 2004, DEP submitted revisions to the human health criteria for mercury at 38 M.R.S. § 420(1-B.A.(2)) to EPA for review and approval or disapproval. On January 11, 2006, Maine DEP submitted numeric Human Health Criteria ("HHC") for toxic pollutants, among other revisions, to EPA for review and approval or disapproval (the "2006 HHC").[23] These criteria replaced Maine's previous regulation that incorporated EPA's CWA § 304(a) recommended criteria by reference. The revisions reflected DEP's use of a statewide fish consumption rate ("FCR") of 32.4 g/day (an increase from the 6.5 g/day FCR on which EPA's

[22] Section 303's requirements also apply to tribes that are authorized to implement a WQS program. Since EPA's decision today relates to a state's WQS program, the discussion of general statutory and regulatory requirements and guidance are framed in terms of state actions only.

[23] HHC are established to protect human health from exposure to pollutants that occur through the ingestion of water and/or contaminated fish and shellfish. Any human health criterion for a toxicant is based on at least three interrelated considerations: cancer potency or systemic toxicity, exposure (e.g., fish consumption rate), and risk characterization. http://water.epa.gov/scitech/swguidance/standards/handbook/chapter03.cfm#section13

then CWA § 304(a) recommended criteria were based).[24] The HHC revisions included a requirement that HHC for carcinogens be based on a cancer risk level (CRL) of $1x10^{-6}$. DEP Rule Chapter 584 § 4. Accordingly, all of the HHC for carcinogens submitted to EPA in 2006 were calculated using a 10^{-6} CRL. EPA approved the mercury criteria for waters outside of Indian lands on January 25, 2005, and approved the other criteria for waters outside of Indian lands on July 7, 2006 and September 18, 2006. EPA is today addressing these criteria for waters in Indian lands.

On January 13, 2014, DEP submitted new HHC for acrolein and phenol, and revised criteria for arsenic (discussed separately below), to EPA for review and approval. Similar to the 2006 HHC, the new HHC for acrolein and phenol were based on the statewide fish consumption rate of 32.4 g/day and a CRL of 10^{-6}. EPA is addressing these criteria in its decision today for all waters in the State, including in Indian lands.

In 2011, Maine's legislature enacted LD 515, which required DEP to revise Maine's HHC for arsenic by basing it on a CRL of 1 in 10,000 ($1x10^{-4}$) rather than the previous CRL of 1 in 1,000,000 ($1x10^{-6}$). DEP adopted the new criteria based on the 10^{-4} CRL and a revised FCR of 138 g/day, in order to protect highly exposed state subpopulations, and on January 14, 2013, submitted them to EPA for review and approval. EPA approved the revised arsenic criteria only for waters outside of Indian lands on May 16, 2013. EPA is addressing these criteria in its decision today for waters in Indian lands.

4.2.2 EPA's Analysis of the Adequacy of Maine's HHC for Waters in Indian Lands

4.2.2.1 EPA Guidance

As explained in EPA's *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health* (the "2000 Human Health Methodology" or "2000 Guidance"), EPA recommends that states provide adequate protection from adverse health effects to the general population, as well as to highly exposed populations, such as recreational and subsistence fishers, two distinct groups whose fish consumption rates may be greater than the general population.[25] EPA provides national default fish consumption rates ("FCR") of 17.5 grams per day ("g/day") for the general population and recreational anglers, and of 142.4 g/day for subsistence fishers.[26] However, because the level of fish consumption in highly exposed populations varies by geographic location, EPA strongly recommends that states use local or regional data over the default values. EPA has also recently explained that in order to provide for safe fish consumption, it is important that HHC avoid any suppression effects that may occur

[24] Although not explicitly stated in DEP Regulation Chapter 584, the mercury criteria in 38 M.R.S. § 420(1-B.A.(2)) were based on the Maine Bureau of Health Fish Tissue Action Level of 0.2 mg/Kg, which was derived using a fish consumption rate of 32.4 g/day. See *Development of Ambient Water Quality Criteria for Mercury, A Report to the Joint Standing Committee on Natural Resources,* by DEP, dated January 15, 2001.
[25] EPA. 2000. *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health.* U.S. Environmental Protection Agency, Office of Water, Washington, D.C. EPA-822-B-00-004, p. 2-2. Available at: http://www.epa.gov/waterscience/criteria/humanhealth/method/complete.pdf
[26] Id., pp. 1-12 and 1-13.

when a group's consumption rate is artificially diminished due to perceptions of pollutant contamination of the fish.[27]

4.2.2.2 Tribal Sustenance Fishers to be Protected as the Target Population in Tribal Waters

EPA concludes that when analyzing how the WQS program applies to the sustenance fishing use in the waters of Indian lands in Maine, the tribal population must be considered to be the "target population" for the purpose of determining whether the State's human health criteria are adequate to protect the tribes' health, including determining the appropriate fish consumption rate applicable in those waters and weighing the risk level to which tribal members should be exposed. Congress set aside Indian lands to provide a place for the Tribes to reside and to exercise their sustenance practices. Therefore, that tribal population and its sustenance fishing use must be the focus of the risk assessment supporting water quality criteria to adequately protect that use. To do otherwise risks undermining the purpose for which Congress established and confirmed the Tribes' land base.

EPA's 2000 Human Health Methodology provides that when developing in-stream water quality criteria to protect human health, states have some flexibility in determining which populations the state's criteria are designed to protect. Generally the guidance recommends that states consider how to protect both susceptible and highly exposed populations when setting criteria.

> When choosing exposure factor values [including fish consumption rates] to include in the derivation of a criterion for a given pollutant, EPA recommends considering values that are relevant to population(s) that is (are) most susceptible to that pollutant. In addition, highly exposed populations should be considered when setting criteria.[28]

EPA's approach in this guidance is to recommend protection of the general population based on fish consumption rates designed to represent "the general population of fish consumers," and then to recommend that states assess whether there might be more highly exposed subpopulations or "population groups" that require the use of a higher fish consumption rate to protect them as the "target population group(s)." *Id*. at 4-24 – 25. The guidance leaves states considerable discretion in determining which populations to target for protection using either statewide criteria or more geographically focused site-specific criteria.

The 2000 Guidance does not directly speak to the unique situation EPA confronts in this action, where 1) a state has authority to set human health criteria for waters in Indian lands, and 2) those lands have been set aside by Congress for, among other reasons, the preservation of tribal cultural practices, including sustenance fishing. Nevertheless, it is possible to apply the principles outlined in the 2000 Guidance to this situation, informed by the settlement acts. As discussed below, the settlement acts lead EPA to consider the Tribes to be the general target population in their waters, and the Guidance's recommendations on exposure and cancer risk for the general target population can be applied accordingly.

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[27] EPA 2013, Human Health Ambient Water Quality Criteria and Fish Consumption Rates: Frequently Asked Questions, page 2. Available at: http://water.epa.gov/scitech/swguidance/standards/criteria/health/methodology/upload/hhfaqs.pdf

[28] EPA 2000 Human Health Methodology at 4-17.

In Maine, the State has authority to set WQS for the waters in tribal lands where tribal members are the exclusive or predominant population. See 30 M.R.S. § 6206(1) (Penobscot Nation and Passamaquoddy Tribe control "the right to reside within the respective Indian territories" as an internal tribal matter.) Some of those lands and the waters in them are subject to a statutorily reserved tribal fishing right; some are set aside for the purpose of giving the resident tribe a land base on which to exercise traditional sustenance practices. What all the waters in these Indian lands have in common is, as explained above, that the fishing activity on them will involve tribal members, and may be predominated by tribal members, who have the right to, and desire to, fish for their sustenance. Also as explained above, consistent with the purpose of the settlement acts to preserve the Tribes' culture, these tribal members intend to fish for their sustenance. They are not a highly exposed or high-consuming subpopulation in their own lands; they are the general population for which the federal set-aside of these lands and their waters was designed.[29]

Therefore, as described above, EPA has identified and approved a designated sustenance fishing use applicable to waters in these Indian lands. That designated use requires the Agency to focus its analysis on sustenance fishers as the target general population. In effect, the settlement acts have determined how EPA and Maine must analyze the use of these waters and the population to be targeted for protection, because those acts established Indian lands in Maine for the clearly identifiable purpose of allowing the Tribes to sustain themselves on their own lands and waters.

A similar analysis applies to another critical factor in deriving human health criteria, the cancer risk level. For carcinogenic pollutants, EPA's 2000 Guidance recommends that states protect the general population to a level of risk no greater than one in one hundred thousand to one in one million (1×10^{-5} to 10^{-6}) of an additional cancer occurring in that population. Maine DEP has selected 10^{-6} as the level of risk that must be used to establish human health criteria for carcinogenic pollutants, with the exception of arsenic. Maine Rule Chapter 584 § 4. EPA's 2000 Guidance indicates that if there are highly exposed groups or subpopulations within that target general population, such as subsistence consumers, water quality standards should protect those consumers to a level of risk no greater than one in ten thousand (1×10^{-4}).[30] EPA and Maine relied on this aspect of the guidance in approving Maine's recently submitted revision to its human health criterion for arsenic as it applies to waters outside Indian lands. The Agency analyzed whether the State's revised arsenic criterion adequately protected subsistence consumers *outside* tribal waters as a *subpopulation* to a risk level of 10^{-4}.

Again, EPA concludes that it would be inconsistent with the intent of the settlement acts to treat the Tribes as a subpopulation of the State when developing HHC for waters in their own lands, and to expose them to levels of risk above what would be reasonable for the general population of the State. Therefore, the CWA requires that when establishing WQS for these waters, the tribal members must be considered to be the target general population for the purposes of setting

[29] EPA recognizes that tribal members will not be the only population fishing from some of these waters. On major rivers such as the Penobscot River, for example, the general population has the right to pass through the waters in Indian lands. The presence of some nonmembers fishing on these waters, however, does not change the fact that the resident population in the Indian lands is made up of tribal members who expect to fish for their sustenance in the waters in Indian lands pursuant to the settlement acts.

[30] EPA 2000 Human Health Methodology at 2-6.

risk levels to protect the sustenance fishing use. In Maine, the State has codified a risk level of 10^{-6} for all but one carcinogen, and EPA is today approving that provision in Chapter 584 to apply to waters in Indian lands, as discussed further below.

4.2.2.3 Fish Consumption Rate

In evaluating the adequacy of Maine's HHC to protect the sustenance fishing designated use for waters in Indian lands, EPA reviewed the basis for the FCR used by Maine, and also considered whether other localized information exists that would be relevant and appropriate to consider in determining an adequate sustenance fishing consumption rate that is not artificially suppressed by pollution concerns.

4.2.2.3.1 ChemRisk Study

DEP derived the 32.4 g/day FCR, used for all of its HHC except arsenic, in part[31] from the results of a 1990 study conducted by McLaren/Hart – ChemRisk, of Portland, Maine (the "ChemRisk Study"[32]). While DEP considered several sources of information about fish consumption rates to develop the 2006 HHC, the ChemRisk Study contains the only localized data that DEP used. EPA reviewed the ChemRisk Study as well as additional information about the Study contained in comments from a primary author of the Study and responses to comments from DEP, contained in DEP's May 25, 2012 Response to Comments document submitted to EPA on January 14, 2013, to determine the Study's relevance to the target tribal populations' sustenance fish consumption rates in waters in Indian lands.

In 1990, to characterize the rates of freshwater fish consumption by Maine's resident anglers, ChemRisk conducted a statewide mail survey of Maine residents holding a valid Maine fishing license in 1989. The survey asked respondents to report the number of freshwater fish caught in Maine, their species, and the average length of each fish that was eventually consumed by them, including fish caught by other members of the respondent's household and by individuals outside the household. Along with other demographic information, respondents were asked to self-identify their ethnic background (white/non-Hispanic, Hispanic, Native American, Asian/Pacific Islander, Black, or other). Of the 2,500 surveys mailed, 1,612 were completed and returned. Of these, 1,053 anglers reported having consumed freshwater and anadromous fish obtained from Maine inland waters during the 1989-1990 ice fishing season or 1990 open water fishing season. The 95th percentile FCR (as calculated by rank without any assumption of statistical distribution) for the fish consuming anglers was 26 g/day.

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[31] Maine Bureau of Health, *Fish Tissue Action Levels,* February 20, 2001, published at https://www1.maine.gov/dhhs/mecdc/environmental-health/eohp/fish/documents/action-levels-writeup.pdf

[32] ChemRisk, A Division of McLaren Hart, and HBRS, Inc., *Consumption of Freshwater Fish by Maine Anglers,* as revised, July 24, 1992. See also Ebert, E.S., N.W. Harrington, K.J. Boyle, J.W. Knight, R.E. Keenan, *Estimating Consumption of Freshwater Fish among Maine Anglers*, North American Journal of Fisheries Management, 13:4, 737-745 (1993); http://dx.doi.org/10.1577/1548-8675(1993)013<0737:ECOFFA>2.3.CO;2

According to the Study, 148 Native Americans participated in the survey (11% of total participants), and 96 of those reported consuming freshwater fish that had been sport-caught.[33] The consumption rate for the Native American participants equaled or exceeded the rate of all other population groups at the 66th, 75th, and 90th percentiles[34], and the 95th percentile for Native Americans was nearly double the 95th percentile for the next highest population group.[35] However, the maximum rate reported by the Native Americans respondents (162 g/day) was lower than the maximum rate reported by the entire surveyed population (182 g/day).[36]

Ultimately, DEP used a statewide fish consumption rate of 32.4 g/day to establish its HHC, which is the equivalent of one 8-oz. fish meal per week, and, according to DEP, represents the 97th percentile FCR for Maine recreational anglers for all waters, and the 94th percentile for Native American anglers in Maine.[37] It was "designed to protect the subpopulation of recreational anglers that frequently consume sport-caught fish….."[38]

As explained above, in evaluating whether the sustenance fishing designated use for waters in Indian lands is protected by Maine's HHC, EPA considers the tribal sustenance fishers to be the "target" general population for such waters. This means that the FCR for the applicable HHC must reflect, as accurately as possible, the Tribes' sustenance level FCR, and the CRL must be protective of the sustenance fishers as a general population rather than as a highly exposed subpopulation.

Maine's FCR is based primarily on statewide data, which EPA's 2000 HH Methodology generally prefers over the use of national data. However, it is not based on localized data for the specific waters in Indian lands or the target tribal populations. The ChemRisk Study was not intended to be, nor was it, a survey of tribal sustenance fishers in tribal waters. The survey was sent to state-licensed recreational anglers, but tribal sustenance fishers are not required to have state licenses to fish in waters in Indian lands.[39] Therefore, EPA is unable to conclude that the Study results are representative of a fish consumption rate for tribal sustenance fishers in tribal waters.

In addition, the Study does not reflect unsuppressed fish consumption levels. At the time the ChemRisk survey was conducted, Maine had issued fish consumption advisories for the main stem of the Penobscot River, where the Penobscot Nation reservation is located, the Androscoggin River (1985), and the Kennebec River, (1987), and it issued advisories for the Presumpscot River and West Branch of the Sebasticook River in 1990.[40] DEP has acknowledged that "public awareness of historical pollution in industrialized rivers can be expected to have suppressed fish consumption on a local basis," and that the ChemRisk

[33] ChemRisk Study, Tables 5 and 6a..
[34] Id., Table 6a.
[35] Id., as revised (see comment by Ellen Ebert in DEP's Response to Comments, May 25, 2012, page 16).
[36] Written comments from Ellen Ebert, primary author of the Chemrisk Study, to Maine DEP, as reported in DEP Response to Comments dated May 25, 2012 and submitted to EPA January 14, 2013.DEP, page 16.
[37] Maine RTC, May 25, 2012, page 20.
[38] Maine DEP testimony to the Maine Legislature, April 25, 2011, p. 3.
[39] Id., p. 19.
[40] Id., p. 20.

"estimates of fish consumption for rivers and streams as well as the inclusive 'all waters' category are likely to have been affected to some degree."[41]

Although the responses were not tallied and not analyzed in ChemRisk's report, the ChemRisk survey did include questions regarding the impact of fish consumption advisories. EPA analysis of the survey response data[42] indicates that 35% of respondents (556 individuals) were aware of the advisories during the time of the survey. Of the 160 respondents who reported that they ate fish from locations covered by fish consumption advisories, 82% (135) reported that the advisories affected whether they kept the fish caught at those locations.[43] It is not clear (because the question was not asked) whether anglers avoided certain waters in the 1989/1990 fishing season because of the fish advisories and whether that avoidance affected their total fish consumption. Nonetheless, it is clear that the existence of the advisories did result in some anglers reducing their take from those rivers.

EPA also reviewed the results of the Penobscot Nation's draft 1991 Penobscot River Users Survey.[44] While the survey was small (210 respondents) and the response rate was only 25%, and it was limited to Penobscot Nation members and their use of the Penobscot River, it does contain information that reinforces EPA's conclusion that the ChemRisk Study does not reflect unsuppressed sustenance fish consumption in tribal waters. For example, 72.9 % of the respondents stated they did not eat fish from the Penobscot River, and a majority (66.7%) stated that they had concerns about eating fish from the river.[45] The vast majority of those concerns were related to pollution.[46] In addition, of the 37.1% who reported not using the river at all, 16.3% identified the reason as concerns about pollution.[47]

4.2.2.3.2 Wabanaki Traditional Cultural Lifeways Exposure Scenario

In considering whether there are other sources of local data to inform EPA's determination of what FCR is representative of sustenance fishing in the waters in Indian lands, EPA reviewed the Wabanaki Cultural Lifeways Exposure Scenario ("Wabanaki Study"), which was completed in 2009. This peer reviewed Study was produced under a Direct Implementation Tribal Cooperative Agreement (DITCA) awarded by EPA to the Aroostook Band of Micmac Indians on behalf of all of the Maine Tribes. The purpose of the Study was to use available anthropological and ecological data to develop a description of Maine Tribes' traditional cultural uses of natural resources, and to present the information in a format that could be used by EPA to evaluate whether or not tribal uses are protected when EPA reviews or develops water quality standards in Indian lands in Maine.[48] It is relevant to contemporary water quality because another purpose of

[41] Id., pp. 20-21.
[42] Provided by the study author, Ellen Ebert, to EPA via email October 3, 2013.
[43] EPA, *Analysis of Suppression Questions from Chemrisk Study,* Memo to File*,* January 30, 2015.
[44] 1991 Penobscot River Users Survey conducted by the Penobscot Nation's Department of Natural Resources (draft).
[45] Id., Appendix A, §§ A.5 and A.6
[46] Id., Appendix A, § A.6
[47] Id., Appendix A, §A.1.a
[48] Harper, Barbara and Darren Ranco, *Wabanaki Traditional Cultural Lifeways Exposure Scenario*, prepared for EPA in collaboration with the Maine Tribes, p.7, July 9, 2009.

the Study "is to describe the lifestyle that was universal when resources were in better condition and that some tribal members practice today (and many more that are waiting to resume once restoration goals and protective standards are in place)."[49] It provides a numerical representation of the environmental contact, diet, and exposure pathways of the traditional tribal lifestyle, including the use of water resources for food, medicine, cultural and traditional practices, and recreation. The Study acknowledges that "the Wabanaki homelands extended further west and south into areas with different plants and climate and where farming was possible," but notes that "the scenario itself covers only areas most heavily used by Tribal members at present, and where farming is marginal due to climate."[50]

The report used anthropological and ecological data to identify major activities that contribute to environmental exposure and then to develop exposure factors related to traditional diet, drinking water, soil and sediment ingestion, inhalation rate and dermal exposure. Credible ethno historical, ecological, nutritional, archaeological, and biomedical literature was reviewed through the lens of natural resource use and activities necessary to survive in the Maine environment and support tribal traditions. Along with single, best-professional judgment estimates for direct exposures (inhalation, soil ingestion, water ingestion) as a reasonable representation (central tendency) of the traditional cultural lifeways, the Wabanaki Study provides an estimated range of diets that reflect three major habitat types.[51]

In developing the dietary component of the exposure scenario, the Wabanaki Study authors assembled information about general foraging, seasonal patterns, dietary breadth, abundance, and food storage. From these they evaluated the relative proportion of major food groups, including fish, as well as nutritional information, total calories and quantities of foods. This resulted in an estimate of a nutritionally complete diet for the area east of the Kennebec River, which is the area most heavily used by tribal members today and where farming is marginal due to climate.[52]

With regard to the consumption of fish, the Wabanaki Study identifies three traditional lifestyle models, each with its own diet:

1. Permanent inland residence on a river with anadromous fish runs ("inland anadromous"),
2. Permanent inland residence with resident fish only ("inland non-anadromous"), and
3. Permanent coastal residence ("coastal").

The study provides estimates of average consumption of aquatic resources, game, fowl, and plant based foods for each lifestyle model. Aquatic resources were divided into two categories: "resident fish and other resources" and "anadromous and marine fish and shellfish." Table 1 summarizes the consumption of aquatic resources for each lifestyle model.

[49] Id., p. 9
[50] Id.
[51] Id., p. 16.
[52] Id., pages 8-9.

Table 1 – Consumption of Aquatic Resources by Lifestyle Model[53]

Lifestyle Model	Resident Fish & Other Aquatic Resources(g/day)	Anadromous & Marine Fish, Shellfish (g/day)[54]
Inland Anadromous	114	400
Inland Non-anadromous	286	0
Coastal	57	457

The Wabanaki Study provides a range of fish consumption rates specifically for Maine Indians using natural resources for subsistence living and reduces the uncertainties associated with a lack of knowledge about tribal exposure in Maine Indian waters. On their own, these fish consumption rates could form the basis for criteria protective of sustenance fishing. Alternatively, they could be the starting point that could be modified, based on additional information, to take into account present day circumstances related to the species composition of available fish. For example, in developing its 2014 tribal water quality criteria, the Penobscot Nation used a FCR of 286 g/day. The Nation explained that it chose the inland non-anadromous total FCR of 286 g/day because, although the Penobscot lands are in areas that would have historically supported an inland anadromous diet (with total FCR of 514 g/day), the contemporary populations of anadromous species in Penobscot waters are currently too low to be harvested in significant quantities. [55]

4.2.3 Disapproval of Maine's HHC Because They Are Based on FCRs that Fail to Protect Sustenance Fishing

EPA is today disapproving, for waters in Indian lands, the mercury human health criteria in 38 M.R.S. § 420(1-B.A.(2)) submitted to EPA on May 14, 2004; the fish consumption rate of 32.4 g/day specified in DEP Rule Chapter 584 § 5.C and all human health criteria in DEP Rule Chapter 584, Surface Water Quality Criteria for Toxic Pollutants, Appendix A, submitted to EPA on January 11, 2006; and the human health criteria revisions related to arsenic, acrolein, and phenol in DEP Rule Chapter 584, Surface Water Quality Criteria for Toxic Pollutants, Appendix A, as well as the last sentence in Ch. 584, § 5.C related to the fish consumption rate, submitted to EPA on January 14, 2013. The basis for the disapproval is that the HHC do not protect the sustenance fishing use in those waters. For the reasons discussed above, Maine's 32.4 g/day FCR is not representative of an unsuppressed sustenance fish consumption rate by tribal members in waters in Indian lands.

In the absence of a local survey of current fish consumption, adjusted to account for suppression, that documents fish consumption rates for sustenance fishing in the tribal waters, EPA finds that the Wabanaki Study contains the best currently available information for the purpose of deriving an FCR for HHC adequate to protect sustenance fishing for such waters. It is local, focused on the areas most heavily used by tribal members today. It identifies historic FCRs based on

[53] Id., pp. 61-66.
[54] Includes marine mammals for coastal lifestyle model only.
[55] Penobscot Nation, Department of Natural Resources, *Response to Comments on Draft Water Quality Standards*, September 23, 2014, p. 9.

reasonable estimates for total calories and protein intake per day. Heritage rates provide reliable evidence of what unsuppressed rates would be for tribal populations.[56] The Study uses a sound methodology (peer reviewed, written by a range of experts in risk assessment and anthropology). It presents a range of FCRs from 286 g/day (freshwater fish only) to 514 g/day (combinations of freshwater, anadromous, and marine species), which can provide the basis for choosing an FCR that reflects traditional cultural practices in light of present day circumstances related to, for example, the species composition of available fish (as the Penobscot Nation recently did in adopting an FCR of 286 g/day).

Because the Wabanaki Study documents a substantially higher tribal sustenance fish consumption rate than the FCR on which Maine's HHC are based, EPA cannot conclude that the HHC are based on a sound scientific rationale consistent with 40 C.F.R. § 131.11(a) and protect the sustenance fishing use for the waters in Indian lands. EPA is therefore disapproving the HHC.

4.2.3.1 Remedy to Address EPA's Disapproval

Under CWA § 303(c)(3) and EPA's implementing regulations at 40 C.F.R. §§ 131.21 and 131.22, when the EPA disapproves a state's new or revised water quality standard, it must "specify the changes" necessary to meet the applicable requirements of the Act and EPA's regulations. The CWA requires that this disapproval of Maine's human health criteria for waters in Indian lands be addressed in a timely manner. In the first instance, the CWA and EPA's regulations provide the State up to 90 days to revise its WQS, and EPA prefers that Maine address this disapproval under its regulatory development process. However, if the State does not adopt necessary changes, EPA will propose and promulgate appropriate human health criteria for waters in Indian lands in Maine.

To address this disapproval action, Maine must develop new human health criteria for waters in Indian lands that protect tribal sustenance fishers as the target general population and are based on a fish consumption rate that represents unsuppressed sustenance fishing by tribal members.

Among the available existing information on fish consumption, the Wabanaki Study is most relevant for Maine to consider in revising human health criteria in Indian lands. As discussed in section 4.2.2.3, the Wabanaki study is directly applicable to the Maine Tribes fishing in waters on Indian lands. The fish consumption rates developed in the Wabanaki study are estimates of unsuppressed tribal fish consumption that could be used in the derivation of criteria protective of contemporary tribal sustenance fishing. In addressing the disapproval, Maine should use the fish consumption rates developed in the Wabanaki study either on their own or modified, based, for instance, on information that may be provided by the Maine Tribes, to take into account changes in species composition in tribal fisheries and contemporary tribal sustenance fishing goals.

[56] National Environmental Justice Advisory Council, *Fish Consumption and Environmental Justice,* November 2002 (revised), page 49.

4.2.4 Approval of Maine's Cancer Risk Level of 10^{-6} and No Action on Maine's Arsenic CRL of 10^{-4}

Maine's water quality regulations specify that water quality criteria for carcinogens be based on a CRL of 10^{-6} for all pollutants except arsenic. DEP Rule Chapter 584 § 4. This CRL is consistent with the range of CRLs that EPA considers to be appropriate for the general population and is the risk level that EPA uses when publishing its CWA § 304(a) recommended criteria.[57] As explained above, EPA has determined that the Tribes are the target general population for waters in Indian lands. EPA is therefore today approving Maine's requirement to use 10^{-6} CRL for all carcinogens except arsenic (discussed further below) for the waters in Indian lands. Criteria based on this low level of cancer risk, along with other appropriate factors (including an appropriate FCR), will protect the sustenance fishing use for waters in Indian lands.

EPA recognizes that the Maine Legislature enacted a law that requires DEP to use a CRL of 10^{-4} when establishing arsenic criteria,[58] and that DEP Rule Chapter 584 was revised in 2012 to reflect this requirement. Since EPA is disapproving Maine's arsenic criteria along with all of the other HHC for waters in Indian lands due to an inadequate FCR, EPA is not acting on Maine's CRL for arsenic (i.e., the last sentence in Ch. 584, § 4, related to the cancer risk level to be used to calculate human health criteria for inorganic arsenic, and the first sentence of Footnote aME in Table I of Appendix A of Chapter 584). However, we note that when Maine revises its arsenic criteria, it must ensure that the criteria protect the Tribes as the general target population in these waters, not as a subpopulation. Based on the analysis above, the use of a sustenance level FCR developed for all of the HHC, in combination with a CRL of 10^{-4} for arsenic, would not protect the designated use of sustenance fishing.

4.3 EPA's Decision to Approve Maine's Human Health Criteria for Acrolein for the Consumption of Organisms Only and for the Consumption of Water and Organisms, and Phenol for the Consumption of Organisms Only, and to Take No Action on Phenol for the Consumption of Water and Organisms, in Waters Outside Waters in Indian Lands

For all waters in Maine *except* for waters in Indian lands, EPA approves the following water quality criteria contained in DEP Rule Chapter 584, Surface Water Quality Criteria for Toxic Pollutants, Appendix A, submitted to EPA on January 14, 2013:

- Human health criteria for the consumption of water plus organisms for acrolein; and
- Human health criteria for the consumption of organisms only for acrolein and phenol.

Maine's revised human health criteria for acrolein and phenol were derived using the same methodology and equations used to calculate EPA's current 304(a) recommended criteria for non-carcinogens. EPA updated recommended human health criteria for acrolein and phenol in 2009 based on new Integrated Risk Information System Reference Doses (RfDs) for the pollutants[59]. Consistent with EPA's criteria derivation, Maine has made no changes to the

[57] *2000 Human Health Methodology*, p. 1-8.
[58] 38 M.R.S. § 420(1-B.J).
[59] Federal Register: June 10, 2009 (Volume 74, Number 110)

parameters incorporated into these criteria or to the equations used other than the new RfDs. The criteria calculations are summarized in attached Tables 1 and 2 below.

Table 1 – Calculation of Approved Acrolein Human Health Criteria

Parameter	**2012 criteria**
Reference Dose (RfD)	0.0005 mg/(kg-d)
Body Weight (BW)	70 kg
Water Consumption (DW)	2 L/day
Bioconcentration Factor (BCF)	215 L/kg
Fish Consumption Rate (FCR)	0.0324 kg/day
Criteria to protect human health for consuming fish and drinking water (water + organism) $= \frac{1{,}000\ \mu g/mg \times RfD \times BW}{DW + (BCF \times FCR)}$	3.9 µg/L
Criteria to protect human health for consuming fish only (organism only) $= \frac{1{,}000\ \mu g/mg \times RfD \times BW}{BCF \times FCR}$	5.0 µg/L

Table 2 – Calculation of Approved Phenol Human Health Criteria

Parameter	**2012 criteria**
RfD for Phenol	0.30 mg/(kg-d)
Body Weight (BW)	70 kg
Water Consumption (DW)	2 L/day
Bioconcentration Factor (BCF)	1.4 L/kg
Fish Consumption Rate (FCR)	0.0324 kg/day
Criteria to protect human health for consuming fish only (organism only) $= \frac{1{,}000\ \mu g/mg \times RF \times BW}{BCF \times FCR}$	462,963 µg/L

EPA's approval of Maine's revisions to its human health criteria for acrolein and to the human health criteria for phenol for the consumptions of organisms only is based on a review of whether the criteria protect the applicable designated uses, including consideration of EPA's National Recommended Water Quality Criteria published pursuant to Section 304(a) of the CWA. EPA finds that the revised criteria are scientifically defensible and are protective of designated uses for waters outside of Indian lands, for the reasons explained in the EPA criteria documents for each chemical constituent.

EPA understands that DEP will be revising the phenol criteria for the consumption of water and organisms to address a mathematical error made in the criteria derivation. Therefore, at this time EPA is not taking action on the human health criteria for phenol for the consumption of water and organisms, for waters outside of Indian lands, with the anticipation that the revised phenol criteria will be adopted and submitted to EPA for review and action within the coming months.

4.4 EPA's Decision to Approve Maine's Aquatic Life Criteria for Acrolein, Diazanon and Nonylphenol for waters throughout the State of Maine, including in Indian Lands

EPA's review of Maine's new aquatic life criteria for acrolein, diazanon and nonylphenol, submitted to EPA on January 14, 2013, is based on whether the criteria protect aquatic life uses, including consideration of EPA's National Recommended Water Quality Criteria published pursuant to Section 304(a) of the CWA. EPA finds that the revised criteria are scientifically defensible and are protective of designated uses for the reasons explained in the EPA criteria documents[60] for acrolein, diazanon and nonylphenol.

4.5 EPA's Decision to Approve Maine's Aquatic Life Criteria Tables I and II in DEP Rule Chapter 584, except for Ammonia, Approve Aquatic Life Criteria in 38 M.R.S. § 420(1-B.A.(1)), (1-B.C), (1-B.D), and (1-B.E), and Approve Biological Criteria in DEP Rule Chapter 579 for Waters in Indian lands

EPA's review of the aquatic life criteria, other than ammonia, in DEP Regulation Chapter 584 Tables I and II, submitted to EPA on January 11, 2006, and in 38 M.R.S. § 420(1-B.A.(1)), (1-B.C)[61],(1-B.D), and (1-B.E), submitted to EPA on May 14, 2004 (related to mercury and referenced in Table I of Chapter 584), for waters in Indian lands, is based on whether the criteria protect aquatic life uses, including consideration of EPA's National Recommended Water Quality Criteria published pursuant to Section 304(a) of the CWA. EPA finds that the revised criteria are scientifically defensible and are protective of designated uses for the reasons explained in the EPA criteria documents[62] for those pollutants. EPA approved these criteria for waters outside Indian lands on January 25, 2005 and July 7, 2006, and is now approving them for waters in Indian lands.

DEP Rule Chapter 579 provides numeric biological criteria that quantify aquatic life standards for Class AA, A, B and C waters. The rules use the benthic macroinvertebrate community as a surrogate to determine conformance with statutory aquatic life standards. EPA approves of these criteria because they are based on sound scientific rationale and are protective of designated aquatic life uses, as required by Section 303(c)(2)(B) of the CWA and 40 C.F.R. § 131.11. EPA approved this rule for waters outside Indian lands on January 25, 2005, and is now approving it for waters in Indian lands.

4.6 EPA's Decision to Approve Maine's Narrative Criteria for Toxic Pollutants and Implementation Policies Regarding the Development of Statewide Criteria and Site-Specific Criteria, except for Specified Fish Consumption Rates, in DEP Rule Chapter 584, for Waters in Indian Lands

EPA's review of Maine's narrative water quality criteria, as expressed in Chapter 584, §§ 1, 2, and 3.A(1), and submitted to EPA on January 11, 2006, is based on whether those provisions are protective of designated uses, as required in 40 C.F.R. § 131.11. Since the narrative criteria specifically call for waters to be free of pollutants in concentrations that cause waters to be

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[60] See http://water.epa.gov/scitech/swguidance/standards/criteria/current/index.cfm#altable for National Recommended Water Quality Criteria and access to criteria documents for each pollutant.

[61] Not including 38 M.R.S §420(1-B.C.(1)) and (1-B.C.(2)), which are not WQS requiring EPA review and approval – see section 4.9 below.

[62] See http://water.epa.gov/scitech/swguidance/standards/criteria/current/index.cfm#altable for National Recommended Water Quality Criteria and access to criteria documents for each pollutant.

unsuitable for the designated uses of the water body, EPA finds that they are consistent with the requirements. EPA approved these provisions for waters outside Indian lands on July 7, 2006, and is now approving them for waters in Indian lands.

EPA's review of Maine's implementation policies regarding the development of statewide criteria and site specific criteria in Chapter 584 §§ 3 and 5 (other than the fish consumption rates of 32.4 g/day and 138 g/day, which EPA is disapproving as discussed above) is based on whether the criteria developed from those policies would protect the applicable designated uses including a consideration of EPA's ambient water quality criteria guidance, published pursuant to Section 304(a) of the CWA. The implementation policies include requirements for developing scientific bases for new or revised criteria as well as assumptions regarding ambient waters characteristics (such as pH, temperature, and salinity), and human health (such as water consumption rate and average body weight). EPA approved these policies for waters outside Indian lands on July 7, 2006 and now approves the implementation policies in Chapter 584 §§ 3 and 5 (other than the fish consumption rates) for waters in Indian lands because they require criteria to protect designated uses, and since the procedures and numeric assumptions are consistent with currently published EPA guidance.

EPA is not taking action on the procedures described in Chapter 584 § 3 which describe how alternative statewide and site-specific criteria are to be initiated, reviewed and adopted under state law.[63] Such procedures are not WQS requiring review and approval by EPA. Any new or revised criteria developed under the procedures for statewide, alternative statewide, or site-specific criteria must be submitted to EPA for review and approved by EPA pursuant Section 303(c)(3) of the Clean Water Act and 40 C.F.R. part 131 in order to be effective for Clean Water Act purposes.

4.7 EPA's Decision to Approve Maine's Dissolved Oxygen (DO) Criteria for Class C waters, Requirements for Compliance with DO criteria in Riverine Impoundments, Requirements for Instream Design Flows, the Requirement to Hold a WQS Review Hearing Every Three Years and Provisions that Allow for Pesticide Discharges into Class B and SB Waters for Mosquito Control, for Waters in Indian Lands

EPA's review of the revision to the DO criteria for Class C waters in 38 M.R.S. §465(4.B), submitted to EPA on January 11, 2006, is based on whether the criteria protect aquatic life uses, particularly cold waters species. For the reasons provided in our July 7, 2006 approval of these criteria for waters that are not in Indian lands, EPA finds that the criteria are protective of aquatic life uses and approves them in Indian lands as well.

EPA's review of the revision to DO measurement requirements for riverine impoundments in 38 M.R.S. §464(13), submitted to EPA on August 26, 2003, is based on whether the criteria protect existing and designated uses for waters in Indian lands. As explained in our February 9, 2004

[63] Specifically, these provisions are: the requirement in Chapter 584 § 3(A.(2)) that "statewide criteria must be initiated in accordance with the petition for rulemaking provisions of the State Administrative Procedures Act, 5 M.R.S.A., Section 8055"; the provision in the first paragraph of Chapter 584 § 3(B) that site specific criteria "must only be adopted by the Board as part of a waste discharge license proceeding pursuant to 38 M.R.S.A. Sections 413, 414 and 414-A"; and the first two sentences of the second paragraph of Chapter 584 § 3(B).

approval of this revision for waters that are not in Indian lands, EPA finds that the narrative standard that accompanies the measurement requirements ("dissolved oxygen concentration in existing riverine impoundments must be sufficient to support existing and designated uses of these waters") ensures that, notwithstanding the measurement restrictions in this provision, the revision is consistent with the requirements of the Clean Water Act.

EPA's review of the revisions to DEP Rule Chapter 530 § 4(B), which contains instream design flows for the application of water quality criteria for aquatic life and human health, submitted to EPA on January 11, 2006, is based on whether the provision protect existing and designated uses for waters in Indian lands. The instream design flows (1Q10 low flow for acute aquatic life criteria, 7Q10 for chronic aquatic life criteria, and harmonic mean flow for human health criteria), are consistent with guidance intended to ensure protection of uses provided in Section 5.2 of EPA' Water Quality Standards Handbook[64]. EPA approved this provision for waters outside Indian lands on April 17, 2006, and is now approving it for waters in Indian lands.

EPA's review of the revision to provisions in 38 M.R.S. § 464(3.B), that ensure that a hearing will be held at least every three years for the purpose of reviewing Maine's WQS, and revising them, as appropriate, submitted to EPA on May 14, 2004, is based on whether the provision is consistent with federal WQS review requirements. This revision reversed a previous change to 38 M.R.S. § 464(3.B)[65] that specified hearings only every four years. Since CWA § 303(c)(1) and 40 C.F.R. § 131.20 require states to hold public hearings every three years, the revision is consistent with federal WQS requirements. EPA approved this provision for waters outside Indian lands on January 25, 2005, and is now approving it for waters in Indian lands.

Revisions submitted on April 8, 2008 included the addition of 38 M.R.S. § 465(3.C.(2)) and § 465-B(2.C) which allow the discharge to Class B and SB waters of aquatic pesticides approved by DEP for control of mosquito-borne diseases. EPA's review is based on whether the provision will protect existing and designated uses for waters in Indian lands and is consistent with the requirements of the Clean Water Act. Given the requirements that the methods and materials used be protective of non-target species, EPA anticipates that no degradation of water quality would occur due to the discharge of aquatic pesticides authorized under these revisions. EPA approved these provisions for waters outside Indian lands on August 19, 2009 and is now approving it for waters in Indian lands.

4.8 EPA's Decision to Take No Action on Maine's Ammonia and Recreational Bacteria Criteria for Waters in Indian lands; on the Reclassification of Long Creek; and on Certain Bacteria and Pesticide Provisions for Waters throughout Maine, Including Waters in Indian Lands

EPA understands that Maine will be conducting a comprehensive triennial review in the coming months and will be reviewing the ammonia criteria for protection of aquatic life and the bacteria

[64] EPA-820-B-14-004, September 2014, provided on line at http://water.epa.gov/scitech/swguidance/standards/handbook/chapter05.cfm#section52.
[65] EPA did not act on the previous revision (calling for hearings every 4 years) which DEP submitted to EPA on August 26, 2003, since DEP agreed at that time to propose changing the requirement back to hearings every 3 years.

criteria for the protection of primary contact recreation, in light of EPA's recommendations[66] for these widespread pollutants, issued in 2013 and 2012, respectively. EPA expects that DEP will be revising these criteria for all waters in Maine, including waters in Indian lands, so that they are based on sound science and protective of the designated uses. For this reason, for waters in Indian lands, we are not taking action at this time on Maine's ammonia criteria for the protection of aquatic life in DEP regulation Chapter 584, Appendix A, and the numeric bacteria criteria for the protection of primary contact recreation for Class B and C waters in 38 M.R.S. §465(3.B) and (4.B), and the extension of the applicability of bacteria criteria for Class SB and SC waters to include bacteria of domestic animal origin in 38 M.R.S. § 465-B(2.B) and (3.B). For the same reason, we are not taking action for waters throughout the State, including waters in Indian lands, on the revisions to 38 M.R.S. §465(3.B) and (4.B) and 38 M.R.S. § 465-A(1.B), which extended the applicability of the bacteria criteria for Class B, C, and GPA waters to include bacteria of domestic animal origin. EPA would be happy to provide assistance to DEP as it develops the new criteria.

In addition, EPA is not taking action on the reclassification of a section of Long Creek (which is a water outside of Indian lands) from Class B to Class C. This downgrade in classification was adopted to achieve consistency in the Creek where the upstream and downstream reaches were already Class C waters. EPA agrees with DEP that it is unusual for a downstream section of a flowing water to be at a higher classification that the upstream section, However, EPA would like to discuss this reclassification further with DEP in the coming months to explore whether there are other means to remedy the inconsistency, such as reclassifying the upstream section to Class B if the restoration of Long Creek and Class B uses there are attainable.

EPA also reviewed the provisions related to certain pesticide discharges submitted to EPA in 2006, 2008 and 2014 and finds that many of these are not water quality criteria requiring review and approval by EPA (as discussed in the section that follows) and two are WQS that we have approved herein (as discussed in the preceding section). However, EPA finds that some of these revisions are WQS which EPA has not yet acted on for waters anywhere in Maine. The revisions related to pesticides that are WQS that we are continuing to take no action on are:

- The revisions made in L.D. 1304 at 38 M.R.S. § 464(4.A.(3)(a)), and § 465((3.C.(1)) and (4.C), related to certain pesticide discharges, submitted to EPA on January 11, 2006;
- The revision made in L.D. 1430 at 38 M.R.S. § 464(4.A.(3)(b)), related to certain pesticide discharges to tributaries of GPA waters, submitted to EPA on February 27, 2014.

The revisions made at 38 M.R.S. § 464(4.A.(3)(a) and (b)), would allow, in GPA waters and tributaries to GPA waters, the impairment of characteristics and designated uses and increase in trophic state due to discharges of aquatic pesticides or chemical discharges for the purpose of restoring biological communities affected by an invasive species or that are the unintended or incidental result of the spraying of pesticides. The revision made at 38 M.R.S. § 465((3.C.(1)) would allow, in Class B waters, impairment of the resident indigenous biological community due to discharges of aquatic pesticides or chemical discharges for the purpose of restoring biological

[66] See December 2, 2013 letter from EPA Region 1 Office of Ecosystem Protection Director, Ken Moraff to DEP Bureau of Land and Water Quality Director, Michael Kuhns.

communities affected by an invasive species. Similarly, the revision made at 38 M.R.S. § 465(4.C) would allow impairment of the function and structure of the indigenous biological community due to discharges of aquatic pesticides for the purpose of restoring biological communities affected by and invasive species. EPA understands from recent discussion with DEP, that Maine will be revising these provisions during the upcoming months to ensure that they are protective of designated uses. For this reason EPA is not taking action on these revisions at this time.

4.9 EPA's Determination That Various Provisions Submitted to EPA from 2004 through 2014 Are Not Water Quality Standards and Therefore EPA is Taking No Action on These Provisions

EPA has reviewed the following provisions and determined that they are not water quality standards and therefore EPA is taking no action on these provisions:

- Revisions made at 38 M.R.S. § 465(1.C.(2)) and (2.C.(2)), enacted as Chapter 574, L.D. 1833 "An Act to Amend Water Quality Laws to Aid in Wild Atlantic Salmon Restoration," submitted to EPA on May 14, 2004;
- Revisions made at 38 M.R.S. § 420(1-B.B) related to discharger compliance, submitted to EPA on May 14, 2004;
- Revisions made at in 38 M.R.S. § 420(1-B.C.(1)) and (1-B.C.(2)) that describe the state regulatory procedures for establishing site-specific bioaccumulation factors, submitted to EPA on May 14, 2004;
- Procedures in DEP Rule Chapter 584 that describe how alternative statewide and site-specific criteria are to be initiated, reviewed and adopted under state law, submitted to EPA on January 11, 2006;[67]
- Revisions made at 38 M.R.S. § 361-A(1-J) and (1-K), enacted as Chapter 330, L.D. 1588, Sections 7 and 8, which updated the definitions of "Code Of Federal Regulations" and "Federal Water Pollution Control Act" to include their amendments through January 1, 2005, submitted to EPA on January 11, 2006;
- Revisions made at 38 M.R.S. § 464(4.A.(1)(c) and (d)); § 465(1.C.(3)) and (2.C.(3)); and § 465-A(1.C), enacted as Chapter 182, L.D. 1304 "An Act Concerning Invasive Species and Water Quality Standards," submitted to EPA on January 11, 2006;
- Revisions made at 38 M.R.S. § 464(4.A.(1)(e)); § 465(1.C.(4)) and (2.C.(4)); § 465-A(1.C.(4)); and § 465-B(1.C.(2)), enacted as Chapter 291, L.D. 1274, "An Act to Allow the Discharge of Aquatic Pesticides Approved by the Department of Environmental Protection for the Control of Mosquito-borne Diseases in the Interest of Public Health and Safety," submitted to EPA on April 8, 2008;
- Revisions made at 38 M.R.S. § 420(1-B.F) and § 464(4.J) and (4.K), related to testing and licensing requirements for waste discharges that were included in LD 515, submitted to EPA on January 14, 2013; and

[67] Specifically, these provisions are: the requirement in Chapter 584 § 3(A.(2)) that "statewide criteria must be initiated in accordance with the petition for rulemaking provisions of the State Administrative Procedures Act, 5 M.R.S.A., Section 8055"; the provision in the first paragraph of Chapter 584 § 3(B) that site specific criteria "must only be adopted by the Board as part of a waste discharge license proceeding pursuant to 38 M.R.S.A. Sections 413, 414 and 414-A"; and the first two sentences of the second paragraph of Chapter 584 § 3(B).

- Revisions made at 38 M.R.S. § 464(4.A.(1)(f)); § 465(1.C.(5)) and (2.C.(5)); § 465-A (1.C.(5)); and § 465-B(1.C.(4)), enacted as Chapter 193, L.D. 1430, "An Act to Clarify the Permitted Use of Aquatic Pesticides," submitted to EPA on February 27, 2014.

Since many state and tribal laws that establish WQS include related provisions that are not themselves WQS, as defined by the Clean Water Act and EPA's regulations, EPA routinely reviews state submissions and identifies revisions that, while an important element of state law, are not WQS requiring EPA review and approval or disapproval pursuant to Section 303(c)(2) of the Clean Water Act and 40 C.F.R. part 131. EPA has in the past considered certain discharge prohibition exceptions, discharge licensing requirements, and alternative criteria adoption procedures in Maine to be WQS revisions and acted on them accordingly.[68] However, since the Region last considered such a revision in Maine, EPA has clarified how it determines what is or is not a new or revised WQS, as summarized in EPA's 2012 Frequently Asked Questions (FAQ) publication on the subject.[69] After careful review of Maine's submissions in light of this clarification, EPA finds that the provisions listed above are not WQS requiring EPA review and approval or disapproval.

As noted in the FAQ, one salient feature of a water quality standard is that it includes or addresses one of the three core components of WQS: designated uses, water quality criteria (narrative or numeric) to protect designated uses, and/or antidegradation requirements for waters of the United States. The provisions listed above, in contrast, do not establish, alter, or in any other way include or address designated uses, criteria or antidegradation requirements. Rather, most of the provisions allow the DEP to issue discharge licenses for certain previously prohibited discharges to occur in certain waters, and address compliance and testing requirements for certain discharges. In all cases, such discharges would still need to satisfy all applicable water quality standards. Therefore, the provisions are more accurately characterized as permit implementation provisions rather than water quality standards. The remaining provisions are purely procedural in nature, updating federal statutory and regulatory references, and establishing processes for adopting alternative criteria and establishing bioaccumulation factors, but they do not themselves alter uses, criteria, or antidegradation requirements, or mandate how they must be expressed or established in the future.

EPA has previously written approval letters for some of the above-listed provisions as applied in state waters, assuming that they were WQS (such as the discharge prohibition exceptions), or without calling out embedded non-WQS language in a longer narrative (such as the state adoption procedures in DEP rule Chapter 584). However, under CWA §303(c), EPA only has authority to approve or disapprove new or revised state WQS. Therefore, EPA's prior "approval" letters related to these provisions have no legal effect. EPA is hereby clarifying that

[68] The latest example of EPA action on discharge prohibition exemptions in Maine as WQS was EPA's August 19, 2008 approval of discharge prohibition exemptions related to the discharge of aquatic pesticides for the control of mosquito-borne diseases in the interest of public health and safety using methods and materials that provide for the protection of non-target species.

[69] EPA, *What is a New or Revised Water Quality Standard Under CWA 303(c)(3)? Frequently Asked Questions*, October 2012.

in spite of letters that might indicate otherwise, the Agency has not taken action pursuant to CWA §303(c) on any of these provisions.

With respect to the new provisions enacted in L.D. 1304, submitted to EPA on January 11, 2006, and L.D. 1430, submitted to EPA on February 27, 2014 (both listed above), it is important to note that federal antidegradation regulations and Maine's WQS require that water quality in Outstanding National Resource Waters (ONRWs) be "maintained and protected" (*See* 40 C.F.R. § 131.12(a)(3) and Title 38 M.R.S. § 464(4)(F)(2)). EPA has interpreted that language to mean that states may only allow "some limited activity which may result in temporary and short-term changes in water quality" (*See* 48 FR 51402, November 8, 1983 preamble to changes in 40 C.F.R. part 131). The new provisions enacted in L.D. 1430 do not alter antidegradation requirements. Therefore, in any review of a request to apply pesticides to Class AA or other ONRWs, DEP must ensure that such application will result in no more than temporary and short term changes in water quality, as well as comply with all other CWA applicable WQS requirements.

4.10 List of Submissions from 2003 through 2014

DEP submissions from 2003-2014 to which EPA is responding in today's decision are:

- August 26, 2003 submission which included enacted legislative chapters from the 2002-2003 legislative session;
- May 14, 2004 submission which included statutory amendments and rulemakings from 2000 to 2004 that had not been previously submitted to EPA ;
- January 11, 2006 submission which included statutory amendments and rulemakings from 2004 and 2005;
- April 8, 2008 submission which included statutory amendments from the 2007 legislative session;
- December 7, 2009 submission which included statutory amendments from the 2009 legislative session;
- May 16, 2013 submission which included statutory amendments from the 2011-2012 legislative session and 2012 rulemaking; and
- February 27, 2014 submission which included statutory amendments from the 2013 legislative session.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION 1
5 POST OFFICE SQUARE SUITE 100
BOSTON, MASSACHUSETTS 02109-3912

February 2, 2015

Patricia W. Aho, Commissioner
Maine Department of Environmental Protection
17 State House Station
Augusta, ME 04333-0017

Re: Review and Decision on Water Quality Standards Revisions

Dear Commissioner Aho:

By letter of January 14, 2013, the Maine Department of Environmental Protection ("DEP") submitted revisions of the State's surface water quality standards ("WQS") to Region 1 of the United States Environmental Protection Agency ("EPA" or "Region") for review and approval or disapproval. The revisions were adopted by the DEP on July 13, 2012. By letter to EPA dated January 9, 2013, Maine's Assistant Attorney General in the Natural Resources Division certified the revisions as having been duly adopted pursuant to state law. By letter of May 16, 2013, EPA approved the revision to the arsenic criteria to protect human health in state waters outside of Indian territories and lands, but did not act on the arsenic criteria for waters in Indian territories and lands. In the approval letter EPA also indicated that the additional revisions submitted by DEP were still under review.

I commend DEP for the 2012 adoption of revisions to its water quality standards that strengthen the ability to protect Maine's waters including the adoption of new aquatic life criteria for acrolein, diazinon, and nonylphenol.

DEP submitted additional revisions of the State's surface water quality standards to the Region for review and approval or disapproval by letter of February 27, 2014. The revisions were certified on February 26, 2014, by Maine's Assistant Attorney General in the Natural Resources Division as having been duly adopted pursuant to state law. Before now, EPA had not acted on any of these revisions for any waters in Maine.

In both of the above-referenced submission letters, DEP requested that EPA approve Maine's WQS in Indian territories and lands ("Indian lands"). As discussed in the attached Decision Support Document (Attachment A), EPA has concluded that the State of Maine has the authority to adopt WQS that are applicable to waters in Indian lands. Accordingly, EPA is herein responding to the remaining unapproved elements of the 2013 and 2014 WQS revisions for waters throughout the State, including in Indian lands.

In addition to the 2013 and 2014 submissions, DEP submitted numerous WQS revisions to EPA from August 26, 2003, through July 8, 2011, for review and approval or disapproval.[1] In EPA's letters approving WQS revisions contained in those submissions, EPA noted that it was not taking action on the WQS with respect to any waters in Indian lands. In light of EPA's determination that the State of Maine has the authority to adopt WQS for waters in Indian lands, EPA is herein responding to those WQS revisions for those waters.[2]

Many of the WQS revisions under review for approval or disapproval for waters in Indian lands are water quality criteria, and the Clean Water Act ("CWA") requires that criteria be protective of designated uses. As discussed in the Decision Support Document, EPA has not yet approved any WQS, including designated uses, for waters in Indian lands.

Therefore, in order to evaluate whether the submitted criteria are protective of designated uses, EPA must first approve designated uses for these waters. Accordingly, EPA is herein approving Maine's surface water classifications and corresponding designated uses for waters in Indian lands.[3] Because EPA has not previously approved these WQS for waters in Indian lands, EPA considers them to be "new" WQS as applied to such waters. EPA is also approving 38 M.R.S. § 6207(4) and (9) (a provision of the Maine Implementing Act, or MIA, which settled the Maine Indian land claims as a matter of Maine law), as an explicit designated use for certain waters in Indian lands.

The following paragraphs state EPA's decisions on Maine's new and revised WQS described above. The decisions include approvals and disapprovals, and the detailed explanations for the decisions are provided in Attachment A. EPA has also identified several provisions that EPA is not taking action on, primarily because DEP is planning to update them soon, and some provisions that EPA is not taking action on because we have concluded that they are not WQS requiring EPA review and approval; these are also explained in Attachment A. EPA is not responding to new or revised Maine WQS other than those explicitly identified in this letter.

Approvals

Pursuant to Section 303(c)(3) of the Clean Water Act and 40 C.F.R. part 131, I hereby approve the following new or revised WQS:

Classifications and Designated Uses

For all waters in Indian lands:

- Maine's standards for classification and corresponding designated uses in 38 M.R.S. § 465(1.A), (2.A), (3.A) and (4.A)(for fresh waters); § 465-A(1.A) (for great ponds and natural lakes and ponds less than 10 acres in size, and impoundments of rivers that are

[1] A list of these submissions is provided in Section 4.10 of Attachment A.
[2] Maine's July 8, 2011 submission was for EPA's review of a reclassification of the Kennebec River. Although EPA's July 20, 2011 letter approving the reclassification included the caveat about not acting with respect to waters in Indian lands, the Kennebec River is nowhere near Indian lands. Therefore, EPA is taking no further action today with respect to that submission.
[3] EPA intends to review and approve or disapprove all remaining Maine WQS that could apply to waters in Indian lands, such as dissolved oxygen criteria, definitions, antidegradation provisions, etc., as soon as possible.

defined as great ponds pursuant to 38 M.R.S. § 480-B), including the definition of "great ponds" in 38 M.R.S. § 480-B(5); and § 465-B(1.A), (2.A) and (3.A) (for estuarine and marine waters);

- The classification of specific waters in 38 M.R.S. § 467 (Classification of major river basins) and § 468 (Classification of minor drainages); and § 469 (Classification of estuarine and marine waters);
- The addition of agriculture as a designated use to freshwaters (Classes AA, A, B, C, and GPA), submitted to EPA on August 26, 2003; and
- The reclassifications, submitted to EPA on December 7, 2009, of Otter Creek, a tributary of Seboeis Stream, Alder Stream, and South Branch Stream, a tributary to the Mattamiscontis Stream, from Class B to Class A; and of Grand Falls Flowage between Route 1(Princeton and Indian Township) and Black Cat Island from Class B to Class GPA.

Criteria

For waters throughout the State of Maine, including in Indian lands, the following water quality criteria provisions contained in DEP Rule Chapter 584, Surface Water Quality Criteria for Toxic Pollutants, Appendix A, submitted to EPA on January 14, 2013:

- Freshwater and marine aquatic life criteria for diazinon and nonylphenol;
- Freshwater aquatic life criteria for acrolein;
- Corrections of Federal Register Cites/Sources in Tables I and II of Appendix A; clarifications in footnote ll in Table I, and footnotes A and C and Additional Note 4 in Table II; and
- Footnote aME in Table I of Appendix A *except* for the first sentence related to arsenic, which EPA is taking no action on.

For all waters in Maine *except* for waters in Indian lands, the following water quality criteria contained in DEP Rule Chapter 584, Surface Water Quality Criteria for Toxic Pollutants, Appendix A, submitted to EPA on January 14, 2013:

- Human health criteria for the consumption of water plus organisms for acrolein; and
- Human health criteria for the consumption of organisms only for acrolein and phenol.

For all waters in Indian lands, the following water quality criteria provisions:

- The provision regarding dissolved oxygen measurement requirements in riverine impoundments contained in 38 M.R.S. § 464(13), submitted to EPA on August 26, 2003;
- Aquatic life criteria provisions in 38 M.R.S. § 420(1-B.A.(1)),(1-B.C),(1-B.D), and (1-B.E), submitted to EPA on May 14, 2004, *except for* revisions made at in 38 M.R.S. § 420(1-B.C.(1)) and (1-B.C.(2)) that describe the state regulatory procedures for establishing site-specific bioaccumulation factors and which are not WQS (see below);
- The Classification Attainment Evaluation Using Biological Criteria for Rivers and Streams, contained in DEP Rule Chapter 579, submitted to EPA on May 14, 2004;
- All provisions of DEP Rule Chapter 584, Surface Water Quality Criteria for Toxic Pollutants, including Appendix A, submitted to EPA on January 11, 2006, *except for:*
  - All human health criteria in Appendix A, which EPA is disapproving (see below);

- the ammonia aquatic life criteria in Appendix A and 7.C, on which EPA is taking no action at this time (see below); and
- provisions which are not WQS (see below);

- The 30-day average dissolved oxygen criterion of 6.5 ppm for certain Class C waters, contained in 38 M.R.S. § 465(4.B), submitted to EPA on January 11, 2006;
- The instream design flows for the application of water quality criteria for aquatic life and human health protection, which are consistent with EPA's current guidance (lQ10 low flow for acute aquatic life criteria, 7QlO low flow for chronic aquatic life criteria, and harmonic mean flow for human health criteria), contained in DEP Rule Chapter 530, § 4.B, submitted to EPA on January 11, 2006; and
- Revisions at 38 M.R.S. § 465(3.C.(2)) and § 465-B(2.C) enacted in Chapter 291, L.D. 1274, "An Act to Allow the Discharge of Aquatic Pesticides Approved by the Department of Environmental Protection for the Control of Mosquito-borne Diseases in the Interest of Public Health and Safety,"), submitted to EPA on April 8, 2008.

General

For all waters in Indian lands:

- The provisions in 38 M.R.S. § 464(3.B) that ensure that a hearing will be held at least once every three years for the purpose of reviewing Maine's water quality standards, and revising them as appropriate, consistent with 40 C.F.R. § 131.20, submitted to EPA for review on May 14, 2004.

Disapprovals

Pursuant to Section 303(c)(3) of the CWA and 40 C.F.R. part 131, I hereby disapprove the following new and revised water quality standards:

For all waters in Indian lands:

- The mercury human health criteria revision at 38 M.R.S. § 420(1-B.A.(2)), submitted to EPA May 14, 2004;
- All human health criteria in DEP Rule Chapter 584, Surface Water Quality Criteria for Toxic Pollutants, Appendix A, submitted to EPA on January 11, 2006; and
- Human health criteria revisions related to arsenic, acrolein, and phenol in DEP Rule Chapter 584, Surface Water Quality Criteria for Toxic Pollutants, Appendix A, and the last sentence in Ch. 584, § 5.C related to the fish consumption rate, submitted to EPA on January 14, 2013.

Revisions for Which EPA is Not Making a Decision at This Time

EPA is not deciding to approve or disapprove the following new or revised WQS at this time:

For all waters in Indian lands:

- The ammonia criteria for protection of aquatic life in DEP Rule Chapter 584, Appendix A, submitted to EPA on January 11, 2006;

- The recreational (bacteria) numeric criteria for the protection of primary contact recreation for Class B and C waters in 38 M.R.S. § 465(3.B) and (4.B), submitted to EPA on January 11, 2006;
- The revisions made in L.D. 1450 at 38 M.R.S. § 465-B(2.B) and (3.B), which extended the applicability of the bacteria criteria for Class SB and Class SC waters to include bacteria of domestic animal origin, submitted to EPA on January 11, 2006; and
- The first sentence of Footnote aME in Table I of Appendix A and the last sentence in Ch. 584, § 4 (the cancer risk level to be used to calculate human health criteria for inorganic arsenic).

For all waters throughout Maine, including in Indian lands:

- The revision made in L.D. 1304 at 38 M.R.S. § 464(4.A(3)(a)), and § 465((3.C.(1)) and (4.C), related to certain pesticide discharges, submitted to EPA on January 11, 2006;
- The revisions made in L.D. 1304 at 38 M.R.S. § 465(3.B) and (4.B), which extended the applicability of the bacteria criteria for Class B and Class C waters to include bacteria of domestic animal origin, submitted to EPA on January 11, 2006;
- The revision made in L.D. 1778 at 38 M.R.S. § 465-A(1.B), which extended the applicability of the bacteria criteria for Class GPA waters to include bacteria of domestic animal origin, submitted to EPA on April 8, 2008;
- The phenol criteria for the protection of human health consumption of water plus organisms, in DEP Rule Chapter 584, Appendix A, submitted to EPA on January 14, 2013; and
- The revision made in L.D. 1430 at 38 M.R.S. § 464(4.A(3)(b)), related to certain pesticide discharges to tributaries of GPA waters, submitted to EPA on February 27, 2014.

For waters outside of waters in Indian lands:

- The reclassification of a 0.3 mile segment of Long Creek that flows through Westbrook from Class B to Class C, submitted to EPA on December 7, 2009.

Revisions That are not WQS and do Not Require an EPA Decision

I have concluded that the following revisions, which relate to exemptions from discharge prohibitions, testing and licensing provisions related to discharges, updates of federal statutory and regulatory references, and procedural provisions that establish processes for adopting alternative criteria and establishing site-specific bioaccumulation factors, are not water quality standards requiring EPA review and approval or disapproval:

- Revisions made at 38 M.R.S. § 465(1.C.(2)) and (2.C.(2)), enacted as Chapter 574, L.D. 1833 "An Act to Amend Water Quality Laws to Aid in Wild Atlantic Salmon Restoration," submitted to EPA on May 14, 2004;
- Revisions made at 38 M.R.S. § 420(1-B.B) related to discharger compliance, submitted to EPA on May 14, 2004;
- Revisions made at in 38 M.R.S. § 420(1-B.C.(1)) and (1-B.C.(2)) that describe the state regulatory procedures for establishing site-specific bioaccumulation factors, submitted to EPA on May 14, 2004;

- Revisions made at 38 M.R.S. § 361-A(1-J) and (1-K), enacted as Chapter 330, L.D. 1588, Sections 7 and 8, which updated the definitions of "Code Of Federal Regulations" and "Federal Water Pollution Control Act" to include their amendments through January 1, 2005, submitted to EPA on January 11, 2006;
- Revisions made at 38 M.R.S. § 464(4.A.(1)(c) and (d)); § 465(1.C.(3)) and (2.C.(3)); and § 465-A(1.C), enacted as Chapter 182, L.D. 1304 "An Act Concerning Invasive Species and Water Quality Standards," submitted to EPA on January 11, 2006;
- Revisions made at DEP Rule Chapter 584 § 3, submitted to EPA on January 11, 2006, regarding adoption procedures for alternative statewide and site specific criteria. This includes: the requirement in Chapter 584 § 3(A.(2)) that "statewide criteria must be initiated in accordance with the petition for rulemaking provisions of the State Administrative Procedures Act, 5 M.R.S.A., Section 8055"; the provision in the first paragraph of Chapter 584 § 3(B) that site specific criteria "must only be adopted by the Board as part of a waste discharge license proceeding pursuant to 38 MRSA Sections 413, 414 and 414-A"; and the first two sentences of the second paragraph of Chapter 584 § 3(B);
- Revisions made at 38 M.R.S. § 464(4.A.(1)(e)); § 465(1.C.(4)) and (2.C.(4)); § 465-A(1.C.(4)); and § 465-B(1.C.(2)), enacted as Chapter 291, L.D. 1274, "An Act to Allow the Discharge of Aquatic Pesticides Approved by the Department of Environmental Protection for the Control of Mosquito-borne Diseases in the Interest of Public Health and Safety," submitted to EPA on April 8, 2008;
- Revisions made at 38 M.R.S. § 420(1-B)(F) and § 464(4)(J) and (K), related to testing and licensing requirements for waste discharges that were included in LD 515, submitted to EPA on January 14, 2013; and
- Revisions made at 38 M.R.S. § 464(4.A.(1)(f)); § 465(1.C.(5)) and (2.C.(5)); § 465-A (1.C.(5)); and § 465-B(1.C.(4)), enacted as Chapter 193, L.D. 1430, "An Act to Clarify the Permitted Use of Aquatic Pesticides," submitted to EPA on February 27, 2014.

EPA looks forward to continued cooperation with Maine in the development, review and approval of water quality standards pursuant to our responsibilities under the Clean Water Act. EPA would like to begin discussions with DEP as soon as possible about the criteria that EPA is disapproving and those about which EPA is making no decision. EPA will contact you next week to schedule such discussions. In the meantime, please contact Ellen Weitzler (at weitzler.ellen@epa.gov or 617-918-1582) if you have any questions.

Sincerely,

H. Curtis Spalding
Regional Administrator

From: EIM_Reporting@ecy.wa.gov [mailto:EIM_Reporting@ecy.wa.gov]
Sent: Tuesday, December 08, 2015 9:48 AM
To: James Tupper <tupper@tmw-law.com>
Subject: EIMSearch Download Request Confirmation (COMPLETED)

Your request for EIMSearch Download is COMPLETED.

Following is your request information:

Download Type : EIMSearch
Download Description : Puget Sound Phase 3 Study
Download Record Count : 23359
Email Provided : tupper@tmw-law.com

You can download your file using the hyperlink
https://fortress.wa.gov/ecy/eimdownload/tupper474119.zip

The download file will be available for 7 days, then it will be removed.

Docket Number: 58-0102-1201
Effective Date: 2016 Sine die
Rules Title: Water Quality Standards
Agency Contact and Phone: Barry Burnell, 373-0194

Public Notice
Hearings: [ ]Yes [X] No
Locations and Dates: N/A
Written Comment Deadline: 9/4/15

Descriptive Summary of Rule as Initially proposed: On May 10, 2012, the United States Environmental Protection Agency (EPA) disapproved the July 7, 2006 Idaho DEQ water quality standard rule submittal. The disapproval affects 167 of Idaho's revised human health criteria for 88 toxic pollutants. In addition to incorporating newer toxicity information, DEQ's 2006 rule changed the fish consumption basis for determining the toxic standard from 6.5 g/day to 17.5 g/day, based on EPA's nationally recommended fish consumption rate. EPA disapproved the proposed criteria because EPA believes that the resulting criteria do not protect Idaho's designated uses. As a result, EPA was unable to determine that the 17.5 g/day fish consumption rate was consistent with 40 CFR 131.11(a). EPA identified several sources of information on local and regional fish consumption, which they claim that Idaho did not consider before using the national default fish consumption rate. According to EPA, the information that EPA reviewed suggests that fish consumption among some Idaho population groups is greater than 17.5 g/day.

Over the span from October 2012 to August 2015, DEQ met with interested parties in eighteen negotiated meetings. DEQ planned a statewide Idaho fish consumption survey then executed a yearlong survey and, while the survey was underway, discussed the various policy decisions involved in derivation of criteria protective of human health. At the same time as Idaho's fish consumption survey was being conducted, the Nez Perce Tribe and Shoshone-Bannock Tribes were conducting similar surveys to inform DEQ's knowledge of the potential magnitude of exposure to toxic substances through consumption of fish with the help of EPA and the intent that this information would also inform DEQ's revision of human health criteria. In May 2014 EPA proposed updates to its national 304(a) criteria, recommendations to states and tribes, for protection of human health. These updates were based on a new national fish consumption rate of 22 g/day, as well as new information on body-weight, drinking water intake, chemical toxicity, bioaccumulation of toxins in fish tissue, and the relative magnitude of contribution to exposure to toxins from various sources other than fish and water. EPA's proposal was finalized on June 29, 2015, providing new or updated criteria for 94 chemicals, some not currently present in Idaho's rules.

EPA's national action expanded what DEQ considered in its rulemaking. In addition to recent information on fish consumption in Idaho, these criteria changes also incorporate new information on body-weight, drinking water intake, toxicity, bioaccumulation, and relative source contribution. DEQ is also updating more criteria than just those EPA acted on in 2012.

The current rule proposal is to update Idaho's human health criteria for 104 toxic substances (10 of which are new), plus an additional fish-plus-water criterion for copper based on the drinking water maximum contaminant level (MCL). There are 208 revised or new criteria, consisting of 94 revised and 10 new criteria based on exposure to toxic substances from the consumption of fish and ingestion of water plus an additional fish-plus-water criterion for copper, and 94 revised and 10 new criteria based on exposure to toxic substances from the consumption of fish alone. In addition, although new input values were used, the values for the antimony fish only criterion and the bromoform fish-plus-water criterion did not change; these are counted as revised criteria. With this proposal, Idaho will have updated all of its human health criteria except those for arsenic, methylmercury, and asbestos.

Negotiated Rule Making: [X] Yes [ ] No
The text of the proposed rule has been drafted based on discussions held and concerns raised during negotiations conducted pursuant to Idaho Code § 67-5220 and IDAPA 58.01.23.810-815. The Notice of Negotiated Rulemaking was published in the September 2012 Idaho Administrative Bulletin, Vol. 12-9. Eighteen meetings were held between October 2012 and August 2015. A preliminary draft rule was made available for public review in August 2015. Members of the public participated in this negotiated rulemaking process by attending the meetings and by submitting written comments. A record of the negotiated rule drafts, written comments, documents distributed during the negotiated rulemaking process, and the negotiated rulemaking summary is available at www.deq.idaho.gov/58-0102-1201.

Costs to the Agency: None anticipated.

Costs to the Regulated Community: Dischargers of NPDES regulated pollutants may have stricter limits with which to comply.

Relevant Statutes: Sections 39-105, 39-107, and 39-3601 *et seq.*, Idaho Code

Idaho Code § 39-107D Statement: The standards included in this rule are not broader in scope, nor more stringent, than federal regulations and do not regulate an activity not regulated by the federal government.

Fiscal Impact Statement: The following is a specific description, if applicable, of any negative fiscal impact on the state general fund greater than ten thousand dollars ($10,000) during the fiscal year: Not applicable.

DEQ recommends that the Board adopt the rule, as presented in the final proposal, as a pending rule with the final effective date coinciding with the adjournment *sine die* of the Second Regular Session of the Sixty-third Idaho Legislature. The rule is subject to review by the Legislature before becoming final and effective.

Temporary Rule	[ ] Necessary to protect public health, safety or welfare [ ] Compliance with deadlines in amendments to governing law or federal programs [ ] Conferring a benefit

Docket Number: 58-0102-1201

Response to Comments Attached

Section	Section Title	Summary of Rule Changes Based on Public Comment
010.	**Definitions.**	This section has not been changed.
070.	**Application of Standards.**	This section has not been changed.
210.	**Numeric Criteria for Toxic Substances for Waters Designated for Aquatic Life, Recreation, or Domestic Water Supply Use**	This section has been changed.
284.	**South Fork Coeur d'Alene Subbasin, Subsection 110.09, HUC 17010302, Aquatic Life Criteria for Cadmium, Lead and Zinc.**	This section has not been changed.
400.	**Rules Governing Point Source Discharges.**	This section has not been changed.

Commenter 1 – Darcy James
Commenter 2 – Columbia River Intertribal Fish Commission
Commenter 3 – National Association of Clean Water Agencies
Commenter 4 – Northwest Pulp & Paper Association
Commenter 5 – Northwest Food Processors Association
Commenter 6 – Association of Idaho Cities
Commenter 7 – Idahoans for Sensible Water Regulation
Commenter 8 – Idaho Farm Bureau Federation
Commenter 9 – Idaho Council on Industry & Environment
Commenter 10 – Nez Perce Tribe
Commenter 11 – J.R. Simplot Company
Commenter 12 – American Forest & Paper Association
Commenter 13 – Spokane Riverkeeper
Commenter 14 – Coeur d'Alene Tribe
Commenter 15 – Shoshone-Bannock Tribes
Commenter 16 – Confederated Tribes of the Umatilla Indian Reservation
Commenter 17 – Federal Water Quality Coalition
Commenter 18 – Pentachlorophenol Task Force
Commenter 19 – Idaho Conservation League
Commenter 20 – EPA Reg 10 Regional Tribal Operations Committee
Commenter 21 – Environmental Protection Agency Region 10
Commenter 22 – Idaho Association of Commerce & Industry
Commenter 23 – Clearwater Paper
Commenter 24 – Upper Snake River Tribes
Commenter 25 – 76 Citizen Letters

Rule Section / Topic(s)	Commenter	Comment	Response
Survey design, target population	1	I am troubled that the survey of fish consumption was taken on "a random sample of Idahoans" without apparent consideration of tribal members for whom Idaho fish are a staple. We must protect their treaty rights to fish at "all the usual and accustomed places" without being poisoned. Water in our streams must be pure enough to be a fit food source for those who depend on the fish, not for the average occasional consumer. This will bring collateral health benefits to the rest of us, who fish, wade, and float on the rivers. Being in business or owning property should not convey a right to pollute water that everyone uses.	Random sampling of a population is a standard statistical method to assure a representative sample. Tribal members were considered, both through inclusion in Idaho's survey and through separate tribal fish consumption survey's. The criteria proposed provide a high level of protection even for those whose fish consumption is well above average.
	21	The EPA contracted with Westat, a well-known statistical consulting firm, to review DEQ's fish consumption survey results as reported in the Fish Consumption Survey report prepared by Northwest Research Group. Westat identified a number of issues that DEQ should review (see attached memoranda from Westat), and EPA is available to discuss this information further. For example, Westat determined that the frequency of fish consumption declined over the seven day recall period. DEQ did not account for this trend, which could result in an underestimation of fish consumption. As previously noted, it is important for DEQ's fish consumption survey results to be peer reviewed by individuals with the necessary expertise. The Westat review provides information that DEQ should consider along with the results of its peer review. In particular, it is important that the National Cancer Institute (NCI) analysis, which involves many assumptions and employs statistical methodology not generally accessible to the lay person, be adequately reviewed. In addition, it is important that DEQ's final peer review findings be readily available and distributed to support the credibility of DEQ's survey results.	We have passed Westat's comments on to our contractor's for their response along with the comments from the ongoing peer review we arranged. We will post the peer review comments and response as soon as they are ready. We understand that the NCI method involves sophisticated statistical analysis and have the utmost confidence that Information Management Services performed the analysis correctly.
	22	Also, unlike Oregon, Washington or Alaska, Idaho conducted a state-wide fish consumption survey. Oregon established a state-wide FCR based on a subpopulation study of four Native American tribes published by the Columbia River Inter-Tribal Fish Commission (CRITFC).15 This study has a number of uncertainties which include the origin and species of consumed fish (locally harvested or commercial) and the type of local harvested (anadromous, non-anadromous) fish. Furthermore, the raw data from the study have never been available for public review. Though EPA has implied that studies such as CRITFIC (1994) provide information that can be used to	We concur that recent fish consumption surveys conducted by Idaho and EPA on behalf of Idaho tribes provide the best information available of which to base a regulatory fish consumption rate to be used in deriving human health criteria.

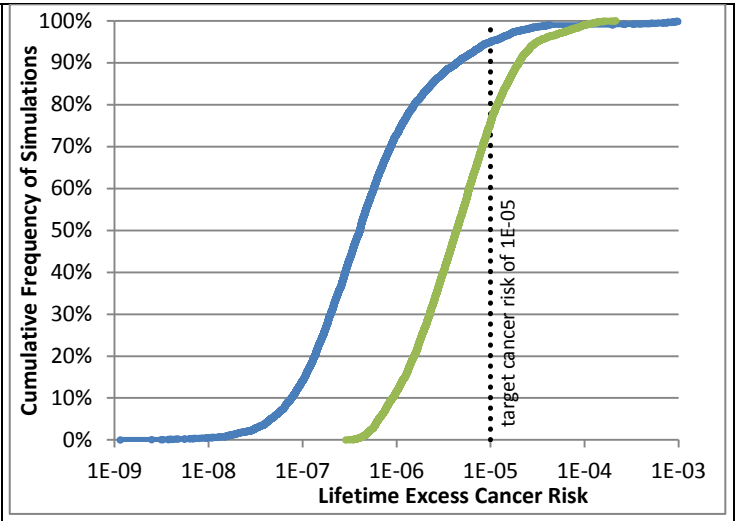
		establish a FCR for the State of Idaho, such a study does not represent the Idaho population, geography, and fish availability. The survey conducted by the state of Idaho provides a scientifically sound basis for FCR for Idaho residents.	
	24	Target Population – Although we have requested that Indian tribes be considered part of the general population, IDEQ continues to subjugate them to a lesser status.	Idaho has considered three high end consuming groups ***within*** the general population: Idaho resident anglers, the Nez Perce Tribe and the Shoshone-Bannock Tribes. Our survey of the general population included members of Idaho's Indian tribes. Moreover, our proposed criteria are based on Nez Perce Tribal exposure to contaminants in fish and water. We are disheartened that you view our consideration as subjugation.
level of protection / allowable risk	2	Written comments delivered to DEQ from tribes were unambiguous - if Idaho's water quality standards are not specifically calculated to protect the health of the majority of tribal members, the standards have the potential to limit the amount of fish that may safely be eaten by tribes. Despite knowing this, DEQ has proposed water quality standards for Idaho's waters that were calculated using substantially reduced levels of protection for tribal people as compared to the general population.	The proposed human health criteria are calculated to provide a high level of protection to the majority of tribal members. It is not possible to equalize the level of protection for tribal people as compared to the general population – for any given criterion or contaminant level respective risks will differ by differences in fish consumption.
	4	NWPPA would like to emphasize Clearwater Paper's comments on risk policy and reiterate that we also believe the Department should reassess their risk policy choices on carcinogens and non-carcinogens based on the recommendations of Clearwater.	DEQ has carefully considered comments received regarding risk policy decisions and has modified the risk level applied, but at the same time, has incorporated other more conservatives inputs to ensure the resulting criteria continue to be protective within the range that EPA provides is acceptable. Please see response to comments below regarding this issue.
	5	As a part of this rulemaking, DEQ has made decisions about the level of protection for different segments of the population. DEQ is currently proposing to apply the 1x10-6 risk management goal to the 95th percentile of the general population. The State's currently proposed risk management goal results in the average Idahoan having an excess lifetime cancer risk of about 1x10-7. These risk management decisions can greatly influence criteria values. NWFPA is concerned that the level of protection should assure preserving designated uses and ensure risk thresholds that allow for balance. Therefore, we encourage the DEQ to look at how the allowable risk decisions affect the calculated criteria value: more stringent risk management benchmarks lead to more stringent criteria. Depending upon the calculation methodology and allowable risk decisions, calculated values may result in criteria that are not achievable and would result in significant financial resources to try to achieve such values. It should be noted that these unrealistic risk thresholds will result in significant expenditures to meet criteria that, at best, will provide negligible improvements for human or ecological health. These costs do not just impact the regulated community, but will impact all Idaho businesses and residents. Idaho state law requires divisions of government, including DEQ, to estimate and evaluate economic costs and benefits of proposed rules. NWFPA would encourage DEQ to look at their risk policy decisions in balance with health values and economic costs of the resulting criteria. We would recommend that this sort of analysis should be performed at both the proposed target risk value and with a target risk value of 1x10-5 , to better examine the difference in benefits versus costs.	While there is direct relation between level of protection and criteria values there are other factors that also have such a direct influence on the criteria – i.e. toxicity, bioaccumulation rate, relative source contribution, and fish consumption rate. DEQ has determined to use a 10^{-5} cancer risk level, but has also determined to use the Nez Perce mean fish consumption rate of group 2 fish, which includes all near coastal, estuarine, freshwater and anadromous fish. This increases the fish consumption rate used to calculate criteria from 16.1 to 66.5 g/day. While including salmon and other anadromous fish, DEQ continues to generally use a RSC of .2, thus double counting some marine fish, and is using the 2015 EPA recommended toxicity values, bioaccumulation rates and other input values, such as water intake. In addition, DEQ has shifted from the use of a probabilistic risk assessment method of calculating criteria to a deterministic method. The deterministic method compounds the conservative nature of the input values. DEQ believes that the resulting criteria are protective of both the higher fish consuming population and the general population of Idaho. DEQ's approach to determining the human health criteria, including the choice of a 10^{-5} cancer risk level, is consistent with EPA national guidance. EPA has emphasized that the choice of a cancer risk rate and the percentage of the population to protect are risk management policy decisions for States to make. EPA believes that both 10^{-5} and 10^{-6} risk levels are acceptable for the general population as long as the risk level for higher exposed populations does not exceed 10^{-4}. EPA also provides that States may choose to use either high-end values or average values for an identified population. For EPA's 304(a) recommended criteria, EPA uses the 90^{th}% of the general population fish

			consumption, while using the average fish consumption for more highly exposed populations. DEQ's approach is very consistent. DEQ has used a 10^{-5} risk level for the Nez Perce Tribe, which results in a lower risk range for the general population. Also, similar to EPA's approach nationwide, DEQ has used the mean of the tribal fish consumption. In addition, while EPA excludes salmon as a marine fish in its 304(a) criteria development, *DEQ has included salmon* in its fish consumption rate. Also, while EPA directs States to alter the RSC in the event a State chooses to include salmon or other marine species, DEQ has determined to retain the very conservative default RSC recommended by EPA. Finally, DEQ has used all the latest EPA recommended toxicity values, bioaccumulation rates and other inputs. In sum, DEQ's approach is both consistent with EPA's national guidance, and in some respects, reflects a more conservative approach then EPA has recommended. We are aware of the fact that some criteria may not be immediately or easily achievable, and thus have allowed for implementation tools, including the new tool of intake credits to ease the transition. We also know that few discharges in Idaho currently have permit limits based on achieving human health toxics criteria. Though this can certainly change, we do not expect it to change soon or quickly. The Idaho Administrative Procedures Act, Idaho Code sections 67-5221 and 67-5224, require State agencies include in the notice of proposed rulemaking and in the notice of the adoption of a pending rule a description, if applicable, of any negative fiscal impact on the State general fund greater than $10,000 during the fiscal year when the rule will become effective. It should be noted, however, that the absence or accuracy of this fiscal statement does not affect the validity or enforceability of the rule. DEQ complied with these provisions in its notice of proposed rulemaking, and will do so in its notice of the adoption of a pending rule. DEQ believes there will be no impact on the general fund in excess of $10,000.
	6	The proposed state science updates, risk management, and policy decision as a package are consistent with the EPA methods and guidance for derivation of human health criteria and new updated EPA science and policy. While individual science or policy choices may cause individual stakeholders participating in the rulemaking concern for being over or under protective, the proposed policy choices in aggregate, are clearly well within and consistent with EPA science, guidance, state's policy choices and therefore fully comply with CWA obligations for state development of human health water quality standards.	We agree; thank you for stating so.
	7	The members of ISWR do have a strong concern with DEQ setting a risk standard at one in one million (10^{-6}). The state does have the discretion under the Federal Guidance to set a risk factor in the range of 10^{-4} to 10^{-6}. ISWR recommends a factor of 10^{-5}. There is no significant difference in protection of the public health by utilizing the less conservative standard, while there is significant difference in the cost of compliance by both industry and the tax paying public. The Idaho Legislature has supported the idea that IDEQ should consider a range of risks in other environmental programs. *See* Idaho Code § 39-7210 (Idaho Land Remediation Act).	Please see response to commenter number 5 above.
	8	Our members do not support the policy decision DEQ has made to set the risk standard at 10-6. The state does have the discretion under EPA's Clean Water Act Guidance to set a risk factor in the range of 10-4 to	Please see response immediately above.

		10-6. While the risk factor choice DEQ has made is within the allowable range, our members do not believe the miniscule additional protection from risk associated with the 10-6 risk factor provide additional benefits anywhere close to the significant additional costs that will be borne by industry, municipalities and ultimately the taxpayers and citizens of Idaho. It is our understanding that a reduction in the risk factor from 10-6 to 10-5 would be similar to the risk associated with every Idaho citizen driving an additional 11 miles per year. This tiny, incremental amount of associated risk however, stands to save our state economy an estimated $14 billion or more, which will have far more devastating consequences directly on our citizens and economy through a loss of jobs, higher prices for goods, and higher costs of water treatment. As an example, we have been told that the average water bill in Boise City would need to increase by at least $79 per month to pay for the required new treatment works to reach the nearly impossibly high new standards as proposed by DEQ. That is more than double the current rates and would be a significant burden on all families; but especially on fixed-income seniors who would accrue virtually no benefit from the greater expense. Our members do not believe the significant financial burdens are worth the tiny incremental reduction in risk. Furthermore, this higher standard does not meet the state's long-held view that costs and benefits must be carefully weighed when proposing new rules.	
	10	The Nez Perce Tribe has consistently emphasized throughout IDEQ's negotiated rulemaking process that any water quality standards that are developed - and ultimately approved by EPA - must be protective of fish consumption levels and needs of our tribal members given the United States' treaty and trust obligations to the Nez Perce Tribe. The Nez Perce Tribe is disappointed to find that Idaho's proposed water quality standards are orders of magnitude less protective than those of all other states in the Columbia River basin region, and are not protective of the fish consumption levels and needs of our members thereby resulting in unacceptable health risks to our members who rely heavily on fish.	We believe our combination of risk management choices is protective of even those that consume high quantities of fish. In addition, DEQ has determined to include the tribal consumption of salmon, near coastal, estuarine and freshwater fish See also response below to commenter 2 under topic of "Tribal treaty right and designated uses"
	11	One of the key factors in calculating HHWQC is a policy decision for the Department in setting a human health risk target. Inherent in discussing risk is the recognition that risk varies across all Idahoans and that this has implications for what target risk goals can be achieved. EPA recognizes this variation in potential risk and provides guidance on how to address it: "With AWQC derived for carcinogens based on a linear low-dose extrapolation, the Agency will publish recommended criteria values at a 10^{-6} risk level. States and authorized Tribes can always choose a more stringent risk level, such as 10^{-7}. USEPA also believes that criteria based on a 10^{-5} risk level are acceptable for the general population as long as States and authorized Tribes ensure that the risk to more highly exposed subgroups (sport fishers or subsistence fishers) does not exceed the 10^{-4} level." The Department should utilize the flexibility provided in EPA guidance to allow for a range of risks. This is especially important in that certain chemicals, which are highly bioaccumulative and may have a low toxicity threshold, could have a very low calculated HHWQC depending on the risk target selected by the Department. Such criteria may not be achievable. Thus, the Department needs to carefully consider the target risk factor so that human health protection is provided without excessive conservatism (i.e., unrealistic risk scenarios) that would result in criteria that are not achievable without considerable expenditures of resources. Therefore, we urge the Department to consider a one in 10^{-5} risk target for both Idaho and tribal populations.	The policy decision on acceptable risk is definitely a key factor, but by no means the only factor that can greatly affect calculated criteria. DEQ has determined to use the flexibility allowed by EPA and use a 10^{-5} risk level, while also using other more conservative input factors. Please see response to commenter 5 above in this section on "level of protection / allowable risk."

	12	AF&PA also supports IDEQ's risk management decision to use a mean fish consumption rate to represent the higher-consuming populations. We are concerned, however, about two critical aspects of the IDEQ methodology. First, IDEQ is developing its state-wide standards on the basis of the fish consumption rate for one higher-consuming population – the Nez Perce Tribe. We believe that using this higher fish consumption rate for a particular population to derive state-wide criteria is not appropriate as it leads to even greater "compounded conservatism" and results in criteria that are unnecessarily stringent to protect human health. We also do not support IDEQ's choice to apply an incremental cancer risk level of 1x10-6 in deriving its criteria, especially when coupled with the other conservative assumptions used to derive the criteria. While we recognize that under Federal guidance, the State has the discretion to make that choice, we note that under that guidance, IDEQ could also use a risk level of 1x10-5. Setting human health water quality criteria in Idaho based on a theoretical excess lifetime cancer risk level of 1x10-6 is a poor public policy choice. This policy would reduce potential cancer incidence by a fraction of a cancer case per year compared to criteria set at 1x10-5 (see below). But, such a policy also imposes costs on cities, counties, rate payers and industry of potentially several billion dollars, harming the economy of the state. In addition, as noted above, these risk calculations contain needlessly conservative assumptions such as that people drink 2.4 liters (about 2.5 quarts) of untreated surface water. This policy choice actually harms public health because it diverts resources from reducing other risks that are much more significant. Comments submitted by the Idaho Association of Commerce and Industry (IACI) on August 21, 2015, citing material previously submitted by ARCADIS, demonstrate that there is no measurable difference in the number of excess cancers expected for Idaho residents under criteria based on 1x10-5 versus 1x10-6. Specifically, deriving criteria based on a 1x10-5 allowable excess lifetime cancer risk management goal for the population size of Idaho in 2012 would be expected to lead to an increase of 0.23 cancers per year among average Idahoans-- from 2570.00 to 2570.23 cancers per year in Idaho in 2012. Using a 1x10-6 excess lifetime cancer risk, the increase in annual cancer incidence would be 0.023 cancers—or going from 2570.00 to 2570.023 cancers per year. The difference in the number of excess cancers resulting from the application of criteria based on the different risk levels is so small it is not measureable, and would be lost in the year-to-year variation in cancer incidence. Yet, as noted, it could cost several billion dollars, harming local governments and industry in the state	In accordance with EPA's 2000 human health criteria methodology, DEQ has chosen a 10^{-5} cancer risk level, but also feels that it is appropriate to look at the tribal consumption of salmon, freshwater and estuarine species. The use of the 10^{-5} risk for the higher consuming tribes will result in a more protective risk level for the general population, but that will be the case no matter what approach DEQ uses—risk will always be uneven across populations that have different consumption patterns.
	13	The proposed standards are calculated to protect only 50% of tribal fish consumers, as opposed to the 95th percentile for the general population. A water quality standard must protect all consumers and cannot disproportionately impact a discrete and vulnerable community (such as tribal communities). That is an issue of environmental justice that will not pass any legal muster.	The criteria proposed will protect the designated recreational use that includes fishing for the population of Idaho, and at very low level of risk – high degree of protection. Different portions of the population and each individual therein will necessarily have different risk, but this is by virtue of differing fish consumption habits, not the criteria. Unequal risk in this situation is due to unequal exposure, not unequal or unfair application of water quality criteria. This reality of differing risk due to differing fish consumption cannot be changed through criteria, would exist absent criteria. It is not injustice. The mean consumption rate for the Nez Perce tribe corresponds is closer to the70th %tile, not the 50th.
	14	DEQ has proposed water quality standards for Idaho's waters that were calculated using substantially reduced levels of protection for tribal people as compared to the general population. Idaho's choice to limit the protection levels for tribal populations in Idaho threatens our tribal waters and the current and future ability of tribal members to safely practice a subsistence lifestyle. DEQ's proposed standards are also weaker than those proposed by all other states and tribal governments in	As explained immediately above and in response to commenter 2 in this section, we are being protective and it is not possible to equalize risks. If you actually compare criteria, not fish consumption rates, you will find that DEQ's proposed standards are not weaker than those adopted or proposed by all other states and tribal governments in the region.

		the region.	
	15	IDEQ's choice to set a less protective, acceptable cancer risk level and hazard quotient for tribes by subcategorizes tribes from the general population and utilizing the mean consumption rate at cancer risk level of 10^{-6} amounts to an unacceptable health risk to Tribal members.	Idaho's risk management choice recognizes the inherent differences in risk among segments of the general population and goes above EPA's national guidance on the matter that speaks to an allowable incremental cancer risk level of 10^{-4} : *"EPA also believes that criteria based on a 10-5 risk level are acceptable for the general population as long as States and authorized Tribes ensure that the risk to more highly exposed subgroups (sportfishers or subsistence fishers) does not exceed the 10-4 level."* EPA goes on to say in chapter 2 of their 2000 human health methodology: *"EPA believes that both 10-6 and 10-5 may be acceptable for the general population and that highly exposed populations should not exceed a 10-4 risk level. States or Tribes that have adopted standards based on criteria at the 10-5 risk level can continue to do so, if the highly exposed groups would at least be protected at the 10-4 risk level. However, EPA is not automatically assuming that 10-5 will protect "the highest consumers" at the 10-4 risk level. Nor is EPA advocating that States and Tribes automatically set criteria based on assumptions for highly exposed population groups at the 10-4 risk level. The Agency is simply endeavoring to add that a specific determination should be made to ensure that highly exposed groups do not exceed a 10-4 risk level. EPA understands that fish consumption rates vary considerably, especially among subsistence populations, and it is such great variation among these population groups that may make either 10-6 or 10-5 protective of those groups at a 10-4 risk level."* Idaho has looked at Idaho specific data for both the general population and three more highly exposed subgroups of the general population. With our proposal an individual would have to eat more than 665 g/day of fish from Idaho's waters *every day for 70 years* to exceed a cancer risk level of 10^{-4}.
	16	In calculating water quality criteria, Idaho has chosen to set the cancer and non-cancer protection levels for the general population at the 95th percentile, but for tribal populations the levels would only be for the mean. This is discriminatory, would result in disproportionate and disparate risk to tribal members, and would provide unequal protection as a direct product of state action. Idaho's standards must eventually be submitted to and accepted by the U.S. Environmental Protection Agency (EPA), but it is highly questionable (to say the least) whether standards based on this obvious differential treatment will obtain the necessary approval. The CTUIR DNR would encourage EPA to reject such standards.	It is impossible to equalize risks among populations or all people in a population. Please see response immediately above. The inherent difference in risk distribution is illustrated in the graph below comparing the risk distribution for two populations:

			 Changing water quality criteria (if it changes fish quality) will shift these curves left or right, but it will do nothing to close the gap between them.
	17	First, IDEQ has taken the fish consumption rate for one higher consuming population – the Nez Perce Tribe – and applied that rate to develop state-wide standards. For fish-only criteria, that Tribe's rate drives all of the derived levels, since it is substantially above both the general population exposure level and the exposure levels for other high-consuming populations. We believe that using this higher fish consumption rate for a particular population to derive state-wide criteria is not appropriate. We are also concerned with IDEQ's choice to apply an incremental cancer risk level of 10-6 in deriving its criteria. While we recognize that under Federal guidance, the State has the discretion to make that choice, we note that under that guidance, IDEQ could also use a risk level of 10-5. We see no basis for applying 10-6 instead of 10-5, when there is no significant difference in risk posed to the public, and the difference in compliance costs to regulated parties – and to the public that must eventually bear those costs - could be very significant. Finally, we encourage IDEQ to use the best available science for determining Relative Source Contribution (RSC) values, rather than simply relying on EPA's recommended values.	Although the Nez Perce Tribe's fish consumption ended up driving our proposed criteria that was not a predetermined outcome, but rather a consequence of considering higher end consumers per EPA guidance. DEQ used the group 2 fish for the Nez Perce tribe. There was no comparable fish group in Idaho's general population survey results. The survey did record all fish. While this includes a broader range of fish than the group 2 fish, it is the most comparable fish grouping. The mean tribal fish consumption rate is comparable to the 95% of the general population consumption of all fish. This is consistent with, while more conservative than, EPA's national guidance in which they used the 90% of the general population's consumption of freshwater + estuarine fish while using the average consumption for higher consuming populations. DEQ has determined to use a 10^{-5} risk level. See response to commenter 5 in the section "level of protection/allowable risk."
	19	Our most significant point of objection here is the final Fish Consumption number that DEQ has chosen to integrate into its standards. The number that is being used is not protective of human health. As a result, this proposed rule incorporates water quality standards for numerous pollutants that are not sufficiently protective. This is especially true with regard to how these rules will affect the health of Tribal Members. It is totally unacceptable to intentionally develop standards that are protective for 95% of Idaho's white population and only protective for the mean of Tribal members. While there might be some means to rationalize this with statistics, it is immoral and wrong for the State of Idaho to develop standards that fail to provide Tribal members with the same level of protection as is provided for Idaho's larger white population.	The protectiveness on the proposal should be determined by the resultant criteria, not any particular component of the criteria calculation. As noted above, it is not possible to equalize risk, provide the same level of protection to all. In addition, DEQ is adopting state wide criteria. Inherent in the development of criteria for all Idaho residents is the unavoidable fact that some individuals or groups of individuals will be affected differently by the criteria. EPA's 304(a) recommended criteria are based upon the 90th percentile

		We urge you to revisit this decision. … We are concerned that certain high consuming subpopulations will be placed at an unacceptable risk if DEQ provides 10-6 level of protection only to the mean of the overall subpopulation. We advocate that DEQ instead provides this level of protection to the 95th percentile of the high consumer subpopulation. Failure to do so creates environmental justice issues as it exposes Tribal members and all fishing/angling Idahoans to elevated levels of risk. These high consuming members of the public are specifically the people that need to be protected – they are the people eating larger quantities of fish.	consumption rate for the general population, while the default fish consumption rates used for higher consuming populations reflect the average consumption rate. Our proposal is well within EPA's guidance in its level of protection afforded high end consumers. Please see responses above, particularly to commenters 2, 13, & 15.
	20	The proposed standards are fundamentally flawed in two significant ways. First, the proposed water quality standards were calculated using substantially reduced levels of protection for tribal people as compared to the general population. The RTOC believes the utilization of the mean consumption figure for tribal populations fails to protect the health of a great number of Idaho residents and those who fish in Idaho. Moreover, the decision to protect the average person, as opposed to most of the vulnerable population, is a significant environmental justice matter – one that makes this proposal significantly flawed and beyond the possibility of EPA approval. According to EPA, environmental Justice is the fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies. Fair treatment means that no group of people should bear a disproportionate share of the negative environmental consequences resulting from industrial, governmental and commercial operations or policies. This proposal is anything by "fair treatment" because a disproportionate burden of the impact of toxic pollution will fall upon tribal communities. … Given these concerns, the RTOC would urge IDEQ to "go back the drawing board" and look to the process utilized in the State of Oregon, which adopted a rate of 175 grams per day of fish consumption. We believe that the Oregon rate is appropriately protective of subsistence use of fish in our Region and should be considered in any effort to review Idaho's consumption rate. In short, we believe that IDEQ should adopt a rate that is protective of human health. If IDEQ is unable to fully consider the impacts of toxics on tribal health, we would urge IDEQ to allow EPA to step in and to promulgate standards that are protective of the health of all fish consumers in the State.	Basing the criteria for carcinogens on a 10^{-5} incremental risk level is a very high level of protection that goes above what EPA guidance suggests is acceptable. More importantly there is no "disproportionate share of the negative environmental consequences resulting from" these criteria. The criteria are applied equally across the landscape regardless of who uses the water. While there are differences in risk, these are due to immutable differences in consumption habits; consumption habit differences that are unrelated to water quality criteria, existed prior to water quality criteria, and would persist at lower (or higher) criteria, or even absent criteria. We firmly believe that the criteria we proposed are protective of all in Idaho, even high end consumers. We urge you to evaluate our proposal on the whole, not just by its fish consumption rate.
	21	The EPA supports DEQ's proposed policy decision to retain its 10-6 cancer risk level to derive human health criteria.	
	22	As a part of setting human health water quality criteria, DEQ also has policy decisions to make, especially in regards to selecting a risk target. The selection of a risk target significantly influences the final calculated human heath water quality criteria. There are a number of aspects of selecting the risk target, such as ensuring the criteria are protective of Idaho residents (including subpopulations that have high fish consumption rates), consideration of conservatism that is inherent in risk calculations, how the resulting calculated criteria compare to background and ubiquitous chemicals (such as PCBs) and the feasibility of achieving the criteria. EPA guidance provides latitude to DEQ in selecting risk targets. IACI recommends that a risk factor of one to 10^{-5} for both the Idaho and tribal populations provides the "balance" among these different aspects for determining human health water quality criteria.	Please see response to commenter 5 above in this section on "level of protection / allowable risk."

		… EPA chose to use the one-in-one million (10^{-6}) risk level as the default value when calculating HHWQC because it believes this risk level "reflects an appropriate risk for the general population." However, EPA also notes that risk levels of 10^{-5} for the general population and 10^{-4} for highly exposed populations are acceptable. A target risk level of 10^{-4} is sometimes interpreted as meaning that highly exposed populations are not as well protected. However, as discussed in a paper by Kocher, "if only a small population would be at greatest risk, the expected number of excess cancers corresponding to individual risks at the de minimis level of 10^{-4} would still be (essentially) zero." Given that the 10^{-4} risk level has been identified as an acceptable/de minimis risk level for highly exposed populations, it may be useful to consider exactly what that risk level represents in terms of fish consumption rates. If the default fish consumption rate is 17.5 g/day represents a 10^{-6} target risk level, then a highly exposed population that eats as much as 1,750 g/day will still be protected at a 10^{-4} risk level.	
	23	We urge IDEQ to reassess its proposed risk policy choices on carcinogens and non-carcinogens. Based on material previously submitted by ARCADIS, a nationally recognized environmental consulting firm, there is no measurable difference in the number of excess cancers expected for Idaho residents under criteria based on a 10^{-5} versus 10^{-6} excess lifetime cancer risk (ELCR). Specifically, deriving criteria based on a 10^{-5} (instead of 10^{-6}) allowable ELCR management goal for the population size of Idaho would be expected to lead to an increase of 0.23 cancers in total per year—from 2570.00 to 2570.23 (based on the 2012 Idaho population). If a $1x10^{-6}$ ELCR were used, the increase would be 0.023—from 2570.00 to 2570.023 (based on the 2012 Idaho population). The difference in the number of excess cancers resulting from the application of criteria based on the different risk levels is so small that it is basically immeasurable and statistically without meaning because of the year-to-year variation in cancer incidence. Moreover, as noted in the IACI comments, these calculations do not reflect that IDEQ is currently proposing to apply the 1x10-6 risk management goal to the 95th percentile of the general population, an <u>even more</u> stringent benchmark than used in the above example and much more stringent than the EPA's national risk policy guidance. Clearwater Paper urges IDEQ to modify the ELCR used in selecting carcinogenic HHWQC's to the more stringent of 1 in a 100,000 at the 95th risk percentile of either the general population or the tribal risk distributions <u>assuming</u> the very important statistical correction discussed below (and in Attachment A) is adopted by IDEQ. With this adjustment, spurious 303(d) listings will be avoided and only those water bodies posing elevated and unacceptable risk would be listed thereby avoiding unneeded TMDL's and unwarranted NPDES allocations that provide no measureable improvement in public health. To provide some perspective, the added risk from the proposed risk policy change is the equivalent of the average Idahoan *driving an additional 11 miles a year*. Noted below is a discussion of the cost implication of the proposed standard—**<u>$16 billion</u>** over the next 25 years for municipal and industrial dischargers in Idaho, with no guarantee of even achieving the de minimis benefit represented by the proposed HHWQC based on an ELCR of 10^{-6} (when compared to 10^{-5}). … Because the appropriate level of risk is a matter of policy, IDEQ and the Idaho Legislature represent the appropriate bodies to establish the state's policy on risk.	Because acceptable risk is a matter of public policy, we concur that such decisions are appropriately made locally, and note that EPA has said so as well: *"EPA believes that ambient water quality criteria inherently require several risk management decisions that are, in many cases, better made at the State, Tribal, or regional level."* EPA, 2000 Please see response to commenter 5 above in this section on "level of protection / allowable risk."
	24	The lack of acknowledgement for the future health of tribal members exhibited by IDEQ in proposing to only protect them at the mean consumption rate at a cancer risk level of 10^{-6} is without merit. The policy position that Idaho has taken to set a less protective, acceptable cancer risk level and hazard quotient for tribal	We are sorry that you so misunderstand the range of risk that we cannot alter through water quality criteria, and our effort to reasonably protect all.

		people is troubling and counter to federal laws and mandates that were developed with the sole purpose of preventing exactly this type of disparate impact. That a state agency would be so influenced by outside forces that care little to nothing about human health and water quality that it would propose standards that specifically protects one sector of the general population less than another is really disgraceful! … Our position has not changed. USRT and its member tribes believe that criteria should be derived by that portion of the general population (our definition of the general population includes tribal members, as should IDEQ's) who eats the most fish (including anadromous/market fish) and thus is exposed to the most risk.	Please see our response to commenters 2, 13, 15 and 20. Please also see our response to you above under topic heading 'Survey design, target population.' As we have noted in our response to the above comments, DEQ's policy choices are entirely consistent with federal law and guidance.
	25	IDEQ has proposed an incremental cancer risk at a level that will protect 95% of the "general" population but only 50% of high fish-consuming Idaho residents. The draft rule perpetuates an ongoing environmental injustice by subjecting tribal people to disproportionately higher risks simply from exercising our rights to harvest First Foods and practice our religion and culture.	As discussed throughout the rulemaking process and above, there is no way to equalize risk- higher fish consumption rates will always carry a greater exposure to fish-borne contaminants. Furthermore, criteria cannot change these inherent differences in risk. Please see our response to commenters
Included fish	2	Idaho's proposed water quality standards were derived following a state policy decision that excludes market fish and anadromous fish except for steelhead from its analysis of general and tribal fish consumption. Excluding anadromous fish from the state's fish consumption rate has had the effect of significantly decreasing the protectiveness of the state's water quality standards. This exclusion ignores the fact that treaties with the federal government have guaranteed the right of tribal members "to take fish" and does not limit in any way the particular mix or species of fish. Tribal people are free to determine what species they wish to harvest and consume and the state must not undermine this treaty-protected right.	DEQ has chosen to use a fish consumption rate that includes salmon to develop the human health criteria. This decision is not based upon tribal treaty fishing rights. Please see response to commenter 5 below.
	5	The exclusion of salmon, other marine fish and market fish is justified for a number of reasons. Several research studies have shown that anadromous fish acquire the majority of the contaminant burden in marine waters, providing good science to support the exclusion of salmon from the fish consumption rate. Arguments have been made for consistency with other Northwest states. However, Idaho water quality rules can't regulate estuarine and marine waters, and where most market fish come from; thus Idaho regulations can't influence concentrations of chemicals present in such waters. As an inland or non-coastal state, Idaho is significantly different from the other Northwest states. The exclusion of salmon clearly recognizes the best science on sources of contaminants for salmon and the inland nature of our state and waters. In Idaho, the inclusion of salmon will not improve public health by decreasing risks associated with chemicals in anadromous fish. In addition, Idahoans could be faced with substantially increased compliance costs that would not result in improved public health benefits.	DEQ has chosen to use a fish consumption rate that includes salmon and all freshwater and estuarine fish no matter the source to develop the criteria. DEQ made this choice in order to be consistent with EPA guidance and for the other reasons set out below. EPA expects standards to be set to enable residents to safely consume from local waters the amount of fish they would normally consume from all fresh and estuarine waters. Therefore, DEQ felt it was important to include more than just local freshwater fish as it had originally proposed. In addition, in its national guidance, EPA allows States the choice to include salmon and other marine fish. While EPA excluded almost all salmon from the fish consumption rate used to develop its 304(a) recommended criteria, EPA has emphasized the need to use local rather than national information, if local data is available. EPA has raised questions concerning whether salmon that are consumed in Idaho pick up some pollutant load from regional waters within the jurisdiction of the CWA, and even in Idaho waters. EPA has provided DEQ very little information regarding the recent research and modeling that it asserts shows the source of pollutants in Idaho salmon.[1] Nevertheless, DEQ believes it is appropriate to include salmon, like DEQ did with respect to steelhead, because of the uncertainties regarding the source of pollutants. In addition, using a broader more inclusive range of fish and thus a

			higher consumption rate, along with other conservative factors, while using a higher risk level, helps to ensure that DEQ's criteria remain protective. In other words, DEQ believes it has chosen an appropriate balance of more conservative and less conservative factors that it believes results in human health criteria that are protective of human health and while reasonably achievable. [1]While DEQ is using the group 2 fish, DEQ is concerned about the accuracy of the modeling performed by Gobas because Gobas used incorrect criteria in the modeling exercise
	7,8	1. **Market Fish:** ISWR fully supports IDEQ's determination that the only market fish to have any rational connection to Idaho water quality would be the Rainbow Trout. The members of ISWR strongly feel that the inclusions of any market fish not found in Idaho's waters would yield a standard that would be difficult for municipalities and industries to meet and would have no impact on the toxics found in those fish. 2. **Anadromous Fish:** ISWR supports IDEQ's decision to exclude anadromous fish in setting the HHWQC standards. Anadromous fish present in Idaho's waters can potentially collect only a negligible amount of contaminants (if any) from their time in Idaho waters, so to include their consumption in a risk assessment associated with setting criteria for Idaho waters would be inaccurate, overly conservative and not consistent with the state's goal of using best available science in rule makings.	Please see response directly above.
	9	There was a great deal of discussion about anadromous fish and Idaho's fresh water species. We support DEQ's decision to base the update of the rules on consumption of Idaho's fresh water species since our rules would have no impact on fish which spend most of their life cycle in the waters of other states and the ocean. The same logic applies to Idaho fish versus market fish.	While we agree that the effect of Idaho's water quality criteria on fish that grow up outside Idaho waters is limited, Idaho does contribute pollutants to downstream waters and thus has some effect. By including these other fish we recognize a shared responsibility among all states in the nation. In addition, please see response to comment above.
	11	A foundational assumption in this rulemaking is that Idaho water quality standards influence the contaminant levels in fish and water. When considering the different sources of fish consumed by Idaho residents, such questions arise such as to where do these different sources of fish acquire contaminants and can Idaho water quality rules change the levels of contaminants in these fish? The Department, for the purpose of the FCR study, decided that the fish included in the survey need to be fish, in which the contaminant levels can be influenced by Idaho quality criteria. This definition of "Idaho fish" excludes marine fish, most market fish (except rainbow trout), and salmon.' Though salmon spend a part of their life history in Idaho water's, studies have definitely shown that greater than 95% of the contaminants accumulated by salmon occur in marine water. Since the purpose of the establishing a fish consumption rate for Idaho residents is to help determine appropriate water quality criteria for Idaho waters, such regulations will have no effect on the levels of contaminants acquired by such fish as salmon. Simplot believes that the Department has appropriately selected the fish species to be included to determine fish consumption rates for Idaho residents.	Please see also responses to other commenters in this section.
	13	Second, the rate excludes anadromous fish, including salmon, because the State does not believe it can impact waters outside of Idaho. This ignores the fact that Idaho water and its pollution contributes to water quality in the Snake and Columbia Rivers outside of the state. It also ignores Idaho's legal obligation to avoid causing and contributing to water quality issues downstream. 40 C.F.R. § 122.4. Turning a blind eye to anadromous fish ignores these facts and leaves one of Idaho's most treasured natural resources – salmon – without protection that they deserve.	DEQ has chosen to use a fish consumption rate that includes salmon in calculating the human health criteria. DEQ is not, however, including salmon in order to protect salmon as the commenter asserts. The criteria at issue are human health criteria; they are not developed to protect aquatic life. DEQ has separate aquatic life criteria for toxic pollutants. The proposed criteria are about protecting human health; there are separate aquatic life criteria set to protect fish, including salmon.

	16	The CTUIR DNR disagrees with your decision to exclude market fish and anadromous fish (except for steelhead) from your analysis of general and tribal fish consumption. This fails to accurately reflect the reality of fish consumption patterns and will substantially decrease the degree of protection afforded by the state's water quality standards.	DEQ has chosen to use a fish consumption rate that includes salmon and all freshwater and estuarine fish in the consumption rate used to calculate the criteria. The reasons for this decision are set forth in response to commenter 5 above.
	19	Market Fish We disagree with DEQ's decision to exclude the consumption of market fish when calculating Idaho's fish consumption rate and urge the Department to reconsider this matter and include market fish. The consumption of Idaho fish must be considered within the context of the actual (surveyed) eating patterns of Idahoans. If Idahoans are consuming market fish, and thus being exposed to contaminants in these fish, Idaho water quality standards must be set such that the consumption of Idaho fish does not add to a consumer's pollutant burden in a way that results in physical harm to the consumer. Idaho consumers should not have to choose between eating market fish and eating Idaho fish; Idaho's standards should be set in such that a consumer can consume fish from both sources and do so at the levels that they are accustom to. In order to do so safely, Idaho standards should be set in a manner that accounts for the consumption of both local and market fish. Anadromous Fish We disagree with DEQ's decision to exclude the consumption of anadromous fish when calculating Idaho's fish consumption rate and urge the Department to reconsider this matter and include anadromous fish. Our decision to support the inclusion of anadromous fish in the calculation of Idaho's fish consumption rate is based in part on the fact that various species of anadromous fish spend varying lengths of time in Idaho waters and/or in waters that could be affected by Idaho water quality standards. The duration of such residency of anadromous fish varies from one to three years and there is scant scientific evidence to determine what proportion of a fish's pollutant burden comes from its time in Idaho or in downstream waters affected by Idaho water quality standards. As such, it does not seem to be defensible to lump all anadromous fish together and exclude them from inclusion.	DEQ has chosen to use a fish consumption rate that includes all freshwater and estuarine fish consumption. Please see response to commenter 5 in the above section.
	20	Second, the proposal is fundamentally flawed because it excludes market fish and anadromous fish, except for steelhead, from its analysis of general and tribal fish consumption. Excluding anadromous fish, such as salmon, from the consumption rate significantly decreases the protection afforded to human health by the standard. This also ignores the subsistence use of salmon and other anadromous fish that is a legally-protected right of many Tribes both in Idaho and outside of the State, who have treaty rights to fish within state boundaries.	Pease see response to commenter 5 above.
	21	**Market Fish (Other than Rainbow Trout)** Idaho's approach is to exclude from the FCR the fraction of the consumption of freshwater and estuarine fish and shellfish that is currently associated with fish originating from waters outside of Idaho. Idaho justifies its approach on the grounds that Idaho lacks regulatory authority over fish caught outside of its borders. Based on the information and rationale EPA has received from Idaho to date, we note the following reasons why Idaho's justification for this approach is not scientifically sound: • The purpose of including consumption from waters outside of Idaho's borders in the FCR is not to support any purported regulation of such waters by Idaho. Rather, the purpose of including this fish consumption in	DEQ has chosen to use a fish consumption rate that included freshwater and estuarine fish, consistent with EPA national guidance. See response to commenter 5 in the above section.

		the FCR is so that a determination that a particular Idaho water body is "fishable" will result in adequate health protection for Idahoans should they consume, from local waters, the amount of fish they would normally consume from all inland and near shore waters. • The approach of excluding "market fish" appears to assume that there is no exposure to pollutants from fish that were sourced outside of Idaho. This is because the full allowance for acceptable pollutant levels is given exclusively to local state waters. Consider if every state took this approach. For a non-carcinogenic pollutant with a specified Reference Dose, the criteria development equation would allocate this full dose to fish originating from the individual state. If a person then consumes overall 25 grams/day (glday) of fish, comprised of 5 glday each from 5 different states (and each state set a state-specific consumption rate of 5 glday), then the consumer could potentially receive five times the acceptable pollutant dose.	
	21	**Anadromous Fish** The EPA recognizes that Idaho has included steelhead, an anadromous species, in the calculation of its FCR. However, the EPA continues to have concerns with DEQ's proposed policy decision to exclude all other anadromous fish from the FCR, and recommends that DEQ either include all other anadromous fish in the FCR or provide additional demonstration of how criteria derived using a lower FCR that excludes anadromous fish will protect downstream shared waters in the Columbia River basin and protect the tribal populations exercising their treaty-reserved rights (see comments below regarding consideration of tribal reserved fishing rights). While the EPA's 304(a) recommended criteria account for exposures to non-carcinogens and nonlinear carcinogens in anadromous fish using the relative source contribution (RSC), the EPA supports and recommends that states include anadromous fish in the FCR when there is credible and compelling evidence of significant consumption of anadromous fish. For example, Oregon and Washington chose to include salmon in the FCR used to derive human health criteria due to, amongst other reasons, the large amounts of salmon consumed by tribes, the variation in individual market basket preferences (i.e., the types of fish that people purchase and consume), and uncertainties in the sources of salmon contaminant body burdens from inland and near shore waters (e.g., salmon residing in Puget Sound). The EPA approved Oregon's human health criteria in 2011. Similarly, the EPA supports Washington's decision to develop human health criteria using a FCR that includes anadromous fish consumption. The EPA also has reviewed recent work related to salmon contaminant acquisition from near coastal waters of the Pacific Northwest and recommends that DEQ also consider this available information. For example, the research conducted by Sandra O'Neill, James West, David Herman, and Gina Yitalo provides evidence that certain Pacific Northwest salmon species, most notably chinook and coho, acquire organic pollutants from near coastal marine waters. O'Neill et al. assayed salmon and herring for several classes of persistent organic pollutants (POPs). The POPs of interest included polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), hexachlorobenzene (HCB), and the insecticide DDT. An analysis of these POPs in herring populations identified unique regionally-specific patterns of these chemicals or "fingerprints," thus showing herring are acquiring contaminants from waters under CW A jurisdiction. Chinook salmon harvested from specific locations were found to have the same contaminant "fingerprints" as those exhibited by co-located herring samples, suggesting that they are feeding on herring in near coastal waters. This work provides evidence that certain Chinook salmon species are acquiring contaminants from near coastal waters of Washington and Oregon, as well as California and British Columbia. Similar but more limited data by O'Neill et al. indicate that coho salmon, which reside in coastal waters and have feeding preferences similar to chinook salmon, are also acquiring contaminants from waters under CW A jurisdiction. In addition, EPA has communicated with Laurie Weitkamp and Peter Lawson from NOAA, who have stated	DEQ is using the mean of the Nez Perce consumption of their Group 2 fish. This includes near coastal, estuarine, freshwater and anadromous fish. Please see DEQ response to commenter 5 in the above section regarding market fish for the reasons for DEQ's decision. As set out above, while Nez Perce Group 2 fish includes salmon DEQ does not believe the tribal treaty fishing rights mandate this result. Instead, DEQ's decision is based on the uncertainties raised by EPA regarding the source of salmon pollutant loads, and the balance of the various input factors DEQ is using to develop the criteria. It should also be noted that DEQ has included a downstream waters provision recommended by EPA. EPA itself has concluded that downstream protection does not mean that all state standards must be identical.

		that chinook (and likely coho) salmon from Idaho reside in near coastal waters off the Oregon coast. Myers at al. 1998, analyzing coated wire tag recovery, has concluded that Snake River Chinook salmon have a coastal residence pattern. O'Neill et al.'s work shows that resident chinook salmon from these waters have regional contaminant fingerprints specific to this area. Given the contaminant fingerprint correlation between herring and coastal resident salmon at all locations where both species were analyzed, it is very likely that coastal salmon originating in Idaho waters are acquiring contaminants from coastal waters under CW A jurisdiction. EP A recognizes that salmon acquire most of their body weight and, therefore, most of their body burden of highly bioaccumulative contaminants during open-ocean feeding. However, it is possible that salmon may acquire less bioaccumulative contaminants directly from water during their return spawning migration as adults. EPA consulted with Frank Gobas, a well-known expert in bioaccumulation and bioconcentration in aquatic food webs, to evaluate this issue and prepare an analysis. The analysis first involved the development of contaminant concentrations in salmon tissue that were associated with either a cancer risk of 1 in 1,000,000 or a non-cancer hazard quotient of 1. These risk-based concentrations assumed a fish consumption rate of 175 grams per day by an 80 kilogram person. Next, bio-concentration modeling was performed to determine the water concentration that results in a salmon tissue concentration associated with the aforementioned risk-levels. The model includes quantitative structure activity relationship biotransformation of chemicals and the impacts of changing lipid content associated with migration energy expenditure. The model also accounts for the time dependent nature of chemical uptake. This modeling utilized a range of migration times for spawning Idaho chinook and sockeye salmon associated with several harvest locations within Idaho. The longer the migration time, the greater the opportunity for contaminants to bioconcentrate. Finally, ratios of Idaho's proposed water quality criteria to modeled water concentrations were computed. The results showed, for example, toxicity ratios of 10 or greater for 13 chemicals with non-carcinogenic toxicity. In other words, for 13 non-carcinogenic chemicals, Idaho's proposed criteria could result in hazard quotients of 10 or more for populations consuming Idaho returning salmon at a rate of 175 grams per day or more. This far exceeds EPA's recommendation of limiting risks to non-carcinogens to a hazard quotient of 1 or less. Therefore, DEQ should consider these results. EP A has enclosed the analysis for your review and consideration (see attached spreadsheets). Idaho cites work by Hope 2012, suggesting that salmon do not acquire contaminants from waters under CW A jurisdiction, to justify excluding anadromous species from the FCR used to develop DEQ's proposed criteria. The Hope study's conclusions are limited by its focus on PCBs and not on other toxics, and the study does not consider salmon acquisition of contaminants from near coastal waters as demonstrated by 0'N eill et al. Central to the modeling is the assumption that contaminant uptake occurs largely through diet. While this is true for PCBs, depending on a chemical's lipophilicity, direct uptake from water may be a significant contributor to an organism's contaminant body burden. The Gobas work on contaminant bioconcentration in migrating adult Idaho salmon, described above, provides evidence that adult Idaho salmon may acquire contaminants directly from the water column through their gills, in addition to dietary uptake. Finally, the Hope study also does not discuss different patterns of contaminant uptake associated with the complex life histories of other salmonids, such as steelhead. In conclusion, DEQ should consider the above-referenced scientific information when making its final decision on whether to include anadromous salmonids, other than steelhead, in calculating the FCR. The EPA remains concerned that Idaho's decision to exclude most anadromous salmonids results in human health criteria that are not adequate to protect Idaho's primary and secondary contact recreation uses.	
	22	The ultimate result of the fish consumption rate rulemaking is the refinement of Idaho's human health water quality criteria (HHWQC) to ensure such criteria are protective of public health. Thus, understanding	Please see response to commenters above.

		the potential exposure of the public to contaminants from eating fish from Idaho's waters and drinking Idaho water is key to setting water quality criteria and subsequent discharge levels for the regulated community. Underpinning this regulatory framework is the assumption that regulation of dischargers in Idaho directly affects the contaminants in Idaho fish and water being consumed. Thus, the substantive question related to fish consumption by Idaho residents is, what fish should be included in determining fish consumption rates for Idaho residents? A number of fish found in the marketplace come from marine sources, international sources or fish that are anadromous. Once again, back to the foundational assumption that Idaho water quality standards influence the contaminant levels in fish and water, where do these different sources of fish acquire contaminants and can Idaho water quality rules change these levels of contaminants in these fish? <u>Anadromous Species</u> Unlike true freshwater species, anadromous fish spend a substantial portion of their life in marine or estuarine environments that are outside the jurisdiction of Idaho. If a substantial fraction of the chemical-specific body burden (mass per fish) found in returning adult salmon is acquired during time spent in the ocean, there is effectively nothing Idaho water quality criteria can do to reduce risks to humans resulting from exposure to chemicals in the salmon they eat. Thus, the ultimate question is, what fraction of the final chemical burden in Idaho's returning adult salmon is acquired in Idaho vs. in the ocean? … IACI supports DEQ's definition of "Idaho Fish" and the decision to exclude market fish (other than rainbow trout), anadromous salmon, marine fish and other non-Idaho resident fish for determining fish consumption rates for the purpose of setting Idaho water quality standards. As discussed earlier, Idaho water quality regulations cannot control the level of contaminants in these excluded fish. For example, the predominant fraction of the ultimate PBT burden found in harvested adult salmon, even salmon passing through highly contaminated fresh and estuarine waters during out migration, is accumulated while in the ocean phase of their life cycle (i.e., Cullon et al. 2009; O'Neill and West 2009). This conclusion is supported by modeling as well (Hope 2012).18 Indeed, HHWQC could be set to zero and human health risks associated with consumption of these fish, assuming such risks are present, would remain unchanged. In short, Idahoans could be faced with substantially increased compliance costs and garner no benefit from such increased costs.	
	23	**Market Fish** Clearwater Paper supports IDEQ's scientifically justified choice of limiting the level of market fish by including only those fish reared naturally or purposefully in Idaho to set HHWQC. To include species not grown in Idaho or Pacific Northwest states in a fish consumption rate would be overly stringent and quite frankly result in risk assessments not rooted in reality. Because it is scientifically based and defensible and would result in an accurate risk assessment outcome, we strongly urge IDEQ to maintain the treatment of market fish as proposed. **Anadromous Fish** As with the issue of market fish, including anadromous fish that spend a negligible amount of time in Idaho waters would result in an overly stringent risk calculation and would have a negligible difference on the actual risk to those eating large amounts of anadromous fish. Forcing Idaho to adopt overly and unnecessarily stringent controls would not affect contaminants in anadromous fish: so to include such fish in the determination of HHWQC is not following a science-based decision process. Because it is scientifically	Please see response to commenters above.

		based and defensible and would result in an accurate risk assessment outcome, we strongly urge IDEQ to maintain the treatment of anadromous fish as proposed.	
	24	Fish Included – Fish group 2 should be used for determining Idaho's fish consumption rate (FCR) and not a cherry-picked group of fish that does not adequately reflect consumption patterns in Idaho, nor leads to protective WQC. Anadromous and market fish must be included in the FCR calculation and we adamantly oppose and reject the back-of-the envelope calculation used by IDEQ to inappropriately manipulate tribal FCR data. USRT and its member tribes reject the manner in which IDEQ derived both the angler/non-angler FCR and the tribal FCR, which was erroneously revised by stripping out anadromous and market fish. As such, we find that the FCR used by IDEQ to be illegitimate and in no way do we support its use.	DEQ has chosen to use group 2 fish.
	25	Salmon is a tribal First Food and the importance of it to the tribes cannot be overstated. The fishery resource is not only a major food source for tribal members, but also an integral part of our cultural, economic, and spiritual well-being. As ceremonial and subsistence fishers, we rely on the State to set reasonable and legitimate water quality standards that will protect our water and the fish that we consume from harmful exposure to toxic pollutants.	DEQ has chosen to use a fish consumption rate that included salmon in its criteria development. DEQ believes it has set criteria that are protective for all Idaho citizens.
Downstream Waters	5	DEQ has proposed rule language on how to apply the standards to the protection of downstream waters. This is a very significant issue which requires very careful examination and discussion. This provision also introduces new concepts that are undefined, therefore restricting our ability to determine potential impacts to this rulemaking to future DEQ rulemakings and any potential water quality decisions made by EPA. We raised this issue in previous comments and would again recommend that DEQ not include this provision in the rulemaking and address this matter in a future, separate rulemaking	Protection of downstream waters is a requirement of the CWA and its implementing regulations. We believe the added language clarifies current practice in Idaho; is not a new concept. While not a new concept, EPA has made addition of language to state and tribal water quality standards a national priority. Failure to address downstream protection directly in rule could give EPA sufficient reason to find fault with Idaho's proposal.
	6	Protection of downstream waters as required at 40 CFR 131.10(b) is an important consideration in designation of uses and associated water quality criteria. In 2015, EPA adopted revisions of the Water Quality Standards Rule that include clarification of six water quality standards items, including protection of downstream waters. EPA guidance on the six water quality rule elements included discussion of acceptable downstream water quality protection options to states, including narrative of numeric approaches. The proposed Idaho water quality criteria include a narrative for protection of downstream waters at 58.01.02.070.08, which appears to be an acceptable approach under the new water quality standards rule. AIC supports the dual approached proposed by EPA for states to comply with the downstream waters protection element of the rule and Idaho's proposed narrative approach, which is consistent with EPA guidance to states for satisfaction of this water quality standards element.	We agree, and see that it is important to address downstream protection clearly and now, in this current rulemaking effort. We believe the narrative language that we have chosen, based on EPA's template language, meets the requirements of the federal regulations while providing flexibility in implementation consistent with current practice in achieving downstream protection.
	15	The Tribes continue to request that IDEQ implement protective downstream water quality standards for each of the watersheds that may have an impact on reservation waters; particularly the mainstem Snake River, Blackfoot River, Portneuf River and Bannock Creek watersheds.	
	16	Unfortunately, IDEQ has chosen to embrace revised standards based on significantly reduced levels of protection for tribal people as compared to those for the general population. Adopting such standards would result in greater amounts of toxic discharges to Idaho waters than those allowed by other regional states and tribes, and those Idaho waters would eventually become the waters of those adjacent or downstream states and tribes. It is unacceptable that such neighboring jurisdictions should have to bear	It is impossible to equalize risks among all people in a population. (see above) As most of our criteria have decreased in value the proposed criteria, to the extent they affect water quality, offer more protection going forward. Our criteria are also lower than many of the criteria currently in place for Oregon and lower than those currently in place in Washington.

		the burden of Idaho's unenthusiastic approach to safeguarding water quality.	When water quality criteria are implemented – e.g. used in a TMDL or NPDES permit – we look at both Idaho water quality standards as well as those of downstream jurisdictions to make sure both will be met.
	19	While we support the inclusion of this clause directing that water quality in downstream waters shall be protected, we believe that the proposed language needs refinement. We advocate that language be added that states that existing and designated uses shall be protected. Doing so more accurately reflects the true extent of what is required to comply with the legal antidegradation requirements of protecting downstream water quality. See proposed additional language inserted into DEQ's proposed rule language below. All waters shall maintain a level of water quality at their pour point into downstream waters that provides for the attainment and maintenance of the water quality standards and protection of existing and designated uses of those downstream waters, including waters of another state of tribe.	The suggested language is not needed as water quality standards include uses, criteria and antidegradation.
	21	The EPA is encouraged by DEQ's inclusion of a downstream protection narrative criterion in the proposed rule, following the language in EPA's "Templates for Narrative Downstream Protection Criteria in State Water Quality Standards" (EPA publication No. 820-F-14-002). However, the EPA's Protection of Downstream Waters in Water Quality Standards: Frequently Asked Questions suggests that states consider a more tailored and specific narrative criterion and/or a numeric criterion in certain situations, such as when more stringent numeric criteria are in place downstream and/or environmental justice issues are relevant. As mentioned above, most of Idaho's waters are in the Columbia River basin and are, therefore, upstream of Washington's and Oregon's portion of the Columbia River. The EPA strongly encourages DEQ to adopt numeric human health criteria (either in addition to or instead of a narrative criterion) that ensure the attainment and maintenance of downstream human health water quality criteria, or to provide additional rationale detailing how use of a narrative downstream protection criterion in combination with Idaho's numeric human health criteria will ensure the attainment and maintenance of downstream human health criteria, consistent with the EPA's regulations at 40 CFR 131.10(b).	We note that EPA itself denied a Sierra Club petition on this matter in the Mississippi River Valley in 2004 (Letter to Maxine I. Lipeles, J.D. dated June 25, 2004) claiming that downstream protection required uniform state standards. EPA's response was basically that different uses and criteria among states is not a contradictory construct. This is perhaps best captured in this quote from EPA's denial: *The federal regulations state, "In designating uses of a water body and the appropriate criteria for those uses, the State shall take into consideration the water quality standards of downstream waters and shall ensure that its water quality standards provide for the attainment and maintenance of the water quality standards of downstream waters." 40 C.F.R. §131.10(b). The regulations do not compel states to adopt the same criteria and uses, nor do they suggest that this is the only way a state can meet these requirements. The water quality program is structured to provide states with flexibility to determine the best way to meet their obligations under § 131.10(b).* Also, adopting numeric human health criteria that ensure the attainment and maintenance of downstream water quality standards – if that means identically valued criteria – would be difficult. This is because Washington's human health criteria are in a state of flux. With Oregon, their human health criteria are based on a different set of inputs than are Idaho's current proposal and EPA's national recommendations – for bioaccumulation, relative source contribution, toxicity, body weight, drinking water intake in addition to fish consumption rate. A comparison of actual criteria (rather than just one of the input factors) will reveal some of Idaho's proposed criteria are lower in value than Oregon's, others are higher. This mismatch is likely to always be the case, or at least often so, as adjacent sates update their criteria on different schedules and with different information and policy decisions each time. As EPA itself noted in the Mississippi case above, this mismatch does not prevent meeting the requirements of 40 C.F.R. §131.10(b). Therefore a narrative approach is best.

	22	IACI requests that proposed Section 070.08 be withdrawn for the reason articulated in our letter of August 21, 2015 as well as Clearwater Paper's letter of August 20, 2015. In sum the downstream waters provision does not appear necessary and if it is in the future, it should be subject to a different negotiated rule-making. The provision also introduces a variety of new and undefined concepts that IACI cannot discern their potential impact to this rulemaking or future activities by DEQ and EPA. Illustrative of this uncertainty, does the proposed human health criteria rule comply with this new provision? As noted above, Oregon has adopted human health criteria that are likely an order of magnitude more stringent than DEQ's proposed rule. Many Idaho waters directly or indirectly flow into Oregon waters. In fact, the Snake River forms the border between the two states for hundreds of miles. Does this new provision mean that Idaho waters must meet Oregon's human health criteria? If so, then it appears that DEQ's efforts in relying upon a science-based approach to setting human health criteria has been a wasted effort. We are hopeful that such is not intent of the downstream water provision and that this provision is not abdicating the state of Idaho's sovereignty to establish designated uses and water quality criteria to downstream states or Tribes. However in light of the vague terms used in this provision, we are concerned that third parties may use this provision to suggest such a result. Accordingly we believe DEQ should withdraw this provision and consider addressing this issue in another negotiated rulemaking.	Our assessment is that addressing downstream protection in this rule is a prudent step. We follow EPA's national template language for a narrative criterion, the most flexible way to address the federal requirement for downstream protection. Please see our response to EPA's comment on downstream protection directly above. Downstream protection does mean that the quality of water leaving Idaho must meet downstream state water quality standards; this does not mean that all water within Idaho must meet those downstream state standards. In developing discharge permits we can look at downstream dilution as well as fate and transport to assure we meet downstream standards even though different standards apply locally, at the point of discharge.
	23	We urge IDEQ to withdraw this provision (IDAPA 58.01.02.070.08) for the reasons specified in our letter of August 20, 2015. In short, we believe this provision raises too many questions as to how it will be implemented and may complicate approval of this rule by the EPA in light of conflicting state and tribal criteria in this area.	To the contrary, we feel quite certain failure to address downstream protection would complicate approval of this rule by EPA. Please see our response above to commenter 22, as well as our response to EPA (commenter 21) on this matter.
	24	The protection of downstream water quality provision is but words on a piece of paper. The inadequate WQC proposed by IDEQ in no way will protect downstream waters under the jurisdiction of tribes, Oregon, and Washington. Should the WQC be approved, they will certainly lead to downstream water quality violations and open Idaho up to enforcement actions.	We are disheartened that you are prejudging us. Please see response to commenter 21 above.
Tribal treaty right and designated uses	2	The CWA sets a single threshold for setting water quality standards – protection of the designated uses. If a state's human health criteria do not protect both the right to safe harvest and the tribes that consume it, then EPA has indicated that they have the authority, and the duty to disapprove standards that do not protect tribal rights. Idaho must make appropriate policy choices that will result in a level of water quality that is adequate to allow the tribes to safely consume fish taken pursuant to their treaty-reserved rights.	Human health criteria in Idaho attach to the designated uses of recreation (fish exposure only) and domestic water supply (fish + water exposure). Idaho's secondary recreation use speaks to fishing but not any particular level of harvest such as subsistence or sustenance. None-the-less, and recognizing that every individual has a different risk, the data from recent Idaho and tribal fish consumption surveys coupled with Idaho's risk management decisions provide a high level of protection to even high end / higher risk consumers of fish, including tribal members taking fish pursuant to treaty-reserved rights. Please see also response to commenter 15 under "level of protection / allowable risk."

	15	Our expectation is that IDEQ will propose a FCR that recognizes the importance of our reserved Treaty rights and subsistence lifestyle by reducing the exposure risk to our high end fish consumers to the level of the General Population. … This final draft rule as it stands today will not meet our intensions or expectations for the membership to continue exercising treaty reserved rights or to utilize one of our first foods regularly without the risk of acute or chronic exposure to toxins.	It is not possible equalize exposure between populations with different fish consumption levels. Please see also response to commenters 2, 13, and 14 under level of protection / allowable risk above. We believe the criteria we have proposed are protective of high end consumers as required by the CWA. This includes tribal members taking fish pursuant to treaty reserved rights.
	16	Fishing is an appropriate and commonly-accepted designated use for Clean Water Act (CWA) regulatory purposes. In the Pacific Northwest, fishing by tribal members, based on various treaties with the federal government, and in a manner and to a degree contemplated by those treaties, is a "designated use" long recognized and acknowledged by numerous court decisions, above and beyond the CWA-specific definition. State water quality standards must be developed that protect the tribal fishing use. The Final Draft Rule does not.	Please see response to commenter 2 above. DEQ does not agree that the treaty reserved fishing rights require DEQ to adjust the fish consumption rate or increase the protectiveness of criteria beyond that required by the CWA. Please see response commenter 21 below.
	21	Per EPA's regulations at § 131.11(a), water quality criteria must contain sufficient parameters or constituents to protect the designated use, and for waters with multiple use designations, the criteria must support the most sensitive use. In determining whether WQS comply with the CW A and EPA's regulations, when setting criteria to support the most sensitive fishing designated use in Idaho, it is necessary to consider other applicable laws, including federal treaties. In Idaho, certain tribes hold reserved rights to take fish for subsistence purposes, including treaty-reserved rights to fish at all usual and accustomed fishing grounds and stations and in unoccupied lands of the United States, which in combination appear to cover the majority of waters under state jurisdiction. Many areas where reserved rights are exercised cannot be directly protected or regulated by the tribal governments and, therefore, the responsibility falls to the state and federal governments to ensure their protection. In order to effectuate and harmonize these reserved rights with the CW A, such rights appropriately must be considered when determining which criteria are necessary to adequately protect Idaho's waters used for consumption of fish (designated as Primary or Secondary Contact Recreation, IDAPA 58.01.02.100.02(a)&(b). Protecting Idaho's fishing designated uses necessitates protecting the population exercising those uses. Where a population exercising such uses has a legally protected right to do so under federal law such as a treaty, the criteria protecting such uses must be consistent with such right. Thus, in order to protect the applicable fishing designated uses in areas where such rights apply, as informed by the treaty-reserved right to continue legally protected culturally important subsistence fishing practices, the state must consider the tribal population exercising their reserved fishing rights in Idaho as the target general population for the purposes of deriving criteria that will protect the subsistence fishing use and allow the tribes to harvest and consume fish consistent with their reserved rights. The data used to determine the FCR are critical to deriving criteria that will protect the subsistence fishing use. The data used to determine a FCR must reasonably represent tribal subsistence consumers' practices that reflect consumption unsuppressed by fish availability or concerns about the safety of available fish. Deriving criteria using an unsuppressed FCR furthers the restoration goals of the CWA, and ensures protection of human health as pollutant levels decrease, fish habitats are restored, and fish availability increases. If sufficient data regarding unsuppressed fish consumption levels are unavailable, consultation with tribes is important in deciding which fish consumption data should be used.	EPA asserts that tribal reserved fishing rights must be taken into consideration by DEQ in adopting human health criteria. The relevant treaty language reserves the "right of taking fish at all usual and accustomed places in common with citizens of the territory…" and the right to "hunt on the unoccupied lands of the United States…" which has been interpreted to include fishing on unoccupied lands. The CWA requires States adopt criteria sufficient to protect designated uses. DEQ includes fishing as part of its secondary contact recreation use. (IDAPA 58.01.02.100.02.b.) Therefore, Idaho's human health criteria must ensure a level of water quality that allows the safe consumption of fish taken by recreational fishermen. DEQ agrees that, in order to ensure criteria are sufficient to protect the secondary contact recreation use, DEQ must take into consideration the amount of fish consumed by both the general population in Idaho and any more highly exposed subpopulations, including the consumption of fish by members of Idaho tribes pursuant to tribal fishing rights. DEQ has done exactly that. It has used the data from both the tribal surveys and the survey of the Idaho general population in order to set criteria that protect the general population and members of Idaho tribes taking fish pursuant to treaty fishing rights. EPA also, however, asserts that DEQ is required by the treaties in Idaho to use a fish consumption rate that reflects tribal subsistence consumption unsuppressed by fish availability or concerns about the safety of available fish. DEQ disagrees with this assertion for a number of reasons. First, it is worth noting that EPA has provided absolutely no legal analysis in their comments regarding the tribal treaties to support their position that the treaties in Idaho require DEQ to use an unsuppressed subsistence fish consumption rate. Second, the treaties do not expressly preserve to the tribes a right to a level of water quality, and no court has found that such a right is an implied part of the tribal fishing rights.[2] Third, EPA's argument is based on the proposition that the right to take fish under

		With these principles in mind, the EPA has concerns with whether DEQ's decision to calculate the FCR based only on current consumption of Idaho fish, and to use a mean FCR for high consuming populations, will adequately protect the treaty-reserved subsistence fishing use. First, in calculating the FCR, DEQ has not considered suppression, specifically suppressed consumption amongst tribal populations in Idaho with reserved rights to fish for their subsistence. Current average FCRs for the Nez Perce and Shoshone Bannock tribes are below heritage rates documented for both of these tribes, as well as heritage rates for the Kootenai and Coeur d' Alene tribes, suggesting that current tribal consumption rates could be suppressed. Second, given that tribal consumption rates are likely suppressed, DEQ has not provided adequate justification for how a rate based on the mean FCR for the tribal target general population will adequately protect tribal fish consumers exercising their treaty-reserved rights, including those whose consumption is not suppressed. Finally, as discussed in greater detail above, the omission of anadromous species from the FCR may result in criteria that are not adequately protective of Idaho's designated uses as informed by the reserved fishing rights of tribal consumers.21 Based on local conditions in Idaho, it is particularly appropriate to include anadromous species in the FCR, because it is well documented that a large proportion of fish consumption for the tribal target population to be protected consists of anadromous species, such as salmon. Accordingly, EPA recommends that DEQ select a FCR that reflects the tribal subsistence consumers' unsuppressed fish consumption, including consumption of anadromous fish. If such data are unavailable at this time, the EPA recommends using an upper percentile of consumer only data to account for uncertainty in the unsuppressed consumption rates of tribal consumers within the state and to help ensure that the resulting criteria protect the tribal target general population exercising their treaty-reserved rights. Additionally, government-to-government communications with affected tribes could inform, among other things, which fish consumption data should be used by DEQ.	the treaties includes a right to take the amount of fish that reflects an unsuppressed subsistence level of consumption. The relevant cases do not support this proposition, and in fact, say just the opposite. The U.S. Supreme Court in Washington v. Washington State Commercial Passenger Fishing Vessel Ass'n, 443 U.S. 658, 99 S.Ct. 3055 (1979), interpreted the off-reservation right to take fish in common to mean that the tribes have a right to "take a fair share of the available fish." The court explained that a fair share is a maximum of 50% of available fish, that can be reduced depending upon changing circumstances. Importantly, the court specifically refused to adopt the tribe's argument that the treaty guarantees a right to take as much fish as necessary to support their subsistence and commercial needs. In addition, the right was to "available fish" and the right was one that was subject to changing circumstances, rather than a right to take fish in the amounts the tribe once had harvested to support a subsistence lifestyle. Other courts have consistently held that the off-reservation right to take fish in common with others does not include a right to take an amount of fish at a level that existed when the treaty was signed. The Idaho district court in Nez Perce v. Idaho Power Company, 847 F. Supp. 791 (1994) held that the Nez Perce treaty does not provide the Nez Perce Tribe with an absolute right to preservation of the fish runs in the condition existing in 1855, free from environmental damage caused by a changing and developing society. Similarly, the Idaho State District Court in the Snake River Basin Adjudication was called upon to determine whether the off reservation right to take fish included a right to an amount of water necessary to support the right. The court found that the Nez Perce treaty language at issue did not guarantee a predetermined amount of fish, establish a minimum amount of fish, or otherwise require maintenance of the status quo. The right is subject to changing circumstances incurred by settlement and development. In Re SRBA (Nez Perce Instream Flow Claims) Order on Motions for Summary Judgement (November 10, 1999). The 9th Circuit Court of Appeals has also confirmed that the treaty right to take fish at the usual and accustomed places does not entitle the tribes to a particular minimum allocation of fish. U.S. v. Washington, 759 P.2d 1353, 1358-59 (9th Cir. 1985) ("Contrary to certain statements in the district court's opinion, the Supreme Court in Fishing Vessel did not hold that the Tribes were entitled to any particular minimum allocation of fish."); See also, U.S. v. Adair, 723 F.2d 1394 (9th Cir. 1983) (court found that the exclusive right to hunt and fish on the Klamath Tribe reservation included the implied reservation of water rights, but that this was only a right to the water to support hunting and fishing rights as currently exercised and "not as these rights once were exercised by the Tribe in 1864.")[3] In short, the underlying premise of EPA's argument that the treaties preserve a right to take and consume fish at a subsistence rate unsuppressed by fish availability or concerns about the safety of available fish is not supported by the treaty language itself or by relevant case law. Therefore, while DEQ recognizes its obligation under the Clean Water Act to develop criteria that are protective of all

			Idaho citizens, including tribal fish consumers, there is simply no support for EPA's position that DEQ is required by tribal treaty fishing rights to use a subsistence fish consumption rate unsuppressed by availability of fish or concerns regarding the safety of the fish. EPA also asserts that because there are tribal reserved fishing rights DEQ must treat the tribes as the general population of Idaho. Again, EPA provides absolutely no legal support for this position, and there is none. DEQ is promulgating state-wide criteria to protect all citizens of the state, including tribal members. The tribes are in fact subpopulations of the state, and the treaty right to share in available fish with the rest of the population does not somehow convert the tribe into the general population. The situation may be different if DEQ was only adopting criteria for waters within tribal jurisdiction. But, DEQ's criteria apply state-wide, except for those areas of the state within tribal jurisdiction. As a result, DEQ is setting criteria taking into account the tribes' consumption of fish taken from waters within the jurisdiction of Idaho where the tribes share fish with the rest of the state population. Under these circumstances, the tribes are clearly a subpopulation of the entire state, and EPA's position to the contrary has no legal, factual or logical basis. [2] In U.S. v. Gila Valley, 920 F. Supp 1444 (D AZ 1996) a tribe's demand for protection of water quality was at issue. But, this case involved the protection of water under prior appropriation law, and did not involve treaty fishing rights at all. Therefore, it does not provide authority for implying water quality protection based on treaty fishing rights. [3] U.S. v. Washington, 20 F.Supp.3d 1000 (W.D.WA 2013), that is currently on appeal to the 9th circuit, involves whether the treaties require Washington to repair or replace culverts that are preventing the passage of fish. The court in this case, however, did not determine whether the treaties preserve a right to any certain quantity of fish.
	24	To claim that treaty rights are an unresolved issue is preposterous. Treaty rights in Idaho exist and hold the force of law. IDEQ's proposed FCR and WQC are a clear violation of treaty rights. A century's worth of federal court decisions has established beyond dispute that treaty fishing rights are permanent in nature and that they secure for the tribes the right to take all species of fish found throughout their reserved fishing areas for subsistence, ceremonial, and commercial purposes. Tribal treaties are the supreme law of the land, and federal agencies including EPA, must interpret the state's designated uses to include subsistence fishing.	Please see response immediately above.
Idaho-specific / Tribal Bioaccumulation Factors (BAFs)	2	While CRITFC supports DEQ's use of BAFs consistent with EPA's 2015 human health criteria recommendations, Idaho has again chosen to use less protective parameters for tribal populations as compared to the general population in developing their Idaho-specific BAFs.	The BAFs (or BCFs) used in our criteria calculations are those provided by EPA in their 2015 Human Health Criteria update. For BAFs EPA's 2015 update provided 3 different values for each chemical depending on trophic level 2, 3 or 4. Since the NCI method fish consumption rates are not parsed by trophic level in either Idaho or tribal fish consumption results, it was necessary reduce the three BAFs per chemical to a single weighted average BAF per chemical. This weighted averaging was done using the trophic level break down reported in EPA's 2014 national fish consumption survey.
	16	The CTUIR DNR does not agree with Idaho's choice to use less protective parameters for tribal populations as compared to the general population in developing its Idaho-specific Bioaccumulation Factors (BAFs).	We have reverted to using EPA's national default FCR trophic level breakdown to derive a trophic level weighted average BAF from EPA's three trophic level specific

		IDEQ used a value of fish intake for the general population that represents the 95th percentile of the general population to determine an Idaho general population BAF, while using a value of fish intake for tribal populations reflecting the mean consumption of tribal members—again, 95th percentile vs. mean; patently unfair on its face. In addition, market and anadromous fish (except for steelhead) were excluded from the evaluation of fish intake.	BAFs. This is described in our TSD as well as each of EPA's chemical specific documents and used where they have relied on BAFs, for example: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OW-2014-0135-0163) , see sections 4.3, 7.1 and 7.2.
	22	Uncertainty in the BAF estimate can be of substantial consequence to the final HHWQC. An overestimation of the BAF predicts higher concentrations in fish tissue at a given water concentration resulting in a HHWQC lower than necessary to protect human health at the target risk level specified by the HHWQC. BAFs are species dependent and those species feeding at a higher trophic level (TL) are generally expected to have more bioaccumulation and thus higher chemical concentrations than those feeding at a lower TL. Therefore BAFs are estimated by TL to reduce uncertainty. Based on intake rates of fish species grouped by TL (i.e. TL2, TL3, and TL4), EPA developed an equation to calculate a BAF that is weighted by expected fish intake within each TL. DEQ (2015), using Idaho fish consumption rates by species data available from the fish consumption survey, devised a similar equation for the general population using Idaho specific weights. (The TL for each species of Idaho fish are provided in Appendix A of IDEQ, 2015). DEQ (2015) also developed separate TL weights for the Nez Perce population using information from the Nez Perce tribal survey (Ridolfi, et al. 2015). However, because the dietary recall data were not available to DEQ at the time the TL weights were developed for the Nez Perce tribe, DEQ used data from the food frequency questionnaire (FFQ). The dietary recall data are generally judged to be more accurate for use in the estimation of usual intake and should be used rather than the FFQ data to derive TL weights for the Nez Perce population. Using, the dietary recall data from the tribal survey, Aracdis was able to calculate the percentage of fish consumption within each trophic level and calculated more accurate weights for use in the BAF weighting equation. A summary of the TL weights used by EPA and DEQ as well as the alternate weights calculated for the Nez Perce by Arcadis are presented in the table below. **Table 1** **Intake Based Weights for Weighted Average BAF Calculation** | Trophic Level | Weights Presented in DEQ, 2015 – EPA Default | DEQ General Population | DEQ Nez Perce | Alternate Nez Perce Based on Dietary Recall Survey Data by Arcadis | | --- | --- | --- | --- | --- | | TL2 | 36% | 9% | 19% | 5% | | TL3 | 41% | 73% | 27% | 70% | | TL4 | 23% | 17% | 55% | 25% | Higher trophic levels have higher estimated BAFs for most compounds, therefore higher weights within a higher trophic level result in a larger BAF than when weights are higher for lower trophic levels. As shown above the weights used by DEQ for the Nez Perce presume higher consumption of fish in TL4. The weights calculated by Arcadis for the Nez Perce based on the dietary recall data indicate that consumption in TL4 is lower and that the highest consumption is within TL3. Therefore, the weighted BAFs, using the alternate weights for the Nez Perce are generally lower than those reported by DEQ for the Nez Perce. A summary	We agree that a trophic level (TL) breakdown of fish consumption based on dietary recall is preferable to one based on food frequency questions. We are intrigued by your analysis and its finding that the Nez Perce Tribe's TL breakdown is quite similar to the one DEQ derived for the Idaho general population. Had we the time to recalculate criteria we would consider using one TL breakdown to weight the BAF for both populations. Because we chose to use Nez Perce Group 2 fish and did not have time to determine a trophic level for Nez Perce Group 2 fish, we have used the trophic level breakdown in EPA's national default FCR to weight BAFs.

		of the BAFs presented by IDEQ (Windward, 2015) along with the BAFs calculated using the alternate weights for the Nez Perce based on dietary recall data are presented in Appendix A. As shown in the table, the alternate BAFs for the Nez Perce (based on dietary recall data) are generally lower than those presented by DEQ, (based on FFQ data). Finally, IACI recommends that where data are available, Idaho specific bioaccumulation factors be developed and used to calculate HHWQC.	
Bioaccumulation	11	Prior to this rulemaking, the Department used bioconcentration factors (BCF) in the calculation of HHWQC. The Department is now proposing to use bioaccumulation factors (BAF). Simplot supports the use of BAF instead of BCF. Simplot recommends that the Department, when data is available, calculate BAF based on Idaho specific data. For example, Simplot has done extensive work looking at selenium in the water column, fish tissue and other trophic levels. Simplot plans to submit such data to the Department for consideration in developing an Idaho specific BAF for selenium.	Thank you for supporting use of BAFs. The Department has relied on national data on bioaccumulation provided in EPA's 2015 human health criteria updates, or earlier BCF work where BAFS are not available. We are open to future consideration of Idaho specific information on bioaccumulation rates representative of Idaho waters.
	21	As stated in DEQ's Technical Support Document (TSD) for the human health criteria, DEQ created an Idaho-specific BAF weighting equation using Idaho fish consumption survey data and stated that the approach they used was similar to the framework that EPA used to derive the BAF weighting in the EPA's 2015 final human health criteria recommendations. According to the TSD, DEQ used food frequency data collected for the Idaho general population and dietary recall data for the tribal population. From these data, DEQ developed a trophic level weighted BAF using the following equation: (FCRm x BAFTl2 + FCRm x BAFTl.3 + FCRTL4 x BAFTL4) / (FCRT12 + FCRTL3 + FCRTL4). This approach is appropriate and addresses the EPA's previous concern that Idaho tribal populations consume larger amounts of high trophic level fish relative to the U.S. general population. However, the EPA recommends that DEQ provide more information on the derivation of the trophic level specific FCRs used to compute weighted BAFs.	We don't know what more information we could provide. Please see comment above prepared by ARCADIS and provided by commenter 22.
	22	DEQ is moving towards the use of bioaccumulation factors (BAFs) instead of bioconcentration factors (BCFs). A bioaccumulation factor (BAF) is an estimate of the ratio of the concentration of a chemical in the tissue of an aquatic organism to its concentration in water. IACI supports the use BAFs instead of BCFs, however as noted below, there are a number of technical considerations in using and determining BAFs.	Thank you. Please see our response to your more detailed comments on trophic level weighting of BAF above.
Relative source contribution	12	For example, other commenters have urged IDEQ not to use the EPA default Relative Source Contribution (RSC) factor of 0.2, and they provide information and data specific to Idaho to support those recommendations. … We urge IDEQ to adopt the RSC recommendations and to maintain its methodology for calculating the FCR.	Although DEQ believes there are logical ways to adjust RSC short of describing "central tendencies and high-ends for relevant exposure source pathways" as directed in EPA's Exposure Decision Tree, it was made clear to us that simple adjustments were not likely to be acceptable to EPA. We regret that we did not have sufficient time to develop, seek comment on and incorporate chemical specific RSC's developed according to EPA's decision tree approach beyond those provided by EPA itself.
	17	Finally, we encourage IDEQ to use the best available science for determining Relative Source Contribution (RSC) values, rather than simply relying on EPA's recommended values.	Please see response above.
	21	In June 2015, the EPA published final updated ambient water quality criteria recommendations for the protection of human health for 94 chemical pollutants. These updated recommendations reflect the latest scientific information and EP A policies, including updated body weight, drinking water consumption rate, FCR, bioaccumulation factors, health toxicity values, and relative source contributions (RSCs). The EPA supports DEQ's proposed approach to use RSC values specified in EPA's 2015 final 304(a) human health	While we appreciate your support, we also believe there are simpler logical adjustments that could and should be made to default RSC based on the role of bioaccumulation in magnifying the exposure due to fish consumption.

		criteria recommendations.	
	22	Along with the use of Idaho specific fish consumption survey results (utilizing Idaho fish), IACI recommends that DEQ use specific chemical data (for relative source contribution) and additional Idaho specific for determining bioaccumulation factors.	Please see response to commenter 12 above. Other than for methylmercury, arsenic and selenium, we are unaware of statewide Idaho specific data on bioaccumulation. The methylmercury and arsenic criteria are not being updated, nor does the current arsenic criterion incorporate bioaccumulation. The selenium criterion uses a bioconcentration factor. We believe adjustment of criteria on a site-specific basis is a future possibility, given site-specific data on bioaccumulation.
	22	DEQ used 2015 EPA recommended relative source contribution (RSC) factors; the default factor of 0.2 (20%) was used for most chemicals. IACI recommends that DEQ use a RSC other than 0.2 based on chemical specific information and the rate of fish consumption. The first, and most recognized instance for using a RSC of greater than 20% is when data indicate that the sources of daily exposure to a chemical, other than the sources regulated by a water quality criteria (HHWQC) (i.e., consumption of fish from a local water or consumption of fish from a local water body to which the HHWQC applies) comprise less than 80% of the allowable daily intake.2 When available data indicate exposures from sources other than local waters are a small fraction of the allowable daily exposure, the RSC can be set at a percentage of the allowable daily intake (i.e., reference dose (RfD)) greater than the USEPA default of 20%. For some chemicals, that percentage can be substantially greater than the default of 20%, sometimes exceeding the USEPA maximum default of 80%. The Florida Department of Environmental Protection (FDEP) recently reviewed the literature and developed RSCs for 21 non-carcinogenic compounds that ranged from 0.2 to 1.0.3 Consistent with these recent developments, the California Office of Environmental Health Hazard Assessment (OEHHA) had previously concluded that the default use of an RSC of 20% is unreasonably conservative for most chemicals.4 In fact, for 22 of 57 chemicals, a RSC of greater than 20% was used in the calculation of California Public Health Goals for those chemicals in drinking water. It also bears pointing out that the development of chemical-specific RSCs is not necessarily time or resource intensive and DEQ should undertake developing RSCs for chemicals with available data. Alternatively, given the availability of recently developed chemical-specific RSCs by FDEP, DEQ can also consider using those when developing HHWQC. ARCADIS has derived chemical-specific RSCs for eleven chemicals: acenaphthalene, anthracene, fluoranthene, fluorene, pyrene, 2-chlorophenol, selenium, diethyl phthalate, chloroform, butylbenzyl phthalate and toluene (see Table 2 and Appendix B). IACI recommends that these RSCs be used to derive Idaho human health water quality criteria. The other instance when the RSC can be substantially greater than EPA's default of 20% is when the fish consumption rate assumed by a HHWQC is large and, therefore, comprises a majority of an individual's daily protein intake. For such situations, the use of the 20% default RSC will underestimate exposures from consumption of fish caught from waters to which the HHWQC is applied. In such instances, particularly for chemicals that tend to bioaccumulate in the food chain and for which dietary exposure is assumed to be the dominant exposure pathway, an assumed high fish consumption rate can effectively mean that virtually all of an individual's daily protein intake is comprised of fish from local waters (waters regulated by the	In principal we agree that RSC should be adjusted and appreciate the work ARCADIS has done to inform the matter. Three things hold us back; 1) we believe that adjustment of RSC needs to be done 'across the board', that is, for all non-carcinogens and not just for selected non-carcinogens, 2) that any adjustment needs to be done in the context of the fish consumption rate being used and how that affects the contribution of fish included in 'water sources' relative to fish in other sources, 3) we ran out of time to do more with RSC.

HHWQC). In such cases, other dietary sources of protein which are also the sources of a bioaccumulative compound in the human food chain, become negligible and are replaced by locally caught fish. When that happens, the RSC can be set at value greater than the USEPA default of 20%, perhaps even close to or equal to 100%.

Table 2
Recommended RSC Factors

	IDEQ Draft RSCs	ARCADIS Proposed RSCs	Idaho Draft HHWQC (ug/L)	Idaho Draft HHWQC Adjusted with ARCADIS RSC (ug/L)
Acenaphthene	0.2	0.99	78	386
Anthracene	0.2	1.00	340	1700
Fluoranthene	0.2	1.00	20	100
Fluorene	0.2	0.99	51	252
Pyrene	0.2	1.00	26	130
2-chlorophenol	0.2	0.91	19	86
Selenium	0.2	0.65	20	65
Diethyl phthalate	0.2	0.97	620	3007
Chloroform	0.2	0.64	39	125
Toluene	0.2	0.31	36	56
Butylbenzyl phthalate	0.2	0.95	0.11	0.54

	23	Please refer to *Attachment C*, which presents an assessment of IDEQ's choices to set more reasonable than "default" RSC's in establishing the HHWQC for non-carcinogens. Clearwater Paper urges IDEQ to use the best available science in setting RSC's that reflect actual (not defaulting to worst case) risks to the citizens of Idaho from drinking untreated surface water and eating local fish.	Please see response above.
Probabilistic Risk Assessment – Additive Toxicity, and criteria calculation	2	Idaho calculated the state's water quality criteria using a probabilistic risk assessment (PRA) approach supplied by ARCADIS. PRA is an alternative to a traditional deterministic method where high-end or maximum values are typically used to calculate criteria. The method has been suggested as an alternative by dischargers because they believe that the deterministic approach can lead to overestimates of risk known as "compounded conservatism". The PRA approach can lead to less stringent standards since variables in the criteria calculations are no longer maximum values. If the PRA approach allows a larger fraction of high-fish consuming individuals to exceed acceptable doses of noncarcinogens or exceed risks of 1 x 10 -6 for carcinogens, then it must be fully evaluated for its use in setting human health criteria before it can be the basis for EPA approval of standards. In the National Toxics Rule, the EPA states: *The importance of the estimated actual risk increases as the degree of conservatism in the selected risk level diminishes."* Stated differently, analyzing and understanding actual risk should be emphasized when a state seeks to make standards less protective. Before the PRA approach should be accepted by EPA for calculating human health criteria, additional review of the actual risks from both the additive and synergistic effects	DEQ has determined to use the deterministic method to calculate its human health criteria. The issue of exposure to multiple toxins exists independent of whether PRA or deterministic methods are used to derive individual chemical specific criteria.

		of toxic compounds that have similar modes of action need to be understood and incorporated into the criteria formulation. When multiple chemicals induce the same effect by similar modes of action, EPA guidance is to assume that the chemicals contribute additively to risk. Evaluating cumulative risks from exposures to multiple chemicals "is especially important in cases where the resulting toxic effect from the mixture has been demonstrated to be greater than the sum of the individual effects". EPA notes that "[c]ertain categories of contaminants, in particular, persistent organic pollutants that share a common mode of action and/or target tissue, are of elevated concern when they co-occur in the fish and drinking water." These risks may be increased further still due to waterborne exposures to carcinogenic chemicals not addressed by the draft criteria, including chemicals in pharmaceuticals, flame retardants, and personal care products. Some flame retardant such as PBDE's are considered possible human carcinogens, although there are no state human health water quality criteria for these chemicals. Diet is a source of the PBDE body burden in humans, and fish have the highest PBDE levels among different types of food." DEQ should balance its PRA approach to countering "compounded conservatism" and fully consider the effects the health effects (both carcinogenic and non-carcinogenic) of exposure to multiple toxic chemicals. Since recommendations from a Scientific Advisory Board will not be available, EPA should also consider these issues before approving the use of PRA for setting human health criteria.	
	7,8	ISWR supports and commends IDEQ for choosing to utilize a probabilistic risk assessment approach in developing Idaho's Human Health Water Quality Criteria. By using the probabilistic approach, IDEQ is better able to develop defensible standards that more closely reflect the population and the Idaho state requirement that IDEQ use the "best available standards" in setting policy.	DEQ has determined to use the deterministic method. While DEQ recognizes the benefits of the PRA approach, DEQ is concerned about EPA's lack of support for this method in determining human health criteria. DEQ agrees that the deterministic approach is believed to compound the conservative nature of the calculation but, DEQ does not believe using this method in conjunction with the other inputs DEQ has chosen, will appreciably affect criteria.
	9	In previous comments, ICIE supported the use of the PRA method as technically sound and used in many research functions. It represents the best science in assessing risk, would represent all Idaho fish consumers, facilitates transparency in this rulemaking, and inherently calculates the risk to all Idahoans. We continue to do so.	Please see response above.
	12	AF&PA supports IDEQ's decision to use a Probabilistic Risk Assessment (PRA) approach for deriving its HHWQC. A PRA-based approach uses distributions of values to represent factors determining exposure and allow for the estimation of a distribution of potential risks. This is preferable to the deterministic method by which EPA derives national criteria because it: is the best science; allows an incorporation of all data for the different inputs that go into calculating HHWQC; avoids compounded conservatism; and, is more transparent, in that it allows the public and stakeholders to see how the range of data affects calculated human health values.	Please see response above.
	16	For the reasons discussed in the CRITFC comments, Idaho should not rely solely or exclusively on a Probabilistic Risk Assessment approach, but should consider and address the overlapping and synergistic health effects of exposure to multiple toxic chemicals.	The issue of additive toxicity is independent of the use of probabilistic risk assessment; it exists in deterministic as well as probabilistic calculations. We acknowledge that exposure to multiple toxins is real, as does EPA is section 2.3 of their 2000 Human Health Criteria Methodology. But there is to this day no solution offered by EPA in the context of setting broadly applied criteria; far too many assumptions would need to me made about the nature, magnitude and number of such exposures across a population over a lifetime.
	22	DEQ is using the probabilistic methodology for Idaho and tribal specific fish consumption rates, Idaho	Please see response to comments above re the PRA. Thank you for your support.

		specific body weight, and a national distribution for drinking water intake. IACI supports the decisions made by DEQ in the use of a probabilistic methodology for these parameters.	
	23	Using a probabilistic risk assessment approach for HHWQC criteria represents the best available science for setting HHWQC. EPA has endorsed PRA as noted in our comment later dated April 18, 2014, and as shown in *Attachment D*. Even the EPA's website advocates for the use of PRA. *See* http://www2.epa.gov/osa/probabilistic-riskassessment-white-paper-and-supporting-documents. Because it is scientifically based and defensible and would result in an accurate risk assessment outcome, we strongly urge IDEQ to maintain the use of PRA as proposed.	Please see response to commenters above.
	24	Criteria Calculation – USRT has not, and continues to not, support the use of PRA. The use of PRA is untested and leads to WQC that is not protective of tribal members. We are particularly dismayed that IDEQ altered course at the 11th hour and abandoned any use of deterministic criteria selection.	Please see responses to commenters above with respect to PRA. We urge you to look at the actual criteria values and compare them to sister states rather than making judgment based on single input values or policy decisions.
Backsliding	2	DEQ dropped its draft "no backsliding" provision which would have maintained current standards if the calculation of criteria by the PRA methodology was less stringent. The National Discharge Elimination System (NPDES) is designed to ratchet down on pollution discharges overtime, with the goal of eliminating pollution and restoring the nations' waters. Under the NPDES program, pollution effluent limits should be reduced as the regulated facility moves through multiple five-year permit cycles. The CWA expressly prohibits the development of NPDES permit effluent limitations that authorize an increase in the discharge of pollutants, stating, "a permit may not be renewed, reissued, or modified to contain effluent limitations which are less stringent than the comparable effluent limitations in the previous permit." This prohibition is known as "anti-backsliding." Although the anti-backsliding provisions of the CWA are subject to some exceptions, such as availability of new data, nothing in the law expressly provides for changes in regulation that result simply from a different calculation methodology.	DEQ used the phrase "no backsliding" to distinguish its proposal at one time to not let Idaho's water quality criteria to become less stringent from "antibackslidiing" as applied in NPDES permits. Basically anitbacksliding as applied to NPDES effluent limits is different than a change in water quality criteria where new science, better understanding of exposure and toxicity, can result in criteria going up or down in value. This is in part evident in the fact that EPA's national human health criteria update resulted in 28% of their new recommended criteria becoming less stringent than previous recommended criteria – although achieving the same target level of protection. This aside, where there effluent limits are based on achieving water quality criteria (WQBELs) antibacksliding may indeed prevent the relaxation of those limits even though the water quality standard has changed. However, the rules regarding NPDES permits do allow exceptions to antibacksliding, see section 7.2.1.3 of EPA's NPDES Permit Writer's Manual: (http://water.epa.gov/polwaste/npdes/basics/upload/pwm_chapt_07.pdf)
	3	The CTUIR DNR is disappointed that you reversed your earlier decision, and have chosen to allow "backsliding," or a weakening of standards, when your calculations using the PRA methodology yielded a less stringent result. Weakened standards will do nothing to remedy our many waterways that already have well-documented pollution issues. We urge Idaho to work collaboratively with other states and tribes in the region to help solve the pervasive water quality problems that plague so many of our rivers and streams that are our shared natural heritage. Not weakening existing standards would be a start.	The decision to allow criteria to rise or fall was a matter of applying best science. It has nothing to do with use of probabilistic risk assessment to derive criteria, and is still the case now that we have gone with deterministic calculations for our proposed criteria. Please see also response directly above.
	24	No Backsliding – We have made ourselves clear on this policy decision and strongly disagree with IDEQ's last minute decision to abandon this principle.	The matter of not hanging onto older criteria is because they were based on outdated input values for bioaccumulation, relative source contribution, toxicity, body weight, and drinking water intake in addition to fish consumption rate. It was hard to justify not using better, more recent scientific information.
Process, best science and	3	State standards must, by law and regulation, reflect the best available science. But the standards development process also incorporates numerous state policy and risk decisions. This is where Idaho has	Thank you for acknowledging Idaho's efforts to do its best to integrate the science of human health effects with public policy to derive protective criteria.

policy decisions		demonstrated a sound and thoughtful process for evaluating what policy and risk decisions will work best for the state and be consistent with the CW A. Idaho has done its homework to consider the current science and EPA guidance and has made the tough policy and risk decisions to develop a rule that it believes protects human health for the citizens of the state and Native American tribes within the state - responsibilities that lie squarely within Idaho's purview.	
	11	Establishing the best data regarding Idaho specific fish consumption rates (FCR) is crucial for having water quality rules based on the most appropriate scientific information. There have been numerous studies determining FCR. Most of these studies are focused on sub populations (Native Americans), involve the consumption of marine and/or anadromous fish or lack information that would be helpful to determining fish consumption rates for Idaho residents. For example, the Columbia River Inter-Tribal Fish Commission 1994 report does not provide Idaho specific consumption information [see attachment for a review of Northwest FCR studies]. The work done by DEQ establishing an Idaho specific fish consumption survey has provided the best information upon which to help base Idaho water quality standards.	Thank you. We believe the combined work done by Idaho, the Nez Perce and the Shoshone-Bannock Tribes has provided us with excellent local information on fish consumption in Idaho, the best available.
	22	DEQ initiated this rulemaking with the approach of collecting Idaho-specific data and applying the best available science in determining new human health criteria. As described in the following comments, we believe the use of the Idaho fish consumption survey data in a probabilistic risk assessment methodology, adjusted RSC factors and Idaho specific BAF will provide the "sound science" to develop the new criteria.	In principal we agree, and appreciate your acknowledgement of our effort. While we would like to have done more with regard to relative source contribution and bioaccumulation, our resources and schedule did not allow this.
	23	IDEQ's use of a state-based fish consumption survey, correction of the data used in the analysis for fish not found in Idaho waters or the waters of nearby states, assumption of minimal anadromous fish and use of a probabilistic risk assessment approach are commendable and scientifically sound. The demand by some to include all market and anadromous fish in Idaho appears to be motivated by factors other than science or human health concerns for Idahoans. Furthermore, it is not based on the data gathered via the Idaho fish consumption survey. We strongly advocate for a science-based outcome on these issues.	Although there is more to criteria setting than just science – also science policy, such as use of toxicity uncertainty factors, and straight up policy, such as acceptable risk – we appreciate the endorsement of science based outcomes.
Public participation / Open process	5	NWFPA appreciates the process that DEQ has provided for extensive participation by interested parties in this rulemaking.	Thank you for saying so.
	6	The Association of Idaho Cities (AIC) has been a participant in all of the Idaho Fish Consumption Rate (FCR) rulemaking meetings and observes that the rulemaking process was robust, science and data based, consistent with EPA guidance, and transparent. AIC commends the IDEQ for conducting the rulemaking in an open, inclusive, transparent, scientifically rigorous, and well documented process.	Thank you for acknowledging our efforts. DEQ has worked hard to make this update of Idaho's human health water quality criteria an open and transparent process and believe as well that we have closely followed EPA's national *guidance*.
	9	We applaud DEQ's efforts to include a wide variety of stakeholders in the effort to review and update Idaho's water quality standards. The use of the best Idaho-based science in completing the review of Idaho's fish consumption and subsequent promulgation of new water quality standards was vital because of the potential impacts on the citizens and the economy of the state.	Thank you.
	22	Determining human health water quality criteria is a complex, technical matter. DEQ has approached this undertaking in a very systematic, technically based manner. The fish consumption survey that DEQ undertook has provided very valuable information for the foundation of this rule and is important for the protection of public health of Idaho's citizens. …	Thank you.

		As stated in earlier comments, IACI commends DEQ for the significant work done in this rulemaking and the opportunity that has been provided to stakeholders to participate in this process.	
210.03, Mixing Zones	1	The proposed rule includes provisions for mixing zones at section 210.03. Mixing zones are an important component for the implementation of the human health water quality criteria. For some pollutants, significant reductions of the pollutant concentration occur due to natural treatment mechanism. Use of a mixing zone for these pollutants provides an important implementation element necessary to appropriately account for pollutant behavior in the environment. AIC supports the inclusion of the mixing zone language at section 210.03 of the proposed rule.	Thank you for your support. We too see mixing zones as an important component of implementing any surface water quality criterion in a discharge permit.
	19	210.03.b. Upon review of this section, it appears that DEQ is proposing language that would allow the exceedance of water quality criteria in streams during periods of low flow. What is the justification for this provision? Periods of extreme low flow are inherently stressful for aquatic life. DEQ's provision to allow WQS to be exceeded during periods of low flow is the exact opposite of what should be happening. Allowing increased concentrations of pollutants during periods of low flow is likely to increase the detrimental impacts of these pollutants.	Low design flows are not new. They correspond with the frequency component of criteria. Specifying a design flow is necessary to develop water quality based effluent limits. By choosing a very low, rare instream flow condition, e.g. 7Q10 For aquatic life criteria, we can assure that while criteria could be exceeded under those rare flow conditions (assuming maximum effluent discharge and quality co-occur), the exceedance will be very infrequent, and very small if it does occur. This thus assures protection of uses.
400.06, Intake credits	7	The proposed rule includes provision for intake credits at section 400.06. Intake credits are an important component of the implementation of the human health water quality criteria. For some pollutants, intake credits will be a very important element of implementation because the source waters contain pollutants at elevated levels (e.g. background pollutant levels not the result of anthropogenic activities). AIC recognizes that Intake Credits will likely be used infrequently; however, in the circumstances where background is elevated, intake credits are an important tool. AIC supports the inclusion intake credit language at section 400.06 of the proposed rule	Thank you for your support. We too see intake credits as an important and reasonable component of implementing any surface water quality criterion in a discharge permit. Intake credits are likely to be especially important in dealing with naturally occurring pollutants like metals, and criteria that in some situations will be below background levels.
Suppression	9	Finally, the concept of "suppression" was thoroughly discussed and we support DEQ's decision not to include "heritage" or "suppression" rates. A review of the available information showed that it had not gone through a rigorous scientific analysis. Use of such information is too speculative and is not required under the Clean Water Act.	We agree that estimation of suppressed rates of fish consumption does not lend itself to the same degree of rigor as estimation of current fish consumption rates. We also agree that the CWA does not require DEQ to use an unsuppressed fish consumption rate. See response to commenter 19 below.
	19	DEQ has decided to not integrate suppression into its determination of a FCR. Establishing the appropriate fish consumption rate is important because Idaho will use this information to establish certain water quality standards. If Idaho underestimates the fish consumption rate then the DEQ will establish water quality standards that are not protective of human health. DEQ should identify a fish consumption rate that reflects the fact that fish consumption is currently being 'suppressed.' DEQ's proposes fish consumption rate should be inflated to account for this suppression. For the purposes of this discussion, we are considering that a suppressing effect occurs when a population, or a subset of the population, experiences a reduction in the amount of fish that they consume; and that this reduction in consumption occurs as a result of some exterior or artificial force beyond the control of the consumer and counter to the wishes of the consumer. There are two primary means of suppressing fish consumption that warrant consideration here. First, suppression based on contamination of the fishery. Second, suppression based on the lack of availability of fish to consume.	The CWA does not require a state to use an unsuppressed fish consumption rate. First, there is no language in the CWA or the federal regulations that addresses the concept of suppression. Second, the express language of the CWA requires states designate uses and adopt criteria to protect those uses. The CWA leaves it up to States to determine appropriate uses, as long as the States designate attainable fishable/swimmable uses. DEQ has adopted a recreational use that requires water quality appropriate for recreation, including fishing, on or about the water. This use has been approved by EPA. DEQ has not designated a traditional subsistence use or some other kind of use that suggests an intent to restore and protect a level of fish harvest that existed historically before dams and other factors restricted the availability of fish. Criteria that ensures water quality sufficient to protect recreational fishing given actual consumption patterns is clearly protective of Idaho's designated use as required by the CWA.

		… Numerous resident fisheries have been determined to be have elevated levels of certain pollutants, especially mercury. Contaminant levels are such that the State has issued a Statewide Fish Consumption Advisory for all bass (largemouth and smallmouth) caught in Idaho and Fish Consumption Advisories for certain other species of fish caught in Priest Lake, Lake Pend Oreille, Lake Coeur d'Alene, Hells Canyon Reservoir, Payette Lake, Brownlee Reservoir, Payette River, Boise River Lake Lowell, Jordan Creek, CJ Strike Reservoir, Grasmere Reservoir, Shoofly Reservoir. Salmon Falls Creek Reservoir, Oakley Reservoir, Weston Reservoir, Bear River, Glendale Reservoir, Chesterfield Reservoir, Portneuf River, American Falls Reservoir, and the South Fork of the Snake River.2 As you can see, these Fish Consumption Advisories are distributed across the entire state and encompass some of Idaho's most popular recreational fishing areas. … Idahoans who abide by the State's fish consumption advisories are suppressing their fish consumption, upon the advice of the State, in order to protect their health. … To avoid this 'downward spiral' the DEQ must take the necessary steps to ensure that the baseline fish consumption rate that is developed takes into consideration the fish consumption suppression that is occurring. Merely relying on the current, reported fish consumption levels recorded via surveys will not accurately capture the fish consumption rate that the DEQ should utilize when setting water quality standards.	Third, the CWA regulations provide that States must use 304(a) guidance, modified 304(a) guidance or other scientifically defensible methods. EPA's 304(a) recommended criteria are based upon fish consumption surveys that reflect actual consumption patterns and do not take into account suppression. The 304(a) recommended human health criteria for toxic pollutants is based upon the 2000 Methodology, and it also includes nothing about suppression. Fourth, EPA has not clearly articulated what is meant by an unsuppressed fish consumption rate, which would force DEQ to guess on what that number would be. Fifth, EPA itself has stated that adopting criteria for a traditional subsistence lifestyle is something more than the CWA requires .When EPA recently approved of the Spokane Tribe of Indians toxic pollutant criteria to protect the Tribes' traditional subsistence lifestyle, EPA considered the adoption of criteria to protect a traditional subsistence lifestyle to be more stringent than required by the CWA, and therefore, reviewed the WQS using a different standard of review. Technical Support Document for Action on the Revised Surface Water Quality Standards of the Spokane Tribes of Indians (December 11, 2013) at page20-22. Sixth, it is inconsistent with the CWA for States to adopt water quality criteria taking into account suppression because suppression due to availability of fish is not caused by inadequate human health criteria, nor can it be corrected by assuming some higher consumption rate and thus lowering human health criteria. Mercury is an interesting example to consider for it is largely a problem of airborne mercury depositing onto the landscape and into water bodies; a source that water quality criteria cannot control. It is worth noting that lower human health criteria would not reduce fish consumption advisories. This is because those advisories in Idaho are arrived at independent of water quality criteria. More importantly, the human health concerns addressed by Idaho fish consumption advisories are, and would continue to be, addressed by those advisories. This is the case regardless of the human heath water quality criteria, but especially where criteria may be exceeded. Finally, the current or proposed water quality criteria are not locked in forever. Within the past decade we are on now our third iteration of fish consumption rates and human health criteria. During this time criteria have mostly gone down and fish consumption has risen or remained steady. We find no evidence of a 'downward spiral' unfolding. It may be odd to consider, but if advisories were based on the human health criteria then lower criteria, at least in the short run, should lead to more fish consumption advisories, more suppression, not less.

	24	IDEQ's adamant refusal to consider suppression is inconsistent with the ultimate goal of the Clean Water Act, which is the restoration of U.S. waters. It would have also lead to more protective criteria, not less protective criteria. There certainly is irony that IDEQ dismisses the "downward spiral" premise and yet, IDEQ is now proposing that some WQC will be less protective moving forward, which will lead to diminished water quality and less fish consumption.	DEQ disagrees that the CWA requires States to take suppression into account. While some of our proposed criteria are higher in value than the criteria they are to replace, this is largely because of better understanding of toxicity. It cannot be said that such criteria changes provide less protection but rather more precisely provide the intended level of protection.
Ability to achieve criteria / Implementation tools	11	In regards to establishing appropriate Idaho water quality criteria, Simplot recommends that the Department conducts further studies looking at PBT's in Idaho waters including (but not limited to) chemicals such as arsenic, mercury and PCBs. Such chemicals have low toxicity threshold values and thus, depending on the factors used in calculating HHWQC, can have very low criteria. The result is criteria that are below background concentrations and or are not achievable. This issue is of the utmost importance to the regulated community (including Idaho residents) as certain of these chemicals exist naturally in Idaho (arsenic being an example), may primarily be a legacy contaminant (such as PCBs) or due to air deposition (which is primary source today of mercury addition to Idaho waters). This issue is discussed in a paper by Judd (2015).	The Department is keenly aware that some proposed criteria may be unachievable, especially in the near term., and possibly even in the long term when it comes to naturally occurring metals such as mercury and arsenic. We also recognize that effluent limitation is not the most efficient way to reduce legacy contaminants, particularly those such as PCBs which have been banned. Nor are water quality criteria effective in reducing mercury that is largely non-water in origin. To deal with these problem contaminants / criteria we have implementation tools; variance and compliance schedules already in rule, and the addition of provision for intake credits in the current rule. We also note that Idaho has not at this time proposed to update it mercury or arsenic criteria for protection of human health.
Consistency with CWA	13	The proposed changes to water quality standards proposed by IDEQ are alarming in that they are inconsistent with the goals of the Clean Water Act of achieving waters that are fishable and swimmable for the public.	Idaho's proposal is well within the guidance provided by EPA, will provide for waters that are fishable.
Stringency / purpose of proposed criteria	15	The Tribes cannot support a final draft FCR that will allow for WQC to become less protective, which will further suppress fish populations by allowing for additional pollution and contributing to the downward spiral of water quality. … According to Idaho's 2012 Integrated Report to the Environmental Protection Agency, 27.9% of the IDEQ sampled stream miles were classified as in poor condition, not fully supporting cold water aquatic life, with the lowest proportion of stream lengths classified as good found in the Pocatello Region. The purpose of the Clean Water Act is to restore degraded waters, not to allow for the back slide of WQC.	Criteria values depend on more than just the FCR (see response to commenter 5 under topic "level of protection / allowable risk" above). About 60% of Idaho's proposed human health criteria are lower in value than their current (2006) values. These are human health criteria, not aquatic life criteria. Human health criteria are based on protecting human health, while aquatic life criteria are for protecting aquatic life. Almost all the impaired waters in Idaho's 2012 IR are impaired for aquatic life unrelated to human health criteria. Within the impairments to aquatic life, most of those are not due to exceedance of any toxics criterion, rather stressors such as sediment or temperature, or direct biological assessment which takes into account factors such as habitat quality for which there are no water quality criteria. The CWA does not prohibit water quality criteria from increasing in value; in EPA's 2015 national update of human health criteria 28% of the criteria became less stringent.

	23	In the proposed rule, IDEQ has applied certain risk policy decisions in setting the proposed criteria that appear contrary to the spirit if not the specific intent of state law. Idaho Code 39-3602 prohibits IDEQ from adopting water quality standards that "impose requirements" beyond the minimum requirements of the CWA. Additionally, Idaho Code 39-107D requires IDEQ to specifically identify those provisions in proposed rules that are "broader in scope or more stringent than" the requirements under the CWA. We believe that these two provisions explicitly or implicitly create a directive to IDEQ to exercise whatever flexibility is afforded the state under the CWA when promulgating water quality standards to avoid overregulation of Idaho citizens.	DEQ disagrees that the proposed criteria are more stringent than or broader in scope than federal law or regulations. DEQ complied and will continue to comply with 39-107D by clearly identifying that the proposed rule is not more stringent than or broader in scope than federal law or regulations, and does not regulate an activity not regulated by the federal government.
BAF for pentachlorophenol (PCP)	18	Specifically, EPA used a log K_{ow} of 5.12 as the denominator in the equation for the Food Chain Multiplication (FCM) factors in the model used to derive the BAFs for each of the three tropic values. This log K_{ow} is incorrect as the log K_{ow} for PCP is pH dependent. The correct log K_{ow} at environmentally relevant pH is no higher than 3.69 and this value should have been used in the BAF calculation. A log K_{ow} of less than 4.0 would result in a FCM of 1.0 rather than the higher FCM used by U.S. EPA in deriving the BAFs for PCP. We urge the Idaho Department of Environmental Quality to rerun the modeling used to derive the BAFs for PCP with the correct log K_{ow} as Idaho cannot simply adopt U.S. EPA's calculations in its rulemaking without independently assuring the correctness of those calculations. We urge the Idaho DEQ to rerun the modeling used to derive the BAFs for PCP with the correct log K_{ow} as Idaho cannot simply adopt U.S. EPA's calculations in its rulemaking without independently assuring the correctness of those calculations.	This comment appears to take issue with EPA's derivation of their national BAF values and thus should be directed to EPA. DEQ is not in a position to rerun EPA's modeling of BAF.
210.05.b.ii	19	We believe that DEQ should state what fish consumption rate is to be utilized to derive water quality criteria, rather than just reference that a fish consumption rate that is representative will be utilized. This level of vagueness is inappropriate in Rules. We are concerned that this section's proposed use of a mean adult body weight value may place children (who weigh less than the mean adult body weight) at greater risk. DEQ should ensure that its criteria are protective of children because the implications of over exposure to children may be direr and longer lasting than the implications of adult exposure. The average Idaho household has just over two children in the home. To protect Idaho children, DEQ should utilize a mean child weight when calculating water quality criteria.	DEQ will put the formula it uses to calculate criteria in section 210 in the rule. However, some factors are chemical specific, and it would be impossible to include all such information in the rule. Also this section of the rule speaks to development of criteria for chemicals not in the table of toxics criteria. The input parameters for the criteria in the table are fully describes in the Technical Support Document referenced in footnote c.
	21	The EPA is concerned that this provision lacks specificity with regard to a fish consumption rate and the target population to be protected that will be used to derive numeric human health criteria in the future, when numeric criteria are not identified in the toxics table. It would seem reasonable to specify an appropriate fish consumption rate as well as the target population and percentile of the target population that would be used to estimate a fish consumption rate consistent with how Idaho's numeric criteria in the table at Section 210 were derived. For example, the language in b.ii refers to using a fish consumption rate that is representative of the population to be protected. The EPA suggests DEQ include specific language identifying the population to be protected consistent with EPA's previous comments.	DEQ will put the formula it uses to calculate criteria in the rule. But, the degree of specificity requested would be difficult to provide in that we do not know what new information the future may bring. We might be able to specify a percentile, i.e. an upper percentile of the general population so long as the mean of a target high end consuming population is also adequately protected, but to specify a target population seems presumptuous given recent history.
Treatment of the Tail	19	In both the WindWard Report generated for DEQ and DEQ's 'Idaho Human Health Criteria: Technical Support Document,' it is reported that certain statistical methods applied to the upper end distribution tail (95th percentile to 100th percentile) of the Nez Perce Tribe data result in a mean value of 19.2 g/day. DEQ has not explained why it chose to use 16.1 g/day instead of the more protective 19.2.	While we are confident that the distribution used in the probabilistic risk assessment is appropriate for describing risk up to the 95th %tile this is no longer material as DEQ has determined to use the deterministic method to calculate its human health criteria.

Fish Consumption Surveys and Data Use	19	As was discussed in great detail at a rulemaking meeting, we do not support DEQ's utilization of only certain aspects of the Tribal data. The Tribes conducted surveys of their members to develop information to aid in the calculation of fish consumption rates. DEQ appears to be dissatisfied with the high fish consumption rate that the Tribes calculated. This dissatisfaction appears to have lead the State to cherry pick certain data out of the Tribal data and then to use this data to develop a fish consumption rate that is significantly different than the rate that the Tribe calculated. This repurposing of Tribal data is inappropriate and at a minimum violates the understanding of how this data was to be used. We ask DEQ to respect the Tribes' wishes with regard to how the State utilizes Tribal data.	DEQ is using the tribal group 2 fish.
	21	Another concern is development of an appropriate tribal fish consumption distribution for PRA. The National Cancer Institute (NCI) method cannot be used to characterize consumption of a particular grouping of fish (e.g., fish caught in Idaho waters) if the data necessary for the method are not available. Idaho has used tribal Food Frequency Questionnaire (FFQ) and NCI data in an attempt to develop "NCI-like" estimates of average tribal consumption of fish caught in Idaho waters. As previously noted, DEQ should include market fish, including anadromous species, in the FCR used to set Idaho's AWQC. The EPA also has methodological concerns about using FFQ and NCI data to derive ''NCI-like'' FCR statistics based on Westat's review of the PRA approach (see attached Westat memoranda). Thus, the EPA recommends that the NCI group 2 (i.e., anadromous, near coastal and inland fish and shellfish) FCR data for the Nez Perce Tribe be used to develop statistics representing current fish consumption.	Tribal 'Group 2' fish, which includes salmon and estuarine species and our 'Idaho Fish' group are clearly much different. So this appears to us to be a comment about included fish rather than a suggestion for an improved adjustment to make the data we were provided more comparable to that generated by Idaho. Please see response to comments above regarding included fish.

	22	As described earlier, DEQ recently completed a state-wide survey on fish consumption in Idaho (NWRG 2015). National Cancer Institute (NCI)-adjusted usual intake distributions for fish consumption, as reported by Buckman et al. (2015), were used to develop FCR distributions for the general population of Idaho. DEQ chose to base its draft HHWQC on consumption of resident freshwater fish, referred to as Idaho Fish. EPA in collaboration with the Nez Perce and Shoshone-Bannock Tribes, recently completed a survey of tribal fish consumption (Ridolfi and Pacific Market Research 2015). Similar methods were used to survey both tribes, and NCI modelling was conducted using data from both tribes with a tribal identifier used as a covariate in the modelling. Information from this survey was used by IDEQ to develop FCR distributions for the Nez Perce tribal population of Idaho. The Nez Perce fish consumption survey data were reported based on different species groupings than the state-wide Idaho fish consumption survey. Arcadis followed the process outlined by DEQ (2015) to derive an adjustment factor using the Nez Perce dietary recall data to calculate consumption of "Idaho Fish" (known as a Group 2 adjustment factor). The calculations were conducted separately for each of the two dietary recalls because there were some missing responses for the second recall. The NCI methodology for estimating usual intake distributions for fish consumption rely on the dietary recall data, and therefore deriving a Group 2 adjustment factor from these data is more appropriate than relying on the FFQ data. The mean adjustment factor for the two recall events is 7.04%. Arcadis applied the alternate adjustment factor to the mean and each fifth percentile of the empirical distribution of Nez Perce Group 2 fish consumption to derive an alternate estimated distribution of Nez Perce Idaho fish consumption. … In lieu of the discrete distributions used by the draft HHWQC that overestimate the arithmetic mean of the empirical FCR data substantially and which require interpolation between existing percentiles with no basis to determine if the interpolation model is correct, Arcadis recommends that DEQ use continuous theoretical curves to model FCR distributions in @Risk when deriving probabilistic HHWQC. This approach, as described in detail in Appendix C, results in theoretical distributions that fit the individual percentiles of the empirical distributions as well as DEQ's discrete distribution, but provide a much closer fit to the arithmetic mean FCRs. It is crucial that both of these statistics be accurately represented when developing distributions to derive probabilistic HHWQC so that risk managers can knowledgeably and appropriately manage risk for the average member of the population as well as any given percentile.	We appreciate the great amount of work you have put into the finer details of the recent fish consumption survey results, the adjustment to make them comparable, and adjustments to improve their utility for probabilistic risk assessment. At this time we have no ability to incorporate your suggestions.
	23	As noted above *Attachment A* describes a statistically necessary adjustment to the tribal fish consumption data set used by DEQ in setting HHWQC. This data only became available from the EPA last week but should be reflected in the final HHWQC criteria that IDEQ adopts and proposes for approval by the IDEQ board and Idaho Legislature. Some of the HHWQC as proposed are now inconsistent with IDEQ's stated risk policy choices.	Please see response above.
210.03.d.ii Use of annual harmonic mean for human health criteria compliance	21	This provision provides a frequency and duration for human health criteria that are not to be exceeded based on an annual harmonic mean. EPA understands DEQ is attempting to clarify the frequency and duration for the state's human health criteria and is supportive of that effort. EPA's 304(a) recommendations for human health criteria are based on long-term average exposure over a lifetime (70 years). Idaho's proposed duration of one year is protective because it represents long-term or chronic exposure but within a reasonable timescale for the purposes of regularly assessing attainment of the criteria. However, the harmonic mean is an inappropriate measure of central tendency in this context, because it is likely to under-represent the presence of pollutants in ambient water. Harmonic means are an appropriate measure of	We appreciate EPA's recognition of the value of filling in a gap, not leaving this un addressed. We consulted with EPA in early 2014 when we were confronted with the rare occasion of how to compare multiple measurements of a concentration to a human health criterion. We are aware that harmonic means are most appropriate to averaging rates and note that while the criteria in water are purely concentrations they are derived based on bioaccumulation rates that lead to

		central tendency when evaluating rates with varying denominators, such as flows or speeds. However, for measures of varying mass per volume, such as concentrations of contaminants in ambient water, the arithmetic (for skewed datasets) or the geometric mean is the more appropriate measure of central tendency. EPA recommends that DEQ delete reference to the harmonic mean and, instead, insert arithmetic mean.	concentrations in fish that create the exposure of concern. This leads us to believe harmonic means are appropriate for water column measurements and that EPA's suggestion of an arithmetic, or geometric mean would better for direct fish tissue measurements.
400.06, Intake Credits	9	This provision refers to the Idaho Pollutant Discharge Elimination System Program (IPDES) rules and is not a water quality standard. However, in EPA's October 2, 2015 letter from Michael Lidgard to Paula Wilson, EPA provided comments on IDAPA 58.01.25 regarding the proposed intake credit rule language as proposed in the IPDES rules. The EPA is continuing to coordinate with DEQ's IPDES program and has recommended that, if DEQ intends to adopt an intake credit provision into the IPDES rules, it be consistent with the Great Lakes Initiative (GLI). Another option is for DEQ to consider Oregon's intake credit provision rule language, as that language is most similar to the GLI and was approved by EPA.	We agree this is not a water quality standard. This is simply an authorizing provision to clearly allow use of intake credits in applying water quality criteria in effluent limitations, referring to the IPDES regulations for details on how that is to be done.

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Effects of Prenatal and Postnatal Methylmercury Exposure From Fish Consumption on Neurodevelopment

Outcomes at 66 Months of Age in the Seychelles Child Development Study

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Context.—Human neurodevelopmental consequences of exposure to methylmercury (MeHg) from eating fish remain a question of public health concern.

Objective.—To study the association between MeHg exposure and the developmental outcomes of children in the Republic of Seychelles at 66 months of age.

Design.—A prospective longitudinal cohort study.

Participants.—A total of 711 of 779 cohort mother-child pairs initially enrolled in the Seychelles Child Development Study in 1989.

Setting.—The Republic of Seychelles, an archipelago in the Indian Ocean where 85% of the population consumes ocean fish daily.

Main Outcome Measures.—Prenatal and postnatal MeHg exposure and 6 age-appropriate neurodevelopmental tests: the McCarthy Scales of Children's Abilities, the Preschool Language Scale, the Woodcock-Johnson Applied Problems and Letter and Word Recognition Tests of Achievement, the Bender Gestalt test, and the Child Behavior Checklist.

Results.—The mean maternal hair total mercury level was 6.8 ppm and the mean child hair total mercury level at age 66 months was 6.5 ppm. No adverse outcomes at 66 months were associated with either prenatal or postnatal MeHg exposure.

Conclusion.—In the population studied, consumption of a diet high in ocean fish appears to pose no threat to developmental outcomes through 66 months of age.

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INORGANIC MERCURY (Hg) discharged into lakes, rivers, and oceans is converted to methylmercury (MeHg) by microorganisms and bioaccumulated up the aquatic food chain.[1] Concern about the potential public health threat from MeHg arose in the United States in the early 1970s when elevated concentrations were found in fish in the Great Lakes. Today, recreational fishing is restricted in many states and Food and Drug Administration guidelines regulate interstate commerce of fish because of their MeHg content.

For editorial comment see p 737.

Mass health disasters in Minamata and Niigata, Japan, caused by consumption of fish highly contaminated with MeHg from an industrial source,[2,3] and in Iraq following consumption of bread containing MeHg fungicide,[4-6] confirmed that MeHg was neurotoxic and that the prenatal period was the most sensitive stage of the life cycle. For example, severe exposures in Iraq (up to 674 ppm of mercury in hair) were associated with microcephaly, seizures, mental retardation, and cerebral palsy. The Iraq outbreak also resulted in less severe outcomes typified by developmental delays and abnormal results of neurological examinations. A dose-response analysis suggested that effects may occur at maternal hair concentrations of mercury as low as 10 ppm,[5,6] although there was considerable uncertainty in this estimate. This compares with an average in the US population of 1 ppm or less.[7]

All fish contain MeHg. Frequent consumption of ocean fish can lead to MeHg levels in excess of 10 ppm and as high as 50 ppm in hair.[1] Epidemiological studies[8-10] on populations consuming fish where Hg was biologically methylated failed to find

clinical cases of MeHg poisoning. The possibility that prenatal MeHg exposure from maternal consumption of a fish diet may be associated with subtle changes in children's cognitive and neurological development has been examined in these studies with inconclusive results.[1,11]

We have followed longitudinally[12,13] a large inception cohort of mother-child pairs in the Republic of Seychelles, a westernized archipelago in the middle of the Indian Ocean where 85% of the population consumes marine fish daily.[14] This article presents the results of the neurodevelopmental examination of the Seychelles Child Development Study (SCDS) cohort at 66 months, an age at which neuropsychological tests may be given that are sensitive enough to assess potential associations between developmental outcomes and MeHg dietary exposure. Our results also include examination of the role of postnatal exposure from fish consumption.

METHODS

Subjects

The cohort consisted of 711 mother-child pairs living in the Republic of Seychelles, representing 91% of the 779 pairs originally enrolled in the SCDS main study.[11] Informed consent was obtained from the caregiver of every participating child. The protocol was approved by human subjects review boards at the University of Rochester, Rochester, NY, and the Ministry of Health, Victoria, Mahé, Republic of Seychelles, before enrollment began. The sample size was sufficient to detect a 5.7-point difference on any test with a mean (SD) of 100 (16) between low (0-3 ppm) and high (>12 ppm) MeHg groups for a 2-sided test ($\alpha = .05$ at 80% power).

Twenty-eight mother-child pairs were excluded because of medical problems that might seriously affect development.[13] An additional 16 pairs had insufficient maternal hair available to accurately recapitulate prenatal exposure, and 24 did not return for testing at 66 months.

Demographic characteristics of the Seychelles and the cohort were reported earlier.[15] At enrollment, the mothers reported eating an average of approximately 12 marine fish meals per week. Sea mammals are not consumed in the Seychelles. We have previously documented that lead levels in whole blood are less than 0.48 µmol/L (10 µg/dL) in a representative group of Seychellois children and mothers.[16]

Procedure Test Battery

Each child was evaluated at 66 months (±6 months) at a child development center staffed by a team of specially trained Seychellois nurses blinded to MeHg levels and the results of testing during previous visits. Five children were tested between 72 months and 79 months of age. All evaluations were conducted between July 1994 and October 1995. The test battery assessed multiple developmental domains[17] and was similar to those used to demonstrate adverse developmental effects of exposure to lead[18] and polychlorinated biphenyls (PCBs)[19] and to those used in earlier studies to measure MeHg exposure effects.[9,20] The tests are sufficiently sensitive and accurate to detect neurotoxicity in the presence of a number of confounding factors.[21]

The test battery included the following 6 primary measures: (1) the General Cognitive Index (GCI) of the McCarthy Scales of Children's Abilities[22] to estimate cognitive ability; (2) the Preschool Language Scale[23] (PLS) total score to measure both expressive and receptive language ability; (3) the Letter and Word Recognition and (4) the Applied Problems subtests of the Woodcock-Johnson (W-J) Tests of Achievement[24] to measure reading and arithmetic achievement; (5) the Bender Gestalt test[25] to measure visual-spatial ability; and (6) the total T score from the Child Behavior Checklist (CBCL)[26] to measure the child's social and adaptive behavior. The CBCL questionnaire was completed by each child's primary caregiver. All tests were given in Creole, the language spoken by 98% of Seychellois at home.

Pure tone hearing thresholds were tested using a portable audiometer. Caregiver IQ was determined using the Raven Standard Progressive Matrices, a nonverbal test designed to minimize the effects of culture on measurement of IQ.[27] When the children were between 42 and 56 months of age, the Home Observation for Measurement of the Environment (HOME) Inventory for Families of Preschool Age Children[28] was administered during home visits. Following procedures described earlier,[17] on-site test administration reliability was assessed by an independent scorer; percentage of disagreement ranged from 0% to 8%. Mean intraclass correlations for interscorer reliability were 0.96 to 0.97. Reliability of final scoring in Rochester was conducted by rescoring a sample of tests; the mean intraclass correlation coefficient was 0.96.

Mercury Exposure

Prenatal exposure was assessed by measuring the concentration of total mercury (THg) in a segment of maternal hair representing growth during pregnancy. Total Hg in maternal hair during pregnancy correlates well with blood levels of MeHg[1] and with THg levels in fetal brain.[29] Methylmercury accounts for over 80% of the THg in hair samples collected from fish-eating populations.[16,29] Maternal hair levels of THg have been the biological indicator of choice in nearly all previous epidemiological studies of fetal exposure to MeHg. There is considerable variation in the relationship between hair and blood THg in different individuals. However, the key relationship, that of hair levels and brain levels, may not show the same variability.[29] Postnatal exposure was determined by measuring THg at 66 months of age from a 1-cm segment of the child's hair nearest the scalp. This age was chosen because it was coincident with the age of testing and all children were postweaning and eating a fish diet. In 25 children, hair samples taken during the HOME administration (at 48 months of age) were used to determine postnatal MeHg exposure because their hair sample at 66 months of age was insufficient for analysis.

Mercury in Fish

Total Hg was analyzed in 5 or more samples of species of fish caught and consumed in the Seychelles, including yellow fin tuna (*Thunnus albacares*), Indian mackerel (*Rastrelleger kanagurta*), brown spotted grouper (*Epinephelus chlorustigma*), green jobfish (*Aprion virescens*), bonito (*Euthynnus affinis*), bludger (*Carangoides gymnostethus*), and spangled emperor (*Lethrinus nebulosus*).

Maternal and Child Mercury Analysis

The analysis of hair samples and fish homogenates for THg and inorganic Hg was done by cold vapor atomic absorption spectrometry. The analysis technique and quality control procedure are given elsewhere.[16]

PCBs in Blood

Polychlorinated biphenyls are known to be present in some ocean fish and may be associated with developmental delays in children. Levels of PCBs in serum of 49 of the children at 66 months of age were analyzed at the laboratories of the US Centers for Disease Control and Prevention, Atlanta, Ga. The analytic method for measuring the PCBs involved deproteinization of the serum with formic acid, elution through a column containing octadodecyl (C18) packing material, elution through a column containing Florisil packing material, concentration of the organic eluents, and analysis by dual capillary column–gas chromatography with electron capture detection.[30]

Statistical Analysis

The effect of prenatal and postnatal MeHg on each outcome variable was adjusted for covariates, specified as part of the study design, and selected because of their potential to bias the assessment of the association between Hg and outcome.[17] Covariates associated with the child included birth weight, birth order, sex, history of breast-feeding, hearing status, and the child's medical history. Covariates associated with the mother and family included maternal age, maternal smoking during pregnancy, maternal alcohol consumption during pregnancy, maternal medical history, caregiver intelligence, language spoken in the home, Hollingshead socioeconomic status (SES), and HOME score. Two multiple linear regression analyses (with 2-tailed significance tests using a significance level of $P \leq .05$) including both prenatal and postnatal THg were performed for each of the 6 primary measures. The first involved all covariates (full model) and the second included only covariates believed to most likely influence child development in the Seychelles (reduced model), including sex, birth weight, child's medical history, maternal age, HOME score, caregiver IQ, SES, and hearing status. Each full and reduced model was run both with and without THg by sex interaction terms to test the hypothesis that males and females have different THg slopes.

All models were examined for statistical outliers and influential points.[31] Each model was run first with outliers, then without outliers, and the results were compared. All of the results were essentially the same with or without outliers. The regression analyses for all 6 primary measures were also repeated without influential points to determine whether the original results were dependent on such points.[31] The final analysis included influential points that were not also outliers. The results without influential points were consistent with the original analysis.

Secondary analyses tested the hypothesis that associations between developmental outcomes and THg exposure might be nonlinear. All regression analyses were repeated, first using the log of the prenatal and postnatal THg values, then classifying THg variables into 5 groups each for prenatal and postnatal exposure.

Table 1.—Neurodevelopmental Test Means (SDs) by Prenatal Exposure Levels*

Test	Subgroupings by Prenatal Total Mercury Exposure Level, Mean (SD), ppm				
	≤3 (Mean, 2-0) (n = 159)	>3-6 (Mean, 4.5) (n = 206)	>6-9 (Mean, 7.4) (n = 156)	>9-12 (Mean, 10.3) (n = 95)	12-26.7 (Mean, 15.3) (n = 95)
McCarthy Scales of Children's Abilities General Cognitive Index	94.0 (12.3)	93.8 (13.1)	94.3 (13.8)	92.4 (11.6)	95.9 (12.6)
Preschool Language Scale total score†	69.6 (6.7)	69.6 (6.7)	69.6 (6.8)	70.2 (6.3)	72.1 (6.6)
Bender Gestalt errors‡	10.2 (3.9)	10.4 (3.7)	10.0 (4.1)	10.5 (3.7)	9.4 (3.9)
Woodcock-Johnson Tests of Achievement					
Letter and Word Recognition	76.1 (10.8)	77.6 (11.1)	76.9 (9.9)	76.1 (9.9)	77.7 (10.9)
Applied Problems	85.6 (17.2)	87.3 (17.7)	87.3 (17.5)	87.0 (18.0)	90.1 (17.9)
Child Behavior Checklist total T score§	60.4 (9.7)	59.7 (10.5)	59.3 (10.2)	59.3 (9.8)	59.7 (8.8)

*N = 711.
†The Preschool Language Scale raw scores were used since the test and its norms were based on English.
‡The Koppitz scoring method was used. The score represents the number of indicator errors.
§The Child Behavior Checklist yields a percentile (T) score. The threshold for abnormality is beyond the 75th percentile.

Table 2.—Neurodevelopmental Test Means (SDs) by Postnatal Exposure Level*

Test	Subgroupings by Postnatal Total Mercury Exposure Level, Mean (SD), ppm				
	≤3 (Mean, 2.2) (n = 73)	>3-6 (Mean, 4.6) (n = 299)	>6-9 (Mean, 7.4) (n = 213)	>9-12 (Mean, 10.2) (n = 76)	12-25.8 (Mean, 14.9) (n = 47)
McCarthy Scales of Children's Abilities General Cognitive Index	90.6 (14.3)	94.0 (12.8)	94.7 (12.5)	95.8 (13.5)	93.0 (10.5)
Preschool Language Scale total score†	68.8 (6.8)	69.6 (6.7)	70.7 (6.5)	70.6 (7.8)	70.1 (4.8)
Bender Gestalt errors‡	10.4 (4.0)	10.2 (3.9)	10.1 (3.6)	10.0 (4.4)	10.1 (4.0)
Woodcock-Johnson Tests of Achievement					
Letter and Word Recognition	74.7 (11.0)	77.8 (11.3)	76.7 (9.5)	76.8 (10.9)	75.6 (9.0)
Applied Problems	85.6 (18.1)	86.7 (17.6)	88.0 (18.2)	90.0 (16.0)	85.0 (16.3)
Child Behavior Checklist total T score§	57.6 (9.4)	60.1 (10.0)	60.2 (10.7)	59.3 (9.3)	59.5 (7.6)

*N = 708.
†The Preschool Language Scale raw scores were used since the test and its norms were based on English.
‡The Koppitz scoring method was used. The score represents the number of indicator errors.
§The Child Behavior Checklist yields a percentile (T) score. The threshold for abnormality is beyond the 75th percentile.

RESULTS

Mercury in Fish

A total of 350 samples of fish were analyzed. The median THg for each of the 25 species ranged from 0.004 ppm to 0.75 ppm, with most medians in the range of 0.05 to 0.25 ppm. These levels are comparable with fish in the US market. The lowest levels occurred in reef fish. Methylmercury accounted for over 90% of the THg in 34 fish homogenates analyzed by gas chromatography–atomic fluorescent detection. This finding confirms many previous observations.[32]

PCBs in Blood

Twenty-eight PCB congeners ranging from congener 28 to 206 were measured in each serum sample. All samples had no detectable levels of any PCB congeners. The detection limit for the PCB analysis was 0.2 ng/mL. These results are typical for persons with no known exposure to PCBs.[33]

Mercury Exposure

The mean (SD) maternal hair level of THg during pregnancy was 6.8 (4.5) ppm (n = 711), and the mean child hair level at 66 months was 6.5 (3.3) ppm (n = 708). The ranges (maternal hair, 0.5-26.7 ppm; child hair, 0.9-25.8 ppm) were sufficient to test for exposure effects using regression analysis. Maternal and child THg concentrations were not highly associated Pearson $r = 0.15$, n = 708, $P < .001$) as observed by others.[20] The exposure levels found in the Seychelles are typical of populations that depend on fish as a major dietary source of protein and calories.[34]

Test Performance

Tables 1 and 2 show test score means and SDs for prenatal and postnatal exposure levels. These results are similar to what would be expected from a healthy, well-developing US population. No test indicated a deleterious effect of MeHg exposure. Four of the 6 measures showed better scores in the highest MeHg groups compared with lower groups for both prenatal and postnatal exposure.

Regression Analyses

Primary Analyses.—The models with all covariates (full models) and limited covariates (reduced models) were both significant (ie, each model was able to describe the data) and yielded similar results for every measure. The THg by sex interaction test for prenatal exposure was not significant in any regression model. The THg by sex interaction was significant for postnatal exposure for the Bender Gestalt test; hence, we report the results of the reduced model with both interaction terms included. For all

Table 3.—Multiple Regression Analysis of 66-Month Test Scores: Parameter Estimates for Reduced Models With Outliers Removed*

	Regression Coefficients (SEs)†					
				Woodcock-Johnson Tests of Achievement‡		
Parameter Estimate	McCarthy GCI‡	PLS Total Score‡	Bender Gestalt Errors§	Applied Problems	Letter and Word Recognition	CBCL Total T Score‡
Maternal MeHg	−0.057 (0.10)	0.13 (0.057)	0.04 (0.05)	0.11 (0.14)	0.02 (0.09)	−0.11 (0.09)
Child MeHg	0.26 (0.14)	0.18 (0.075)	−0.16 (0.06)	0.36 (0.18)	0.15 (0.12)	−0.02 (0.11)
Sex, female	2.5 (0.92)‖	0.97 (0.51)	−0.14 (0.73)	3.99 (1.24)	1.68 (0.78)	0.002 (0.76)
Sex × maternal MeHg	...	...	...	...	...	...
Female subjects × maternal MeHg	...	...	−0.70 (0.046)	...	...	...
Male subjects × maternal MeHg	...	...	0.042 (0.047)	...	...	...
Sex × child MeHg	...	...	...	...	...	...
Female subjects × child MeHg	...	...	0.09 (0.064)	...	...	...
Male subjects × child MeHg	...	...	−0.16 (0.06)	...	...	...
Birth weight	1.4 (0.98)	0.84 (0.54)	−0.34 (0.31)	2.98 (1.31)‖	1.07 (0.82)	−0.08 (0.81)
Child's medical history¶	−0.65 (2.69)	−0.72 (1.40)	−1.09 (0.83)	2.87 (3.51)	3.57 (2.25)	−2.06 (2.16)
Maternal age	0.054 (0.09)	0.008 (0.47)	−0.02 (0.03)	−0.003 (0.11)	0.01 (0.07)	−0.25 (0.07)
HOME (*P* for overall test)‖	<.01	<.01	<.01	>.01 and ≤.05	<.01	<.01
Low (0-31)	−4.4 (1.22)	−3.16 (0.67)	1.39 (0.38)	−4.69 (1.63)	−4.53 (1.02)	2.79 (1.0)
Medium (>31-35)	−3.2 (1.19)	−1.85 (0.65)	00.75 (0.38)	−3.52 (1.59)	−4.45 (1.0)	2.48 (0.98)
SES (*P* for overall test)‖	.11	.15	.48	>.01 and ≤.05	≤.01	.14
Unskilled	−4.1 (1.68)	−2.01 (0.93)	0.72 (0.53)	−6.44 (2.26)	−4.73 (1.4)	3.0 (1.37)
Skilled	−2.9 (1.57)	−1.14 (0.86)	0.41 (0.5)	−4.57 (2.12)	−4.31 (1.31)	2.74 (1.29)
Semiprofessional	−2.41 (1.65)	−0.76 (0.91)	0.14 (0.52)	−3.92 (2.23)	−0.65 (1.38)	1.78 (1.35)
Caregiver IQ (*P* for overall test)‖	>.01 and ≤.05	<.01	<.01	<.01	.78	.59
Lower third	−3.3 (1.26)	−2.22 (0.7)	1.33 (0.4)	−5.55 (1.69)	−0.65 (1.06)	1.06 (1.03)
Middle third	−1.61 (1.14)	−1.06 (0.62)	0.79 (0.36)	−2.23 (1.52)	−0.59 (0.96)	0.57 (0.94)
Hearing level (*P* for overall test)‖	.96	.87	.09	.03	.52	.99
0-25 dB	−0.94 (3.53)	−0.02 (2.22)	2.45 (1.22)	−6.34 (4.92)	−0.44 (3.10)	0.20 (2.9)
26-35 dB	−1.2 (4.03)	−0.02 (2.48)	1.60 (1.36)	−3.81 (5.56)	−2.38 (3.50)	0.43 (3.3)

*GCI indicates General Cognitive Index; PLS, Preschool Language Scale; CBCL, Child Behavior Checklist; MeHg, methylmercury; HOME, Home Observation for Measurement of the Environment; and SES, socioeconomic status. Ellipses indicate data not applicable.

†Slope-test point/ppm of methylmercury.

‡Model without interaction.

§Model with test for methylmercury by sex interaction.

‖Slopes are provided for the difference between each level of the covariate and the reference (highest) level. Indications of statistical significance are provided for these individual effects as well as for overall effects.

¶Reference group is positive history.

other analyses, we report the results for reduced models without THg by sex interactions.

The regression coefficients for all variables in the 6 sets of analyses are shown in Table 3. Figure 1 shows partial residual plots (end points adjusted for covariates) for prenatal and postnatal exposure for the McCarthy GCI, the PLS total score, and the W-J Applied Problems test score. For the McCarthy GCI analysis, the model (F [15, 628] = 4.41, $P<.001$, $R^2 = 0.10$) indicated that slopes for both THg exposures did not differ from 0 ($P = .59$ and .06 for prenatal and postnatal exposure, respectively). For the PLS analysis, the model (F [15, 590] = 6.25, $P<.001$, $R^2 = 0.14$) showed effects of both prenatal and postnatal THg exposure ($P = .02$ for both), but the effects were very small and in a direction of enhanced performance. The total increase in scores across the entire range of THg exposures was less than 4.5 points. The W-J Applied Problems model (F [15, 625] = 5.38, $P<.001$, $R^2 = 0.11$) indicated that the slope for prenatal exposure did not differ significantly from 0 ($P = .41$). There was a significant beneficial postnatal exposure effect ($P = .05$), but no evidence for an adverse effect. The postnatal exposure slope for the W-J Applied Problems test was 0.36 ppm, representing a 9.7-point increase over the full exposure range, or a 10% improvement in performance.

Figure 2 shows partial residual plots for the Bender Gestalt test, separating male from female subjects. The model (F [17, 613] = 4.53, $P<.001$, $R^2 = 0.11$] showed no significant association with prenatal exposure. The interaction of postnatal THg with sex was significant ($P = .004$). The slightly positive slope for female errors was not significant ($P = .14$). The regression coefficient of −0.16 ppm for male subjects was significant ($P = .009$), resulting in a reduction of 4.3 errors over the entire exposure range (a 40% performance improvement given that the average score for the lowest-exposure group was about 10 errors).

Although the models for the W-J Letter and Word Recognition achievement score and the CBCL yielded significant overall F statistics, none of these was significantly associated with either prenatal or postnatal exposure.

The data for covariate effects shown in Table 3 indicate that test scores were frequently influenced by sex (female subjects scored higher than male subjects), and were directly related to SES, quality of home stimulation, and caregiver IQ, as would be expected in westernized cultures. These data also indicate that performance by Seychellois children on these tests was similar to what would be expected of US children.

Table 4 gives the partial R^2 values for the effects of prenatal and postnatal THg exposure on each developmental measure and the 95% confidence intervals for the effect of a 10-ppm increase in hair THg concentration. The small partial R^2 values shown in Table 4 indicate that THg exposure accounted for little of the variance associated with each test. For the McCarthy GCI and the CBCL, the magnitude of the negative lower confidence limit might be of clinical significance, at least over a greater range of hair THg levels. However, the inclusion of 0 in the confidence intervals shows

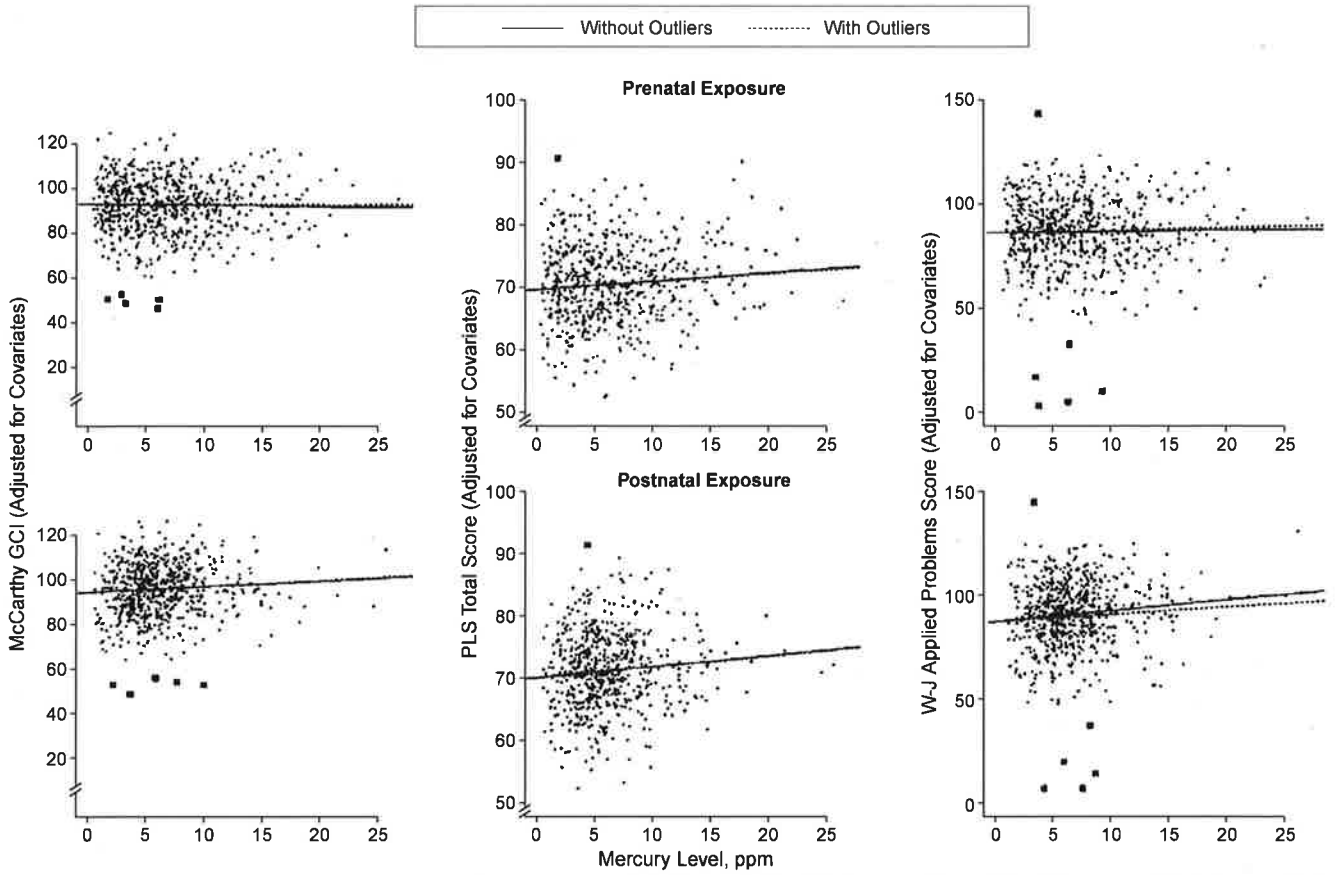

Figure 1.—Partial residuals for prenatal and postnatal exposure. The measures are the McCarthy Scales of Children's Abilities General Cognitive Index (GCI), the Preschool Language Scale (PLS) total score, and the Woodcock-Johnson (W-J) Applied Problems subtest. Each test score was adjusted for all reduced model predictors except the exposure value used in the plot. For graphical representation, the overall mean test score was added to the resulting partial residual. The slope of the line in the plot is the regression coefficient for the multiple regression model. Slopes are shown for the model with and without outliers. Black squares indicate outliers.

that the effects are not statistically significant.

Secondary Analysis.—Log transformations of the 2 THg variables did not alter the direction of any effects. In the categorical analyses, test scores for children with an MeHg exposure level greater than 12 ppm were not significantly different than for children with exposure levels of 3 ppm or less.

COMMENT

Results from this study are relevant for the United States and other countries with similar dietary intake of fish. The major source of MeHg in the Seychelles is ocean fish and the average fish levels are similar to those on the US market. Seychellois MeHg levels are 10 to 20 times higher than in the United States because the Seychellois consume more fish, not because they eat a few fish with abnormally high MeHg levels. Thus, any potential adverse effects of MeHg in fish should be detected in the Seychelles long before such effects would be seen in the United States. Our findings confirm our earlier report in which no adverse developmental effects were found in toddlers following prenatal MeHg exposure.[12] Our data extend preliminary results from the SCDS Pilot Study,[35] involving a less statistically powerful, less well-controlled developmental evaluation of 217 Seychellois children at 66 months using most of the same measures but lacking many of the covariates used here.

We applied multiple regression analysis to our data as has been done in other studies on the effects of mercury,[9-13] lead,[18,36] or PCBs[19] on child development. Although our models showed no negative associations between MeHg and outcome scores, our test procedures did detect other factors known to be associated with child development. The HOME test indicated that the quality of the home environment had a substantial impact on child performance, significantly affecting the results of all tests. The SES of the family, the caregiver's IQ, and the child's sex were all found to have an influence on performance scores, in keeping with the literature on child development.[37,38] These results increase confidence in the sensitivity of our tests to child development functions. Postnatal exposure to MeHg at 66 months of age was associated with a small but statistically significant increase on several developmental outcomes. Our hypothesis did not predict positive effects, since there are no reasons to suppose that such effects are associated with exposure to MeHg. However, MeHg levels in hair are known to correlate closely with fish intake, and other factors or agents associated with fish, such as omega-3 fatty acids, may have beneficial effects. A large cohort study under way in the Faroe Islands found enhancement of developmental milestones in suckling infants exposed to MeHg in breast milk.[39] They suggested that MeHg levels in the infant were a surrogate for the length of breast-feeding, which is reported to have a positive association with developmental outcomes.[40]

In contrast with the conclusions from this and our earlier studies of the main Seychellois cohort,[12,13] the Faroe Islands study found evidence of cognitive deficits associated with prenatal exposure to THg when children were tested at 7

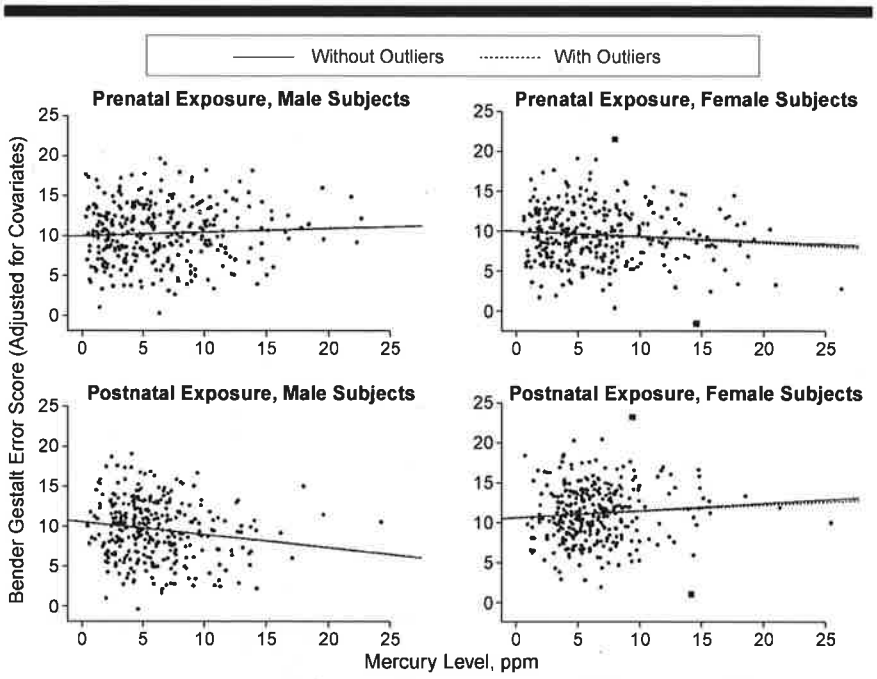

Figure 2.—Partial residuals for prenatal and postnatal exposure. The measures are Bender Gestalt error scores for male and female subjects. Each test score was adjusted for all reduced model predictors except the exposure value used in the plot. For graphical representation, the overall mean test score was added to the resulting partial residual. The slope of the line in the plot is the regression coefficient for the multiple regression model. Slopes are shown for the model with and without outliers. Black squares indicate outliers.

Table 4.—Partial R^2 Values for Total Mercury and 95% CIs for a 10-ppm Increase in Both Prenatal and Postnatal Total Mercury Hair Levels From the Regression Analysis of 66-Month End Points*

	Partial R^2 Value, %		95% CIs for a 10-ppm Increase	
Developmental End Point	Prenatal	Postnatal	Prenatal	Postnatal
McCarthy GCI	0.047	0.55	(−2.58 to 1.45)	(−0.12 to 5.29)
PLS total score	0.91	0.96	(0.22-2.41)	(0.34-3.24)
Woodcock-Johnson Tests of Achievement				
Letter and Word Recognition	0.0062	0.26	(−1.51-1.86)	(−0.79 to 3.75)
Applied Problems	0.11	0.61	(−1.57 to 3.84)	(0.02-7.23)
CBCL total T score	0.24	0.0058	(−2.72 to 0.61)	(−2.43 to 2.00)
Bender Gestalt error score				
Male subjects	0.13	1.11	(−0.50 to 1.34)	(−1.58 to 0.18)
Female subjects	0.38	0.35	(−2.76 to −0.41)	(−0.29 to 2.18)

*Data are from reduced models without interaction (except for those for the Bender Gestalt error score) and with outliers removed. CI indicates confidence interval; GCI, General Cognitive Index; PLS, Preschool Language Scale; and CBCL, Child Behavior Checklist.

years of age.[20] Important differences between the 2 populations may explain the divergent outcomes (eg, nutritional practices, housing, and lifestyle). However, the major difference between our study and the Faroe Islands study is the source of exposure. Ocean fish are the source of MeHg in the Seychelles, whereas pilot whales are the predominant source in the Faroe Islands.[20] The average MeHg level in the meat of pilot whales sampled in the Faroe Islands was 1.6 ppm,[41] approximately 10 times higher than the average level in fish consumed in the Seychelles. Approximately the same level of inorganic Hg is also present in whale meat.[41] In addition, whale blubber is also consumed by the Faroese[41] and is heavily contaminated with fat-soluble pollutants.[42] The average PCB concentration in pilot whale blubber from Faroese waters is elevated (about 30 ppm).[43] In general, fatty tissues of marine mammals in the North Atlantic also contain elevated levels of persistent organochlorine compounds including dibenzofurans and dioxins, DDT and its metabolites, and other pesticides. It is difficult to determine the relative toxicological impact of individual compounds. Some of these contaminants are believed to affect child development.[44] The Faroese study may be relevant to populations consuming large, perhaps episodic, amounts of marine mammals, but its relevance to people consuming ocean fish remains to be established.

A Swedish expert group conducted the first extensive evaluation of human health risks from MeHg in fish in 1971.[45] They concluded the lowest toxic level in hair was 50 ppm in adults. The World Health Organization (WHO) expert group[46] subsequently reaffirmed the Swedish conclusion and applied a safety factor of 10 to cover risks to the most sensitive subgroup of the population, assumed to be those who are prenatally exposed. Thus, 5 ppm in hair was adopted as the international standard for the upper tolerable level of Hg in hair. Subsequent epidemiological studies of human populations prenatally exposed to MeHg from fish have given strong support to the WHO guideline.[8,10,12,13] Our results add further support to the validity of this longstanding guideline.

In summary, the results of extensive performance tests conducted with cohort children at 66 months of age strongly support our findings reported at younger ages. The development of these children is proceeding well without any detectable adverse influence of MeHg. Our results support Egeland and Middaugh's observation[47] that it would be inadvisable to forgo the health benefits of fish consumption to protect against a small risk of adverse effect at the levels of MeHg found in ocean fish on the US market.

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Washington State Toxics Monitoring Program: Contaminants in Fish Tissue from Freshwater Environments in 2004 and 2005

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Washington State Toxics Monitoring Program: Contaminants in Fish Tissue from Freshwater Environments in 2004 and 2005

by

Keith Seiders, Casey Deligeannis, and Patti Sandvik

Environmental Assessment Program
Washington State Department of Ecology
Olympia, Washington 98504-7710

June 2007

Waterbody Numbers: Statewide

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Abstract

The exploratory monitoring component of the Washington State Toxics Monitoring Program (WSTMP) has characterized toxic contaminants in freshwater fish since 2001, primarily from sites never before sampled. Contaminants assessed include persistent, bioaccumulative, and toxic chemicals such as mercury, PCBs, dioxins and furans, chlorinated pesticides, and PBDE flame retardants.

During the 2004-2005 study, a total of 52 sites across the state were sampled which yielded 104 fish tissue samples representing 19 species. Detection frequencies ranged from 59% to 100% for mercury, PCBs, dioxins and furans, DDT pesticides, and PBDEs. Older and larger fish showed higher concentrations of organic contaminants.

Contaminants were detected in Chinook salmon from three coastal rivers with most results being near reporting limits. Levels of PCBs and DDTs in coastal fish were lower than levels found in fish from Puget Sound and the Columbia River. Total PCBs, 2,3,7,8-TCDD TEQ, and toxaphene were detected at levels higher than (exceeding) EPA's Screening Values for Subsistence Fishers.

A total of 45 sites had 93 fish tissue results that exceeded the National Toxics Rule (NTR) criteria for contaminants in fish tissue. Four contaminants accounted for 85% of the exceedances: PCBs, 2,3,7,8-TCDD, 4,4'-DDE, and dieldrin. Other NTR exceedances were due to mercury and four pesticides: 4,4'-DDD, total chlordane, hexachlorobenzene, and toxaphene.

This study recommends that these 45 sites be added to the federal Clean Water Act Section 303(d) List for Washington State.

This study also recommends that the Washington State Department of Health, local health jurisdictions, and affected Tribes should (1) evaluate the results from this study, and (2) assess the risks to human health from the consumption of contaminated fish.

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Introduction

Various monitoring efforts by the Washington State Department of Ecology (Ecology) and others have found toxic chemicals in water, sediment, and fish throughout Washington's freshwater and marine environments. Many of these chemicals are persistent, bioaccumulative, and toxic compounds (PBTs). For many areas of Washington, there is little information about the levels of toxic contaminants in the environment

Ecology and the Washington State Department of Health (DOH) are developing strategies to address PBTs in our environment. These strategies involve learning more about the sources, uses, risks, and fate of these compounds. Mercury and flame retardants were the first PBTs for which chemical action plans were developed (www.ecy.wa.gov/programs/eap/toxics/PBT_strategy.html).

Fish are an important indicator of contaminant levels in the environment. Fish tissue contaminant data collected by various agencies are evaluated by DOH and local health jurisdictions to determine whether fish consumption advisories are needed. While many areas of Washington do not warrant consumption advisories, a number of site-specific and statewide fish consumption advisories have been issued. (www.doh.wa.gov/ehp/oehas/fish/advisoriesmap.htm).

Ecology evaluates fish tissue contaminant data to determine whether state water quality standards are being met. Contaminant concentrations in fish tissue that do not meet water quality standards are not necessarily high enough to warrant advice about eating less fish. DOH evaluates the need for consumption advice based on multiple factors including the benefits of eating fish as part of a healthy diet.

Background

During the 1980s and 1990s, Ecology and other agencies found toxic contaminants in fish, water, sediment, and soil throughout Washington at varied levels of concern (www.ecy.wa.gov/toxics.html). In 2000, renewed concern about toxic contaminants in the environment led Ecology to revitalize a program to address toxic contaminants: the Washington State Toxics Monitoring Program (WSTMP).

The goals of the WSTMP are to:

- Conduct exploratory monitoring to characterize toxic contaminants in freshwater fish across Washington where historical data are lacking.
- Conduct trend monitoring for persistent toxic chemicals.
- Improve access to information about monitoring contaminants in Washington: www.ecy.wa.gov/programs/eap/toxics/index.html.
- Establish cooperative efforts with other agencies and develop monitoring efforts to address issues of concern.

Between 2001 and 2005, 150 fish tissue samples from over 70 sites were analyzed for various contaminants as part of the WSTMP's Exploratory Monitoring component. Three annual reports were published (Seiders et al, 2006; Seiders and Kinney, 2004; Seiders, 2003) and over 27,000 results are now available in Ecology's Environmental Information Management database (EIM) at www.ecy.wa.gov/eim/.

This report summarizes results from fish samples collected in 2004 and 2005.

Sampling occurred at 21 sites in 2004 and at 31 sites in 2005 (Figure 1 and Appendix A). These 52 sites yielded 104 samples representing 18 freshwater and one marine (Chinook salmon) species.

Study Design

The study targeted a broad range of contaminants in fish tissue from multiple sites. Site selection involved reviewing existing information on fish contaminants in Washington and choosing sites and species where historical data were lacking or were more than ten years old. The project plan for the WSTMP describes the selection of sites, species, and analytes in more detail (Seiders and Yake, 2002).

Contaminants Assessed

Target analytes included persistent, bioaccumulative, and toxic chemicals (PBTs) described below. Lipid content of samples was also determined. A brief description of contaminants is given here. More detailed information about individual analytes is available through internet links in EIM.

Mercury

Mercury occurs in the earth's crust and is released to the environment from natural events (e.g., volcanoes, weathering, and forest fires) and human activities (e.g., fossil fuel combustion, mining, and industrial processes).

Methylmercury is the toxic form of mercury which persists in the environment as it accumulates in the food web. Eating fish and shellfish contaminated with methyl-mercury is the primary route for exposure to mercury for most people (ATSDR, 1999; Ecology and DOH, 2003; EPA, 2007).

PCBs

PCBs are synthetic organic compounds historically used as cooling fluids in electrical equipment, and in inks, paints, and plastics. PCBs are stable, have low solubility in water, and have a high affinity for sediments and animal fats. The production of PCBs was banned in the U.S. in 1979 due to their persistence and toxicity (ASTDR, 2000).

There are 209 individual PCBs, or congeners. Commercial mixtures of PCB congeners were known in the United States by the trade name Aroclor. PCB Aroclors were analyzed in all WSTMP samples from 2004 and 2005; individual PCB congeners were analyzed in about half of these samples.

Dioxins and Furans (PCDD/Fs)

Dioxins and furans, or polychlorinated dibenzo-p-dioxins and -furans (PCDD/Fs), are unintentional byproducts of combustion processes (e.g., burning household trash, forest fires, waste incineration), chlorine bleaching in paper production, and chemical and pesticide manufacturing. Agent Orange, used as a defoliant in the Vietnam War, contained dioxins (ATSDR 2006).

About half of the 2004-2005 samples were analyzed for the 17 most toxic congeners. These congeners have different levels of toxicity compared to 2,3,7,8-TCDD, the most toxic congener. The cumulative toxicity of mixtures of congeners in a sample can be expressed as a toxic equivalent (TEQ) to 2,3,7,8-TCDD.

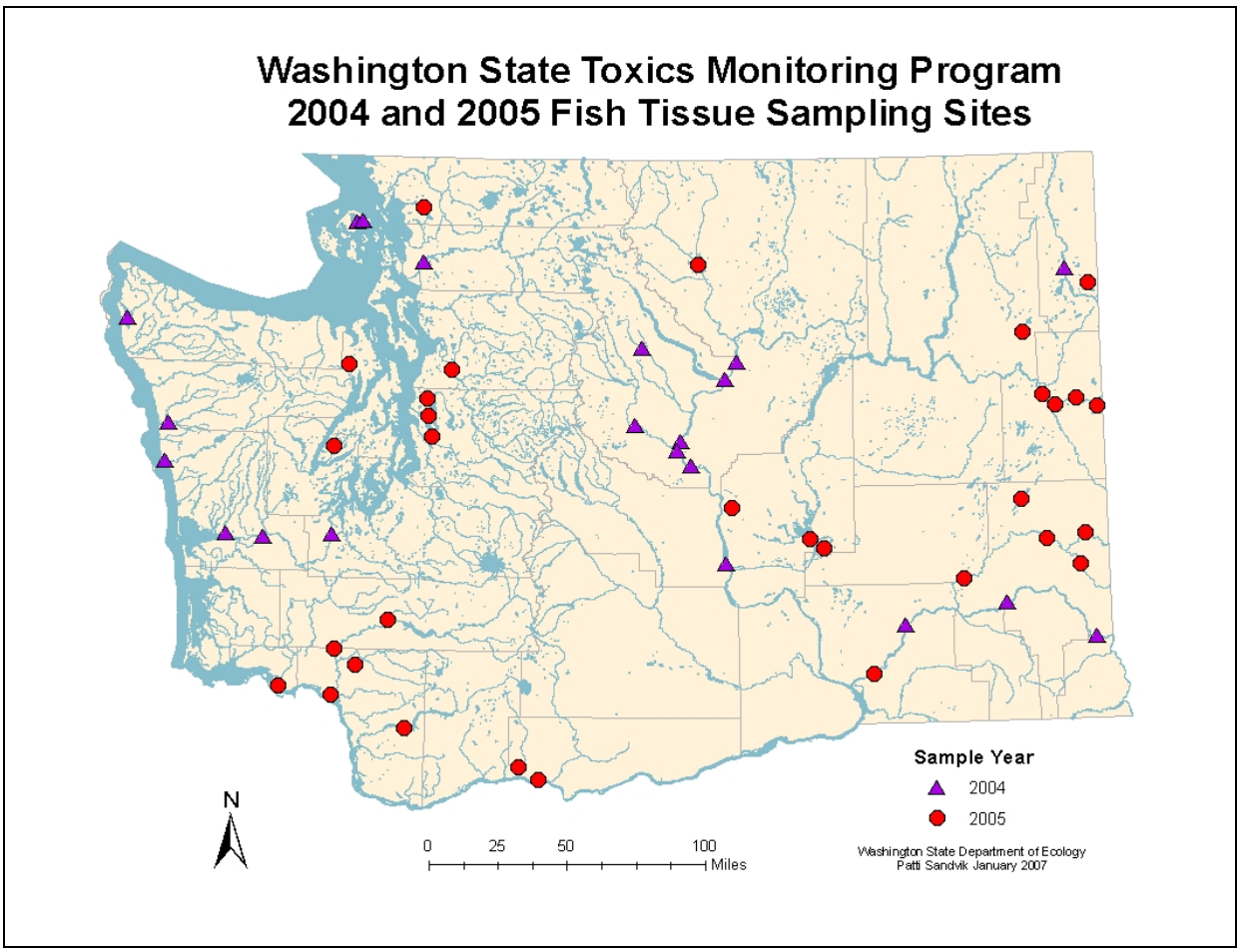

Figure 1. Sample Sites for the WSTMP, 2004-2005.

Chlorinated Pesticides

Pesticides include insecticides, herbicides, fungicides, and related chemicals used to control pests. Chlorinated pesticides were analyzed for in this study because of their widespread occurrence and persistence in the environment.

Many of these pesticides are neurotoxins and are suspected or known carcinogens (EPA, 2000). Some were banned from use in the United States during the 1970s and 1980s as their hazards became evident (e.g., DDT, chlordane, and dieldrin).

PBDE Flame Retardants

Flame retardants, specifically poly-brominated diphenyl ethers (PBDEs), are compounds added to plastic and foam products such as electronic enclosures, wire insulation, adhesives, textile coatings, foam cushions, and carpet padding. Increasing concentrations of PBDEs in humans and wildlife worldwide continue to raise concerns about their health effects. The highest levels of PBDE in human tissue have been found in the U.S. and Canada (Ecology and DOH, 2006).

Site Selection

Sites were selected by examining various factors, such as the type of species present, the presence or absence of historical data, the value of the site for fishing, and the ability to coordinate with other monitoring or watershed planning efforts. Site location information is further described in EIM.

Other monitoring efforts provided tissue samples to the WSTMP which helped enlarge the sampling area of the WSTMP. Using fish from other sites allowed analyses of these already-collected samples for analytes targeted by the WSTMP but not examined by the other studies. These additional tissue samples were from the Pend Oreille and Wenatchee Rivers (Era-Miller and Kinney, 2005; and Era-Miller, 2004); Palouse River (Johnson et al., 2007); Spokane River (Serdar and Johnson, 2006); and Lake Washington (DOH, 2007). These studies provide more detailed information about fish tissue contaminants in their respective geographic areas.

Field Procedures

Target fish species were chosen based on recommendations from the U.S. Environmental Protection Agency (EPA, 2000) and previous experience with fish collection efforts. Most fish were collected in late summer or fall by electro-fishing, gill netting, angling, or trapping. Fish kept for analyses were given a unique identifying code, measured for length and weight, individually wrapped in aluminum foil and put in plastic bags, and transported to freezer storage.

Fish were later processed at Ecology facilities. Composite samples were made up of skin-on fillets from five to ten fish of the same species from the same site. For catfish, skin was removed from the fillet before processing. The sex and age of each fish was determined. Samples were then sent to laboratories for chemical analyses. Sample collection and processing details are described in a standard operating procedure (SOP) (Ecology, 2006a).

Analytical Methods

Table 1 describes analytical methods. Most analyses were performed by Manchester Environmental Laboratory (MEL). Pacific Rim Laboratories, Inc. of Surry B.C. conducted analyses for PCB congeners and PCDD/Fs. At Ecology's request, PCDD/Fs results were reported down to the method detection limit (MDL). Values were qualified as estimates if they were between the MDL and the quantitation limit.

Fish tissue was analyzed for total mercury because analytical costs for methylmercury are prohibitive. Methylmercury is the predominant form of mercury in fish tissue (Bloom, 1995). EPA's National Recommended Water Quality Criteria and EPA's Screening Values are based on methylmercury.

Table 1. Analytical Methods for Fish Tissue Samples, WSTMP 2004-2005.

Parameter	Description	Method	Reporting Limit
PCB Aroclors	GC/ECD	EPA 8082	0.5 ug/kg, wet wt
PCB Congeners	HiRes GC/MS	EPA 1668A	0.02 - 0.08 ug/kg, wet wt
Chlorinated pesticides	GC/ECD	EPA 8081 [1]	0.25 -15 ug/kg, wet wt
PBDEs	GC/MS SIM	EPA 8270 [2]	0.5 - 1.0 ug/kg, wet wt
PCDD/PCDFs	HiRes GC/MS	EPA 1613B	0.1 - 1.0 ng/kg, wet wt
Mercury (total mercury)	CVAA	EPA 245.6	0.017 mg/kg, wet wt
Lipids - percent	gravimetric	MEL SOP 700009	0.1 percent

1 - MEL SOP 730073, a modification of EPA 8081 and others, was used in sample analyses.
2 - MEL SOP 730096, a modification of EPA 8270, was used in sample analyses.

Quality Assurance

Data quality was assessed by reviewing laboratory case narratives, analytical results, and field replicate data. Case narratives were written by the laboratory's analytical staff. The narratives described conditions of the samples upon receipt, analytical quality control procedures, and data qualifications.

Overall, the 2004 and 2005 data met most quality control criteria defined by MEL and the quality assurance project plan. Some data were rejected, and many results were qualified. Estimates of precision for six field replicates were typical for samples of fish tissue. Detailed quality assurance information is available by contacting the authors.

Water Quality Criteria

Fish tissue results were compared to Washington's water quality standards to determine how sites should be assessed in Washington's Statewide Water Quality Assessment (the 303(d) assessment).

Washington's water quality standards for toxic compounds (the National Toxics Rule criteria) are one set of values that can be used in helping to gauge the potential for human health risks from eating contaminated fish. EPA developed more recent criteria and guidance values which are summarized below (*EPA Recommended Water Quality Criteria* and *EPA Screening Values*).

Report results are not compared to these EPA criteria because Ecology lacks authority to begin corrective actions where these criteria are exceeded. Yet these EPA criteria can be used by state, tribal, and local health jurisdictions in evaluating risks to human health from the consumption of contaminated fish.

These EPA criteria and guidance values are compared with Washington's water quality standards criteria in Appendix B. Appendix C describes how Ecology and DOH evaluate fish tissue data.

These Washington State and EPA criteria and guidance values exist because of changing knowledge about the toxic effects of chemicals and subsequent risks to consumers of fish. The various criteria and guidance values are often based on different assumptions used in determining risk, such as daily consumption rates, toxicological data used in calculations, and risk levels.

National Toxics Rule (NTR)

Washington State's water quality standards for toxic substances (WAC 173-201A-040[5]) define human health-based water quality criteria by referencing 40 CFR 131.36, also known as the National Toxics Rule (NTR).

The NTR criteria were issued by EPA to Washington State in 1992. These criteria are designed to minimize the risk of adverse effects occurring to humans from chronic (lifetime) exposure to toxic substances through the ingestion of drinking water and contaminated fish and shellfish obtained from surface waters. The NTR criteria are regulatory values used by Ecology for a number of different purposes, including permitting wastewater discharges and assessing when waterbodies are adversely impacted by contaminants.

The NTR criteria values are based on a daily fish consumption rate of 6.5 grams/day and a risk level of 10^{-6}.

A risk level is an estimate of the number of cancer cases that could be caused by exposure to a specific contaminant. At a risk level of 10^{-6}, one person in a million would be expected to contract cancer due to long-term exposure to a specific contaminant.

EPA Recommended Water Quality Criteria

EPA has published *National Recommended Water Quality Criteria* for some substances such as mercury and pesticides (EPA, 2001, 2002a, and 2003). These recommended criteria are updates to previously developed criteria that occur on an ongoing basis. EPA recommends these criteria be used when states and tribes revise their regulatory criteria. These EPA recommended criteria are not regulatory levels. Most of EPA's Recommended Water Quality Criteria are based on a daily fish consumption rate of 17.5 grams/day and a risk level of 10^{-6}.

EPA Screening Values

Screening values (SVs) for carcinogenic and non-carcinogenic substances were developed by EPA to help prioritize areas that may present risks to humans from fish consumption. The EPA SVs are considered guidance only; they are not regulatory thresholds (EPA, 2000).

The approach in developing the EPA SVs was similar to that used for developing the NTR, yet differ in two key assumptions:

- A cancer risk level of $10^{-5.}$
- Two consumption rates: 17.5 grams/day for recreational fishers and 142.4 grams/day for subsistence fishers.

Results and Discussion

In 2004 and 2005, 52 sites were sampled and yielded 104 samples representing 18 freshwater and one anadromous species (Chinook salmon). Results for the Chinook salmon are discussed later in this report, separately from results for freshwater fish.

The concentrations of contaminants in fish tissue are expressed in wet weight basis using these units of measure:

- mg/kg = ppm, or parts per million
- ug/kg = ppb, or parts per billion
- ng/kg = ppt, or parts per trillion

Table 2 shows summary statistics for key contaminants in freshwater fish. Detection frequencies ranged from 59% to 100% for PCBs, DDTs, PBDEs, PCDD/Fs, and mercury. Contaminant levels in samples

frequently exceeded the NTR criteria for PCBs (58-82% of samples) and 2,3,7,8-TCDD (73% of samples) in resident species. Appendix D shows results for key analytes in fish tissue samples.

The 2004-2005 WSTMP results were within the range of values detected in other studies of fish tissue in Washington. The 2004-2005 median values for PCBs, PBDEs, DDTs, and 2,3,7,8-TCDD TEQs were generally lower than median values derived from other fish tissue studies in Washington.

Contaminants in Freshwater Fish

Mercury

Mercury was detected in all but one of 97 samples, with 4% of samples exceeding the NTR criterion of 0.825 mg/kg. The range of values was similar to those seen in other mercury monitoring efforts in Washington (Serdar et al., 2001; Fischnaller et al., 2003; Furl et al., 2007). Larger and older piscivorous fish tended to have higher mercury levels. The highest levels of mercury (> 0.500 ug/kg) were found in (1) northern pikeminnow from the Chehalis, Cowlitz, Pend Oreille, Palouse, Snohomish, and Columbia Rivers, and Lake Washington, and (2) largemouth bass from Ozette, Leland, and Silver Lakes.

Other species having levels greater than EPA's Recommended Water Quality Criterion for methylmercury of 0.300 mg/kg (EPA, 2001) were smallmouth bass, yellow perch, cutthroat trout, and channel catfish.

PCBs

PCB levels in excess of 40 ug/kg were found in fish from the Columbia, Snake, Spokane, Palouse, and Cowlitz Rivers, and Lake Washington. Species having higher levels of PCBs include channel catfish, common carp, mountain whitefish, northern pikeminnow, and cutthroat trout.

Table 2. Summary Statistics for 2004-2005 WSTMP Fish Tissue Sample Results.

Parameter	n	Min	Max	Median	Mean	Standard Deviation	Detection Frequency	No. Exceeding NTR Criteria
Total PCB Aroclors[1] (ug/kg)	101	4.2 U	1339	10.9	65.2	196.0	59%	59
Total PCB congeners[1] (ug/kg)	49	0.91	1632	21.1	92.7	250.3	100%	40
Total DDT[2] (ug/kg)	98	0.21	509	5.8	56.0	118.7	88%	-
Total PBDE[3] (ug/kg)	100	0.17	1136	5.5	22.7	114.0	87%	-
Total Chlordane[4] (ug/kg)	98	0.22	68	1.0	3.4	10.7	33%	6
2,3,7,8-TCDD TEQ[5] (ng/kg)	48	0.01	12	0.30	0.88	2.02	98%	-
2,3,7,8-TCDD (ng/kg)	48	0.03 UJ	1.9	0.10	0.183	0.316	69%	35
Mercury (mg/kg)	97	0.017 U	0.964	0.154	0.231	0.225	99%	4

1 - Total PCBs is the sum of the individual Aroclors or congeners.
2 - Total DDT is the sum of 4,4' and 2,4' isomers of DDT, DDD, and DDE.
3 - Total chlordane is the sum of cis- and trans- chlordane, cis- and trans- nonachlor, and oxychlordane.
4 - Total PBDE is the sum of the individual congeners.
5 - 2,3,7,8-TCDD TEQ is the sum of the 17 PCDD/F congener results using TEFs by Van den Berg et al. (1998).
The summing process used values without qualifiers and values qualified as estimates. Non-detect values were excluded.
U = The analyte was not detected at or above the reported value.
UJ = The analyte was not detected at or above the estimated reported value.

The highest levels of PCBs were found in fish from Lake Washington and the Wenatchee River. PCB levels in Lake Washington fish were: common carp (1339 ug/kg Aroclors and 611 ug/kg congeners), northern pikeminnow (375 ug/kg Aroclors and 241 ug/kg congeners), and cutthroat trout from the south and north basins (370 and 232 ug/kg Aroclors, and 292 – 383 ug/kg congeners), respectively.

PCB levels in Wenatchee River fish were 1300 ug/kg Aroclors and 1632 ug/kg congeners for mountain whitefish from the Leavenworth area, and 542 ug/kg Aroclors for mountain whitefish near Wenatchee. Similarly high levels of PCBs were documented in previous studies (Era-Miller, 2004; Davis et al., 1995; and Hopkins et al., 1985).

Dioxins and Furans (PCDD/Fs)

Dioxins and furans were detected in 98% of 48 samples tested. 73% of samples exceeded the NTR criterion for 2,3,7,8-TCDD. The highest levels of 2,3,7,8-TCDD were found in the four samples from Lake Washington (0.68 – 1.9 ng/kg). Catfish from the Snake River at Central Ferry had the next highest levels at 0.37 ng/kg. Corresponding 2,3,7,8-TCDD TEQ values for Lake Washington samples were 4.6 – 12 ng/kg and 1.1 ng/kg for catfish from the Snake River at Central Ferry.

The Lake Washington carp result of 12 ng/kg for 2,3,7,8-TCDD TEQ is the highest value found in Washington since 1990, based on data from EIM. Fish from upper Lake Roosevelt had TEQ values up to 17 ng/kg in 1990 which have decreased since a pulp mill in Celgar, Canada improved wastewater treatment processes (Serdar et al., 1994; Munn, 2000).

Chlorinated Pesticides

The most frequently detected chlorinated pesticides were 4,4'-DDE, 4,4'-DDD, 4,4'-DDT, hexachlorobenzene, trans-nonachlor, dieldrin, and cis-chlordane. Eleven other pesticides were detected at frequencies less than 4%.

The highest levels of total DDT were found in fish from the Columbia, Snake, and Wenatchee Rivers, and in fish from Lake Washington. Northern pikeminnow, mountain whitefish, walleye, and peamouth from the mid- to upper-Columbia River sites had total DDT levels from 112 to 509 ug/kg. Lake Washington carp contained 418 ug/kg total DDT which was the third highest level found during this study. Most of the remaining 2004-2005 samples had lower levels of total DDT, with 75% of samples having less than 29 ug/kg total DDT.

Haven Lake, Snake River, and Lake Washington fish had some of the highest levels of hexachlorobenzene found in Washington (5-12 ug/kg). Largemouth bass from Haven Lake exceeded the NTR criteria for hexachlorobenzene, with a level of 12 ug/kg. Rainbow and cutthroat trout had hexachlorobenzene levels of 5 and 6 ug/kg, respectively, which are slightly below the NTR criterion.

Chlordane was detected in 33% of the 98 samples, of which six samples exceeded the NTR criterion. These exceedances included four samples from Lake Washington, with chlordane levels from 36 – 68 ug/kg, and catfish from two sites on the Snake River (Central Ferry and downstream of Lower Monumental Dam) which had 9.1 and 9.9 ug/kg. Fish from Lake Washington appear to contain the highest chlordane levels found in Washington, based on review of data in Ecology's EIM database.

11% of samples exceeded the NTR criterion for dieldrin. The highest levels (2.0-3.9 ug/kg) were found in fish from four lakes (Bead, Potholes, Rock, and Whatcom) and four rivers (Snake, Methow, Snohomish, and Cowlitz).

PBDE Flame Retardants

Like PCBs, higher levels of PBDEs (> 7 ug/kg) were found in fish from the Columbia, Snake, Spokane, Palouse, and Cowlitz Rivers, and Lake Washington.

Fish from the Spokane River had the highest levels of PBDEs (102-1136 ug/kg), followed by fish from Lake Washington (54-102 ug/kg). PBDE levels in these areas are described in more detail by Serdar and Johnson (2006) and DOH (2007). Generally, PBDE levels from the 2004-2005 WSTMP were within the range of values seen in a recent survey of PBDEs in Washington (Johnson et al., 2006).

Contaminants in Chinook Salmon

Chinook salmon were sampled to supplement data collected for this species by EPA in the Columbia River basin, WDFW in Puget Sound, and the U.S. Fish and Wildlife Service in two coastal fish hatcheries and two hatcheries in Puget Sound.

Table 3 shows contaminants detected in returning fall Chinook salmon from the Queets, Quinault, and Chehalis Rivers in 2004. Most results were near the reporting limit, yet PCBs, 2,3,7,8-TCDD TEQ, and toxaphene were detected at levels exceeding one or more of the NTR criteria, EPA's Recommended Water Quality Criteria, and EPA's Screening Values for Subsistence Fishers.

Contaminant levels detected in Chinook salmon from coastal rivers during this study were lower than levels found in several other studies.

Levels of PCBs in Chinook salmon collected in 2004 for the WSTMP were about six times lower than levels in Columbia River fall and spring Chinook salmon (37-38 ug/kg) sampled in 1996-98 (EPA, 2002b). Similarly, 2004 levels of 2,3,7,8-TCDD TEQs in coastal Chinook salmon were two to three times lower than levels found in fall and spring Chinook salmon (mean of 0.4 – 0.6 ng/kg) from the Columbia River basin during 1996-98 (EPA, 2002b).

Levels of total PCBs and total DDTs in coastal Chinook salmon collected during this study in 2004 were nearly ten times lower than the mean value (54 ug/kg PCBs and 21 ug/kg DDTs) of over 200 muscle tissue samples from Puget Sound Chinook salmon collected by WDFW during the 1990s (O'Neill et al., 1998; West et al., 2001; and Hardy and Palcisko, 2006). Mercury levels in Puget Sound Chinook salmon were about two times higher than those found in Chinook salmon from coastal rivers in 2004.

Missildine et al (2005) reported PCBs levels of 16-19 ug/kg in Chinook salmon that returned to the Makah National Fish Hatchery and the Quinault Tribal Hatchery in 2003. These hatcheries are located in the coastal Sooes and Quinault River basins. These PCB levels were about three times higher than levels found during the 2004 WSTMP.

Table 3. Contaminants in Chinook Salmon from Three Coastal Rivers.

Parameter	Chehalis		Queets		Quinault	
Total PCB Aroclors (ug/kg)	5.00		5.60		6.30	
Total PCB congeners (ug/kg)	5.12		4.71		4.44	
Total DDT (ug/kg)	2.63		2.56		3.53	
Total PBDE (ug/kg)	2.30		0.28		0.42	
Total Chlordane (ug/kg)	0.76		1.26		1.68	
2,3,7,8-TCDD TEQ (ng/kg)	0.09		0.23		0.22	
2,3,7,8-TCDD (ng/kg)	0.10	U	0.10	U	0.10	U
Mercury (mg/kg)	0.049		0.041		0.030	
Toxaphene (ug/kg)	5.7	J	9.7	NJ	9.7	U
Lipids (percent)	3.6		2.8		3.5	
Mean Age (years)	4.8		4.8		4.0	

U - not detected at given reporting limit.
J - The analyte was positively identified. The reported result is an estimate.
NJ - The analysis indicates the presence of an analyte that has been tentatively identified. The reported result is an estimate.

Comparisons to Historical Data

There were only two sites where the 2004-2005 results could be compared to historical data because the exploratory monitoring component of the WSTMP focuses on sites where no data exist. The two sites were the mid-Columbia River and the Cowlitz River. Comparison of recent and historical walleye results from Potholes Reservoir was not pursued because of dissimilar fish sizes.

Historical data were obtained from published EPA and Ecology reports or Ecology's EIM database. The same methods for deriving summed values were used among the recent and historical data to allow comparisons (e.g., total PCB Aroclors).

Columbia River: Hanford Reach to Wanapum Dam

Figure 2 shows that levels of DDTs and PCBs in one sample of mountain whitefish collected in 2004 just downstream of Wanapum Dam were lower than the mean value from three samples collected by EPA (2002b) in 1997 from the Hanford Reach by factors of about 2 and 9, respectively. The level of 2,3,7,8-TCDD TEQ in the 2004 sample was about five times lower than the mean 1997 value. The 2004 and 1997 samples contained fish having similar size, weight, and lipid content.

Dioxin/furan levels in a sample of walleye collected downstream of Wenatchee in 2004 were slightly lower than levels found in 1990 (Serdar et al., 1991). The TEQ for the 2004 sample of 0.13 ng/kg was about half of the 1990 mean TEQ of 0.25 ng/kg. The TEQ calculation for this comparison used only the TCDD and TCDF congeners. The fish used in the 2004 samples were also older and larger than those used in the 1990 sample; this strengthens the interpretation that contaminant levels have decreased over time.

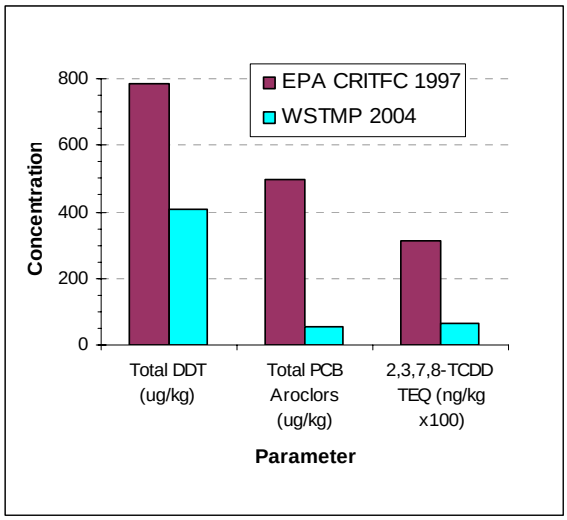

Figure 2. Comparison of Historical to Recent Data for Mountain Whitefish from the Mid-Columbia River: Hanford Reach to Wanapum Dam.

Cowlitz River near Vader

Levels of total PCB Aroclors in cutthroat trout and mountain whitefish from the Cowlitz River were slightly lower in the WSTMP 2005 samples (55 and 46 ug/kg) than in samples collected in 1995 (84 and 60 ug/kg) (Davis et al., 1998). Levels of total DDT in these two species were also lower in 2005 compared to those seen in 1995. The 2005 fish were also larger and had higher lipid content than those analyzed in 1995; this strengthens the interpretation that contaminant levels have decreased over time.

Water Quality Standards Exceeded

A total of 45 of the 49 sites where resident fish were collected had 93 fish tissue results exceeding the NTR criteria. Four contaminants accounted for 85% of these exceedances: total PCBs, 2,3,7,8-TCDD, 4,4'-DDE, and dieldrin. Other contaminants that exceeded criteria were 4,4'-DDD, mercury, total chlordane, hexachloro-benzene, and toxaphene. Table 4 shows the 93 cases recommended for Category 5 classification, *Does Not Meet Criteria*, in Ecology's 303(d) assessment (Ecology, 2006b).

Chinook salmon are excluded from the 303(d) assessment because they accumulate contaminants in the ocean environment which is outside of Ecology's ability to address contaminants in these fish.

A total of 36 sites had fish with 2,3,7,8-TCDD TEQs levels exceeding the NTR criterion for 2,3,7,8-TCDD. Ecology recently changed how dioxin/furan data are assessed (Ecology, 2006b), and TEQ values are no longer used for Category 5 classification. Therefore, these cases are recommended for Category 2 classification, *Waters of Concern* (Table 4).

A total of 159 analyses for toxaphene, aldrin, and dieldrin could not be compared to NTR criteria because the analyte was not detected at reporting limits that were greater than the respective criteria. These cases are recommended for a Category 3 classification, *Lack of Sufficient Data*. The remaining results (n=1761) that met NTR criteria are recommended for Category 1 classification, *Meets Tested Criteria*.

Site Ranking

In order to compare results across many species and sites, a scoring and ranking method was created. The scoring method used results for key contaminants that had high frequencies of detection and/or exceeded their respective benchmark values. The sample and site scores give an overall picture of how far contaminant levels in fish are above benchmark values.

This scoring and ranking method has not been applied to results from other fish tissue

Table 4. Recommended 303(d) Listings for 2004-2005 WSTMP Fish Tissue Sample Results.

Recommended Category for 303(d) Assessment -->			5									2
Site Name	Species Exceeding NTR Criteria	Sum Cat. 5	Total PCBs	2,3,7,8-TCDD	4,4'-DDE	4,4'-DDD	Dieldrin	Total Chlordane	Hexachloro-benzene	Toxaphene	Mercury	2,3,7,8-TCDD TEQ
Bead Lake	PEA, KOK, NPM	2	x	x								x
Black Lake	RBT	1	x									
Chehalis R, near Satsop	CTT, NPM	2	x								x	x
Columbia R, above Rock Island Dam	NPM, WAL, PEA	3	x		x	x						x
Columbia R, below Rocky Reach Dam	MWF	2	x		x							x
Columbia R, below Wanapum Dam	MWF	3	x		x	x						x
Columbia R, below Wells Dam	MWF	3	x		x	x						x
Columbia R, near Beebe Bridge	NPM, PEA	3	x		x	x						
Columbia R, near Cathlamet	NPM, PEA	2	x	x								x
Cowlitz R, near Vader	CTT, MWF, NPM	3	x	x							x	x
Haven Lake	RBT, CTT, LMB	2	x						x			x
Lake Washington, Entire	CCP, NPM	5	x	x	x	x		x				x
Lake Washington, North	CTT	2	x	x								x
Lake Washington, South	CTT	2	x	x								x
Leland Lake	LMB	3	x	x							x	x
Liberty Lake	SMB	1	x									
Long Lake, near Othello	SMB, WAL	1					x					
Loon Lake	LMB	2	x				x					x
Mayfield Reservoir	LMB, NPM	1	x									
Merwin Lake	NPM	1	x									x
Methow R, SE of Winthrop	CTT, MWF	1		x								x
Mountain Lake, Orcas Island	KOK	1	x									x
Northwestern Lake	RBT	1	x									x
Ozette Lake	NPM, LMB	1									x	x
Palouse R, Lower	NPM	2	x		x							x
Palouse R, North Fork	NPM	2	x		x							x
Palouse R, South Fork	NPM	3	x		x		x					x
Pend Oreille R, South	NPM	1	x									
Potholes Reservoir	LWF, SMB, WAL	4	x	x	x		x					x
Rock Lake	LMB, YP	1					x					
Sacajawea Lake, at Longview	GCP, LMB	1	x									
Silver Lake, near Castle Rock	CCP, LMB	2	x	x								x
Skagit R, near Burlington	CTT, MWF	1	x									x
Snake R, at Central Ferry	CC, LMB, PEA	5	x	x	x		x	x				x
Snake R, below Lower Monumental Dam	CC	6	x	x	x		x	x		x		x
Snake R, below Clarkston	MWF, PEA	3	x		x		x					x
Snake R, above Ice Harbor Dam	CCP, PEA	3	x	x	x							x
Snohomish R, above Snohomish	CTT, MWF, NPM	2	x	x								x
Spokane R, at Monroe St.	RBT	0										x
Spokane R, above Ninemile Dam	MWF	1		x								x
Spokane R, at Plante Ferry	RBT	1		x								x
Stan Coffin Lake	CC	1		x								x
Wenatchee R, near Leavenworth	MWF	2	x		x							x
Wenatchee R, near Wenatchee	MWF	2	x		x							
Whatcom Lake	CTT	2	x	x								x
Count of Recommended Category 5 or Category 2 Listings:		93	37	18	16	5	8	3	1	1	4	36
Percent of Recommended Category 5 Listings:			40%	19%	17%	5%	9%	3%	1%	1%	4%	

Species Codes: CC = Channel catfish, CCP = Common carp, CTT = Cutthroat trout, GCP = Grass carp, KOK = Kokanee salmon, LMB = Largemouth bass, LWF = Lake whitefish, MWF = Mountain whitefish, NPM = Northern pikeminnow, PEA = Peamouth, RBT = Rainbow trout, SMB = Smallmouth bass, WAL = Walleye, YP = Yellow perch.

Recommendations for listing are based on 2004/2005 data only. Some sites already listed are based on previous studies (example= Spokane River for PCBs)

studies conducted in Washington, so a statewide perspective is limited to sites sampled in 2004 and 2005 by the WSTMP.

Contaminant scores were first developed from results for each sample as described below. Sample contaminant scores from each site were then averaged to produce a site contaminant score. Site contaminant scores were then ranked from high to low to help show the relative amount of contamination in fish from sampled sites (Figure 3).

Table 5 shows the benchmark values that were used and the contaminant scores generated for three samples from one site. Levels of contaminants in each sample were divided by the benchmark value which produced a ratio of the contaminant concentration to the benchmark value. These ratios show whether individual contaminants are higher or lower than the benchmark values and by how much. These ratios were then summed to give a sample contaminant score, which is an overall indicator of the amount of toxic pollutants in each sample. Appendix D shows the fish species sampled at each site and the results for key contaminants. Results for Chinook salmon were excluded from this ranking process.

Contaminant scores for individual samples ranged from 1.1 for Silver Lake bluegill, where samples did not exceed any benchmark values, to 446 for Lake Washington carp, where benchmark values were exceeded for all contaminants except mercury. The median score for all samples was 4.6. PCBs, dioxin/furans, and total DDT contributed most to these scores. For example, the total PCB value of 1339 ug/kg in Lake Washington carp exceeded the benchmark value of 5.3 ug/kg by a factor of 253, accounting for about 57% of that sample's contaminant score of 446.

Table 5. Example Calculation of Contaminant Scores for Samples and Sites Using the Columbia River Site above Rock Island Dam.

		Sample Result Value			Ratio of Sample Result to Benchmark Value		
Contaminant	**Benchmark Value [1]**	**NPM**	**PEA**	**WAL**	**NPM**	**PEA**	**WAL**
Total PCB Aroclors (ppb)	5.3	52.0	15.0	46.0	9.81	2.83	8.68
Total DDT (ppb)	32	415	151	343	13.0	4.71	10.7
Total PBDE (ppb) [3]	31.0	10.8	6.18	21.9	0.35	0.20	0.71
Total Chlordane (ppb)	8.3	0.78	0.23	0.84	0.09	0.03	0.10
2,3,7,8-TCDD TEQ (ppt) [2]	0.07	0.442	na	0.318	6.31	na	4.54
Mercury (ppm)	0.825	0.515	0.110	0.644	0.62	0.13	0.78
Dieldrin (ppb)	0.65	nd	nd	nd	nd	nd	nd
Sample Contaminant Score:					**30.2**	**7.9**	**25.5**
Site Contaminant Score: [4]					**21.2**		

1 - Benchmark values are NTR criterion unless noted otherwise.
2 - Benchmark value is the NTR criterion for 2,3,7,8-TCDD.
3 - Benchmark value is the 90th percentile from statewide study of PBDEs (Johnson et al., 2006).
4 - The site contaminant score is the mean of the sample contaminant scores from that site.
na - Not analyzed, excluded from calculations. nd - Not detected, excluded from calculations.
Species Codes: NPM - northern pikeminnow, PEA - peamouth, WAL - walleye

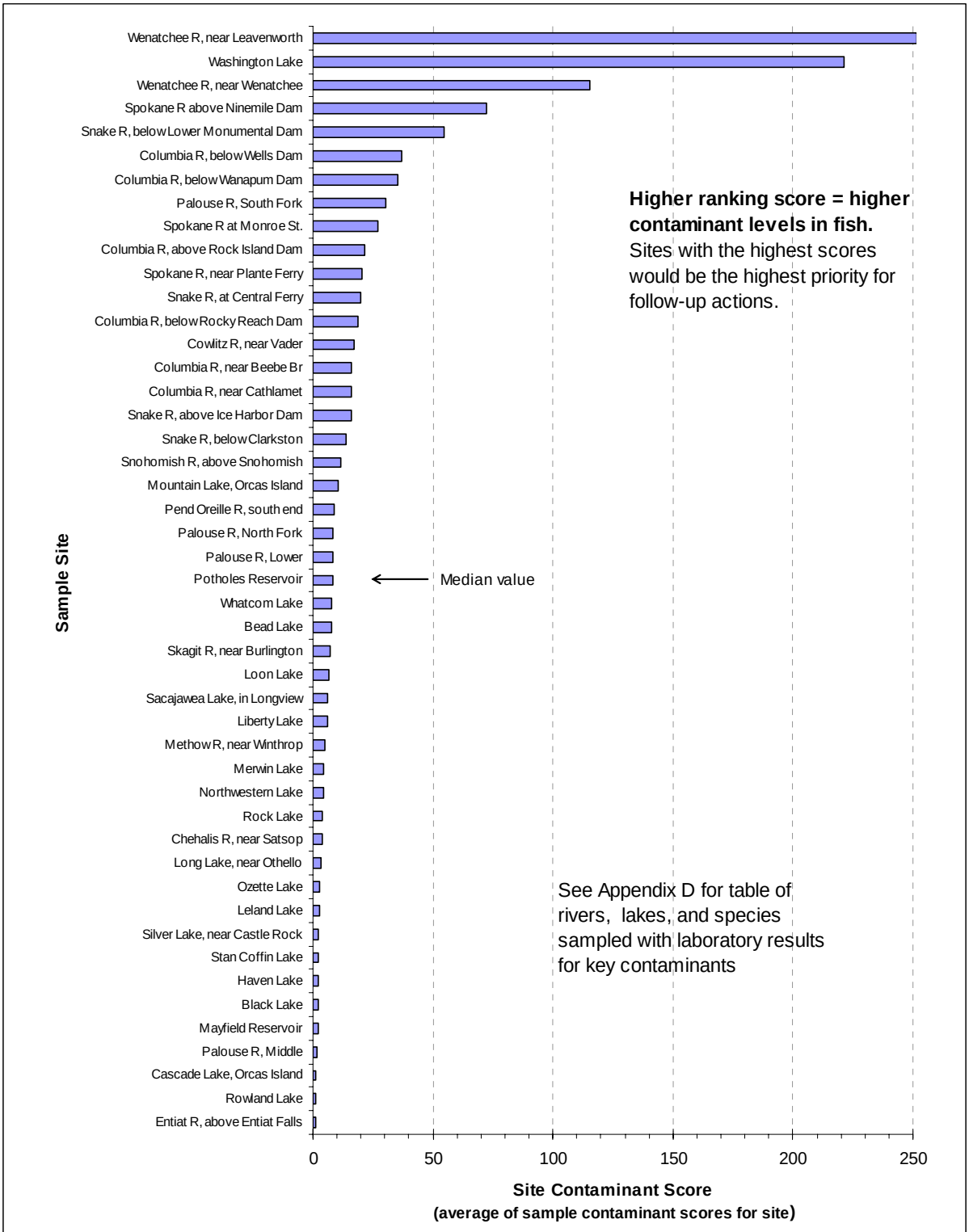

Figure 3. Site Ranking for the 2004-2005 WSTMP Fish Tissue Results.

Site contaminant scores ranged from 1.1 (Entiat River) to 252 (Wenatchee River near Leavenworth): the median score for sites was 8.1. Most sites had at least one sample that exceeded NTR criteria as described earlier and shown in Table 4.

The sites with the highest contaminant scores include Lake Washington and the Wenatchee, Spokane, Snake, Columbia, Palouse, and Cowlitz Rivers. The species having higher levels of contamination at these sites include mountain whitefish, common carp, northern pikeminnow, cutthroat trout, and channel catfish.

Chinook salmon from three coastal rivers had lower levels of contaminants than Chinook salmon from the Puget Sound basin and the Columbia River. Nevertheless, total PCBs and dioxin/furan levels in coastal river Chinook salmon exceeded NTR criteria and EPA's Screening Values for Subsistence Fishers.

Comparison of recent data to historical data was possible in two cases: (1) Levels of PCBs, dioxins/furans, and DDTs have likely decreased in fish from the mid-Columbia River area, and (2) Levels of PCBs and DDTs appear to have decreased in fish from the Cowlitz River near Vader.

Conclusions

PCBs, dioxin/furans, chlorinated pesticides, flame retardants, and mercury were frequently detected in 104 samples of fish from 52 lakes and rivers across Washington during 2004-2005.

A total of 45 sites had 93 fish tissue results that exceeded National Toxics Rule (NTR) criteria for contaminants in fish tissue. Four contaminants accounted for 85% of these exceedances: total PCBs, 2,3,7,8-TCDD, 4,4'-DDE, and dieldrin. Other contaminants exceeding NTR criteria were 4,4'-DDD, mercury, total chlordane, hexachloro-benzene, and toxaphene.

The highest levels of contamination were in fish from Lake Washington and the Wenatchee, Spokane, Snake, Columbia, Palouse, and Cowlitz Rivers. Larger rivers and highly urbanized lake basins (e.g., Lake Washington) generally had fish with higher levels of contaminants. Older, larger, and more piscivorous fish generally had greater occurrences and levels of contaminants.

Recommendations

The Washington State Department of DOH, local health jurisdictions, and affected Tribes should evaluate the results from this study and determine the need for additional sampling in order to assess the risks to human health from the consumption of contaminated fish.

Ecology should review the fish tissue data from the 45 sites listed in Table 4 for placement in Categories 5 and 2 of Washington State's 303(d) assessment. Other results from this 2004-2005 sampling effort should be reviewed and corresponding sites placed in Categories 1 and 3 of the 303(d) assessment.

Ecology should determine what action to take for the most contaminated sites identified in this study, particularly Lake Washington and the Wenatchee, Spokane, Snake, and Columbia Rivers.

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Appendices

Appendix A. Site and Species Sampled for the WSTMP, 2004-2005

Site	County	WRIA	Species
2004 WSTMP Sample Year			
Black L	Thurston	23	RBT
Cascade L, Orcas Is	San Juan	2	KOK, LMB, RBT
Chehalis R, nr Aberdeen	Grays Harbor	22	CHK
Chehalis R, nr Satsop	Grays Harbor	22	CTT, NPM
Columbia R, abv Rock Is Dam	Chelan-Douglas	44	NPM, PEA, WAL
Columbia R, blw Rocky Reach Dam	Chelan-Douglas	45	MWF
Columbia R, blw Wanapum Dam	Kittitas-Grant	41	MWF
Columbia R, blw Wells Dam	Chelan-Douglas	47	MWF
Columbia R, nr Beebe Bridge	Chelan-Douglas	47	NPM, PEA
Entiat R	Chelan	46	RBT
Mountain L, Orcas Is	San Juan	2	KOK
Ozette L	Clallam	20	CTT, LMB, NPM, YP
Pend Oreille R, South	Pend Oreille	62	NPM
Queets R	Jefferson	21	CHK
Quinault R	Grays Harbor	21	CHK
Skagit R, nr Burlington	Skagit	3	CTT, MWF, PEA
Snake R, at Central Ferry	Columbia-Garfield-Whitman	35	CC, LMB, PEA, YP
Snake R, blw Lower Monumental Dam	Franklin-Walla Walla	33	CC
Snake R, ds of Clarkston	Whitman-Asotin	35	LMB, MWF, PEA
Wenatchee R, nr Leavenworth	Chelan	45	MWF
Wenatchee R, nr Wenatchee	Chelan	45	MWF
2005 WSTMP Sample Year			
Bead L	Pend Oreille	62	BUR, KOK, NPM, PEA
Columbia R, nr Cathlamet	Wahkiakum	25	NPM, PEA
Cowlitz R, nr Vader	Cowlitz	26	CTT, MWF, NPM
Haven L	Mason	15	CTT, LMB, RBT
Lake Washington, Entire	King	8	CCP, NPM
Lake Washington, North	King	8	CTT
Lake Washington, South	King	8	CTT
Leland L	Jefferson	17	BC, BG, LMB, YP
Liberty L	Spokane	57	SMB
Long L, nr Othello	Grant	41	SMB, WAL
Loon L	Stevens	59	LMB
Mayfield Res.	Lewis	26	LMB, NPM, YP
Merwin L	Lewis	27	KOK, NPM
Methow R, SE of Winthrop	Okanogan	48	CTT, MWF
Northwestern L	Skamania-Klickitat	29	RBT
Palouse R, Lower	Whitman-Adams	34	NPM
Palouse R, Middle	Whitman	34	SMB
Palouse R, North Fork	Whitman	34	NPM
Palouse R, South Fork	Whitman	34	NPM
Potholes Res	Grant	41	LWF, SMB, WAL
Rock L	Whitman	34	BNT, LMB, YP
Rowland L	Klickitat	29	BG, LMB, YP
Sacajawea L, at Longview	Cowlitz	25	GCP, LMB
Silver L, nr Castle Rock	Cowlitz	26	BG, CCP, LMB
Snake R, ups of Ice Harbor Dam	Franklin-Walla Walla	33	CCP, PEA, YP
Snohomish R, ups of Snohomish	Snohomish	7	CTT, MWF
Spokane R, at Monroe St.	Spokane	57	RBT
Spokane R, at Ninemile	Spokane	54	MWF
Spokane R, at Plante Ferry	Spokane	57	RBT
Stan Coffin L	Grant	41	CC, LMB, YP
Whatcom L	Whatcom	1	CTT, PEA, SMB, YP

Species Codes: BC = Black crappie, BG = Bluegill, BNT = Brown trout, BUR = Burbot, CC = Channel catfish, CCP = Common carp, CHK = chinook salmon, CTT = Cutthroat trout, GCP = Grass carp, KOK = Kokanee salmon, LMB = Largemouth bass, LWF = Lake whitefish, MWF = Mountain whitefish, NPM = Northern pikeminnow, PEA = Peamouth, RBT = Rainbow trout, SMB = Smallmouth bass, WAL = Walleye, YP = Yellow perch.

Appendix B. National Toxics Rule Criteria, National Recommended Water Quality Criteria, and EPA Screening Values for the Protection of Human Health for Contaminants Detected in Fish Tissue, WSTMP 2004-2005

Analyte (ppb ww)[1]	National Toxics Rule	National Recommended Water Quality Criteria [2]	EPA Screening Values			
			Subsistence Fishers		Recreational Fishers	
			Non-carcino-gens	Carcino-gens	Non-carcino-gens	Carcino-gens
Mercury	825	300	49	-	400	-
Total PCBs [3]	5.3	2.0	9.83	2.45	80	20
2,3,7,8-TCDD [4]	0.07	-	-	-	-	-
2,3,7,8-TCDD TEQ [4, 5]	-	0.026	-	0.0315	-	0.256
4,4'-DDD	45	17	-	-	-	-
4,4'-DDE	32	12	-	-	-	-
4,4'-DDT	32	12	-	-	-	-
Total DDT [6]	-	-	245	14.4	2000	117
Chlordane [7]	8.3	11	245	14.0	2000	114
Aldrin	0.65	0.23	-	-	-	-
Alpha-BHC	1.7	0.64	-	-	-	-
Beta-BHC	6.0	2.2	-	-	-	-
Chlorpyriphos	-	-	147	-	1200	-
Chlorthal-Dimethyl (Dacthal)	-	-	-	-	-	-
Dieldrin	0.65	0.25	24	0.307	200	2.5
Endosulfan Sulfate	540	24000	-	-	-	-
Endrin	3200	230	147		1200	
Heptachlor Epoxide	1.2	0.44	6.39	0.54	52	4.39
Hexachlorobenzene	6.7	2.5	393	3.07	3200	25.0
gamma-BHC (Lindane)	8.2	230	147	3.8	1200	30.7
Methoxychlor	-	-	-	-	-	-
Mirex	-	-	98	-	800	-
Pentachloroanisole	-	-	-	-	-	-
Toxaphene	9.8	3.7	122	4.46	1000	36.3
PBDEs	-	-	-	-	-	-

1. Values in parts per billion wet weight (ug/kg ww) unless otherwise noted.
2. EPA 2001 for methylmercury, EPA 2003 for endrin and gamma-BHC, EPA 2002 for others.
3. Total PCBs is sum of Aroclors or congeners.
4. Values in parts per trillion wet weight (ng/kg ww).
5. The cumulative toxicity of a mix of congeners is expressed as Toxic Equivalent (TEQ) to 2,3,7,8-TCDD.
6. Total DDT is the sum of 2,4'- and 4,4'- isomers of DDD, DDE, and DDT.
   DDD = p,p'-dichlorodiphenyldichloroethane. DDE = p,p'-dichlorodiphenyldichloroethylene.
   DDT = p,p'-dichlorodiphenyltrichloroethane
7. The NTR criterion for chlordane is interpreted as the sum of five chlordane components: these can be individually quantified through laboratory analyses while chlordane cannot. The EPA Screening Values are for "Total chlordane" which is the sum of five compounds: cis- and trans- chlordane, cis- and trans- nonachlor, and oxychlordane.

Note: The NTR Criteria and National Recommended Water Quality Criteria for fish tissue are calculated using water column concentrations (the human health water quality criteria for consumption of organisms only: column D2 of the matrix in 40 CFR 131.36) and bioconcentration factors from EPA's 1980 Ambient Water Quality Criteria documents.

Appendix C. Data Evaluation by Ecology and DOH

Several state and federal agencies collect and evaluate fish tissue data in Washington State. These include the Washington State Departments of Ecology, Health (DOH), and Fish and Wildlife; the U.S. Environmental Protection Agency; and the U.S. Geological Survey. Tissue data are evaluated differently by these agencies because their mandates and roles are varied. These multiple evaluations often lead to confusion and misunderstanding among agencies and the public on how fish tissue data are used and interpreted. Adding to potential confusion are the numerous criteria or screening values derived to provide guidance for determining the risks of consuming contaminated fish and protecting public health.

Most fish tissue contaminant data from Washington fish, regardless of who conducted the study, make their way to DOH for evaluation regarding the safety of consuming contaminated fish. The following is an overview of how Ecology and DOH evaluate fish tissue data to meet different needs.

For the WSTMP and many other Ecology studies, fish tissue data are evaluated primarily to determine two things (1) if Washington State water quality standards are being met, and (2) if potential risks to human health from consuming contaminated fish warrant further study and/or development of a fish consumption advisory. Ecology's role is to determine whether water quality standards are met and to begin the process to correct problems where standards are not met. DOH and local health departments are responsible for developing fish consumption advisories in Washington. There is some overlap in these evaluations because the water quality standards that fish tissue data are compared to were developed for the protection of human health.

Washington State Water Quality Standards

Washington's water quality standards criteria for toxic contaminants were issued to the state in EPA's 1992 National Toxics Rule (NTR) (40CFR131.36). The human health-based NTR criteria are designed to minimize the risk of effects occurring to humans from chronic (lifetime) exposure to substances through the ingestion of drinking water and consumption of fish obtained from surface waters. *The NTR criteria, if met, will generally ensure that public health concerns do not arise, and that fish advisories are not needed.*

The NTR criteria are thresholds that, when exceeded, may lead to regulatory action. When water quality criteria are exceeded, the federal Clean Water Act requires that the waterbody be put on a list and that a water cleanup plan be developed for the pollutant causing the problem. This list is known as the 303(d) list, and the water cleanup plan results from a Total Maximum Daily Load (TMDL) study and public involvement process. Ecology uses the TMDL program to control sources of the particular pollutant in order to bring the waterbody back into compliance with the water quality standards.

Risk Management Decisions

While DOH supports Ecology's use of the NTR criteria for identifying problems and controlling pollutant sources so that water quality will meet standards, DOH does not use the NTR criteria to establish fish consumption advisories (McBride, 2006). DOH uses an approach similar to that in EPA's *Guidance for Assessing Chemical Contaminant Data for use in Fish Advisories Vol. 1-4* for assessing mercury, PCBs, and other contaminants (EPA, 2000). These guidance documents provide a framework from which states can evaluate fish tissue data to develop fish consumption advisories, based on sound science and established procedures in risk assessment, risk management, and risk communication. Neither the NTR criteria, nor the Screening Values found in the EPA guidance documents above, incorporate the varied risk management decisions essential to developing fish consumption advisories.

- **Risk Assessment** involves calculating allowable meal limits based on known fish contaminant concentrations. These calculations are conducted for both non-cancer and cancer endpoints using the appropriate Reference Dose (RfD) or Cancer Slope Factor (CSF), if available. These initial calculations are the starting point for evaluating contaminant data to determine whether a fish advisory is warranted. Additionally, known or estimated consumption rates help determine the potential magnitude of exposure and highlight the sensitive groups or populations that may exist due to elevated consumption rates.

- **Risk Management** includes (but is not limited to) consideration of contaminant background concentrations, reduction in contaminant concentrations through preparation and cooking techniques, known health benefits from fish consumption, contaminant concentrations or health risks associated with replacement foods, and cultural importance of fish. Other considerations are the possible health endpoints associated with a contaminant, the strength or weaknesses of the supporting toxicological or sampling data, and whether effects are transient or irreversible.

- **Risk Communication** is the outreach component of the fish advisory. The interpretation of the data from the risk assessment and risk management components drives how and when the fish advisory recommendations are issued to the public dependent on whether the message is targeted toward a sensitive group or a population or the general public. DOH's dual objective in messaging is how best to provide guidance to the public to increase fish consumption of fish low in contaminants to gain the benefits of eating fish while at the same time steering the public away from fish that have high levels of health-damaging contaminants.

Appendix D. Summary of Fish Tissue Sample Results

Site	Species Code	MEL Sample ID	WSTMP Study Year	Date collect	Total PCB aroclors (ug/kg)	q	Total PCB congeners (ug/kg)	q	T-DDT (ug/kg)	q	Total PBDE (ug/kg)	q	Total Chlordane (ug/kg)	q	2378 TCDD TEQ (ng/kg)	q	2378 TCDD (ng/kg)	q	Mercury (mg/kg)	q	Lipid MEL (%)	q	Lipid CL (%)	q	Mean Total Length (mm)	Mean Weight (g)	Mean Age (years)
Bead L	BUR	05514700	2005	10/26/05	5.0	U			1.4		6.2	UJ	1.0	U					0.130		0.4				650	1846	5.6
Bead L	KOK	05514701	2005	10/26/05	16				16		2.6		0.95	U					0.030		1.7				267	178	3.0
Bead L	NPM	05514702	2005	10/26/05	36		21		29		4.1		0.99	U	1.04		0.134		0.260		8.2		8.1		503	1643	11.0
Bead L	PEA	05514703	2005	10/26/05	5.7				2.5		0.29		0.88	U					0.170		1.4				245	107	7.4
Black L	RBT	05084284	2004	9/16/04	9.1				1.1		4.8		0.29						0.100		1.9				292	229	1.9
Cascade L, Orcas Is	KOK	05084286	2004	9/30/04	4.8	U			0.53		1.6		0.96	U					0.199		2.8				415	686	2.0
Cascade L, Orcas Is	KOK	05084285	2004	9/30/04	4.9	U			0.32		2.9		0.97	U					0.241		5.3				205	87	1.0
Cascade L, Orcas Is	LMB	05084287	2004	9/29/04	4.7	U			0.33		0.39		0.94	U					0.194		1.0				304	448	2.3
Cascade L, Orcas Is	RBT	05084288	2004	9/29/04	4.9	U	1.1		0.49		2.4	UJ	0.94	U					0.201		0.7		1.3		303	280	1.1
Chehalis R, nr Aberdeen	CHK	05084289	2004	10/18/04	5.0		5.1		2.6		2.3		0.76		0.089		0.100	U	0.049		3.6		3.3		910	7938	4.8
Chehalis R, nr Satsop	CTT	05084280/4290	2004	9/8/04	9.6	m	13	m	8.9	m	0.88	m	0.36	m	0.099	m	0.100	U	0.054	m	4.0	m	5.6	m	330	376	3.0
Chehalis R, nr Satsop	NPM	05084291	2004	9/8/04	13		17		4.5		2.7		0.49						0.964		0.6		1.4		415	650	8.9
Columbia R, abv Rock Is Dam	NPM	05084292	2004	11/2/04	52		88		415		11		0.78		0.442		0.100	U	0.515		1.8		2.0		400	614	8.4
Columbia R, abv Rock Is Dam	PEA	05084293	2004	11/2/04	15				151		6.2		0.23						0.110		2.3				257	159	4.0
Columbia R, abv Rock Is Dam	WAL	05084294	2004	11/3/04	46		108		343		22		0.84		0.318		0.100	U	0.644		2.6		6.4		652	3601	9.0
Columbia R, blw Rocky Reach Dam	MWF	05084295	2004	11/3/04	36		75		112		10		0.39		0.550		0.100	U	0.022		3.0		3.3		279	187	1.6
Columbia R, blw Wanapum Dam	MWF	05084296	2004	11/4/04	54		91		406		50		2.4		0.652		0.150		0.042		6.9		6.7		355	472	3.3
Columbia R, blw Wells Dam	MWF	05084281/4297	2004	10/28/04	71	m	92	m	430	m	40	m	1.5	m	0.606	m	0.115	U	0.073	m	4.3	m	5.4	m	353	454	3.6
Columbia R, near Cathlamet, RM 38-42	NPM	06024738	2005	8/30/05	76		46		32		17		2.5		0.345		0.110		0.596		2.0		2.5		466	956	9.2
Columbia R, near Cathlamet, RM 38-42	PEA	05524720	2005	8/30/05	47				27		13		1.0	U					0.140		1.6				275	189	6.4
Columbia R, nr Beebe Br	NPM	05084298	2004	10/26/04	31		65		509		18		0.51						0.456		2.4		4.6		431	766	7.4
Columbia R, nr Beebe Br	PEA	05084299	2004	10/26/04	14				197		4.4		0.23						0.130		1.4				259	155	4.3
Cowlitz R, 8 mi N Castle Rock, RM 24-27	CTT	05514704/4705	2005	8/29/05	55	m	24	m	29	m	5.0	m	0.97	U	0.303	m	0.131	m	0.087	m	4.7	m	5.3	m	360	493	3.0
Cowlitz R, 8 mi N Castle Rock, RM 24-27	MWF	05514706	2005	8/29/05	46				6.2		24		0.88	U					0.205		6.8				441	859	5.6
Cowlitz R, 8 mi N Castle Rock, RM 24-27	NPM	05514707	2005	8/29/05	92		56		21		18		0.93	U	0.410		0.124		0.859		1.8		1.7		427	656	10.6
Entiat R, abv Entiat Falls	RBT	05084300	2004	10/12/04	4.9	U	3.8		2.8		0.99		0.22						0.037		2.8		5.0		169	42	3.0
Haven L	CTT	06054771	2005	11/29/05	5.0	U			1.3		2.5		0.99	U					0.192		2.3				250	137	2.0
Haven L	LMB	06054770	2005	11/29/05	4.7	U			1.3		2.3		0.94	U					0.079		1.3				315	528	1.6
Haven L	RBT	06054769	2005	11/29/05	5.0	U	6.3		1.2		1.1		1.0	U	0.186		0.068		0.130		1.0		1.1		365	463	1.2
Leland L	BC	06054752	2005	9/14/05	4.7	U			0.95	U	0.43		0.95	U					0.120		0.8				227	185	2.0
Leland L	BG	06054753	2005	9/14/05	4.8	U			0.97	U	6.0	UJ	0.97	U					0.130		0.8				168	101	2.0
Leland L	LMB	05514708	2005	9/14/05	11		6.2		1.9		1.5		0.96	U	0.181		0.122		0.834		0.9		1.0		481	1776	11.0
Leland L	YP	06054754	2005	9/14/05	4.9	U			0.98	U	6.1	UJ	0.98	U					0.196		0.5				217	131	2.2
Liberty L	SMB	06054755/4756	2005	10/11/05	24	m	11		23	m	3.2	m	0.99	m	0.048		0.044	J	0.154	m	1.6	m	1.7		375	764	3.8
Long L, 8 mi N of Othello	SMB	05514709	2005	8/24/05	4.9	U			3.0		6.1	UJ	0.98	U					0.110		1.0				303	397	3.2
Long L, 8 mi N of Othello	WAL	05514710	2005	8/24/05	4.5	U			9.6		0.34		0.90	U					0.207		1.3				437	765	3.4
Loon L	LMB	06054757	2005	10/26/05	16		11		5.7		1.7		0.92	U	0.084		0.066		0.280	n	1.4		2.0		455	1767	10.2
Mayfield Res.	LMB	05524721	2005	9/15/05	5.5		3.4		0.97	U	2.0		0.97	U	0.050	UJ	0.030	UJ	0.242		0.9		1.0		328	610	4.2
Mayfield Res.	NPM	05524722	2005	9/15/05	8.9		5.0		2.5		2.3		0.98	U	0.009		0.030	UJ	0.474		1.5		1.7		312	244	6.4

Site	Species Code	MEL Sample ID	WSTMP Study Year	Date collect	Total PCB aroclors (ug/kg)	q	Total PCB congeners (ug/kg)	q	T-DDT (ug/kg)	q	Total PBDE (ug/kg)	q	Total Chlordane (ug/kg)	q	2378 TCDD TEQ (ng/kg)	q	2378 TCDD (ng/kg)	q	Mercury (mg/kg)	q	Lipid MEL (%)	q	Lipid CL (%)	q	Mean Total Length (mm)	Mean Weight (g)	Mean Age (years)
Mayfield Res.	YP	05524723	2005	9/15/05	5.0	U			1.0	U	0.38		1.0	U					0.084		0.5				237	164	4.0
Merwin Lake	KOK	06054758	2005	11/1/05	5.0	U			1.5		5.7		1.0	U					0.078		1.5				370	487	2.0
Merwin Lake	NPM	06054759	2005	11/1/05	20		10		4.9		5.6		0.95	U	0.219		0.059		0.373		2.1		1.4		436	919	6.8
Methow R, 2 mi SE of Winthrop, RM 47-49	CTT	05524724	2005	10/20/05	4.9	U	1.9		9.2		2.6		0.98	U	0.304		0.097		0.028		2.4		2.0		291	241	4.2
Methow R, 2 mi SE of Winthrop, RM 47-49	MWF	06024740	2005	10/20/05	4.9	U	1.3		1.4		11		0.99	U	0.214		0.083		0.037		3.9		2.5		358	505	4.8
Mountain L, Orcas Is (natural repro)	KOK	05084301	2004	9/29/04	4.8	U	10		3.4		0.75		0.47		0.627		0.100	U	0.076		3.7		3.8		271	179	3.1
Northwestern Lake	RBT	06054760	2005	11/2/05	8.7		5.7		3.7		0.76		0.98	U	0.133		0.046	J	0.295		1.7		0.9		349	426	2.4
Ozette L	CTT	05084302	2004	10/6/04	4.8	U			0.21		6.0	UJ	0.96	U					0.279		1.7				273	171	3.7
Ozette L	LMB	05084303	2004	10/6/04	4.9	U			0.98	U	6.1	UJ	0.98	U					0.910		0.7				371	840	4.4
Ozette L	NPM	05084304	2004	10/6/04	5.0	U	0.9		0.57			R	1.0	U	0.195		0.100	U	0.724		0.9		3.0		371	464	7.2
Ozette L	YP	05084305	2004	10/6/04	4.7	U			0.95	U	5.9	UJ	0.95	U					0.240		0.5				211	108	2.0
Palouse R, Lower	NPM	05514711	2005	6/23/05	20		11		44		7.5		0.97	U	0.128		0.033	J	0.749	p	2.0		1.9		458	940	7.0
Palouse R, Middle	SMB	05514712	2005	6/6/05	5.0	U			7.6		3.8		0.99	U					0.120	p	0.5				178	72	2.0
Palouse R, North Fork	NPM	05514713	2005	6/9/05	22				80		6.9		0.94	U	0.101		0.030	UJ			2.9		3.0		351	419	7.1
Palouse R, South Fork	NPM	05514714	2005	5/24/05	109		35		57		42		0.97	U	0.211		0.055		0.465	p	1.1		0.4		354	442	9.8
Pend Oreille R, south end	NPM	05084319	2004	8/18/04	38		34		8.1		11		0.53						0.825		2.5		4.8		391	758	12.1
Potholes Res	LWF	06024741	2005	10/25/05	17		6.0		60		1.9		6.7		0.326		0.153		0.046		17		18		576	2524	6.2
Potholes Res	SMB	06024742	2005	10/26/05	4.4	U			4.3		0.62		0.88	U					0.118	n	1.9				451	1386	5.8
Potholes Res	WAL	06024743	2005	10/25/05	5.2				18		0.46		1.0	U					0.170		1.7				578	1999	4.2
Queets R	CHK	05084306	2004	10/18/04	5.6		4.7		2.6		0.28		1.3		0.233		0.100	U	0.041		2.8		4.7		932	7983	4.8
Quinault R	CHK	05084307	2004	10/18/04	6.3		4.4		3.5		0.42		1.7		0.218		0.100	U	0.030		3.5		4.9		868	7892	4.0
Rock L	BNT	05524725	2005	8/23/05	4.9	U			8.5		0.60		0.97	U					0.021		4.2				259	187	1.0
Rock L	LMB	05524726	2005	8/23/05	4.9	U			2.7		0.58		0.98	U					0.044		1.0				272	346	2.8
Rock L	YP	05524727	2005	8/24/05	4.7	U			7.9		0.44		0.94	U					0.160		0.8				316	499	6.0
Rowland L	BG	06054761	2005	9/7/05	4.9	U			0.98	U	6.1	UJ	0.98	U					0.044		0.6				175	106	3.1
Rowland L	LMB	06054762	2005	9/7/05	4.9	U			3.6		1.1		0.98	U					0.120		0.8				370	740	3.6
Rowland L	YP	06054763	2005	9/7/05	4.9	U			0.98	U	6.1	UJ	0.98	U					0.036		0.7				218	119	2.5
Sacajawea L @ Longview	GC	05514715	2005	9/14/05	30				2.2		0.56		1.0	U					0.017	U	1.2				447	1249	1.0
Sacajawea L @ Longview	LMB	06024744	2005	9/14/05	29		17		2.3		0.86		0.95	U	0.068		0.049	J	0.059		1.0		0.5		342	692	2.0
Silver L, near Castle Rck	BG	06054764	2005	9/22/05	4.8	U			0.96	U	0.28		0.96	U					0.020		1.7				164	95	2.0
Silver L, near Castle Rck	CCP	05514716	2005	9/22/05	6.8		5.6		1.3		0.33		0.94	U	0.130		0.083		0.043		2.0		1.8		521	2313	4.8
Silver L, near Castle Rck	LMB	06054765	2005	9/22/05	4.8	U	2.7		1.4		0.34		0.95	U	0.094		0.030	UJ	0.079	n	0.7		0.8		352	695	3.6
Skagit R, nr Burlington	CTT	05084308	2004	10/4/04	36		22		7.3		14		0.69		0.220		0.100	U	0.140		3.1		6.3		370	501	4.0
Skagit R, nr Burlington	MWF	05084309	2004	10/5/04	19		12		6.1		7.8		0.62		0.299		0.100	U	0.076		1.4		6.5		245	103	2.5
Skagit R, nr Burlington	PEA	05084310	2004	10/5/04	4.9	U			3.0		2.6		0.99	U					0.241		1.6				250	151	6.2
Snake R, at Central Ferry (L Bryan)	CC	05084311	2004	12/1/04	148		65		389		14		9.9		1.12		0.370		0.283		13		11		565	1842	12.0
Snake R, at Central Ferry (L Bryan)	LMB	05084312	2004	12/1/04	11				9.3		0.47		1.0	U					0.092		0.7				295	399	2.1
Snake R, at Central Ferry (L Bryan)	PEA	05084313	2004	12/1/04	10				29		2.1		0.91	U					0.264		2.2				284	186	5.1
Snake R, at Central Ferry (L Bryan)	YP	05084314	2004	12/1/04	5.0	U			5.9		6.2	UJ	1.0	U					0.196		0.5				258	232	3.3

Site	Species Code	MEL Sample ID	WSTMP Study Year	Date collect	Total PCB aroclors (ug/kg)	q	Total PCB congeners (ug/kg)	q	T-DDT (ug/kg)	q	Total PBDE (ug/kg)	q	Total Chlordane (ug/kg)	q	2378 TCDD TEQ (ng/kg)	q	2378 TCDD (ng/kg)	q	Mercury (mg/kg)	q	Lipid MEL (%)	q	Lipid CL (%)	q	Mean Total Length (mm)	Mean Weight (g)	Mean Age (years)
Snake R, blw Lower Monumental Dam	CC	05084283/4315	2004	11/8/04	111	m	165		373	m	26	m	9.1		1.11		0.520	U	0.347	m	7.2	m	7.3		491	1162	11.5
Snake R, ds Clarkston at Chief Timothy park	LMB	05084316	2004	11/30/04	4.2	U			22		1.8		0.85	U					0.140		0.7				283	346	1.9
Snake R, ds Clarkston at Chief Timothy park	MWF	05084317	2004	11/29/04	106		70		38		9.4		0.98	U	0.413		0.100	U	0.120		2.0		1.4		299	231	2.5
Snake R, ds Clarkston at Chief Timothy park	PEA	05084318	2004	11/30/04	26				86		12		0.47						0.296		1.9				273	155	4.3
Snake R, ups Ice Harbor Dam, RM 11-12	CCP	06024751	2005	11/14/05	115		65		146		30		5.1		0.417		0.100		0.180		5.4		1.7		675	4207	13.6
Snake R, ups Ice Harbor Dam, RM 11-12	PEA	05524731	2005	11/14/05	43				22		2.5		0.98	U					0.190		1.8				286	4207	5.4
Snake R, ups Ice Harbor Dam, RM 11-12	YP	05524730	2005	11/14/05	4.9	U			6.7		0.60		0.99	U					0.045		0.6				204	94	1.2
Snohomish R, ups Snohomish, RM 15-18	CTT	05524728	2005	9/1/05	42		32		4.7		26		0.99	U	0.304		0.097		0.120		3.6		6.2		375	526	3.4
Snohomish R, ups Snohomish, RM 15-18	MWF	06024749/4745	2005	9/1/05	20	m	9.5	m	3.2	m	32	m	0.98	U	0.243	m	0.077	m	0.076	m	4.1	m	3.5	m	304	268	3.8
Snohomish R, ups Snohomish, RM 15-18	NPM	06024746	2005	9/1/05	48		30		3.7		12		1.5		0.100		0.077		0.696		2.5		1.8		332	372	4.4
Spokane R nr Monroe St., RM 75.2	RBT	05524735	2005	9/28/05	120	s					30	s			0.248		0.032	J			1.5		1.8		358	433	3.0
Spokane R nr Ninemile, RM 64.0	MWF	05524736	2005	9/29/05	129	s					1136	s			0.809		0.083				3.4		2.3		335	337	4.7
Spokane R nr Plante Ferry, RM 85.0	RBT	05524737	2005	8/23/05	58	s					102	s			0.448		0.096				3.4		2.2		400	625	2.7
Stan Coffin L	CC	06054766	2005	9/6/05	4.6	U	2.4		7.2		0.55		0.92	U	0.175		0.082		0.029		3.5		5.1		548	1589	6.6
Stan Coffin L	LMB	06054767	2005	9/6/05	5.0	U			1.8		6.2	UJ	2.0	U					0.150		0.7				349	732	5.0
Stan Coffin L	YP	06054768	2005	9/6/05	4.9	U			0.99	U	6.2	UJ	0.99	U					0.042		0.4				187	76	2.6
Washington L	CCP	05524717	2005	6/28/05	1339		611		418		54		68		11.9		1.93		0.160		9.0		11		698	5559	17.0
Washington L	NPM	05524734	2005	3/9/05	375	w	241		103	w	61	w	37	w	5.75		0.684		0.531	w	3.8		4.8		430	917	5.7
Washington L, North	CTT	05524732	2005	3/3/05	233	w	292		117	w	64	w	37	w	4.64		0.741		0.277	w	3.8		4.2		433	934	3.4
Washington L, South	CTT	05524733	2005	3/1/05	370	w	384		115	w	102	w	66	w	4.88		0.876		0.308	w	3.1		5.9		437	1027	4.0
Wenatchee R, nr Leavenworth	MWF	05084320	2004	11/18/03	1300		1632		43		7.2		3.4	UJ	0.315		0.100		0.028		3.0		3.3		271	182	2.4
Wenatchee R, nr Wenatchee	MWF	05084321	2004	11/18/03	542				378		40		0.32						0.050		3.9				297	226	3.4
Whatcom L	CTT	06024747	2005	10/12/05	40		23		7.2		13		6.2		0.563		0.156		0.364		2.8		2.7		401	615	4.2
Whatcom L	PEA	05524729	2005	10/12/05	18				3.7		1.9		1.6						0.245		2.1				266	183	10.8
Whatcom L	SMB	06024750	2005	10/12/05	29				2.3		5.4		4.2						0.425		2.4				417	1178	6.0
Whatcom L	YP	06024748	2005	10/12/05	4.9	U			0.97	U	0.17		0.97	U					0.423		0.5				331	496	6.2

Data Qualifiers and Notes

U = The analyte was not detected at or above the reported value.

UJ = The analyte was not detected at or above the reported estimated result.

R = Rejected (due to poor data quality and apparent spurious value of 31.62 ppb)

m = mean value from analyses of field duplicates where two results are available. Where analysis was not done on only one sample, that sample result is given. Where both values were non-detect, the highest value was used. Where one duplicate was qualified as a non-detect (U, UJ), the reported value was used in determining the mean value.

n = mean value of 10 individuals: individual fish results from Mercury Trends in Fish project, (C. Furl, in preparation).

s = values from Spokane R study by Serdar and Johnson, ECY pub # 06-03-025. Values are means from multiple samples from other study that were combined to make a WSTMP sample for contract lab analyses of PCB congeners and PCDD/Fs.

p = values from Palouse R study by Johnson et al (in preparation). Values are from corresponding sample or from means from multiple samples from other study that were combined to make a WSTMP sample for contract lab analyses of PCB congeners and PCDD/Fs. Value for sample 05514711 is based on result from analyses of 4 of 7 fish used. All fish were of same size and weight range.

w = values from Lake Washington study by DOH (in preparation). Values are means from multiple samples from other study that were combined to make a WSTMP sample for contract lab analyses of PCB congeners and PCDD/Fs.

For completeness, included values for some parameters that were analyzed by MEL for different studies: Spokane R, Palouse R, Lake Washington. These are qualified as "s","p", or "w", and are explained above.

Size and age data were obtained from studies that shared fish: 303d Ver. Studies (Wenatchee, Pend Oreille) and Lake WA DOH study, Spokane, and Palouse studies.

Species Codes: BC = Black crappie, BG = Bluegill, BNT = Brown trout, BUR = Burbot, CC = Channel catfish, CCP = Common carp, CHK = Chinook salmon, CTT = Cutthroat trout, GCP = Grass carp, KOK = Kokanee salmon, LMB = Largemouth bass, LWF = Lake whitefish, MWF = Mountain whitefish, NPM = Northern pikeminnow, PEA = Peamouth, RBT = Rainbow trout, SMB = Smallmouth bass, WAL = Walleye, YP = Yellow perch.

Appendix E. Health Information about Fish

Fish is good food. Trying to balance the health benefits of fish with concerns about contaminant levels can be challenging, yet information is available to help consumers make healthy choices. Contaminants are found in most foods, and choosing fish wisely can be an excellent health choice. The key is to make smart choices and choose fish that are low in mercury, PCBs, and other contaminants.

The American Heart Association recommends eating fish twice a week because fish are a great source of protein, vitamins, and nutrients. Fish are loaded with omega-3 fatty acids, which provide protection from heart disease and are great "brain food" for adults and children.

A valuable source of information about eating fish is the Washington State Department of Health (DOH) website:

www.doh.wa.gov/ehp/oehas/fish/default.htm

- Advice for women and children who eat fish.
- Waterbody-specific fish consumption advisories in Washington.
- How contaminants get into fish (mercury, PCBs, PBDEs, DDTs).
- How you can help reduce contaminants.

www.doh.wa.gov/ehp/oehas/fish/fishchart.htm

- Healthy fish eating guide.
- Checklist to reduce contaminant exposure including the proper way to fillet and prepare fish meals.
- Health benefits of fish/recipes.

www.doh.wa.gov/ehp/oehas/fish/advisoriesmap.htm

- Fish and shellfish consumption advisories.

The U.S. Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA) also provide information on health benefits of fish:

www.epa.gov/waterscience/fish/

- What you need to know about mercury - 10 frequently asked questions.

www.cfsan.fda.gov/seafood1.html

- Seafood information and resources.

Concentrations of Mercury and Other Trace Elements in Walleye, Smallmouth Bass, and Rainbow Trout in Franklin D. Roosevelt Lake and the Upper Columbia River, Washington, 1994

By M.D. Munn, S.E. Cox, and C.J. Dean

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1995

U.S. DEPARTMENT OF THE INTERIOR

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CONVERSION FACTORS AND VERTICAL DATUM

[SI = International system of units]

Multiply	By	To obtain
Inch-pound to international system units		
inch (in)	25.4	millimeter
foot (ft)	30.48	centimeter
mile (mi)	1.609	kilometer
acre	0.4047	hectacre
International system units to inch-pound units		
centimeter (cm)	0.3937008	inch
millimeter (mm)	0.03937	inch
gram (g)	0.03527	ounce avoidupois
Factors for converting SI metric units to other miscellaneous units		
Concentration, in water		
milligrams per liter (mg/L)	1	parts per million
micrograms per liter (µg/L)	1	parts per billion
Concentration, in tissue and bed sediment		
milligrams per kilogram (mg/kg)	1	parts per million
micrograms per gram (µg/g)	1	parts per million

CONCENTRATIONS OF MERCURY AND OTHER TRACE ELEMENTS IN WALLEYE, SMALLMOUTH BASS, AND RAINBOW TROUT IN FRANKLIN D. ROOSEVELT LAKE AND THE UPPER COLUMBIA RIVER, WASHINGTON, 1994

By M.D. Munn, S.E. Cox, and C.J. Dean

ABSTRACT

Three species of sportfish—walleye, smallmouth bass, and rainbow trout—were collected from Franklin D. Roosevelt Lake and the upstream reach of the Columbia River within the state of Washington, to determine the concentrations of mercury and other selected trace elements in tissue. Concentrations of total mercury in walleye fillets ranged from 0.11 to 0.44 milligram per kilogram, with the higher concentrations in the larger fish. Fillets of smallmouth bass and rainbow trout also contained mercury, but generally at lower concentrations. Other selected trace elements were found in fillet samples, but the concentrations were generally low depending on species and the specific trace element. The trace elements cadmium, copper, lead, and zinc were found in liver tissue of these same species with zinc consistently present in the highest concentration.

INTRODUCTION

Grand Coulee Dam was constructed on the Columbia River in Washington in the late 1930's and early 1940's to supply irrigation water, control flooding, and produce hydroelectric power. The reservoir it formed, Franklin D. Roosevelt Lake, commonly called Lake Roosevelt, has become a major recreational and economic resource for the surrounding area due in large part to sport fishing. The dominant sportfish in the Lake Roosevelt system includes walleye, rainbow trout, kokanee, yellow perch, and smallmouth bass (McDowell and Griffith, 1993). The Colville Confederated Tribes and the Spokane Tribe, whose reservations border parts of the reservoir, and local citizens and businesses also benefit from the reservoir fishery and its economic opportunities.

Several studies have raised concerns about whether concentrations of trace elements that bioaccumulate in fish from Lake Roosevelt are elevated to levels of concern to human and environmental health. This concern first surfaced when the U.S. Fish and Wildlife Service reported that concentrations of cadmium in whole fish collected from Lake Roosevelt were the largest of the 112 sites studied nationwide during the period of 1978 to 1980 (Lowe and others, 1985). While additional studies varied as to the species and type of tissue analyzed, arsenic, cadmium, copper, lead, mercury, and zinc were found in fish collected from Lake Roosevelt.

A 1992 study by the U.S. Geological Survey (USGS) reported that, relative to background reference sites, concentrations of arsenic, cadmium, copper, lead, mercury, and zinc were elevated in the bed sediments of Lake Roosevelt and of the Columbia River, its principal source of inflow (Bortleson and others, 1994). Of the trace elements measured, concentrations of copper, lead, and zinc most often exceeded the sediment-quality guidelines developed by the Ontario Ministry of Environment and Energy (Persaud and others, 1991). The elevated concentrations of trace elements in sediments of Lake Roosevelt and the upstream reach of the Columbia River are largely attributable to the transport of metallurgical waste and slag from a smelter discharging to the Columbia River in Canada (Bortleson and others, 1994).

Of the trace elements present, mercury is believed to be the element that most likely poses a threat to human health in Lake Roosevelt because mercury can bioconcentrate to elevated levels in fillets of fish that are then consumed by people (U.S. Environmental Protection Agency, 1992). Serdar (1993) reported that the concentrations of mercury in fillets of fish from Lake Roosevelt were elevated and that the largest concentrations were in walleye. Because of human health concerns, the USGS, in cooperation with Region 10 of the U.S. Environmental Protection Agency (USEPA) and the Lake Roosevelt Water Quality Council, designed and implemented a study to determine the concentrations of total mercury and other trace elements in fillets of selected sportfish in Lake Roosevelt and the upstream reach of the Columbia River (fig. 1). In order to increase the information gained from this study, the livers from the fish collected were also removed and were analyzed for concentrations of cadmium, copper, lead, and zinc. This part of the study was done in cooperation with the Colville Confederated Tribes.

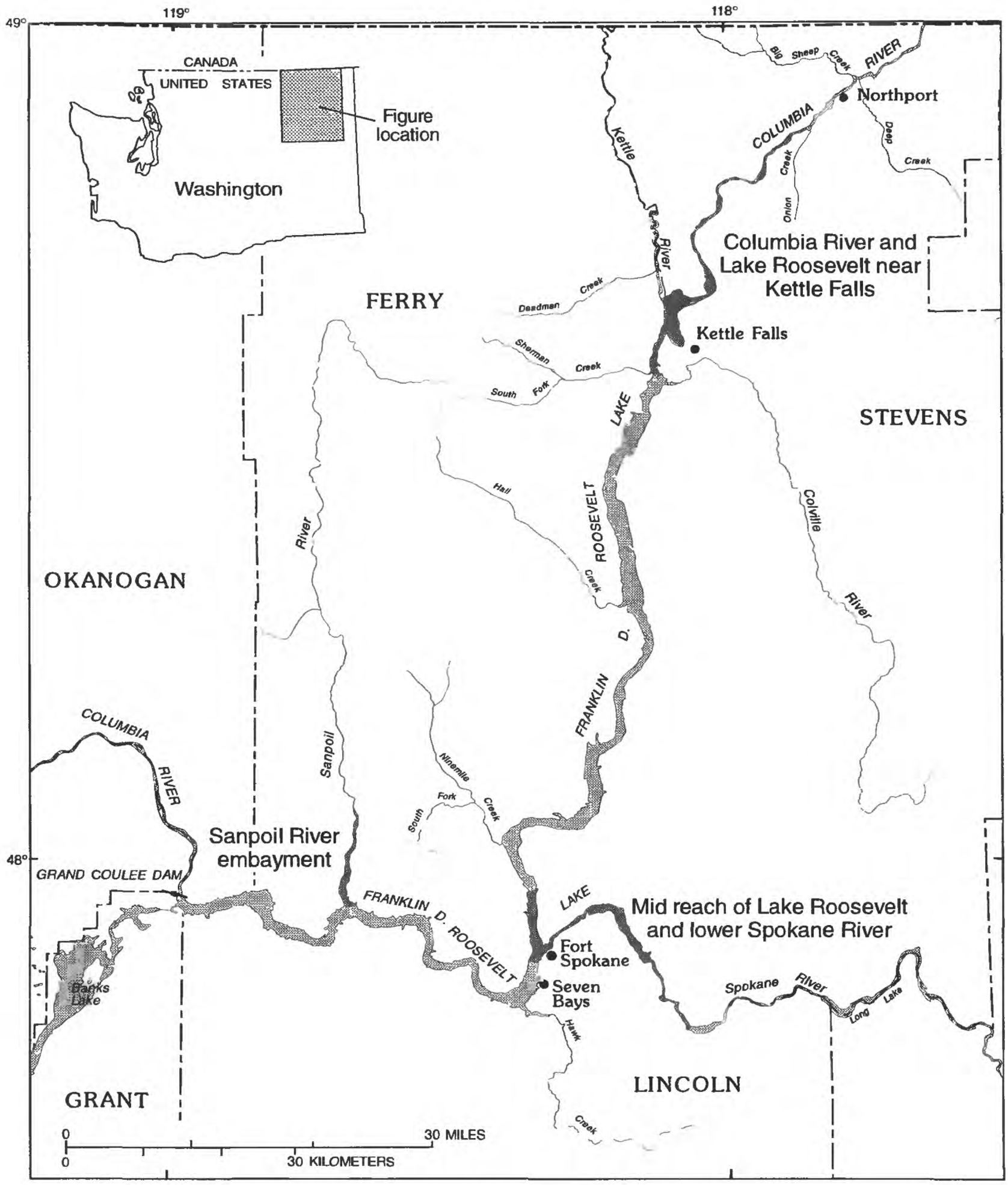

Figure 1.--Map showing location of Franklin D. Roosevelt Lake and sampling locations.

Purpose and Scope

This report presents the data from the 1994 study on the bioaccumulation of trace elements in walleye (*Stizostedion vitreum*), smallmouth bass (*Micropterus dolomieui*), and rainbow trout (*Oncorhynchus mykiss*) in Lake Roosevelt and the upstream reach of the Columbia River. The primary objectives of this study were to:

1. Determine the concentrations of total mercury and other selected trace elements in fillets of walleye, smallmouth bass, and both native and net-pen rainbow trout; and

2. Determine the concentrations of cadmium, copper, lead, and zinc in the liver tissue of the same species.

Data obtained for the first objective will permit the USEPA (Region 10) and the Washington State Department of Health (WDOH) to assess the potential human health effects from the consumption of fish. Data obtained for the second objective will provide baseline data on the concentrations of cadmium, copper, lead, and zinc in fish livers. Both data sets provide a basis for assessing changes in contaminants over time.

Description of the Study Area

Lake Roosevelt is the largest reservoir by volume in Washington and one of the largest in the Nation in total storage. Located in north-central Washington, Lake Roosevelt extends about 135 miles upstream from the dam, reaching to within 15 miles of the international boundary with Canada, several miles below the town of Northport, Wash (fig. 1). The surface area of the lake is about 80,000 acres with a full-pool elevation of 1,289 ft. The stage level of the lake varies as much as 50 feet due to operation of Grand Coulee Dam. Historically, the mean annual retention time of water within the lake has been about 40 days. Additional data regarding Lake Roosevelt are provided by Bortleson and others (1994).

The study area included Lake Roosevelt and the part of the Columbia River upstream from the reservoir to Northport, Wash. The three sampling areas were the Sanpoil River embayment, the mid reach of Lake Roosevelt and lower Spokane River, and Columbia River and Lake Roosevelt near Kettle Falls.

Acknowledgments

This study could not have been completed without the assistance of many individuals and organizations. We thank the Spokane Walleye Club for collecting most of the walleye. We also thank Elizabeth Block of the U.S. Fish and Wildlife Service, Steven Goodbred of the National Biological Survey, David Terpening of the USEPA, and the Spokane Tribe for their assistance in the collection and processing of fish. The National Park Service at Fort Spokane provided accommodations for processing samples. The Washington State Department of Fish and Wildlife aged the fish used in this study.

MERCURY AND OTHER SELECTED TRACE ELEMENTS IN FILLETS

During May 16-21 and June 17-19, 1994, fish were collected for the study from three areas in the Lake Roosevelt and Columbia River system: the Sanpoil River embayment, the mid reach of Lake Roosevelt and lower Spokane River, and the Columbia River and Lake Roosevelt near Kettle Falls (fig. 1). These areas were selected for three primary reasons. (1) They are areas where walleye spawn, or pass through to spawn, and therefore contained a larger percentage of the older individuals required for the study. (2) The areas are commonly fished recreationally. (3) The geographical distribution of sites permitted a general assessment of the distribution of trace elements in fish within the entire reservoir and river system. Because the fish species used in this study move throughout part of (smallmouth bass) or all (rainbow trout and walleye) of the system, individual fish collected in one of the three areas are exposed to trace metals from much larger areas than the area of collection.

Walleye, one of the most commonly harvested species in Lake Roosevelt, were chosen because past studies have shown them to have the highest concentrations of mercury (Serdar, 1993). Smallmouth bass and rainbow trout were also chosen because they are popular sportfish, but were collected in a smaller sampling effort. Both native and net-pen rainbow trout were collected, but were analyzed separately in this study because native rainbow trout are exposed to trace metals throughout their life cycles in the reservoir, whereas net-pen rainbow trout spend their first year in suspended enclosures and are fed commercial food.

Field Procedures

The field procedures apply generally to collection of fish used for both fillet and liver analyses in this study. Specific methods for collecting fish livers are described in the section "Cadmium, Copper, Lead, and Zinc in Liver Tissue". The size class of fish accepted for this study and the type of sample used (composite versus individual) varied depending on the species and availability (table 1). Walleye were collected from four size classes: 10 to 13 in., greater than 13 to 16 in., greater than 16 to 19 in., and greater than 19 to 22 in. A total of 34 walleye composite samples were collected, each composite consisting of 8 individual fillets from fish of the same size class. To determine whether the concentration of mercury from a composite sample was similar to the average mercury concentration from individual fish samples, a single composite sample from each of the three sampling areas was selected from the size class greater than 13 to 16 in. For these three composite samples, the fillets on the opposite side of the fish were removed and analyzed individually for total mercury.

Smallmouth bass were sampled the same as the walleye, except that fish were collected in a single size class of 8 to 12 inches (table 1). Rainbow trout were not sorted into size class, but were analyzed as individuals. All samples were analyzed for concentrations of total mercury. All smallmouth and rainbow samples were also analyzed for other trace elements, but only a subset of the walleye samples were analyzed (table 1).

Fish were collected using two methods. Most of the walleye were collected with hook and line, and individuals of all three species were collected using an electroshock boat. The total length of each fish was measured in order to assign it to size class. Any fish not needed to complete a composite sample within a specific size class was released. The fish that were used were sacrificed, placed in a labelled and sealed plastic bag, and stored on ice in a cooler until processed. Contacts between fish and other objects were minimized.

Fish were transported to a USGS mobile laboratory at Fort Spokane for processing before being sent to the analytical laboratory; all fish were processed within 24 hours of collection. The first processing step was to collect basic physical information on each fish: total length, from the anterior-most part of the fish to the tip of the longest caudal fin ray when the lobes of the caudal fin are compressed dorsoventrally, in millimeters; and total weight, in grams. Fish scales were collected and sent to the Washington State Department of Fish and Wildlife for age determination.

Field processing equipment was made of glass, plastic, or stainless steel. Strict guidelines were followed in the cleaning of all equipment that came into contact with samples, and equipment was cleaned between each composite or individual sample. Cleaning procedures for glass and plastic included washing equipment with phosphate-free laboratory detergent solution, rinsing in Type I reagent-grade water, rinsing in 5-percent nitric acid, rinsing in pesticide-grade methanol, permitting to air dry, and then storing in sealed containers. All dissection equipment was stainless steel and was cleaned using the above cleaning procedures, except for the 5-percent nitric acid rinse.

Fillet samples were removed in accordance with procedures in U.S. Environmental Protection Agency (1993), which included the belly flap. Filleting was done on glass or teflon cutting boards with stainless steel dissecting equipment. Once the fillet was obtained and the skin was removed, the fillet was then weighed (grams) and placed in a plastic bag that was sealed and placed on dry ice for shipment. Individual fish were then opened to determine sex and to remove the liver. All tissue samples were shipped to the USGS National Water Quality Laboratory (NWQL) in Arvada, Colo.

Table 1.--*Samples collected for the analysis of total mercury and other selected trace elements in fillets of walleye, smallmouth bass, native rainbow trout, and net-pen rainbow trout*

[mg/kg, milligrams per kilogram; nc, none collected; RM, river mile; >, greater than]

Species	Size class, in inches (centimeters in parentheses)		Sanpoil River embayment[1]		Mid reach of Lake Roosevelt and lower Spokane River[2]		Columbia River and Lake Roosevelt near Kettle Falls[3]	
			Number of samples	Number of fillets per sample	Number of samples	Number of fillets per sample	Number of samples	Number of fillets per sample
Walleye	[4]10-13	(25.4-33)	1	8	5	8	1	8
	[4]>13-16	(>33-40.6)	2	8	7	8	6	8
	[5]>13-16	(>33-40.6)	8	1	8	1	8	1
	[6]>13-16	(>33-40.6)	1	8	1	8	1	8
	[4]>16-19	(>40.6-48.3)	2	8	3	8	4	8
	[4]>19-22	(>48.3-55.9)	nc	nc	2	8	1	8
Smallmouth bass	[4,6]8-12	(20.3-30.5)	3	5	2	5	nc	nc
Native rainbow trout	[4,6]19-22	(48.3-55.9)	4	1	nc	nc	2	1
Net-pen rainbow trout	[4,6]17-20	(43.2-50.8)	2	1	nc	nc	nc	nc

[1]Sampling reach included the Sanpoil River embayment from its confluence with the Columbia River to the inflow of the Sanpoil River into the embayment.

[2]Sampling reach included Lake Roosevelt from RM 638.9 to RM 644.5 and the lower Spokane River from RM 0 to RM 17.

[3]Sampling reach included Lake Roosevelt below Kettle Falls (RM 705) to Columbia River at Northport (RM 735).

[4]Samples were analyzed for total mercury at a detection limit of 0.05 mg/kg.

5 Individual fillet samples were removed from the opposite side of a fish used in a composite sample of the same size class.

[6]Samples were analyzed for (detection limits) arsenic (0.1 mg/kg), cadmium (0.03 mg/kg), copper (0.1 mg/kg), lead (0.05 mg/kg), manganese (0.01 mg/kg), selenium (0.2 mg/kg), and zinc (0.3 mg/kg).

Laboratory Procedures

The USGS NWQL homogenized the fillets in stainless steel blenders using clean procedures. Homogenized muscle tissue samples were placed in pre-cleaned and certified sample jars, labelled, and shipped frozen (packed on dry ice) to the USEPA laboratory in Manchester, Wash., for chemical analysis; a chain-of-custody form accompanied each sample. For mercury samples, the USEPA laboratory used cold vapor atomic absorption spectrometry, as outlined in Method 245.6 (U.S. Environmental Protection Agency, 1991a). The detection limit for this procedure is 0.05 mg/kg (parts per million, wet weight). The USEPA Laboratory in Manchester used ICP-MS for the analysis of arsenic (at a detection of 0.1 mg/kg), cadmium (0.03 mg/kg), copper (0.1 mg/kg), manganese (0.01 mg/kg), lead (0.05 mg/kg), selenium (0.2 mg/kg), and zinc (0.3 mg/kg). Laboratory analyses followed methods outlined in Method 200.8 (U.S. Environmental Protection Agency, 1991b).

Quality Assurance and Control

Quality assurance and control were used to insure the collection, processing, and analysis of data of a known and acceptable quality. Quality assurance of sample data included initial examination of captured fish, review by laboratory personnel of calibration standards and laboratory generated quality-assurance samples, and review by project quality-assurance personnel of field and laboratory generated quality-control samples. Potential for contamination was minimized by using clean field procedures (described earlier) and by using dedicated field equipment for each sample. Samples were transported to a field laboratory where they were processed within 24 hours; a chain-of-custody form accompanied all samples. Field quality-control samples permitted an assessment of whether field procedures used were "clean". Laboratory quality control was established to assess sample contamination that might occur during the analytical process, and to assess analytical accuracy and precision.

A variety of quality-control samples was used to assess data quality, including field and laboratory blanks to assess potential contamination; laboratory matrix spike samples to assess analytical procedures; and analysis of duplicate sample material to assess analytical accuracy and data precision.

Field blanks were used to assess contamination that might have occurred during sample collection, field processing, and the homogenization of samples in the laboratory. Nine "clean" hatchery-reared fish were used to make up field and process blank samples. The field-blank fish were rainbow trout provided by the USEPA laboratory in Manchester which had been reared under controlled conditions. The field-blank fish were sacrificed, wrapped individually, and taken to the field on ice, along with the sampling and processing equipment. "Clean" rainbow trout were inserted in the sample group at the point of fish capture from the lake and processed identically to field-gathered samples. Individual fillets from three field-blank fish were combined into a single composite sample for each sampling site. The three composite field-blank samples were processed, homogenized, and analyzed in the same manner as the study samples.

Analytical procedures were assessed for accuracy through the analysis of procedural blanks and matrix spike samples. Matrix spike samples were prepared by the addition of a known quantity of the analyte to a duplicate sample. Recovery efficiency is based on the comparison of the results from the analysis of the matrix spike sample with the expected concentration. The acceptance criterion used in this study for the matrix spike recovery was from 80 to 120 percent.

The accuracy of the mercury and trace element data was assessed by analyzing DORM-2 standard reference material and by comparing the results of four duplicate samples analyzed by three independent laboratories. The DORM-2 standard is composed of dogfish muscle tissue and was selected because it more closely resembles the sample matrix of this study than other available standard reference material. These standards are prepared by the National Research Council of Canada.

Interlaboratory duplicate samples were prepared for comparative analysis during the homogenization procedures. The interlaboratory comparison samples were submitted to the project lab (USEPA Manchester Laboratory) and two additional laboratories (Battelle Marine Sciences Laboratory in Sequim, Wash., and Frontier Geosciences Laboratory in Seattle, Wash.). Data accuracy was considered acceptable if the relative percent difference of concentrations of mercury from the USEPA project laboratory was within 20 percent of the reported analysis of both Battelle Marine Science Laboratory and Frontier Geosciences Laboratory.

The precision of sample processing, including sample homogenization and analytical determinations, was determined by comparing duplicate analyses of environmental samples. Duplicate samples were generated under two conditions. Laboratory duplicate samples were prepared

by the analyzing laboratory, whereas blind duplicates were prepared during the homogenization process and submitted to the analytical laboratory as blind samples. Analytical precision was considered acceptable if the relative percent difference between duplicate samples was within 20 percent.

Results

Mercury

Data on the concentrations of total mercury in fillets of walleye are shown in table 2. Concentrations ranged from 0.11 to 0.44 mg/kg with the lowest concentrations reported from the 10 to 13 inches size class and the highest concentrations found in the greater than 19 to 22 inches size class. Table 3 compares data on the concentrations of total mercury in three composite samples with the average concentration of mercury from individual fillets from the same composite samples. As shown, the concentration of mercury in composite samples closely approximates the average value based upon eight individual fillets from the same fish used in the composite samples. Percent moisture was also similar between composite samples and average values for the same fish.

Data on total mercury in smallmouth bass, native rainbow trout and net-pen rainbow trout are presented in table 4. Concentrations of total mercury in smallmouth bass ranged from 0.16 to 0.62 mg/kg (n=5), native rainbow trout from 0.16 to 0.24 mg/kg (n=6), and net-pen rainbow trout from 0.11 to 0.16 mg/kg (n=2). All field data collected on individual fish are presented in Appendix A.

The results of the quality-control samples associated with samples analyzed for the concentration of mercury in fish tissues were all within the quality-assurance criteria. This indicated that the mercury data are acceptable with respect to the absence of contamination and to the reliability of data accuracy and precision.

The concentrations of mercury and other selected trace elements in the three rainbow trout composite field-blank samples are shown in table 5. The concentration of mercury in all three field blank composite samples was below the detection limit of 0.05 mg/kg, indicating no detectable mercury contamination had resulted from sample handling. Procedural blanks were included in each group of samples analyzed. Analysis of all laboratory procedural blank samples resulted in concentrations of mercury and the selected trace elements below the detection levels, indicating no detectable contamination had occurred during analysis.

Data accuracy was assessed through interlaboratory comparison of duplicate samples and the analysis of standard reference materials. The results of the analysis of mercury and the analysis of the DORM-2 standard in duplicate samples by independent laboratories are shown in table 6. The relative percent differences in the reported concentration of mercury from duplicate samples submitted to the USEPA project lab and two outside laboratories were within the 20-percent acceptance range. All labs reported the concentration of mercury in the DORM-2 standard reference material within the acceptable range; two of the labs reported concentrations within the certified range, which is the 95-percent tolerance limit cited by the supplier. These data indicate that the reported mercury concentrations are accurate and reliable. The acceptability criterion for the analysis of the DORM-2 standard was 80-120 percent of the certified value.

Blind replicate samples were sent to the USEPA project laboratory to assess the precision of the analysis of mercury concentrations. The identity of the blind quality-assurance samples was not known to the USEPA project laboratory. Data from the blind replicate samples, as well as duplicate samples generated within the laboratory, are shown in table 6. The relative percent difference of the six blind duplicate pairs ranged from 0.5 to 11.4 percent. The relative percent difference of six duplicate laboratory-generated sample pairs ranged from 1.3 to 12.5 percent. The relative percent differences of replicate analyses were within the quality-assurance criteria of 20 percent, indicating acceptable laboratory analytical precision.

Table 2.--*Physical characteristics and age of walleye in composite samples and results of tissue analysis for total mercury by sampling location and size class. A sample consisted of compositing eight fillets with skin removed.*

[USGS, U.S. Geological Survey; cm, centimeter; mg/kg, milligram per kilogram; >, greater than]

Size class (inches, centimeters in parentheses)	Composite replicate	USGS sample number	Physical characteristics and age: Mean composite length (cm)	Physical characteristics and age: Mean composite weight (grams)	Physical characteristics and age: Mean composite age (years)	Laboratory analysis: Percent moisture	Laboratory analysis: Mercury (mg/kg,wet weight)
			Columbia River and Lake Roosevelt near Kettle Falls				
10-13 (25.4-33)	1	30	31.8	261	2	80	0.21
>13-16 (>33-40.6)	1	14	36.5	393	2	81	.21
	2	19	38.9	491	4	78	.29
	3	15	38.0	454	3	79	.21
	4	55	36.5	386	2	79	.28
	5	57	37.9	439	3	79	.26
	6	58	36.5	391	3	80	.29
	Mean		37.4	426	3	79	.26
>16-19 (>40.6-48.3)	1	16	42.9	610	4	80	.35
	2	17	43.4	650	5	80	.29
	3	18	43.0	635	4	80	.25
	4	56	43.8	650	4	80	.36
	Mean		43.3	636	4	80	.31
>19-22 (>48.3-55.9)	1	21	50.3	1,047	5	79	.32
			Mid-reach of Lake Roosevelt and lower Spokane River				
10-13 (25.4-33)	1	3	30.3	206	1	68	.22
	2	4	30.9	219	1	80	.23
	3	8	31.1	233	2	80	.20
	4	51	31.1	235	2	80	.31
	5	52	32.0	251	2	79	.37
	Mean		31.1	229	2	77	.27
>13-16 (>33-40.6)	1	5	36.0	367	2	80	.23
	2	6	35.3	330	2	80	.27
	3	7	35.8	335	2	79	.36
	4	50	34.6	335	2	79	.30
	5	61	35.1	343	2	79	.34
	6	53	35.9	347	2	79	.34
	7	54	35.7	354	2	79	.35
	Mean		35.5	344	2	79	.31

Table 2.--*Physical characteristics and age of walleye in composite samples and results of tissue analysis for total mercury by sampling location and size class. A sample consisted of compositing eight fillets with skin removed--Continued*

Size class (inches, centimeters in parentheses)	Composite replicate	USGS sample number	Physical characteristics and age: Mean composite length (cm)	Physical characteristics and age: Mean composite weight (grams)	Physical characteristics and age: Mean composite age (years)	Laboratory analysis: Percent moisture	Laboratory analysis: Mercury (mg/kg,wet weight)
			Mid-reach of Lake Roosevelt and lower Spokane River--Continued				
>16-19	1	9	43.4	644	4	80	0.36
(>40.6-48.3)	2	10	44.1	666	5	80	.35
	3	59	43.7	632	5	80	.40
	Mean		43.7	647	5	80	.37
>19-22	1	1	50.5	1,034	5	78	.44
(>48.3-55.9)	2	2	51.2	1,021	4	77	.33
	Mean		50.9	1,028	5	78	.38
			Sanpoil River embayment				
10-13 (25.4-33)	1	12	30.4	205	1	79	.11
>13-16	1	11	35.3	344	2	78	.36
(>33-40.6)	2	27	38.0	409	3	80	.37
	Mean		36.7	377	2	79	.36
>16-19	1	13	42.7	617	3	79	.36
(>40.6-48.3)	2	23	43.4	726	3	78	.42
	Mean		43.1	672	3	78	.39

Table 3.--*Concentrations of total mercury in individual fillets of 13- to 16-inch walleye compared to concentrations of total mercury in composite fillet samples. Composite samples consisted of combining eight fillets with skin removed, from the opposite side of the walleye used for the individual fillet samples.*

[USGS, U.S. Geological Survey; mg/kg, milligrams per kilogram, wet weight; RM, river mile]

	Sanpoil River embayment[1]			Mid reach of Lake Roosevelt and lower Spokane River[2]			Columbia River and Lake Roosevelt near Kettle Falls[3]		
Replicate	USGS sample number	Mercury (mg/kg)	Percent moisture	USGS sample number	Mercury (mg/kg)	Percent moisture	USGS sample number	Mercury (mg/kg)	Percent moisture
				Individual value					
1	27.1	0.15	79	6.1	0.31	91	14.1	0.14	80
2	27.2	0.34	78	6.2	0.21	75	14.2	0.16	79
3	27.3	0.43	79	6.3	0.24	80	14.3	0.20	80
4	27.4	0.42	79	6.4	0.26	80	14.4	0.15	74
5	27.5	0.65	80	6.5	0.18	80	14.5	0.22	80
6	27.6	0.36	80	6.6	0.28	78	14.6	0.30	79
7	27.7	0.30	78	6.7	0.27	81	14.7	0.16	80
8	27.8	0.26	80	6.8	0.30	78	14.8	0.18	79
Mean		0.36	79		0.26	80		0.19	79
				Composite value					
	27	0.37	80	6	0.27	80	14	0.21	81

[1]Sampling reach includes the Sanpoil River embayment from its confluence with the Columbia River to the inflow of the Sanpoil River into the embayment.

[2]Sampling reach includes Lake Roosevelt from RM 638.9 to RM 644.5 and the lower Spokane River from RM 0 to RM 17.

[3]Sampling reach includes Lake Roosevelt at Kettle Falls (RM 705) to Columbia River at Northport (RM 735).

Table 4.--*Concentrations of total mercury in smallmouth bass, native rainbow trout, and net-pen rainbow trout. Smallmouth bass samples were a composite of five fillets without skin, whereas rainbow trout samples were single fillets without skin.*

[USGS, U.S. Geological Survey; cm, centimeter; mg/kg, milligrams per kilogram, wet weight]

Site name	USGS sample number	Physical characteristic and age				Laboratory analysis	
		Length		Weight	Age	Percent	Mercury
		(inches)	(cm)	(grams)	(years)	moisture	(mg/kg)
				Smallmouth bass[1]			
Sanpoil River embayment	24	10.3	26.3	244	2	78	0.62
	25	10.3	26.2	263	2	79	0.17
	26	10.2	25.8	239	2	79	0.27
Mid reach of Lake Roosevelt	28	9.8	24.8	236	2	79	0.16
and lower Spokane River	29	10.5	26.6	253	2	79	0.19
				Native rainbow trout[2]			
Sanpoil River embayment	33	20.1	51.0	1,216	5	73	0.24
	34	19.9	50.5	1,086	5	80	0.16
	35	21.3	54.0	1,188	4	80	0.21
	36	19.3	49.0	1,055	4	78	0.20
Columbia River and Lake	31	20.5	52.0	1,245	5	82	0.19
Roosevelt near Kettle Falls	32	20.1	51.0	996	4	82	0.21
				Net-pen rainbow trout[2]			
Sanpoil River embayment	37	17.9	45.5	1,219	3	77	0.16
	38	20.1	51.0	1,563	3	72	0.11

[1]A smallmouth bass sample consisted of a mean value from a composite sample of 5 fish.

[2]Native and net-pen rainbow trout samples are based on single fish samples.

Table 5.--*Concentrations of trace elements in hatchery rainbow trout used as field blanks for part of the quality control program. Each sample consisted of a composite of three fillets.*

[<, less than detectable levels]

Sample	Concentration of trace elements in milligrams per kilogram, wet weight							
	Arsenic	Cadmium	Copper	Lead	Manganese	Mercury	Selenium	Zinc
1	0.4	<0.1	0.66	<0.01	0.19	<0.05	0.37	4.7
2	0.4	<0.1	<0.5	0.13	0.16	<0.05	0.32	4.5
3	0.4	<0.1	<0.5	0.21	0.14	<0.05	0.33	3.7

Table 6.--*Quality control results from the analysis of total mercury in walleye fish tissue and standard reference material*

[mg/kg, milligrams per kilogram; DORM-2, dog-fish muscle tissue; --, analysis not performed; (L), replicate sample prepared by analyzing laboratory; (B), replicate sample prepared by laboratory other than the analyzing laboratory]

Laboratory	Concentration of mercury in fillet tissue (mg/kg, wet weight)							Analysis of mercury in reference tissue (DORM-2)				
	Sample 8027	Sample 8001	Sample 8006	Sample 8014	Sample 8021	Sample 8002	Sample 1505	Recovery, dry-weight (percent)	Dry fraction (percent)	Undried standard (mg/kg)	Dried standard (mg/kg)	Procedural blank (mg/g)
Battelle Marine Sciences Laboratory, Sequim, Wash.	0.298	0.425	0.242	0.182	--	--	--	92	97.0	4.16	4.28	0.003
	--	--	--	0.190 (L)	--	--	--	--	--	--	--	--
U.S. Environmental Protection Agency, Manchester, Wash.	0.373	0.436	0.267	0.207	0.323	0.334	0.230	104	91.7	4.41	4.87	<0.025
	0.336 (B)	0.521 (B)	--	0.206 (B)	0.327 (L)	0.309 (B)	0.207 (B)	96	--	4.08	4.45	--
	--	0.494 (L)	--	--	0.334 (B)			100	--	4.27	4.66	--
Frontier Geosciences, Seattle, Wash.	0.376	0.432	0.262	0.215	--	--	--	102	89.0	4.23	4.75	0.007
	--	0.422 (L)	--	--	--	--	--	102	--	4.22	4.74	--
	--	--	--	--	--	--	--	102	--	4.20	4.72	--

Other Trace Elements

The results of analyzing for other selected trace elements in fillets from walleye, smallmouth bass, and native and net-pen rainbow trout are shown in table 7. Concentrations of both arsenic and cadmium were below detection limits, or only slightly above, for all samples and species. Concentrations of copper in fillet tissue ranged from 0.27 to 0.68 mg/kg, with largest concentrations measured in native rainbow trout collected from Sanpoil River embayment. Concentrations of lead ranged from below the detection limit of 0.05 mg/kg to 0.1 mg/kg; four of the 16 samples had concentrations between 0.06 and 0.1 mg/kg. Manganese ranged from 0.09 to 0.54 mg/kg, with most samples having similar concentrations among sites and species. Five of the samples showed below detection limits for selenium, with the remainder of the samples having concentrations between 0.22 and 0.39 mg/kg. Concentrations of zinc were the highest of all the trace elements measured with values ranging from 3.7 to 6.1 mg/kg; however, 11 of the 16 samples were noted by the laboratory because spike sample recoveries associated with those 11 samples were outside the laboratory control limits. Therefore, concentrations of zinc for these samples are likely overestimated.

The results of the quality-control samples associated with samples analyzed for the concentration of arsenic, cadmium, copper, lead, manganese, selenium, and zinc in fish tissues were generally within the acceptance criteria. However, several quality-control samples were outside of the acceptable range and thus require that the data be noted appropriately. Overall, the data for arsenic, cadmium, copper, lead, manganese, and selenium are acceptable; zinc required some qualifications.

The concentrations of selected trace elements in the three field blanks ("clean" fish) were below detection limits for cadmium, with detections in at least one of the three replicates for each of the other trace elements. Of the trace elements measured, zinc consistently had the greatest concentrations, indicating either consistent contamination of the fish tissue samples with zinc or, more likely, the presence of zinc in the hatchery-reared fish.

Procedural blanks were included as part of the analytical methods in each group of samples analyzed and are shown in table 8. With the exception of zinc, the concentrations determined in the analysis of blanks were less than the detection limit concentration for the analysis. For zinc, the analysis of the blanks resulted in a concentration of 0.3 micrograms per gram which is the detection limit for that analysis and which is more than an order of magnitude smaller than the reported concentrations for zinc in the fish tissue samples. These data indicate no substantial or detectable contamination resulting from the analytical procedures.

Matrix spike recovery data are in table 8. The recovery of matrix spike samples were within acceptable criteria for all trace elements except for one of two matrix spike samples for zinc. The acceptable range for matrix spike recovery data for this study is from 80 to 120 percent of the spike concentrations. Because one of the matrix spike recovery samples for zinc yielded recoveries of 131 and 136 percent, all of the zinc data in table 8 were noted to indicate this condition.

The accuracy of the trace element data was assessed by the analysis of standard reference materials (table 8). The acceptability criteria for the analysis of the standard reference material was 80-120 percent of the certified value. Reported concentrations of arsenic, copper, manganese, selenium, and zinc were within the acceptable range; copper and zinc were within the manufactures' certified range. The concentrations of cadmium and lead in the standard reference material reported by the project laboratory were above the certified concentrations for the standard reference material, indicating a small positive bias in the data. Because all of the cadmium concentrations reported for fish tissue samples were below the detection limit, a small positive bias of the magnitude suggested by the data in table 8 should not substantially affect the interpretation of the results. Similarly, all of the concentrations of lead reported for the fish tissue samples were below or near the detection limits, therefore a small positive bias of the magnitude suggested by the data should not substantially affect the interpretation of the results.

Duplicate analyses were performed for all seven trace elements from sub-samples generated by the project laboratory. All the duplicate analysis were within the relative percent difference guidelines of 20 percent (see table 8).

Table 7.--*Concentrations of selected trace elements in fillets of walleye, smallmouth bass, native rainbow trout, and net-pen rainbow trout*

[USGS, U.S. Geological Survey; <, less than detectable levels; >, greater than]

Species	Size class: Inches	Size class: Centimeters	USGS sample number	Concentration, in milligrams per kilogram, wet weight: Arsenic	Cadmium	Copper	Lead	Manganese	Selenium	Zinc	Percent moisture
Sanpoil River Embayment											
Walleye	>13-16	(>33-40.6)	11	[1]0.12	<0.03	0.27	<0.05	0.54	[1]0.32	[2]4.6	78
Smallmouth bass	8-12	(20.3-30.5)	24	[1]0.14	<0.03	0.40	<0.05	0.16	[1]0.27	[2]5.8	78
			25	[1]0.14	<0.03	0.40	<0.05	0.18	[1]0.28	[2]6.1	79
			26	[1]0.14	<0.03	0.41	<0.05	0.15	[1]0.31	[2]5.3	79
Native rainbow trout	19-22	(48.3-55.9)	33	<0.1	<0.03	0.28	[1]0.05	0.13	[1]0.22	4.6	73
			34	<0.1	<0.03	0.68	0.1	0.14	<0.2	5.4	80
			35	<0.1	<0.03	0.43	<0.05	0.16	<0.2	5.8	80
			36	<0.1	<0.03	0.52	<0.05	0.12	[1]0.37	[2]5.8	77
Net-pen rainbow trout	17-20	(43.2-50.8)	37	<0.1	<0.03	0.48	[1]0.07	0.17	<0.2	[2]3.7	77
			38	<0.1	<0.03	0.40	<0.05	0.12	[1]0.24	[2]4.6	72
Mid-reach Lake Roosevelt and lower Spokane River											
Walleye	>13-16	(>33-40.6)	7	<0.1	<0.03	0.32	<0.05	0.23	[1]0.23	[2]4.7	79
Smallmouth bass	8-12	(20.3-30.5)	28	[1]0.14	<0.03	0.36	[1]0.06	0.18	[1]0.25	[2]5.9	79
			29	[1]0.14	<0.03	0.40	<0.05	0.16	[1]0.26	[2]6.1	79
Columbia River and Lake Roosevelt near Kettle Falls											
Walleye	>13-16	(>33-40.6)	19	<0.1	<0.03	0.38	[1]0.07	0.16	[1]0.39	[2]5.2	77
Native rainbow trout	19-22	(48.3-55.9)	31	<0.1	<0.03	0.31	<0.05	0.09	<0.2	4.1	82
			32	<0.1	<0.03	0.46	[1]0.05	0.16	<0.2	4.9	82

[1]The analyte was detected above the method detection limit but below the reporting limit, and therefore are estimates.

[2]One of the two (see table 8) spike samples recovery is not within control limits.

Table 8.--*Laboratory quality-control data for analysis of selected trace elements in fish fillets from Lake Roosevelt*

[Values are concentrations in micrograms per gram, wet weight, unless otherwise noted; DORM-2, dog-fish muscle tissue; NIES, National Institute for Environmental Studies; <, less than]

	Arsenic	Cadmium	Copper	Lead[1]	Manganese	Selenium	Zinc
			Procedural blank				
Blank	<0.1	<0.03	<0.1	<0.05	<0.01	<0.2	0.3
			Standard reference material				
DORM-2 or	18.0	0.043	2.34	--	3.66	1.40	25.6
NIES mussel	--	--	--	0.91	--	--	--
(95 percent tolerance limits	±1.1	±0.008	±0.16	±.04	±0.34	±0.09	±2.3
Analyzed concentrations in reference material	19.5	0.06	2.48	1.13	3.28	1.64	26.1
Relative percent difference of reference material with certified values	8	[4]33	6	22	11	16	2
			Matrix spike recovery (in percent)				
Spike 1	109	104	102	99	111	116	[4]136
Spike 1 duplicate	111	107	103	101	109	116	[4]131
Spike 2	113	106	108	101	113	112	115
Spike 2 duplicate	109	103	103	99	108	111	95
			Laboratory duplicate analysis				
424	<0.1	<0.03	0.28	[3]0.05	0.134	[3]0.22	4.62
424 duplicate	<0.1	<0.03	.29	[3]<0.05	0.149	[3]0.22	4.89
424 relative percent difference[2]	0	0	3.5	0	10.6	0	5.7
429	<0.1	<0.03	0.40	<0.05	0.119	[3]0.24	4.62
429 duplicate	<0.1	<0.03	.40	<0.05	.114	[3]0.23	4.36
429 relative percent difference[2]	0	0	0	0	4.3	4	5.8

[1]NIES muscle tissue was used as reference material for lead; whereas for the other trace elements DORM-2 tissue was used.

[2]Relative percent difference = ((Lab concentration - certified concentration)/((Lab concentration + certified concentration/2) X 100.

[3]The analyte was detected above the method detection limit but below the established reporting limit, and therefore are estimates.

[4]Values exceeded quality-assurance guidelines.

CADMIUM, COPPER, LEAD, AND ZINC IN LIVER TISSUE

The general procedures for field collection of fish are described in the section "Mercury and Other Selected Trace Elements in Fillets--FIeld Procedures". The field and laboratory procedures used specifically for the assessment of trace elements in liver tissue are presented here.

Field Procedures

Once the fillets were removed from the fish, the fish were opened and their livers removed using stainless steel dissecting equipment. Equipment cleaning procedures were identical to those described earlier; however, a separate set of dissecting equipment was used for extracting liver tissue. After removal, the livers were rinsed with distilled water, weighed, and placed into pre-weighed plastic jars. Samples were placed on dry ice and shipped to the analytical laboratory.

For both walleye and smallmouth bass, livers were composited from the same fish used in the fillet composite sample. Therefore, walleye samples contained eight livers, and smallmouth bass five livers. Rainbow trout livers were analyzed individually. Although all smallmouth bass and rainbow livers were analyzed, only a subset of the walleye composite liver samples were analyzed. Table 9 summarizes the samples collected in this study.

Laboratory Procedures

Once processed in the field, liver samples were frozen on dry ice and shipped to Battelle Marine Science Laboratories in Sequim, Wash., for analysis. Samples were freeze-dried, ground, digested in nitric acid, and analyzed by ICP/MS (Crecelius and others, 1993). Samples were analyzed for four trace elements (detection limits, in micrograms per gram, in parentheses): cadmium (0.01 µg/g), copper (1.0 µg/g), lead (0.01 µg/g), and zinc (1.0 µg/g). Percent moisture was also determined for all samples.

Table 9.--*Samples collected for the analysis of selected trace elements in liver tissue of walleye, smallmouth bass, native rainbow trout, and net-pen rainbow trout. Livers were analyzed for cadmium, copper, lead, and zinc.*

[nc, none collected; RM, river mile; >, greater than]

Species	Size class, in inches (centimeters in parentheses)	Sanpoil River embayment[1]		Mid-reach Lake Roosevelt and lower Spokane River[2]		Columbia River and Lake Roosevelt near Kettle Falls[3]	
		Number of samples	Number of livers per sample	Number of samples	Number of livers per sample	Number of samples	Number of livers per sample
Walleye	10-13 (25.4-33)	1	8	3	8	1	8
	>13-16 (>33-40.6)	2	8	3	8	3	8
	>16-19 (>40.6-48.3)	2	8	3	8	3	8
	>19-22 (>48.3-55.9)	nc	nc	2	8	1	8
Smallmouth bass	8-12 (20.3-30.5)	3	5	2	5	nc	nc
Native rainbow trout	19-22 (48.3-55.9)	4	1	nc	nc	2	1
Net-pen rainbow trout	17-20 (43.2-50.8)	2	1	nc	nc	nc	nc

[1]Sampling reach includes the Sanpoil River embayment from its confluence with the Columbia River to the inflow of the Sanpoil River into the embayment.

[2]Sampling reach includes Lake Roosevelt from RM 638.9 to RM 644.5 and the lower Spokane River from RM 0 to RM 17.

[3]Sampling reach includes Lake Roosevelt at Kettle Falls (RM 705) to Columbia River at Northport (RM 735).

Quality Control and Assurance

Quality-assurance and control were incorporated to assure the collection, processing, and analysis of data of a known and acceptable quality. Quality assurance of sample data included initial screening of captured fish; review by laboratory personnel of calibration standards and lab-generated quality-control samples; and review by project quality assurance personnel of field and laboratory generated quality-control samples. Quality-control samples were used to assess data quality of trace elements concentrations in liver tissue and included laboratory blanks to assess potential contamination, laboratory matrix spike samples to assess analytical procedures, and the analysis of standard reference material. Quality-control procedures included two procedural blanks, two matrix spikes, and two analyses of standard reference material. The standard reference material used in the analysis of liver tissue was DOLT-2 (dogfish liver tissue) prepared by National Research Center for Canada.

Results

The concentrations of cadmium, copper, lead, and zinc in liver tissue collected from the three species are shown in table 10. The concentrations of cadmium in liver tissue ranged from 0.9 to 15.7 µg/g, with highest concentrations measured in walleye and native rainbow trout. Copper was highest in both native and net-pen rainbow trout, with values reaching 140 µg/g in native rainbow trout; smallmouth bass had the lowest concentrations. Concentrations of lead were similar among the three species and ranged from less than 0.03 to 10.9 µ/g. Of the four trace elements, zinc showed the highest concentrations with values ranging from 64.6 to 622 µ/g.

The results of the quality-control samples associated with samples analyzed for the concentration of cadmium, copper, lead, and zinc in fish liver tissues were generally within the quality assurance acceptance criteria. Several extreme values were present in the data, and review of these data with the project laboratory revealed that the results were not the result of analytical or typographical errors. Several of the standard reference material samples were outside of the acceptable range for either lead or zinc. Two standard reference materials were used and the exceedence of the quality control criteria were not found in both of the standard reference material samples. Overall, the data are of generally acceptable quality.

Procedural blanks were included as part of the analytical methods in each group of samples analyzed and are shown in table 11. Concentrations of the selected trace elements in the procedural blank samples were low, resulting in method detections lower than required for the analysis. Overall, the procedural blank data show no substantial or detectable contamination resulting from the analytical procedures.

The accuracy of the trace element data was assessed by the analysis of standard reference materials, the analysis of which are shown in table 11. The acceptance criterion for the analysis of standard reference material was 80 to 120 percent of the certified concentration. Two standard reference materials were used in the analysis of liver tissue: the DOLT-2 of dogfish liver tissue from the National Research Council of Canada and the 1566a oyster tissue from the U.S. National Institute of Standards and Technology. With the exception of one of the lead analyses of the DOLT-2 standard, all results were within the relative percent difference guideline of 20 percent when compared to the certified concentrations. Duplicate analysis of zinc in the oyster tissue resulted in a relative percent difference of 26 percent, which is larger than the acceptability criteria of 20 percent; however, the triplicate analyses of the DOLT-2 standard for zinc were well within the precision guidelines. One triplicate analysis of lead in the DOLT-2 standard was quite low and resulted in relative percent differences larger than 20 percent; however, the remaining four lead analyses of standard reference material were within the precision guidelines. Matrix spike recovery data are shown for four different spiking levels in table 11. The data show acceptable spike recovery at all spiking levels.

Table 10.--*Physical characteristics and age of sportfish and concentrations of cadmium, copper, lead, and zinc in liver tissue. Walleye samples consisted of eight livers per composite sample, smallmouth bass of five livers per composite sample, and rainbow trout of one liver per sample.*

[USGS, U.S. Geological Survey; >, greater than]

Size class, in centimeters; (inches in parenthesis)	Composite replicate	Physical characteristic and age: USGS sample number	Mean composite length (centimeters)	Mean composite weight (grams)	Mean composite age (years)	Laboratory analysis (micrograms per gram, dry weight): Percent moisture	Cadmium	Copper	Lead	Zinc
				Columbia River and upper Lake Roosevelt						
Walleye										
10-13										
(25.4-33)	1	30	31.8	261	2	80	5.0	48.8	0.16	92.9
>13-16	1	14	36.5	393	2	80	7.1	48.9	0.14	97.9
(>33-40.6)	2	19	38.9	491	4	80	6.9	20.5	0.15	77.4
	3	15	38.0	454	3	80	6.5	23.4	0.14	88.2
	Mean						6.8	30.9	0.14	87.8
>16-19	1	16	42.9	610	4	81	10.6	18.5	0.12	84.6
(>40.6-48.3)	2	17	43.4	650	5	81	10.0	24.9	0.13	93.0
	3	18	43.0	635	4	81	8.5	20.9	0.15	82.7
	Mean						9.7	21.4	0.13	86.8
>19-22										
(>48.3-55.9)	1	21	50.3	1,047	5	81	5.0	27.1	0.06	83.4
Native rainbow trout										
19-22	1	31	52.0	1,245	5	83	7.1	27.4	0.89	148.0
(48.3-55.9)	2	32	51.0	996	4	81	[1]15.7	[1]140	[1]1.19	[1]165.0
	Mean						11.4	83.7	1.04	156.5

Table 10.--*Physical characteristics and age of sportfish and concentrations of cadmium, copper, lead, and zinc in liver tissue. Walleye samples consisted of eight livers per composite sample, smallmouth bass of five livers per composite sample, and rainbow trout of one liver per sample.--Continued*

Size class, in centimeters (inches in parenthesis)	Composite replicate	Physical characteristic and age: USGS sample number	Mean composite length (centimeters)	Mean composite weight (grams)	Mean composite age (years)	Laboratory analysis (micrograms per gram, dry weight): Percent moisture	Cadmium	Copper	Lead	Zinc
			Mid-reach Lake Roosevelt and lower Spokane River							
Walleye										
10-13	1	3	30.3	206	1	81	6.5	50.6	0.11	103.0
(25.4-33)	2	4	30.9	219	1	81	4.7	47.8	0.05	90.7
	3	8	31.1	233	2	80	6.1	37.8	0.06	89.1
	Mean						5.8	45.4	0.07	94.3
>13-16	1	5	36.0	367	2	81	8.9	39.1	0.07	87.8
(>33-40.6)	2	6	35.3	330	2	81	8.8	63.9	0.07	101.0
	3	7	35.8	335	2	82	9.1	53.2	0.09	99.7
	Mean						8.9	52.1	0.08	96.2
>16-19	1	9	43.4	644	4	81	11.2	20.3	0.09	79.9
(>40.6-48.3)	2	10	44.1	666	5	81	7.8	18.7	0.07	82.9
	3	59	43.7	632	5	80	15.7	51.1	0.09	101
	Mean						11.6	30.0	0.08	87.9
>19-22	1	1	50.5	1,034	5	81	8.2	29.8	[1]10.9	[1]622.0
(>48.3-55.9)	2	2	51.2	1,021	4	81	6.9	14.8	0.06	69.1
	Mean						7.5	22.3	5.5	345.5
Smallmouth bass										
8-12	1	28	24.8	236	2	81	2.7	20.8	0.03	99.7
(20.3-30.5)	2	29	26.6	253	2	82	3.9	20.6	0.40	94.1
	Mean						3.3	20.7	0.21	96.9

Table 10.--*Physical characteristics and age of sportfish and concentrations of cadmium, copper, lead, and zinc in liver tissue. Walleye samples consisted of eight livers per composite sample, smallmouth bass of five livers per composite sample, and rainbow trout of one liver per sample.--Continued*

Size class, in centimeters (inches in parenthesis)	Composite replicate	Physical characteristic and age: USGS sample number	Mean composite length (centimeters)	Mean composite weight (grams)	Mean composite age (years)	Laboratory analysis (micrograms per gram, dry weight): Percent moisture	Cadmium	Copper	Lead	Zinc
				Sanpoil River embayment						
Walleye										
10-13										
(25.4-33)	1	12	30.4	205	1	79	5.8	50.8	0.06	98.5
>13-16	1	11	35.3	344	2	80	5.8	30.2	<0.03	83.6
(>33-40.6)	2	27	38.0	409	3	82	7.4	17.4	0.04	84.0
	Mean						6.6	23.8	0.04	83.8
>16-19	1	13	42.7	617	3	80	7.9	37.1	0.07	96.3
(>40.6-48.3)	2	23	43.4	726	3	78	2.9	14.9	<0.03	64.6
	Mean						5.4	26.0	0.07	80.4
Smallmouth bass										
8-12	1	24	26.3	244	2	80	5.2	30.7	0.14	87.4
(20.3-30.5)	2	25	26.2	263	2	81	4.0	17.4	<0.03	72.1
	3	26	25.8	239	2	81	3.2	19.6	0.21	94.0
	Mean						4.1	22.6	0.17	84.5
Native rainbow trout										
19-22	1	33	51.0	1,216	5	79	2.5	33.6	0.19	97.8
(48.3-55.9)	2	34	50.5	1,086	5	81	2.0	12.2	0.10	95.9
	3	35	54.0	1,188	4	80	5.8	18.1	0.80	80.4
	4	36	49.0	1,055	4	20	2.6	34.1	0.34	112.0
	Mean						3.2	24.5	0.36	96.5

Table 10.--*Physical characteristics and age of sportfish and concentrations of cadmium, copper, lead, and zinc in liver tissue. Walleye samples consisted of eight livers per composite sample, smallmouth bass of five livers per composite sample, and rainbow trout of one liver per sample.--Continued*

Size class, in centimeters (inches in parenthesis)	Composite replicate	Physical characteristic and age: USGS sample number	Mean composite length (centimeters)	Mean composite weight (grams)	Mean composite age (years)	Laboratory analysis (micrograms per gram, dry weight): Percent moisture	Cadmium	Copper	Lead	Zinc
				Sanpoil River embayment--Continued						
Net-pen rainbow trout										
17-20	1	37	45.5	1,219	3	80	5.1	10.3	0.30	122.0
(43.2-50.8)	2	38	51.0	1,563	3	76	0.9	117.0	0.30	93.0
	Mean						3.0	63.6	0.3	107.5

[1]Samples 01 and 32 were noted by the analytical laboratory as showing concentrations of some trace elements as being higher than other samples. Values were left in table because no quality-control problems were identified.

Table 11.--*Quality-assurance data for the analysis of cadmium, copper, lead, and zinc in liver tissue of walleye, smallmouth bass, and rainbow trout. Inductively coupled plasma mass spectography (ICP/MS) analysis from Battelle Marine Science Laboratory, Sequim, Washington.*

[SL, spiking level not adequate; DOLT-2, dog-fish liver tissue]

Sample description	Concentrations, in micrograms per gram, dry weight			
	Cadmium	Copper	Lead	Zinc
	Blanks			
Blank—Replicate 1	[2]0.005	[2]0.007	[2]0.007	[2]0.783
Blank—Replicate 2	[2]0.007	[2]0.036	[2]0.016	[3]0.8
Blank—Replicate 3	[2]0.003	[2]0.018	[2]0.011	[3]0.8
Mean blank[1]	0.005	0.020	0.011	0.261
Method detection limit	0.02	0.06	0.03	0.8
	Standard reference material			
1566a—Replicate 1	3.79	62.4	0.319	925
1566a—Replicate 2	3.90	56.2	0.320	710
Certified value	4.15	66.3	0.371	830
Range	±0.38	±4.3	±.014	±57
DOLT-2—Replicate 1	18.3	25.5	0.195	76.9
DOLT-2—Replicate 2	17.3	24.8	0.206	73.9
DOLT-2—Replicate 3	18.2	23.1	0.130	71.2
Certified value	20.8	25.8	0.22	85.8
Range	±0.5	±1.1	±0.02	±22.5
	Matrix spike results			
Amount spiked	5.00	5.00	5.00	5.00
755USGS-1 (KF1905WAL8030)	5.01	48.8	0.156	92.9
755USGS-1 + Spike 1	9.62	53.8	5.13	98.2
Amount recovered	4.61	5.00	4.97	5.30
Percent recovery	92	100	99	106
Amount spiked	50.0	50.0	50.0	50.0
755USGS-1 (KF1905WAL8030)	5.01	48.8	0.156	92.9
755USGS-1 + Spike 2	46.0	93.1	46.2	135
Amount recovered	41.0	44.3	46.0	41.8
Percent recovery	82	89	92	84
Amount spiked	0.500	0.500	0.500	0.500
755USGS-10 (SP1505WAL8004)	4.72	47.8	0.052	90.7
755USGS-10 + Spike 1	5.32	50.2	0.531	94.3
Amount recovered	0.60	2.40	0.479	3.60
Percent recovery	120	SL	96	SL

Table 11.--*Quality-assurance data for the analysis of cadmium, copper, lead, and zinc in liver tissue of walleye, smallmouth bass, and rainbow trout. Inductively coupled plasma mass spectography (ICP/MS) analysis from Battelle Marine Science Laboratory, Sequim, Washington.--Continued*

Sample description	Concentrations, in micrograms per gram, dry weight			
	Cadmium	Copper	Lead	Zinc
Amount spiked	50.0	50.0	50.0	50.0
755USGS-10 (SP1505WAL8004)	4.72	47.8	0.052	90.7
755USGS-20 + Spike 2	46.6	97.3	45.6	144
Amount recovered	41.9	49.5	45.5	53.0
Percent recovery	84	99	91	106
Amount spiked	5.00	5.00	5.00	5.00
755USGS-29 (SP1903WAL8059)	15.7	51.1	0.094	101
755USGS-29 + Spike 1	19.4	55.4	4.59	101
Amount recovered	3.70	4.30	4.50	0.00
Percent recovery	SL	86	90	SL

[1]Value used to blank-subtract data.
[2]Analyte reported below reporting limit.
[3]Not detected at or above detection limit shown.

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Appendix A.--*Summary of Parameters on Individual Fish Collected During the Lake Roosevelt Study*

Appendix A.--*Summary of parameters on individual fish collected during the Lake Roosevelt study*

[USGS, U.S. Geological Survey; mm, millimeter; M, male; F, female; U, unknown; yrs, years; Kettle, Columbia River and Lake Roosevelt near Kettle Falls; Spokane, mid reach of Lake Roosevelt and lower Spokane River; Sanpoil, Sanpoil River embayment; size class 1, 10 to 12 inches; 2, greater than 13 to 16 inches; 3, greater than 16 to 19 inches; and 4, greater than 19 to 22 inches--, not applicable]

Species	Site	USGS sample code	Size class	Replicate	Total length (mm)	Total weight (grams)	Gender M-F-U	Fillet weight (grams)	Liver weight (grams)	Age (yrs)	USGS sample code	Fillet weight (grams)
Walleye	Kettle	FDRKF1905-WAF8030	1	1	315	257	U	44	1.4	1	--	--
				2	286	182	U	32	2.8	1	--	--
				3	330	303	U	50	1.2	2	--	--
				4	315	247	U	46	4.6	2	--	--
				5	318	258	U	31	2	1	--	--
				6	322	261	U	34	2.6	2	--	--
				7	320	241	U	47	3.3	2	--	--
				8	334	342	U	34	1.7	1	--	--
Sample mean					318	261		39	2.6	1.5		
Walleye	Kettle	FDRKF1605-WAF8014	2	1	362	350	M	58	4.6	2	F1014.1	63
				2	347	314	M	40	3.6	2	F1014.2	37
				3	374	444	M	71	4.4	2	F1014.3	65
				4	343	354	M	44	3.4	2	F1014.4	47
				5	343	314	U	56	4.3	2	F1014.5	48
				6	404	560	M	63	6.3	3	F1014.6	67
				7	381	409	U	66	3.7	3	F1014.7	52
				8	365	401	U	46	4.7	2	F1014.8	33
Sample mean					365	393		55	4.3	2.3		
Walleye	Kettle	FDRKF1605-WAF8019	2	1	399	541	U	79	6.7	3	--	--
				2	407	517	M	60	5	4	--	--
				3	401	537	M	60	6.7	5	--	--
				4	380	464	U	56	3.7	4	--	--
				5	370	414	F	72	5	2	--	--
				6	387	512	U	59	7.3	4	--	--
				7	389	500	M	66	6.3	4	--	--
				8	378	444	U	47	4	5	--	--
Sample mean					389	491		60	5.4	3.9		
Walleye	Kettle	FDRKF1605-WAF8015	2	1	345	329	M	62	2.9	2	--	--
				2	373	484	M	51	3.8	2	--	--
				3	397	543	F	103	4.7	3	--	--
				4	390	440	M	41	5.1	4	--	--
				5	378	400	M	66	5.9	3	--	--
				6	400	555	M	85	6.3	5	--	--
				7	399	510	M	84	6.4	2	--	--
				8	360	370	M	39	4.1	2	--	--
Sample mean					380	454		67	5.2	2.9		

Appendix A.--*Summary of parameters on individual fish collected during the Lake Roosevelt study--Continued*

Species	Site	USGS sample code	Size class	Replicate	Total length (mm)	Total weight (grams)	Gender M-F-U	Fillet weight (grams)	Liver weight (grams)	Age (yrs)	USGS sample code	Fillet weight (grams)
Walleye	Kettle	FDRKF1906-WAF8055	2	1	395	495	F	79	3.3	4	--	--
				2	340	351	U	39	4.1	2	--	--
				3	355	344	U	42	3.9	2	--	--
				4	395	464	U	90	1.3	3	--	--
				5	370	384	U	36	2.5	2	--	--
				6	337	296	U	40	3	2	--	--
				7	376	452	U	95	5	2	--	--
				8	350	298	U	39	2	2	--	--
Sample mean					365	386		54	3.1	2.4		
Walleye	Kettle	FDRKF1906-WAF8057	2	1	382	473	F	71	3.4	2	--	--
				2	405	523	F	107	3.3	4	--	--
				3	350	337	U	55	2	2	--	--
				4	355	288	F	57	1.8	3	--	--
				5	400	549	M	82	3.8	3	--	--
				6	371	412	F	82	3.6	3	--	--
				7	390	470	U	74	4.5	4	--	--
				8	380	461	F	71	3.2	3	--	--
Sample mean					379	439		75	3.2	3.0		
Walleye	Kettle	FDRKF1906-WAF8058	2	1	365	409	U	62	3.5	2	--	--
				2	400	481	M	105	4.4	3	--	--
				3	365	393	M	54	3.7	4	--	--
				4	370	454	F	87	5.5	3	--	--
				5	351	369	F	50	2.4	2	--	--
				6	345	309	U	36	2.7	2	--	--
				7	346	340	F	46	2.2	2	--	--
				8	380	374	U	72	2.3	3	--	--
Sample mean					365	391		64	3.3	2.6		
Walleye	Kettle	FDRKF1605-WAF8016	3	1	426	594	M	58	6.7	6	--	--
				2	453	726	M	120	7.5	5	--	--
				3	391	498	M	60	4	4	--	--
				4	424	508	M	87	5.4	3	--	--
				5	460	797	M	135	8.6	2	--	--
				6	448	722	M	82	9	3	--	--
				7	415	480	M	79	4.4	5	--	--
				8	414	555	M	58	6.4	4	--	--
Sample mean					429	610		89	65	4.0		

Appendix A.--*Summary of parameters on individual fish collected during the Lake Roosevelt study--Continued*

Species	Site	USGS sample code	Size class	Replicate	Total length (mm)	Total weight (grams)	Gender M-F-U	Fillet weight (grams)	Liver weight (grams)	Age (yrs)	USGS sample code	Fillet weight (grams)
Walleye	Kettle	FDRKF1605-WAF8017	3	1	435	655	M	113	6.9	4	--	--
				2	410	506	M	42	4.9	5	--	--
				3	412	575	M	66	5.3	6	--	--
				4	458	874	M	111	8.1	4	--	--
				5	444	562	F	65	5.1	4	--	--
				6	420	548	M	62	5	4	--	--
				7	430	601	F	83	5.3	3	--	--
				8	460	879	M	85	8.2	7	--	--
Sample mean					434	650		73	6.0	4.6		
Walleye	Kettle	FDRKF1605-WAF8018	3	1	455	813	M	125	9.4	5	--	--
				2	419	543	M	59	5	3	--	--
				3	470	800	M	110	7.9	6	--	--
				4	424	618	U	85	5.8	4	--	--
				5	432	710	U	106	6.7	4	--	--
				6	410	489	M	49	4.8	4	--	--
				7	416	544	F	81	5.4	4	--	--
				8	413	565	M	66	6	3	--	--
Sample mean					430	635		79	5.9	4.1		
Walleye	Kettle	FDRKF1906-WAF8056	3	1	452	668	M	82	6.3	6	--	--
				2	435	626	F	111	6	4	--	--
				3	455	711	M	94	3.5	6	--	--
				4	461	680	F	127	5.3	5	--	--
				5	435	619	F	63	4.7	4	--	--
				6	430	701	F	87	3.9	4	--	--
				7	415	578	F	115	3.4	3	--	--
				8	420	615	U	76	3	2	--	--
Sample mean					438	650		96	4.3	4.3		
Walleye	Kettle	FDRKF1605-WAF8021	4	1	483	755	F	109	9.4	5	--	--
				2	523	1,283	F	133	10.8	5	--	--
				3	501	1,000	F	158	13.2	5	--	--
				4	488	955	U	109	10.3	4	--	--
				5	487	657	F	74	5	5	--	--
				6	520	1,287	F	137	9.8	7	--	--
				7	515	1,063	F	175	10.3	5	--	--
				8	510	1,373	F	163	15.7	4	--	--
Sample mean					503	1,047		136	10.7	5.0		

Appendix A.--*Summary of parameters on individual fish collected during the Lake Roosevelt study--Continued*

Species	Site	USGS sample code	Size class	Replicate	Total length (mm)	Total weight (grams)	Gender M-F-U	Fillet weight (grams)	Liver weight (grams)	Age (yrs)	USGS sample code	Fillet weight (grams)
Walleye	Spokane	FDRSP1505-WAF8003	1	1	310	216	M	33	2.2	1	--	--
				2	306	219	U	32	0.8	1	--	--
				3	290	180	M	32	2	1	--	--
				4	304	210	U	30	1.6	1	--	--
				5	308	220	M	38	2.7	1	--	--
				6	315	222	U	33	1.6	2	--	--
				7	298	194	U	36	2.1	1	--	--
				8	293	188	U	28	0.8	1	--	--
Sample mean					303	206		33	1.7	1.1		
Walleye	Spokane	FDRSP1505-WAF8004	1	1	281	159	U	22	1.5	1	--	--
				2	310	217	U	41	2.8	1	--	--
				3	325	268	U	42	1.8	2	--	--
				4	318	244	U	48	3.3	1	--	--
				5	306	201	U	28	0.9	1	--	--
				6	312	218	U	35	2.1	1	--	--
				7	304	211	U	34	1	1	--	--
				8	318	235	M	42	2.2	1	--	--
Sample mean					309	219		39	2.0	1.1		
Walleye	Spokane	FDRSP1505-WAF8008	1	1	315	219	M	31	1.9	2	--	--
				2	276	156	M	34	1.5	1	--	--
				3	310	258	M	34	1	1	--	--
				4	323	237	M	45	1.6	2	--	--
				5	325	292	M	37	2.5	1	--	--
				6	310	231	U	45	1.5	2	--	--
				7	330	282	M	30	1.7	2	--	--
				8	299	187	M	36	1.7	1	--	--
Sample mean					311	233		37	1.6	1.5		
Walleye	Spokane	FDRSP1706-WAF8051	1	1	326	286	U	43	2.9	2	--	--
				2	275	152	U	18	2.1	1	--	--
				3	325	258	U	36	2.1	2	--	--
				4	305	234	U	25	3	2	--	--
				5	323	260	U	38	2.1	2	--	--
				6	305	216	U	31	1.7	2	--	--
				7	320	251	U	41	1.5	2	--	--
				8	305	222	U	35	3.8	2	--	--
Sample mean					311	235		32	2.3	1.9		

Appendix A.--*Summary of parameters on individual fish collected during the Lake Roosevelt study--Continued*

Species	Site	USGS sample code	Size class	Replicate	Total length (mm)	Total weight (grams)	Gender M-F-U	Fillet weight (grams)	Liver weight (grams)	Age (yrs)	USGS sample code	Fillet weight (grams)
Walleye	Spokane	FDRSP1906-WAF8052	1	1	330	276	U	34	3.5	2	--	--
				2	303	195	U	36	1.4	1	--	--
				3	330	309	U	30	3.8	2	--	--
				4	296	185	U	35	1.8	1	--	--
				5	310	231	U	32	2.5	2	--	--
				6	322	228	U	72	1.4	2	--	--
				7	325	272	U	40	0.1	2	--	--
				8	344	312	U	61	3.4	2	--	--
Sample mean					320	251		44	2.1	1.8		
Walleye	Spokane	FDRSP1505-WAF8005	2	1	365	368	M	53	2.2	2	--	--
				2	356	360	M	58	5.6	2	--	--
				3	360	389	M	57	2.9	2	--	--
				4	359	342	M	64	4.3	2	--	--
				5	350	321	M	43	2	2	--	--
				6	378	428	M	71	5	3	--	--
				7	340	331	M	47	1.3	1	--	--
				8	368	396	M	65	4.3	2	--	--
Sample mean					360	367		58	3.6	2.0		
Walleye	Spokane	FDRSP1505-WAF8006	2	1	341	290	M	38	1.8	2	F1006.1	29
				2	356	338	M	51	4.4	2	F1006.2	48
				3	345	279	M	42	2.4	2	F1006.3	26
				4	362	338	M	60	3.3	2	F1006.4	50
				5	358	358	U	66	3.8	1	F1006.5	52
				6	351	342	U	41	3	2	F1006.6	34
				7	346	266	U	46	2.4	2	F1006.7	45
				8	366	432	U	70	2.1	2	F1006.8	47
Sample mean					353	330		54	3.1	1.9		
Walleye	Spokane	FDRSP1505-WAF8007	2	1	355	335	U	40	1.2	2	--	--
				2	340	269	U	53	3.8	2	--	--
				3	355	370	U	55	2.2	2	--	--
				4	356	337	M	67	4.2	2	--	--
				5	364	367	U	44	2.7	2	--	--
				6	407	466	U	87	5.7	4	--	--
				7	343	258	M	34	1.6	2	--	--
				8	344	279	U	52	2.6	2	--	--
Sample mean					358	335		56	3.3	2.3		

Appendix A.--*Summary of parameters on individual fish collected during the Lake Roosevelt study--Continued*

Species	Site	USGS sample code	Size class	Replicate	Total length (mm)	Total weight (grams)	Gender M-F-U	Fillet weight (grams)	Liver weight (grams)	Age (yrs)	USGS sample code	Fillet weight (grams)
Walleye	Spokane	FDRSP1706-WAF8050	2	1	345	351	M	53	1.5	2	--	--
				2	342	340	U	35	4.3	2	--	--
				3	352	315	M	44	2.8	2	--	--
				4	355	378	M	49	4.1	2	--	--
				5	345	349	F	56	1.7	2	--	--
				6	345	290	U	31	1.5	2	--	--
				7	344	337	U	43	1.7	2	--	--
				8	342	321	M	43	1.2	2	--	--
Sample mean					346	335		43	2.5	2.0		
Walleye	Spokane	FDRSP1706-WAF8061	2	1	340	289	M	45	1.9	2	--	--
				2	375	434	U	46	5.5	4	--	--
				3	335	289	U	41	3.3	2	--	--
				4	381	498	M	57	1.5	3	--	--
				5	355	340	M	39	0.6	2	--	--
				6	340	262	F	29	2.3	2	--	--
				7	340	322	U	44	1.7	2	--	--
				8	342	311	U	37	2.8	2	--	--
Sample mean					351	343		42	2.5	2.4		
Walleye	Spokane	FDRSP1906-WAF8053	2	1	365	372	U	57	0.1	2	--	--
				2	375	400	U	80	2.8	2	--	--
				3	341	305	M	42	2.4	2	--	--
				4	355	304	U	56	3	2	--	--
				5	390	460	M	48	4.2	2	--	--
				6	360	329	U	64	3.4	2	--	--
				7	345	312	M	42	2.4	2	--	--
				8	340	294	U	63	2.7	2	--	--
Sample mean					359	347		56	3.0	2.0		
Walleye	Spokane	FDRSP1906-WAF8054	2	1	350	309	U	40	3	2	--	--
				2	340	300	U	60	3.8	2	--	--
				3	375	416	U	64	2.9	2	--	--
				4	360	362	U	68	4.1	2	--	--
				5	351	343	U	50	2.8	2	--	--
				6	364	382	M	78	4.5	2	--	--
				7	360	318	U	43	3.8	2	--	--
				8	357	399	M	71	3.4	2	--	--
Sample mean					357	354		62	3.6	2.0		

Appendix A.--*Summary of parameters on individual fish collected during the Lake Roosevelt study--Continued*

Species	Site	USGS sample code	Size class	Replicate	Total length (mm)	Total weight (grams)	Gender M-F-U	Fillet weight (grams)	Liver weight (grams)	Age (yrs)	USGS sample code	Fillet weight (grams)
Walleye	Spokane	FDRSP1505-WAF8009	3	1	451	777	F	67	3.6	5	--	--
				2	430	533	M	94	6	3	--	--
				3	411	565	M	81	2.3	2	--	--
				4	428	550	M	87	2.4	6	--	--
				5	440	636	F	97	5.1	6	--	--
				6	452	793	F	139	5.3	6	--	--
				7	442	705	M	127	7.6	4	--	--
				8	421	589	M	117	7	2	--	--
Sample mean					434	644		106	5.1	4.3		
Walleye	Spokane	FDRSP1505-WAF8010	3	1	450	759	F	71	2.7	6	--	--
				2	425	542	M	84	5.2	4	--	--
				3	423	632	M	117	6.6	4	--	--
				4	465	748	F	77	6.1	--	--	--
				5	433	597	M	90	7.1	4	--	--
				6	440	695	M	88	6.2	6	--	--
				7	419	591	M	112	4.7	4	--	--
				8	475	765	M	96	6.7	5	--	--
Sample mean					441	666		95	6.1	4.7		
Walleye	Spokane	FDRSP1906-WAF8059	3	1	443	706	M	135	4.2	4	--	--
				2	454	646	M	102	4	6	--	--
				3	430	625	F	123	4.6	4	--	--
				4	413	527	F	99	5.8	4	--	--
				5	437	557	M	57	6.4	4	--	--
				6	422	582	M	115	3.7	4	--	--
				7	435	648	F	80	4.8	4	--	--
				8	460	766	F	75	4.3	8	--	--
Sample mean					437	632		93	4.8	4.8		
Walleye	Spokane	FDRSP1405-WAF8001	4	1	520	1000	M	67	8.8	5	--	--
				2	510	1006	F	63	7.2	5	--	--
				3	495	1222	M	73	12.8	3	--	--
				4	510	994	M	64	11.4	8	--	--
				5	507	987	M	90	7.7	5	--	--
				6	500	959	F	62	7.2	5	--	--
				7	508	1155	M	82	14.2	4	--	--
				8	490	948	M	86	10.4	5	--	--
Sample mean					505	1,034		74	10.1	5.0		

Appendix A.--*Summary of parameters on individual fish collected during the Lake Roosevelt study--Continued*

Species	Site	USGS sample code	Size class	Replicate	Total length (mm)	Total weight (grams)	Gender M-F-U	Fillet weight (grams)	Liver weight (grams)	Age (yrs)	USGS sample code	Fillet weight (grams)
Walleye	Spokane	FDRSP1405-WAF8002	4	1	495	911	F	62	7	4	--	--
				2	500	939	M	91	9.7	4	--	--
				3	483	747	F	68	6.7	4	--	--
				4	535	1,242	F	103	11.2	4	--	--
				5	540	1,161	F	85	8.4	6	--	--
				6	500	1,019	F	71	11.2	4	--	--
				7	522	987	M	67	11.4	4	--	--
				8	524	1,165	M	108	10.3	4	--	--
Sample mean					512	1,021		85	9.8	4.3		
Walleye	Sanpoil	FDRSA1605-WAF8012	1	1	305	209	U	21	2.1	1	--	--
				2	315	219	U	30	3.3	2	--	--
				3	311	215	U	28	1.5	1	--	--
				4	315	218	U	29	2.6	2	--	--
				5	290	171	U	22	1.6	1	--	--
				6	310	216	U	32	2	2	--	--
				7	303	214	U	34	2	1	--	--
				8	285	176	U	25	0.7	1	--	--
Sample mean					304	205		29	2.0	1.4		
Walleye	Sanpoil	FDRSA1605-WAF8011	2	1	355	370	U	50	3.9	2	--	--
				2	360	379	U	24	2.1	3	--	--
				3	345	293	M	39	3.4	2	--	--
				4	342	304	M	30	2.4	2	--	--
				5	365	369	U	36	4	2	--	--
				6	353	363	U	51	3.2	2	--	--
				7	361	373	M	32	4.4	2	--	--
				8	341	300	U	41	3.4	2	--	--
Sample mean					353	344		36	3.3	2.1		
Walleye	Sanpoil	FDRSA1805-WAF8027	2	1	380	439	M	52	5.8	2	F1027.1	41
				2	373	406	U	61	2.9	1	F1027.2	57
				3	400	466	M	53	4.1	3	F1027.3	41
				4	403	484	M	71	4.3	3	F1027.4	60
				5	395	494	M	50	3.1	4	F1027.5	36
				6	388	401	M	56	4.6	4	F1027.6	49
				7	340	248	F	34	2.9	3	F1027.7	27
				8	359	337	F	54	2.5	2	F1027.8	45
Sample mean					380	409		54	3.5	2.8		

Appendix A.--*Summary of parameters on individual fish collected during the Lake Roosevelt study--Continued*

Species	Site	USGS sample code	Size class	Replicate	Total length (mm)	Total weight (grams)	Gender M-F-U	Fillet weight (grams)	Liver weight (grams)	Age (yrs)	USGS sample code	Fillet weight (grams)
Walleye	Sanpoil	FDRSA1605-WAF8013	3	1	445	658	F	42	4.9	5	--	--
				2	415	481	M	54	3.2	4	--	--
				3	413	594	M	63	3.7	5	--	--
				4	418	568	M	62	5.3	3	--	--
				5	410	570	M	79	5.9	3	--	--
				6	445	795	F	109	8.6	2	--	--
				7	425	621	F	65	5.7	2	--	--
				8	446	649	M	88	8.6	3	--	--
Sample mean					427	617		74	5.9	3.4		
Walleye	Sanpoil	FDRSA1705-WAF8023	3	1	412	638	F	79	5.7	3	--	--
				2	464	922	F	128	11	3	--	--
				3	444	757	F	105	9.1	3	--	--
				4	423	674	F	107	12.3	3	--	--
				5	425	688	U	94	4.9	2	--	--
				6	448	781	M	102	11.4	2	--	--
				7	425	691	U	78	5.6	2	--	--
				8	432	659	M	75	4.3	4	--	--
Sample mean					434	726		98	8.4	2.8		
Small-mouth bass	Spokane	FDRSP1705-SMF5028	--	1	210	136	M	13	1.6	1	--	--
				2	241	201	M	25	2	2	--	--
				3	275	323	F	32	3.9	2	--	--
				4	280	349	F	36	4.7	2	--	--
				5	235	173	M	17	1.3	2	--	--
Sample mean					248	236		25	2.7	1.8		
Small-mouth bass	Spokane	FDRSP1705-SMF5029	--	1	265	246	F	17	2.7	2	--	--
				2	287	286	F	37	3.3	2	--	--
				3	270	300	M	32	4.1	2	--	--
				4	279	278	F	29	3.7	2	--	--
				5	231	157	F	20	1.5	2	--	--
Sample mean					266	253		27	3.1	2.0		
Small-mouth bass	Sanpoil	FDRSA1805-SMF5024	--	1	260	207	F	18	2.1	2	--	--
				2	258	218	M	16	2.9	2	--	--
				3	250	232	F	24	2.5	2	--	--
				4	257	246	M	16	4.1	2	--	--
				5	290	318	M	30	3.9	2	--	--
Sample mean					263	244		21	3.1	2.0		

Appendix A.--*Summary of parameters on individual fish collected during the Lake Roosevelt study--Continued*

Species	Site	USGS sample code	Size class	Replicate	Total length (mm)	Total weight (grams)	Gender M-F-U	Fillet weight (grams)	Liver weight (grams)	Age (yrs)	USGS sample code	Fillet weight (grams)
Small-mouth bass	Sanpoil	FDRSA1805-SMF5025	--	1	250	214	M	13	2.6	2	--	--
				2	281	348	M	31	4.6	2	--	--
				3	252	205	F	22	1.9	2	--	--
				4	258	268	M	17	4	2	--	--
				5	267	278	M	19	4.6	3	--	--
Sample mean					262	263		20	3.5	2.2		
Small-mouth bass	Sanpoil	FDRSA1805-SMF5026	--	1	250	233	F	26	4.7	2	--	--
				2	282	299	F	24	5.2	3	--	--
				3	251	214	M	23	3.9	2	--	--
				4	252	228	F	14	2.7	2	--	--
				5	256	223	M	24	3.4	2	--	--
Sample mean					258	239		22	4.0	2.2		
Native rainbow trout	Kettle	FDRKF1905-RTF1031	--	1	520	1,245	F	142	12.3	5	--	--
Native rainbow trout	Kettle	FDRKF1905-RTF1032	--	1	510	996	F	128	6.6	4	--	--
Native rainbow trout	Sanpoil	FDRSA1905-RTF1033	--	1	510	1,216	F	138	15.7	5	--	--
Native rainbow trout	Sanpoil	FDRSA1905-RTF1034	--	1	505	1,086	M	211	17	5	--	--
Native rainbow trout	Sanpoil	FDRSA1905-RTF1035	--	1	540	1,188	F	121	22.1	4	--	--
Native rainbow trout	Sanpoil	FDRSA1905-RTF1036	--	1	490	1,055	M	200	12.2	4	--	--
Net-pen rainbow trout	Sanpoil	FDRSA1905-RTF1037	--	1	455	1,219	F	91	7	3	--	--
Net-pen rainbow trout	Sanpoil	FDRSA1905-RTF1038	--	1	510	1,563	M	187	20.8	3	--	--

Lake Fish Tissue

Lakes and reservoirs provide important sport fisheries and other recreational opportunities, and lake ecosystems provide critical habitat for aquatic species and support wildlife populations that depend on aquatic species for food. Lakes and reservoirs occur in a variety of landscapes and can receive contaminants from several sources, including direct discharges into the water, atmospheric deposition, and agricultural or urban runoff. A group of contaminants of particular concern are the persistent, bioaccumulative, and toxic (PBT) chemicals. These contaminants are highly toxic, long-lasting chemicals that can accumulate in fish, reaching levels that can affect the health of people and wildlife that eat them.

PBT contaminants can originate from a variety of sources. A primary source of one of the most important PBTs, mercury, is combustion at coal-fired power plants and other industrial operations (see the Mercury Emissions indicator); mercury emitted to the air can then be transported and deposited in lakes and reservoirs. Among other important PBTs, most uses of DDT became illegal in the U.S. in 1972; production and use of PCBs in the U.S. were phased out by 1979; chlordane was banned in 1988; and dioxin levels in the environment have been declining since the early 1970s (U.S. EPA, 2009).

This indicator is based on tissue samples of predator and bottom-dwelling fish species collected and analyzed for EPA's National Study of Chemical Residues in Lake Fish Tissue (U.S. EPA, 2009). The data generated from this probabilistic survey (Olsen et al., 2009; Stahl et al., 2009) are designed to estimate the national distribution of the mean levels of PBT chemicals in fish tissue from lakes (not including the Great Lakes) and reservoirs of the contiguous 48 states. The indicator consists of statistical distributions of the concentrations of 14 PBT chemicals or chemical groups in predator and bottom-dwelling fish tissue, including mercury, arsenic (total inorganic), dioxins/furans, total PCBs, and 10 organochlorine pesticides.

Fish samples were collected from 500 lakes and reservoirs over a 4-year period (2000-2003). Sampling locations were selected from the estimated 147,000 target lakes and reservoirs in the contiguous 48 states based on an unequal probability survey design. The lakes and reservoirs were divided into six size categories, and varying probabilities were assigned to each category to achieve a similar number of lakes in each size category. The lakes and reservoirs ranged from 1 hectare (about 2.5 acres) to 365,000 hectares (about 900,000 acres), were at least 1 meter (3 feet) deep, and had permanent fish populations.

Because no predator or bottom-dwelling species occurs in all 500 lakes and reservoirs, the study focused on 12 target predator species and six target bottom-dwelling species to minimize the effect of sampling different species. These species were chosen because they are commonly consumed in the study area, have a wide geographic distribution, and potentially accumulate high concentrations of PBT chemicals. Sampling teams applied consistent materials and methods nationwide. From each lake or reservoir, teams collected composite samples of five adult fish of similar size for one predator species (e.g., bass or trout) and one bottom-dwelling species (e.g., carp or catfish) where one or both were available (U.S. EPA, 2002). Sampling the 500 lakes and reservoirs yielded 486 composite samples for predator species and 395 composite samples for bottom-dwelling species. Fillets were analyzed for predators, and whole bodies were analyzed for bottom-dwelling fish. Fillet data represent the edible part of the fish most relevant to human health, while whole-body data are more relevant to wildlife consumption. A single laboratory prepared fish tissue samples for analysis in a strictly controlled environment, and tissue samples were sent to four analytical laboratories. The same laboratory analyzed tissue samples for each chemical group (e.g., PCBs or organochlorine pesticides), using the same standard analytical method, for the duration of the study. Concentrations of dioxins and furans were reported on a toxic equivalency quotient (TEQ) basis, which adjusts for the different toxicities of the various dioxin and furan compounds.

Concentrations of mercury, PCBs, dioxins and furans, DDT, and chlordane in predator fillets were compared with human health screening values. The mercury screening value is EPA's tissue-based water quality criterion (U.S. EPA, 2001). The other screening values are risk-based consumption limits from EPA's *Guidance for Assessing Chemical Contaminant Data for Use in Fish Consumption Limits: Volume 2* (U.S. EPA, 2000).

What the Data Show

Mercury, PCBs, dioxins and furans, and DDT are widely distributed in lakes and reservoirs in the contiguous 48 states (Exhibits 1 and 2). Mercury and PCBs were detected in 100 percent of both predator and bottom-dweller composite samples. Dioxins and furans were detected in 81 percent of the predator composite samples and 99 percent of the bottom-dweller composite samples, and DDT was detected in 78 percent of the predator composites and 98 percent of the bottom-dweller composites.

Median concentrations in predator fillets (i.e., half of the lakes and reservoirs had fish with higher values) were as follows: mercury, 0.285 ppm; total PCBs, 2.161 ppb; dioxins and furans, 0.006 ppt [TEQ]; and total DDT, 1.47 ppb (Exhibit 1). Median concentrations in whole, bottom-dwelling fish were lower for mercury (0.069 ppm), but higher for total PCBs (13.88 ppb), dioxins and furans (0.406 ppt [TEQ]), and total DDT (12.68 ppb) (Exhibit 2).

Exhibit 3 shows the proportion of lakes that exceeded human health screening values for five commonly detected chemicals. Mercury was detected above human health screening values in almost 50 percent of the lakes sampled. The percentage of lakes above screening values was much lower for the other chemicals. DDT and chlordane were detected above human health screening values in less than 2 percent and 1 percent of the lakes sampled, respectively.

Limitations

- Survey data are not available for Alaska, Hawaii, or Puerto Rico.
- The Great Lakes and the Great Salt Lake are not included in the target population.
- Because the distribution of sampling sites was based on the frequency of occurrence of lakes and reservoirs, contaminants in lakes and reservoirs in arid states (e.g., Arizona, New Mexico, and Nevada) are not well represented.
- Due to the inaccessibility of some target lakes (e.g., landowner denial of access), the results are representative of the sampled population of lakes (approximately 80,000) rather than the original target population of 147,000 lakes.
- Trend data are not yet available, as this is the first time that a national lake fish tissue survey has been conducted using a probabilistic

sampling design. These data can serve as a baseline for future surveys.

Data Sources

The data for this indicator were obtained from EPA's National Study of Chemical Residues in Lake Fish Tissue (U.S. EPA, 2009). Information about this study is available at http://water.epa.gov/scitech/swguidance/fishstudies/lakefishtissue_index.cfm.

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Exhibit 1. Lake fish tissue PBT contaminant concentration estimates for predators (fillets) in the contiguous U.S., 2000–2003

Contaminant	Number of samples	Number of samples above MDL	Percentiles for fillet tissue concentrations (ppm)						
			5th	10th	25th	50th (median)	75th	90th	95th
Mercury	486	486	0.059	0.089	0.177	0.285	0.432	0.562	0.833
Total PCBs	486	486	0.000351	0.000494	0.001000	0.002161	0.008129	0.018159	0.033161
TEQ dioxins/furans only	486	395	*	*	*	6×10^{-9}	46×10^{-9}	109×10^{-9}	318×10^{-9}
Total inorganic arsenic	486	2	*	*	*	*	*	*	*
Total chlordane	486	96	*	*	*	*	*	0.003617	0.008266
Total DDT	486	378	*	*	*	0.00147	0.00694	0.01966	0.03057
Dicofol	486	15	*	*	*	*	*	*	*
Dieldrin	486	24	*	*	*	*	*	*	0.001193
Total endosulfan	486	18	*	*	*	*	*	*	*

Visit www.epa.gov/roe to see the full exhibit.

Exhibit 2. Lake fish tissue PBT contaminant concentration estimates for bottom-dwellers (whole fish) in the contiguous U.S., 2000–2003

Contaminant	Number of samples	Number of samples above MDL	Percentiles for whole-body tissue concentrations (ppm)						
			5th	10th	25th	50th (median)	75th	90th	95th
Mercury	395	395	0.019	0.020	0.039	0.069	0.124	0.220	0.247
Total PCBs	395	395	0.001579	0.002308	0.005146	0.013876	0.070050	0.130787	0.198324
TEQ dioxins/furans only	395	393	19×10^{-9}	59×10^{-9}	165×10^{-9}	406×10^{-9}	1067×10^{-9}	1770×10^{-9}	2006×10^{-9}
Total inorganic arsenic	395	36	*	*	*	*	*	*	0.037
Total chlordane	395	197	*	*	*	0.001653	0.009313	0.025964	0.030931
Total DDT	395	388	0.00108	0.00182	0.00423	0.01268	0.0353	0.15392	0.21863
Dicofol	395	8	*	*	*	*	*	*	*
Dieldrin	395	73	*	*	*	*	*	0.003436	0.024613
Total endosulfan	395	23	*	*	*	*	*	*	*

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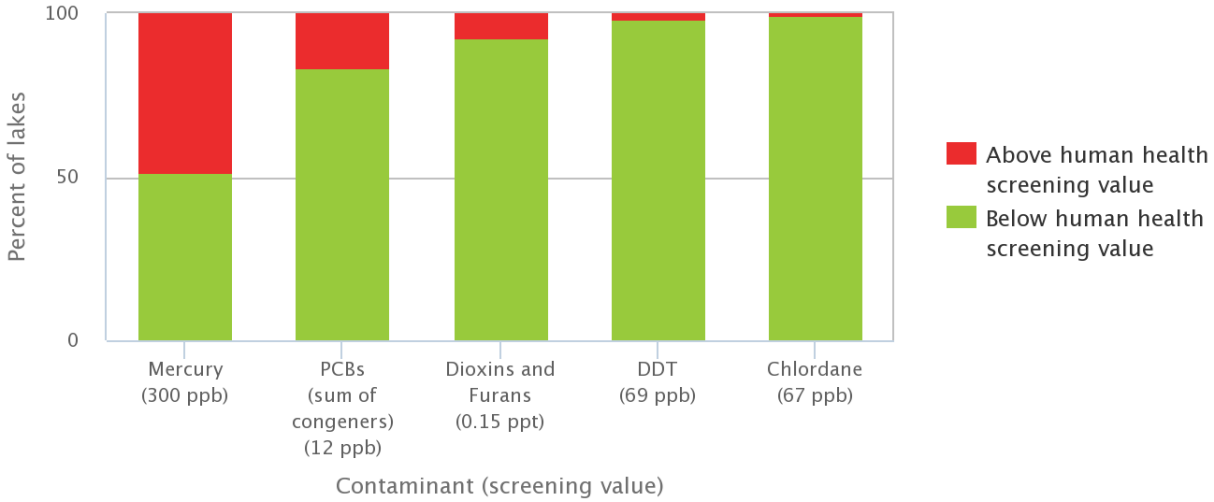
Exhibit 3. Percent of lakes above or below human health screening values for predators (fillets) in the contiguous U.S., 2000–2003



Coverage: Lakes and reservoirs of the contiguous 48 states.

Based on eating one 8-ounce meal of fish per week.

ppb = parts per billion ppt = parts per trillion

Trend analysis has not been conducted because these data represent a single snapshot in time. For more information about uncertainty, variability, and statistical analysis, view the technical documentation for this indicator.

Data source: U.S. EPA, 2009

Fish Intake, Contaminants, and Human Health
Evaluating the Risks and the Benefits

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Context Fish (finfish or shellfish) may have health benefits and also contain contaminants, resulting in confusion over the role of fish consumption in a healthy diet.

Evidence Acquisition We searched MEDLINE, governmental reports, and meta-analyses, supplemented by hand reviews of references and direct investigator contacts, to identify reports published through April 2006 evaluating (1) intake of fish or fish oil and cardiovascular risk, (2) effects of methylmercury and fish oil on early neurodevelopment, (3) risks of methylmercury for cardiovascular and neurologic outcomes in adults, and (4) health risks of dioxins and polychlorinated biphenyls in fish. We concentrated on studies evaluating risk in humans, focusing on evidence, when available, from randomized trials and large prospective studies. When possible, meta-analyses were performed to characterize benefits and risks most precisely.

Evidence Synthesis Modest consumption of fish (eg, 1-2 servings/wk), especially species higher in the n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), reduces risk of coronary death by 36% (95% confidence interval, 20%-50%; $P<.001$) and total mortality by 17% (95% confidence interval, 0%-32%; $P=.046$) and may favorably affect other clinical outcomes. Intake of 250 mg/d of EPA and DHA appears sufficient for primary prevention. DHA appears beneficial for, and low-level methylmercury may adversely affect, early neurodevelopment. Women of childbearing age and nursing mothers should consume 2 seafood servings/wk, limiting intake of selected species. Health effects of low-level methylmercury in adults are not clearly established; methylmercury may modestly decrease the cardiovascular benefits of fish intake. A variety of seafood should be consumed; individuals with very high consumption (≥5 servings/wk) should limit intake of species highest in mercury levels. Levels of dioxins and polychlorinated biphenyls in fish are low, and potential carcinogenic and other effects are outweighed by potential benefits of fish intake and should have little impact on choices or consumption of seafood (women of childbearing age should consult regional advisories for locally caught freshwater fish).

Conclusions For major health outcomes among adults, based on both the strength of the evidence and the potential magnitudes of effect, the benefits of fish intake exceed the potential risks. For women of childbearing age, benefits of modest fish intake, excepting a few selected species, also outweigh risks.

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Since the publication of pioneering studies demonstrating low rates of death from coronary heart disease (CHD) among Greenland Eskimos,[1] fish (used herein to refer to finfish or shellfish) has been considered a healthy food. During ensuing years, evidence from several research paradigms—including animal-experimental, observational, and clinical studies—further supported this hypothesis and identified 2 long-chain n-3 polyunsaturated fatty acids (n-3 PUFAs), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), as the likely active constituents.[2-20] DHA also appears important for neurodevelopment during gestation and infancy.[21-26] Conversely, concern has arisen over potential harm from mercury, dioxins, and polychlorinated biphenyls (PCBs) present in some fish species.[27-34] The public is faced with seemingly conflicting reports on the risks and benefits of fish intake, resulting in controversy and confusion over the role of fish consumption in a healthy diet.[35,36] To elucidate the relative risks and benefits, we reviewed the scientific evidence for adverse and beneficial health effects of fish consumption.

EVIDENCE ACQUISITION

Identification of Studies

A myriad of exposures and outcomes have been related to fish consumption; we focused on populations and topics for which evidence and concern are greatest. We searched MEDLINE, governmental reports, and systematic reviews and meta-analyses to identify reports published through April 2006 evaluating (1) intake of fish or fish oil and risk of cardiovascular events and mortality, (2) effects of methylmercury and fish oil on early neurodevelopment, (3) risks of methylmercury for cardiovascular and neurologic outcomes in adults, and (4) health risks of dioxins and PCBs in fish.

MEDLINE search terms were (*Fish* or *n-3 PUFA* or *omega-3*) and (*coronary* or *cardiac* or *cardiovascular* or *mor-*

See also Patient Page.

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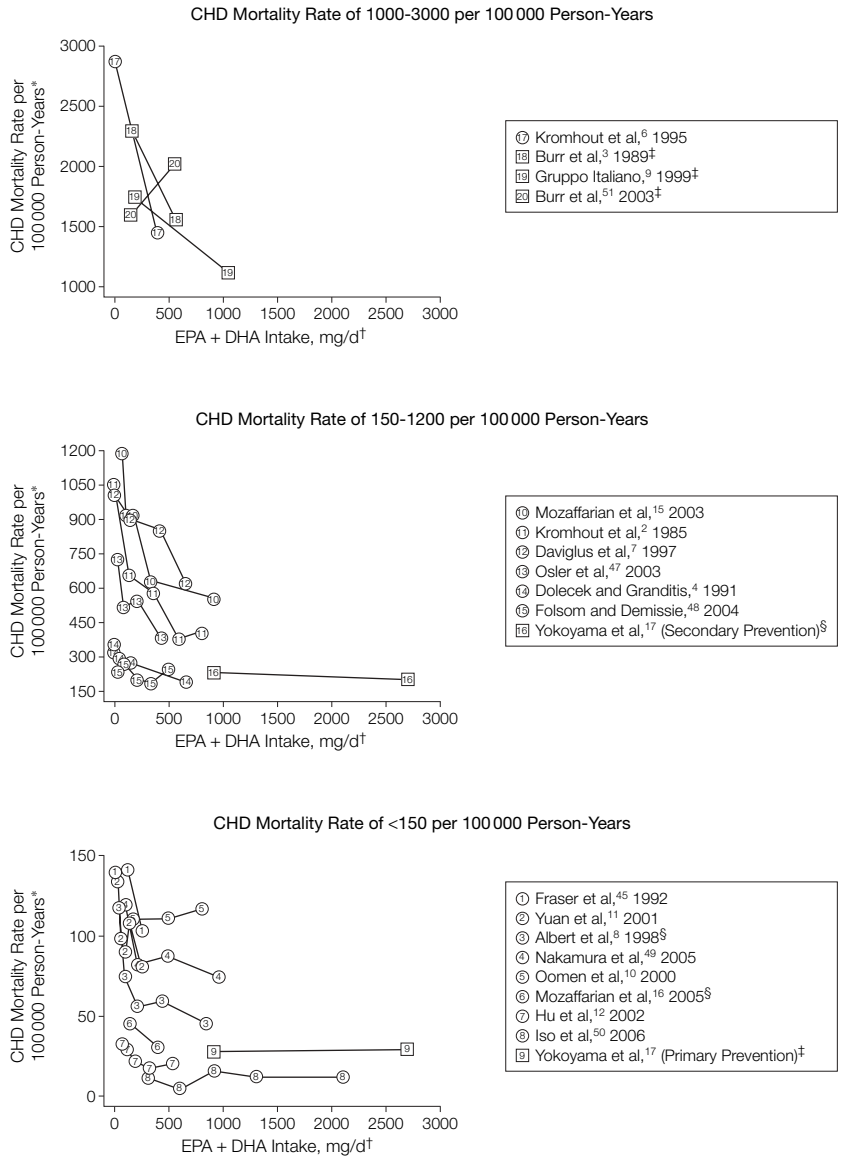
Clinical Review Section Editor: Michael S. Lauer, MD. We encourage authors to submit papers for consideration as a Clinical Review. Please contact Michael S. Lauer, MD, at lauerm@ccf.org.

Figure 1. Relationship Between Intake of Fish or Fish Oil and Rates of CHD Death in Prospective Cohort Studies and Randomized Clinical Trials



Circular data markers indicate prospective studies; square data markers, randomized trials. Absolute coronary heart disease (CHD) mortality rates vary more than 100-fold across different populations (due to differences in age, prior CHD, and other risk factors), but the relative effects of intake of fish or fish oil are consistent, whether for primary or secondary prevention, for cohort studies or randomized trials, or for comparing populations at higher or lower absolute risk. Compared with little or no intake, modest consumption (≈250-500 mg/d eicosapentaenoic acid [EPA] + docosahexaenoic acid [DHA]) is associated with lower risk of CHD death, while at higher levels of intake, rates of CHD death are already low and are not substantially further reduced by greater intake. For instance, populations with very high fish intake (Yokoyama et al[17] [secondary prevention; square 16]) already have much lower CHD death rates than otherwise comparable populations (Gruppo Italiano[9] [square 19]), and additional intake of fish or fish oil produces little further reduction in CHD mortality. Only 1 study (Burr et al[51] [square 20]) found results markedly divergent from this pattern. One study[46] was not included due to limited events data and limited multivariable adjustment.

*Rates in the control and intervention groups (for randomized trials) or rates in the reference group and multivariable-adjusted relative rates (for cohort studies).

†Reported data or estimated from similar populations.

‡Populations with prior CHD (secondary prevention).

§Rates of sudden death, not CHD death.

tality) and (*clinical trial* or *prospective* or *meta-analysis*); (*fish* or *n-3 PUFA* or *omega-3* or *docosahexaenoic* or *mercury* or *methylmercury*) and (*cognitive* or *neurologic* or *neurodevelopment*) and (*clinical trial* or *prospective* or *meta-analysis*); (*mercury* or *methylmercury*) and (*coronary* or *cardiac* or *cardiovascular* or *cognition* or *neurologic*) and (*clinical trial* or *prospective* or *meta-analysis*); (*dioxin* or *polychlorinated biphenyl* or *PCB*) and (*fish* or *seafood*). MEDLINE searches were restricted to identify only English-language reports, studies in humans, and adult or child populations (as appropriate) and were supplemented by searches of related articles of relevant identified manuscripts as well as by hand reviews of references from identified reports and direct contact with investigators.

Study Selection

One author (D.M.) screened all identified studies, and the final articles included were selected by both authors by consensus. Because fish intake is related to exposure to many different compounds, including n-3 PUFAs, mercury, and PCBs and dioxins, as well as to multiple different health outcomes, including cardiovascular diseases, neurologic outcomes, and cancer, a systematic quantitative review of every possible combination was beyond the constraints of this report. We concentrated on studies evaluating or estimating risk in humans, focusing on the evidence, when available, from randomized clinical trials and large prospective studies. Metabolic studies and animal-experimental evidence were also considered to elucidate potential mechanisms of effect. The evidence for risks and benefits was considered overall and among different at-risk populations. When possible, pooled or meta-analyses were performed to characterize effects most precisely.[37-39] Other potential benefits of fish intake (eg, for cognitive decline or dementia,[40] depression or neuropsychiatric disor-

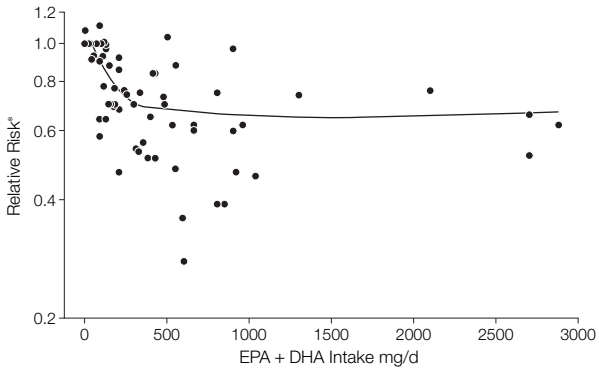
ders,[41,42] and asthma or inflammatory disorders[43,44]) were not reviewed in this report.

EVIDENCE SYNTHESIS

Benefits of Fish Intake

Cardiovascular Outcomes. Death from CHD—ie, documented or suspected fatal myocardial infarction—and sudden death—ie, a sudden pulseless condition of presumed cardiac etiology—are clinically defined entities often sharing the final common pathway of ventricular arrhythmia, often ischemia-induced ventricular fibrillation. The evidence from prospective studies and randomized trials[2-4,6-17,45-51] suggests that consumption of fish or fish oil lowers risk of CHD death and sudden death (FIGURE 1 and FIGURE 2). Across different studies (Figure 1), compared with little or no intake, modest consumption (≈250-500 mg/d of EPA and DHA) lowers relative risk by 25% or more. Higher intakes do not substantially further lower CHD mortality, suggesting a threshold of effect.[52] Pooling all studies, this pattern was clearly evident (Figure 2). At intakes up to 250 mg/d, the relative risk of CHD death was 14.6% lower (95% confidence interval [CI], 8% to 21%) per each 100 mg/d of EPA and DHA, for a total risk reduction of 36% (95% CI, 20% to 50%). At higher intakes, little additional risk reduction was present (0.0% change per each 100 mg/d; 95% CI, −0.9% to +0.8%). This threshold effect explains findings among Japanese populations,[17,50] in whom high background fish intake (eg, median 900 mg/d of EPA and DHA[50]) is associated with very low CHD death rates (eg, 87% lower than comparable Western populations[9,17]), and additional n-3 PUFA intake predicts little further reduction in CHD death; thus, most of the population is already above the threshold for maximum mortality benefits. Comparing different types of fish, lower risk appears more strongly related to intake of oily fish (eg, salmon, herring, sardines), rather than lean fish (eg, cod, catfish, halibut).[10,15] Fish intake may modestly affect other cardiovascular outcomes, but evidence is not as robust as for CHD death (TABLE 1).[17,50,53-66]

Figure 2. Relationship Between Intake of Fish or Fish Oil and Relative Risks of CHD Death in Prospective Cohort Studies and Randomized Clinical Trials



The relationship between intake of fish or fish oil and relative risk of coronary heart disease (CHD) death in a pooled analysis of the prospective studies and randomized trials shown in Figure 1, evaluated nonparametrically using restricted cubic splines[38,39] and adjusted for each within-study relationship. Given the much higher reference group intakes in some studies, the reference relative risk was scaled by 0.7 for studies with reference group intakes between 150-500 mg/d of eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) (n=5) and by 0.6 for studies with reference group intakes >500 mg/d (n=1) based on spline relationships prior to including these studies; exclusion of these studies, or of the few groups with intakes >1000 mg/d, had little effect on the pooled spline relationship. A significant threshold effect ($P<.001$) was evident at intake of 250 mg/d: between 0 and 250 mg/d, mortality risk was lower by 14.6% (95% confidence interval [CI], 8% to 21%) per each 100-mg/d greater intake (total risk reduction, 36%; 95% CI, 20% to 50%; $P<.001$), while at higher intakes, risk was not further lowered (0.0% change per each 100 mg/d; 95% CI, −0.9% to 0.8%; $P=.94$). *Relative risks in the control and intervention groups (for randomized trials) or relative risks in the reference group and multivariable-adjusted relative risks in the comparison groups (for cohort studies).

n-3 PUFAs influence several cardiovascular risk factors.[18,19,43,49,50,60-75,79-84] Effects occur within weeks of intake and may result from altered membrane fluidity and receptor responses following incorporation of n-3 PUFAs into cell membranes[76,77] and direct binding of n-3 PUFAs to intracellular receptors regulating gene transcription.[78] The heterogeneity of the effects of fish or fish oil intake on cardiovascular outcomes is likely related to varying dose and time responses of effects on the risk factors (FIGURE 3). At typical dietary intakes, antiarrhythmic effects predominate, reducing risk of sudden death and CHD death within weeks. At higher doses, maximum antiarrhythmic effects have been achieved, but other physiologic effects may modestly impact other clinical outcomes (possibly requiring years to produce clinical benefits). For instance, nonfatal myocardial infarction may not be significantly affected by lower doses or shorter durations of intake but may be modestly reduced by higher doses or prolonged intake (eg, 1.8 g/d for 5 years[17]).

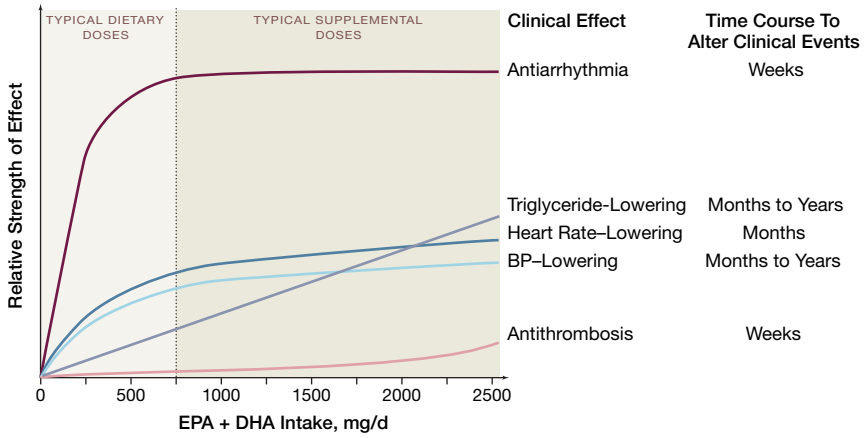
Heterogeneity of clinical effects may also be related to differing pathophysiologies of the clinical outcomes. For instance, disparate pathophysiologies of primary ventricular fibrillation (often ischemia-induced) vs recurrent ventricular tachyarrhythmias (ectopic or reentrant) may explain stronger effects of n-3 PUFAs on the former. Similarly, biological differences in development of atherosclerosis vs acute plaque rupture/thrombosis vs arrhythmia would account for heterogeneous effects of n-3 PUFAs on plaque progression vs nonfatal myocardial infarction vs CHD death. Consumption of fish may displace that of other foods, such as meats or dairy products, in the diet. However, this likely accounts for little of the observed health benefits, because foods replaced would be highly variable among individuals and across cul-

Table 1. Summary of Evidence for Effects of Consumption of Fish or Fish Oil on Cardiovascular Outcomes

Outcome	Clinical Effect	Strength of Evidence	Comment
CHD mortality			
CHD death	≈ 35% decrease	Strong	Probable threshold of effect—most risk reduction occurs with modest intake (≈ 250 mg/d EPA + DHA), with little additional benefit with higher intakes[2-4,6-17,45-51]*
Sudden death	≈ 50% decrease	Strong	
Ischemic stroke	≈ 30% decrease	Moderate	Strong evidence from prospective cohort studies[53,54]; no RCTs
Nonfatal CHD			
Nonfatal MI	Modest benefit?	Equivocal	Possible benefits at very high intakes (≈ 2 g/d n-3 PUFAs)[17,50]
Progression of atherosclerosis	Modest benefit?	Equivocal	Mixed results in cohort studies[55] and RCTs[56-58]
Postangioplasty restenosis	Modest benefit?	Equivocal	Possible benefits in a meta-analysis of RCTs[59]
Recurrent ventricular tachyarrhythmias	Modest benefit?	Equivocal	Mixed results in 3 RCTs[60-62]
Atrial fibrillation	≈ 30%+ decrease	Limited	Mixed results in 2 cohort studies[63,64]; benefit in 1 RCT[65]
Congestive heart failure	≈ 30% decrease	Limited	Benefit in 1 prospective cohort study[66]

Abbreviations: CHD, coronary heart disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MI, myocardial infraction; n-3 PUFA, n-3 polyunsaturated fatty acid; RCT, randomized clinical trial.
*See Figure 1.

Figure 3. Schema of Potential Dose Responses and Time Courses for Altering Clinical Events of Physiologic Effects of Fish or Fish Oil Intake



The relative strength of effect is estimated from effects of eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) on each risk factor and on the corresponding impact on cardiovascular risk.[70-72,79-84] For example, dose response for antiarrhythmic effects is initially steep with a subsequent plateau, and clinical benefits may occur within weeks, while dose response for triglyceride effects is more gradual and monotonic, and clinical benefits may require years of intake. At typical Western levels of intake (eg, <750 mg/d EPA + DHA), the physiologic effects most likely to account for clinical cardiovascular benefits include (1) modulation of myocardial sodium and calcium ion channels, reducing susceptibility to ischemia-induced arrhythmia;[18,19] and (2) reduced left ventricular workload and improved myocardial efficiency as a result of reduced heart rate, lower systemic vascular resistance, and improved diastolic filling.[67-72,80] At higher levels of intake seen with fish oil supplementation or in Japanese populations[49,50] (>750 mg/d EPA + DHA), maximum antiarrythmic effects have been achieved and clinically relevant effects occur on levels of serum triglycerides[79] and possibly, at very high doses, thrombosis.[75] Potentially important effects on endothelial,[73] autonomic,[74] and inflammatory[43] responses are not shown because dose responses and time courses of such effects on clinical risk are not well established. Effects are not necessarily exclusive: eg, antiarrythmic effects may be partly mediated by effects on blood pressure (BP) or heart rate.

tures, and modest intake of such foods is not associated with CHD risk.[85]

Total Mortality. n-3 PUFAs most strongly affect CHD death[5,9,14-16,18] and are unlikely to affect appreciably other causes of mortality. Effects on total mortality in a population would therefore depend on the proportion of deaths due to CHD, ranging from one quarter of deaths in middle-age populations[86] to one half of deaths in populations with established CHD.[9] Thus, given a ≈36% reduction in CHD death (Figure 2), intake of fish or fish oil would reduce total mortality by between ≈9% (36% reduction × 25% CHD deaths) to ≈18% (36% reduction × 50% CHD deaths), or an average of ≈14% in mixed populations. This is consistent with a meta-analysis of randomized trials through 2003[3,9,51,56,57,87-93] that found a nonsignificant 14% reduction in total mortality with n-3 PUFAs (pooled relative risk, 0.86; 95% CI, 0.70 to 1.04).[94] When we added additional placebo-controlled, double-blind, randomized trials[60-62] performed since 2003, marine n-3 PUFAs reduced total mortality by 17% (pooled relative risk, 0.83; 95% CI, 0.68 to 1.00; $P = .046$) (FIGURE 4). This can be compared to effects of statins on total mortality—a 15% reduction—in a meta-analysis of randomized trials (pooled relative risk, 0.85; 95% CI, 0.79 to 0.92).[95]

Neurologic Development. DHA is preferentially incorporated into the rapidly developing brain during gestation and the first 2 years of infancy, concentrating in gray matter and retinal membranes.[26] Infants can convert shorter-chain n-3 fatty acids to DHA,[96] but it is unknown whether such conversion is adequate for the developing brain in the absence of maternal intake of DHA.[22,25]

Effects of maternal DHA consumption on neurodevelopment have been investigated in observational studies and randomized trials, with heterogeneity in assessed outcomes (visual acuity, global cognition, specific neurologic domains) and timing of DHA intake (gestational vs nursing). In a meta-analysis of 14 trials, DHA supplementation

improved visual acuity in a dose-dependent manner.[23] Results for cognitive testing are less consistent, possibly due to differences in neurologic domains evaluated[21,25,26]; a quantitative pooled analysis of 8 trials estimated that increasing maternal intake of DHA by 100 mg/d increased child IQ by 0.13 points (95% CI, 0.08 to 0.18).[24] Most trials evaluated effects of maternal DHA intake during nursing, rather than pregnancy. In a trial among 341 pregnant women, treatment with cod liver oil from week 18 until 3 months postpartum increased DHA levels in cord blood by 50% and raised mental processing scores, a measure of intelligence, at age 4 years.[97] This is consistent with observational studies showing positive associations between maternal DHA levels or fish intake during pregnancy and behavioral attention scores, visual recognition memory, and language comprehension in infancy.[98-100] Thus, while dose responses and specific effects require further investigation, these studies together indicate that maternal intake of DHA is beneficial for early neurodevelopment.

Risks of Mercury

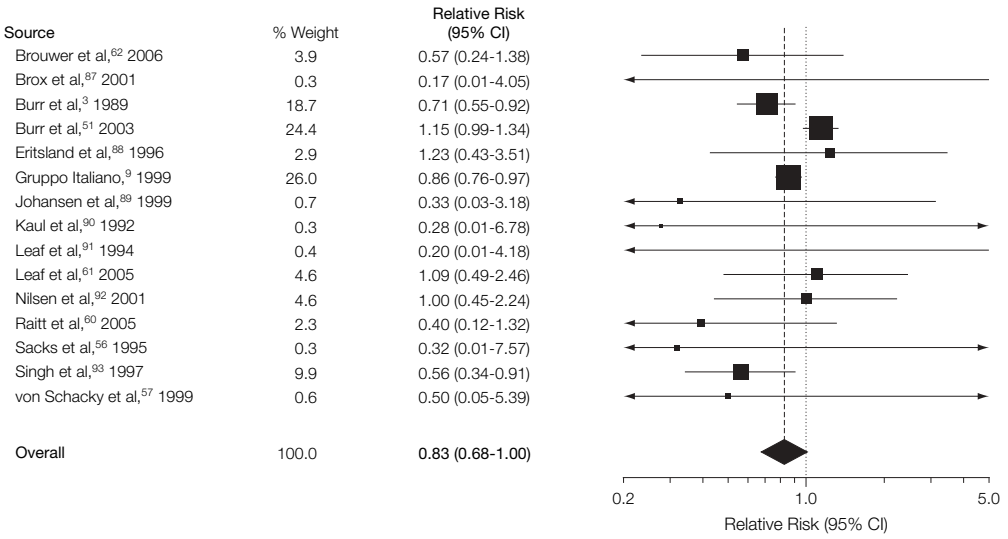
Mercury is a reactive heavy metal emitted from natural sources (volcanoes) and human sources (coal-fired electric power plants, gold mining, institutional boilers, chlorine production, and waste incineration).[101] From the atmosphere, mercury cycles from rainwater into lakes and oceans, where it is converted by microbial activity into organic methylmercury. Inorganic mercury is poorly absorbed following ingestion, and elemental mercury does not readily cross tissue barriers. In contrast, methylmercury is readily absorbed and actively transported into tissues.[27] Thus, methylmercury bioaccumulates in aquatic food chains and has greater potential toxicity than inorganic mercury.[27,28,30] Concentrations of methylmercury in aquatic species depend on levels of environmental contamination and on the predatory nature and lifespan of the species. Larger, longer-living predators (eg, swordfish, shark) have higher tissue concentrations, while smaller or shorter-lived species (eg, shellfish, salmon) have very low concentrations (TABLE 2).[122] Preparation methods have little impact on methylmercury content.[27]

Health effects of very high mercury exposure following occupational or industrial accidents are well documented, including paresthesias, ataxia, and sensory abnormalities in adults, and delayed cognitive and neuromuscular development following in utero exposure.[27,131] Toxicity appears related to binding of methylmercury to sulfhydryl groups of enzymes, ion channels, and receptors, resulting in inhibition of antioxidant systems and production of free radicals and reactive oxygen species.[27,29] Health effects of chronic low-level mercury exposure—ie, that seen with fish consumption—are less well established. The public is aware of the potential harm from mercury in fish but lacks clear understanding of who is at risk or which seafood species contain mercury.[35,36] We review the evidence for health effects below.

Methylmercury and Neurodevelopment

Methylmercury crosses the placenta, and fetal exposure correlates with maternal

Figure 4. Risk of Total Mortality Due to Intake of Fish or Fish Oil in Randomized Clinical Trials



The size of the shaded squares indicates each trial's contribution (inverse-variance weight) to the pooled estimate (dotted line) and 95% confidence interval (CI; diamond), determined by random effects meta-analysis.[37] Intake of fish or fish oil reduced total mortality by 17% ($P=.046$), with evidence for heterogeneity between trials ($P=.04$ for heterogeneity). If 2 trials with methodologic concerns[51,93] were excluded, the pooled relative risk was 0.83 (95% CI, 0.74-0.92; $P<.001$) with little evidence for heterogeneity ($P=.75$). A recently reported trial of fish oil among Japanese individuals[17] was not included in the primary analysis due to very high fish intake in the reference group (estimated eicosapentaenoic acid + docosahexaenoic acid intake, 900 mg/d) which would obviate mortality benefits of additional fish oil intake. When this trial was added to the secondary analysis, the pooled relative risk was 0.87 (95% CI, 0.76-0.99; $P=.048$; $P=.29$ for heterogeneity).

exposure.[132] Marked neurodevelopmental abnormalities occur in children following very high gestational exposure,[27,131] such as from maternal consumption of highly contaminated fish (10-30 ppm mercury) from industrially polluted Minimata Bay, Japan, in the 1950s, or of contaminated grain in Iraq in 1971 (maternal intake, 710-5700 ug/kg per day; 18-598 ppm mercury in maternal hair). More typical methyl mercury exposures are substantially lower: among US women of childbearing age, median (10th-95th percentiles) levels of mercury in hair were 0.19 (0.04-1.73) ppm overall and 0.34 (0.09-2.75) ppm among women consuming 3 or more servings of fish per month.[133]

Table 2. Levels of n-3 Fatty Acids and Contaminants in Commonly Consumed Fish, Shellfish, and Other Foods*

	EPA + DHA, mg/serving (Serving Size†)	EPA + DHA, mg/100 g (3.5 oz)	Selenium, µg/g (ppm)	Mercury, µg/g (ppm)	PCBs, ng/g (ppb)	Dioxins, TEQ pg/g (ppt)‡
FDA action level[33,102]	NA	NA	NA	1.0	2000	None§
Fish						
Anchovy	1165 (2 oz)	2055	0.68	<0.05		0.35 (1997-1998)[103]
Catfish, farmed	253 (5 oz)	177	0.15	<0.05	<50 (1997)[104]	0.53 (1995-1997)[105] 0.51 (1996)[106] 2.09 (1995-1996)[107] 1.65 (1995)[108]
Cod, Atlantic	284 (6.3 oz)	158	0.38	0.10		0.05 (1995-1997)[105] 0.15 (1995-1996)[107]
Fish burger, fast food	337 (2.2 oz)	546	0.17‡	<0.05	8 (2001)[109]	0.01 (2001)[110] 0.11 (2001)[109]
Fish sticks, frozen	193 (3.2 oz)	214	0.17	<0.05		0.04 (2001)[110]
Golden bass (tilefish), Gulf of Mexico	1358 (5.3 oz)	905	0.52	1.45		
Golden bass (tilefish), Atlantic	1358 (5.3 oz)	905	0.52	0.14		
Halibut	740 (5.6 oz)	465	0.47	0.25		1.00 (1995-1997)[105]
Herring, Atlantic	1712 (3 oz)	2014	0.47	<0.05		0.97 (1995-1998)[105]
Mackerel, Atlantic	1059 (3.1 oz)	1203	0.52	0.05		0.87 (1997-1998)[103] 0.32 (1995-1998)[105]
Mackerel, King	618 (5.4 oz)	401	0.47	0.73		
Mahimahi	221 (5.6 oz)	139	0.47	0.15		
Pollock, Alaskan	281 (2.1 oz)	468	0.43	<0.05		0.01 (1998)[105] 0.24 (1998)[111]
Salmon, farmed‖	4504 (6 oz)	2648	0.41	<0.05	21 (2001-2003)[112] 15 (2002)[113] 40 (2002)[115]¶ 26 (2001)[110] 25 (2001)[116] 51 (1999-2000)[117]¶ 38 (1999)[116]	0.50 (2001-2003)[112] 0.87 (2002)[114] 0.45 (2002)[115] 0.33 (2001)[110] 0.50 (1997)[105]
Salmon, wild‖	1774 (6 oz)	1043	0.46	<0.05	3 (2002)[115]¶ 0.5 (2002)[113] 5 (2000)[117]¶	0.03 (2002)[115] 0.34 (2002)[114]
Sardines	556 (2 oz)	982	0.53	<0.05	57 (2001-2003)[112] 22 (2002)[118]	0.44 (2001-2003)[112] 0.18 (2002)[118] 0.60 (1995)[105]
Shark	585 (3 oz)	689	0.34	0.99		
Snapper	546 (6 oz)	321	0.49	0.19		
Swordfish	868 (3.7 oz)	819	0.62	0.98		
Trout	581 (2.2 oz)	935	0.15	0.07	11 (2002)[113]	0.56 (2002)[113]# 0.32 (2002)[114] 0.74 (1998-2000)[119] 0.35 (1998)[105]
Tuna, light (skipjack)‖	228 (3 oz)	270	0.80	0.12	45 (2001)[110]	0.02 (1995-1998)[105]
Tuna, white (albacore)‖	733 (3 oz)	862	0.66	0.35	100 (2001-2003)[112]	0.23 (2001-2003)[112]

(continued)

Table 2. Levels of n-3 Fatty Acids and Contaminants in Commonly Consumed Fish, Shellfish, and Other Foods* (cont)

	EPA + DHA, mg/serving (Serving Size†)	EPA + DHA, mg/100 g (3.5 oz)	Selenium, µg/g (ppm)	Mercury, µg/g (ppm)	PCBs, ng/g (ppb)	Dioxins, TEQ pg/g (ppt)‡
Shellfish						
Clams	241 (3 oz)	284	0.64	<0.05	3 (2001-2003)[112] 2 (2002)[118]	0.05 (2001-2003)[112] 0.05 (2002)[118] 0.10 (1997-1998)[103]
Crab	351 (3 oz)	413	0.40	0.09	6 (2002)[113]	0.55 (2002)[113]# 1.05 (1998)[111]
Lobster	71 (3 oz)	84	0.43	0.31		0.69 (1998)[111] 0.12 (1997-1998)[103]
Mussels	665 (3 oz)	782	0.90	<0.15	7 (2001-2003)[112] 0.8 (2002)[113] 2 (2002)[118]	0.09 (2001-2003)[112] 0.11 (2002)[113]# 0.07 (2002)[118] 0.39 (1998)[105] 0.45 (1995-1996)[107]
Oysters	585 (3 oz)	688	0.77	<0.05	17 (2001-2003)[112] 0.8 (2002)[113]	0.46 (2001-2003)[112] 0.19 (2002)[113]#
Scallops	310 (3 oz)	365	0.28	<0.05		0.16 (1998)[111]
Shrimp	267 (3 oz)	315	0.40	<0.05	2 (2002)[118] 0.2 (2002)[113]	0.06 (2002)[113]# 0.11 (2002)[118] 0.06 (2001)[110] 0.19 (1995-1997)[105] 0.08 (1995-1996)[107]
Other Foods						
Beef	0	0	0.19	0	22 (2001)[110]	0.13 (2001)[110] 0.27 (1995)[120]
Bologna	0	0	0.14	0		0.16 (2001)[110] 0.29 (1995)[120]
Butter, regular	0	0	<0.05	0	70 (2001)[110]	0.22 (2001)[110] 0.31 (1995-1996)[107] 0.66 (1995)[120]
Cheese	0	0	0.22	0		0.25 (2001)[110] 0.77 (1998)[111] 0.34 (1995)[120]
Chicken	0	0	0.23	0	32 (2001)[110]	0.02 (2001)[110] 0.20 (1995)[120]
Eggs	22 (1 egg)	43	0.23	0	19 (2001)[110]	0.05 (2001)[110] 0.52 (1998)[111] 0.31 (1995)[120]
Milk, whole	0	0	0.02	0		0.01 (2001)[110] 0.12 (1995-1996)[107] 0.13 (1995)[120]
Pork	0	0	0.34	0	18 (2001)[110]	0.10 (2001)[110] 0.23 (1995)[120]

Abbreviations: DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FDA, US Food and Drug Administration; NA, not applicable; PCB, polychlorinated biphenyl; ppb, parts per billion; ppm, parts per million; ppt, parts per trillion; TEQ, toxic equivalence.

*Based on data from US Department of Agriculture (USDA),[121] Food and Drug Administration (FDA),[110] Environmental Protection Agency,[122] and other[103-109,111-120,123-126] sources. These values may vary due to methodologic, geographic, temporal, and fish-to-fish differences. Levels of PCBs and dioxins may overestimate current levels because contaminant levels in most foods, including fish species, are decreasing over time[33,110,112,127,128] (eg, TEQs decreased by 33%-81% in meats[127] and 66%-77% in salmon and tuna fish[112] between 1995 and 2003); year of sampling is given in parenthesis.

†Based on USDA serving sizes: 2 oz anchovies or sardines; 1 fillet catfish, cod, mackerel, mahimahi, snapper, or trout; ½ fillet halibut, king mackerel, pollock, or golden bass; 6 oz salmon; 3 oz herring, shark, shellfish, or tuna; 1 piece (3.75 oz) swordfish.[121]

‡The sum of dibenzodioxins (PCDDs) + debenzofurans (PCDFs) (nondetects = 1/2 LOD when multiple estimates available).

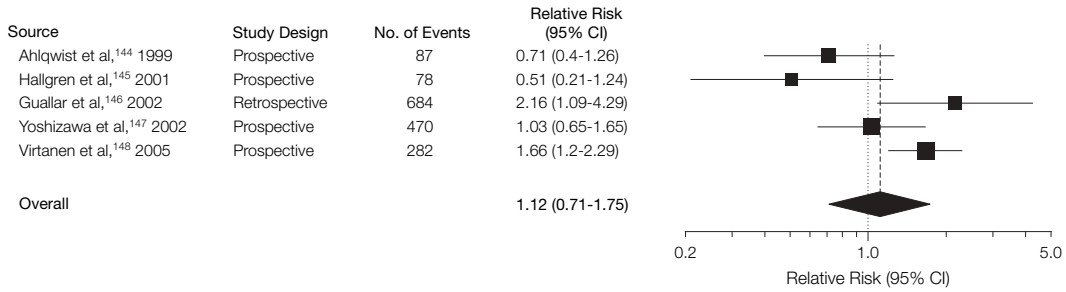
§Due to "numerous questions and uncertainties regarding scientific data on and analysis of dioxin risk."[129]

||For the same specific species, there are minimal differences in nutritional or contaminant content of canned vs fresh salmon or tuna. However, different species are typically canned vs sold fresh. For salmon, differences between species are small compared with differences between farmed and wild salmon. For tuna, canned light (skipjack) tuna and fresh yellowfin/ahi tuna are more similar overall, while canned white (albacore) tuna and fresh bluefin tuna are more similar overall.

¶Measured including the fish skin; levels may be lower in the edible portion.[130]

#Includes dioxin-like PCBs.

Figure 5. Multivariate Risk of Incident Coronary Heart Disease (CHD) With Higher Levels of Mercury Exposure



Relative risk and 95% confidence intervals (CIs) are shown comparing the highest to the lowest quantile of mercury exposure after adjustment for other risk factors. In 2 studies in Sweden, higher mercury levels were associated with trends toward lower risk,[144,145] but findings may have been limited by relatively few numbers of events. In 2 larger European studies, positive associations between mercury levels and CHD risk were reported.[146,148] A large US study observed no association,[147] but most participants were dentists, in whom mercury levels in part represented occupational exposure to inorganic mercury,[149] which may be less toxic than methylmercury in fish.[27,28,30] The overall pooled relative risk (dotted line) and 95% CI (diamond), estimated using inverse-variance random-effects meta-analysis,[37] was 1.12 (95% CI, 0.71-1.75; $P=.62$), with significant heterogeneity between studies ($P=.008$).

These exposure levels do not produce symptomatic neurodevelopmental deficits, but several prospective studies have evaluated whether subclinical effects, detectable with specialized testing, might occur.[98,100,134-140] Among children from the Faroe Islands,[134,135] New Zealand,[136,137] and Poland,[138] higher gestational exposure to mercury was associated with lower scores on some neurologic tests (eg, finger tapping, naming tests) but not others. In contrast, higher gestational exposure to mercury was associated with higher scores on some neurologic tests among Seychellois children.[139,140] In a US cohort, gestational maternal fish intake was positively associated with, but mercury levels in hair were negatively associated with, visual recognition memory scores in infancy,[98] indicating possible opposing effects of overall fish consumption (ie, providing DHA) and methylmercury exposure. In a British cohort, gestational mercury exposure was not associated with, but maternal and infant fish intake was associated with, improved neurodevelopmental scores.[100] Other studies did not detect consistent associations between gestational exposure to mercury and neurologic test scores during childhood.[141]

Comparisons across studies are limited by heterogeneity of study designs (prospective vs cross-sectional), mercury assessment methods, neurologic tests used, timing of assessment (infancy vs childhood), and statistical methods. Some analyses are also limited by multiple statistical testing (eg, ≥30 neurologic variables) or incomplete adjustment for other potential risk factors. Randomized trials to test effects of reducing low-level methylmercury exposure during gestation have not been performed. Nevertheless, given associations with some lower neurologic test scores in some studies, and clinical neurotoxicity of methylmercury following high-level accidental exposures, it is prudent to conclude that subclinical neurodevelopmental deficits may occur at lower exposure levels.

Based on this, the Environmental Protection Agency determined a reference dose, ie, the allowable upper limit of daily intake, for methylmercury of 0.1 ug/kg per day (≈50 µg/wk for a 70-kg woman, calculated from the lower 95% confidence limit at which gestational exposure to mercury may produce abnormal neurologic test scores, multiplied by a 10-fold uncertainty factor)[132] and published a focused advisory for women of childbearing age, nursing mothers, and young children.[142] The advisory specifically advises such individuals to avoid shark, swordfish, golden bass, and king mackerel (each containing >50 µg methylmercury per serving) (Table 2); to eat up to 12 oz/wk (2 average meals) of a variety of fish and shellfish lower in mercury, including up to 6 oz/wk of albacore tuna (30 µg methylmercury per serving); and to consult local advisories for locally caught freshwater fish. This advisory was not intended for the general population, because the importance of this reference dose to health effects in adults was unclear.[143] We review the evidence for such effects below.

Health Effects of Methylmercury in Adults

Cardiovascular Disease. Several studies[144-148] have evaluated the relationship between mercury exposure and incidence of cardiovascular disease (FIGURE 5). The conflicting results provide inconclusive evidence for cardiovascular toxicity of mercury. Notably, in the 2 studies observing higher risk with higher mercury levels, the net effect of fish consumption was still beneficial: greater mercury exposure lessened the benefit associated with consumption of fish or n-3 PUFAs but did not increase overall risk.[146,148,150] Thus, the principal question may not be whether consumption of mercury-containing fish increases cardiovascular risk but whether consumption of such fish would decrease risk even further if mercury were not present. This would be most true for oily fish species containing higher amounts of n-3 PUFAs (ie, most mercury-containing ocean fish), compared with lean freshwater fish. This is an important public

health issue, which requires balancing potentially attenuated benefits of fish intake due to presence of mercury with the costs and practicality of reducing mercury contamination in fish species. Nevertheless, this should not obscure evidence for net cardiovascular benefits of fish consumption, particularly fish richer in n-3 PUFAs.

Neurologic Outcomes. Very high methylmercury exposure from accidents (eg, Minimata)[27,151] or prolonged high intakes of mercury-containing fish (eg, 1-2 fish servings/d, including species high in mercury, for >10 years[152]) can produce sensorimotor symptoms in adults, most commonly paresthesias, which are often reversible when mercury exposure is reduced. Whether lower exposures produce neurologic abnormalities in adults is not clear. Cross-sectional studies have evaluated associations between mercury levels in hair or blood and subclinical neurologic function in adults. Among Amazon basin and Quebec Cree individuals, both positive and inverse associations were seen between mercury levels and some neurologic measures,[153-155] but findings were limited by minimal adjustment for other risk factors and multiple testing (typically ≥20-30 neurologic tests or participant subgroups). Among US adults, mercury levels were associated with lower visual memory scores ($P=.01$) but better motor and manual dexterity scores ($P=.02$) among 20 different outcomes evaluated.[156] Among elderly Swedish adults, no associations were found between mercury levels and cognitive function.[157] Thus, it is unclear whether low-level methylmercury affects subclinical neurologic outcomes in adults and, if so, what quantities or durations of exposure are necessary. Conversely, a growing body of evidence suggests that fish consumption may favorably affect clinical neurologic outcomes in adults, including ischemic stroke,[53] cognitive decline and dementia,[40] and depression and other neuropsychiatric disorders.[41,42]

Possible Mercury-Selenium Interaction. Health effects of mercury may partly result from selenoprotein inactivation, which might be mitigated by adequate intake of selenium, an essential dietary trace element.[158-161] Selenium also may reduce tissue accumulation of mercury in fish[162] and humans.[163] Seafood species are rich dietary sources of selenium.[121] A protective effect of selenium may partly account for conflicting results of studies of mercury exposure and neurodevelopmental indices in children[160] and of mercury exposure and risk of CHD.[164] A potential selenium-mercury interaction would have important public health implications, and additional investigation is warranted.

Risks of PCBs and Dioxins

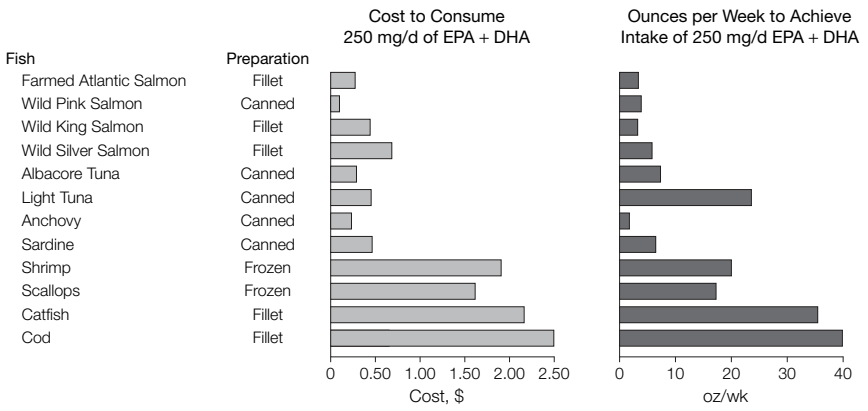
PCBs are synthetic organochlorine compounds previously used in industrial and commercial processes.[34] Dioxins—commonly referring to dibenzodioxins and dibenzofurans—are organochlorine by-products of waste incineration, paper bleaching, pesticide production, and production of polyvinyl chloride plastics.[33] Manufacture and processing of PCBs was prohibited in 1977,[34] and regulatory and industry efforts have reduced dioxin emissions by more than 90% since 1987.[33] Nevertheless, these contaminants persist for long periods in the environment, and thus while levels are steadily declining,[33,110,112,127,128] PCBs and dioxins continue to be present in low concentrations in many foods (Table 2).

Cancer Risks. Animal experiments and some evidence in humans indicate that PCBs and dioxins are carcinogenic, possibly related to effects on the aryl hydrocarbon receptor, a transcription factor affecting gene expression.[32,165] Multiple congeners (structural variants) of PCBs and dioxins exist. Potential toxicities of foods are calculated using toxic equivalence (TEQ): the sum of each congener's level in the food multiplied by that congener's toxic equivalency factor (standardized against 2,3,7,8-tetrachlorodibenzo-p-dioxin). In the United States, PCBs comprise 28% and dioxins 72% of total TEQ exposure.[120] Among adults, major dietary sources of PCBs and dioxins are beef, chicken, and pork (34% of total TEQ); dairy products (30%); vegetables (22%); fish and shellfish (9%); and eggs (5%).[120] Dietary sources are similar for children.[120]

Although major sources of exposure to PCBs and dioxins are meats, dairy products, and vegetables, considerable attention has been given to fish sources (Table 2). When PCBs and dioxins were measured in farmed and wild salmon,[115,166] levels were similar to those in several other foods (Table 2). Farmed and wild salmon also contained substantial levels of n-3 PUFAs: 4504 and 1774 mg of EPA and DHA per 6 oz, respectively.[166] Cancer risks and CHD benefits were evaluated in a quantitative risk-benefit analysis, assuming regular farmed or wild salmon intake to provide 1000 mg/d of EPA and DHA over a 70-year lifetime.[167,168] Per 100 000 individuals, consumption of farmed vs wild salmon would result in 24 vs 8 excess cancer deaths, respectively, while consumption of either farmed or wild salmon would result in 7125 fewer CHD deaths.[167] We further evaluated age-specific estimates, based on allocation of lifetime cancer risks[167] (adjusted for competing risks) by age-specific cancer mortality[169] and 25% reduction in age-specific CHD mortality.[169] For all ages evaluated (25-34 to ≥85 years), CHD benefits outweighed cancer risks by 100- to 370-fold for farmed salmon and by 300- to more than 1000-fold for wild salmon.

Notably, estimated CHD benefits are based on prospective studies and randomized trials in humans (Figures 1 and 2); estimated cancer risks include a 10-fold safety factor and are based on animal-experimental data and limited studies in humans at high doses.[168] Cancer estimates also assumed lifetime salmon consumption to provide 1000 mg/d of EPA and DHA (eg, four 6-oz servings of wild salmon every week for 70 years). However, CHD mortality reduction may be achieved with lower intake: ≈250 mg/d (Figures 1 and 2), or one 6-oz wild salmon serving per week. At this intake, CHD benefits would be

Figure 6. Estimated Costs of Consuming the equivalent of 250 mg/d EPA + DHA From Fish



Costs were calculated for commonly consumed seafood species, based on retail prices (averaging the most commonly sold items in each of 6 US cities in the east, midwest, and south from a national online grocery store[181] or, for wild king and silver salmon, from online retailers[182-184]) and on species-specific eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) content.[121] Least expensive was canned pink salmon (9 cents/250 mg of EPA + DHA); the average cost per 250 mg of EPA + DHA for these 12 types of seafood was 92 cents. The corresponding ounces per week needed to achieve 250 mg/d of EPA + DHA is also shown.

largely unchanged (≈7125 fewer CHD deaths), while lifetime cancer risk would decrease by ≈75% (6 and 2 estimated deaths per 100 000 lifetimes for farmed and wild salmon, respectively). Consistent with these very low cancer risks, prospective studies in humans have seen little evidence for effects of fish intake on cancer risk.[170]

Other Risks. PCBs and dioxins may have noncancer risks in adults, such as immune system or neurologic effects.[32-34] Conversely, fish consumption may also have other benefits, possibly lowering risk of other cardiovascular outcomes (Table 1), dementia,[40] neuropsychiatric disorders,[41,42] and inflammatory disorders.[43,44] If present, such additional possible risks would have to exceed additional possible benefits by more than 100-fold to meaningfully alter the present estimates of risks vs benefits. PCB content in fish can be reduced 12% to 40% by trimming belly and back fat during filleting and by not consuming the skin.[130] Also, contaminant levels are typically measured in unprepared foods, and cooking may reduce PCB and dioxin content.[106]

Prenatal (but not postnatal) exposure to PCBs and dioxins has been associated with childhood neurodevelopmental deficits in several,[171-177] though not all,[178,179] studies. Because most exposure (>90%) generally comes from meat, dairy, and vegetable sources,[120,180] this concern is not specific to fish consumption, particularly since fish also contains potentially beneficial DHA. However, women consuming 1 or more servings/d of commercial freshwater fish or consuming locally caught freshwater fish from highly contaminated inland sources may be more greatly exposed to PCBs and dioxins[180] and should consult regional advisories.

Related Considerations

Costs. We evaluated potential costs of consuming 250 mg/d of EPA and DHA from fish (FIGURE 6). The daily cost was as low as 9 cents, or 63 cents/wk. For combinations of different types of salmon; salmon and tuna; or salmon, tuna, anchovies, and sardines, the average cost was 37 cents/d ($2.59/wk) or less. Actual (net) costs would be lower because intake of fish would replace intake of other foods.

Supplements. Fish oil capsules contain 20% to 80% of EPA and DHA by weight (200-800 mg/g[185,186]), little to no mercury,[187] and variable levels of PCBs (0-450 ng/g,[116,188]) and dioxins (0.2-11 TEQ pg/g[114,189]). Given small amounts of fish oil consumed (1-3 g/d), exposure to PCBs and dioxins from fish oil intake is low. "Functional foods" supplemented with EPA and DHA (eg, dairy products, salad dressings, cereals) can also provide reasonable intake to individuals not consuming seafood.[190] Compared with supplements, fish intake also provides potentially beneficial protein, vitamin D, and selenium.[121]

Commercial Preparation. Commercially-prepared fried fish meals from fast food restaurants or supermarket frozen sections[123,124] are often made using white-meat fish (lower in n-3 PUFAs)[27,123] and prepared with partially hydrogenated oils (containing *trans* fats) or oils reused for multiple frying cycles (introducing oxidative/deteriorative products[191]). Higher cardiovascular risk seen with fried fish intake[15,54,63,66] may relate to this unfavorable balance of benefit vs harm (lower levels of EPA and DHA; higher levels of *trans* fats/deteriorative products) or to residual confounding from other lifestyle factors. While further research is needed, it appears unlikely that most commercially prepared fried fish meals lower cardiovascular risk.

n6:n3 Ratio. Ecologic studies and limited animal-experimental data suggest that linoleic acid (18:2n-6) may counteract potential benefits of n-3 fatty acids,[192,193] but this hypothesis has not been supported by clinical trials or prospective studies in humans.[16,194] A much greater change in the dietary ratio of n-6 fatty acids to n-3 fatty acids can be practically achieved by increasing intake of n-3s (eg, going from no intake of oily fish to 1 serving/wk) compared with lowering intake of n-6s (which are widely consumed in cooking oils, salad dressings, and prepared foods). Thus, for most populations, attention to relative intakes of n-6 vs n-3 fatty acids may be less important than simply increasing n-3 intake.

Aquaculture. Concerns exist about sustainability of some aquaculture and

commercial fishing practices.[195-197] Conversely, aquaculture contributes to global fish production,[198] and sustainability concerns are not unique to aquaculture or fishing but also exist for agricultural, forestry, freshwater, atmospheric, and energy resources.[195,199,200] Some progress has been made, such as changes in fish feeds to reduce dependence on fish meal or oil.[195] Given the importance of n-3 PUFAs for health, balance must be achieved between environmental and economic concerns to allow sustainable, financially viable aquaculture and commercial fishing.[195,196,199]

Plant Sources. Alpha-linolenic acid (ALA) (18:3n-3) is an n-3 fatty acid present in flaxseed, canola, soybeans, and walnuts.[121] In humans, ALA is converted to EPA in small quantities (in women more than men); further conversion to DHA is very limited.[201] Consumption of ALA (eg, 2-3 g/d) may reduce cardiovascular risk[202] or affect neurodevelopment, but benefits are less established compared with those for EPA and DHA.

Optimal Intakes

Optimal intake of n-3 PUFAs may vary depending on population and outcome of interest. In the general population, 250 mg/d of EPA and DHA is a reasonable target intake to reduce CHD mortality. Because dietary n-3 PUFAs persist for weeks in tissue membranes,[203] this can be converted to a weekly intake of ≈1500-2000 mg. This corresponds to one 6-oz serving/wk of wild salmon or similar oily fish, or more frequent intake of smaller or less n-3 PUFA–rich servings (Table 2). For individuals with CHD, 1000 mg/d of EPA and DHA is currently recommended to reduce CHD mortality.[204,205] Our analysis suggests that lower doses may be sufficient, but given this population's higher risk and that most data are from primary prevention studies, a target intake of 500 to 1000 mg/d—consistent with the largest secondary prevention trial to date[9]—appears reasonable. This could be approximated by one 6-oz serving/wk of fish richest in n-3 PUFAs (eg, farmed salmon, anchovies, herring), more frequent consumption of other fish (Table 2), or supplements. Optimal intake levels for other clinical outcomes are not well established.

The effects, if any, of low-level methylmercury exposure in adults are not established; mercury may modestly reduce the cardiovascular benefits of fish intake. One can minimize concerns by choosing fish higher in n-3 PUFAs and lower in mercury or by simply consuming a variety of different seafood. Individuals with high consumption (≥5 servings/wk) should limit intake of selected species highest in mercury (Table 2).

DHA appears important for early neurodevelopment. Women who are or may become pregnant and nursing mothers should avoid selected species (shark, swordfish, golden bass, and king mackerel; locally caught fish per local advisories) and limit intake of albacore tuna (6 oz/wk) to minimize methylmercury exposure.[31,142] However, emphasis must also be placed on adequate consumption—12 oz/wk—of other fish and shellfish to provide reasonable amounts of DHA[31,142] and avoid further decreases in already low seafood intake among women (74% of women of childbearing age and 85% of pregnant women consume <6 oz/wk).[206,207]

Continued efforts to limit environmental contamination from organochlorine compounds are appropriate. However, levels of PCBs and dioxins in fish are low, similar to those in several other foods, and the magnitudes of possible risks in adults are greatly exceeded by benefits of fish intake and should have little impact on individual decisions regarding fish consumption (for locally caught freshwater fish, women of childbearing age should consult regional advisories).

CONCLUSIONS

Potential risks of fish intake must be considered in the context of potential benefits. Based on strength of evidence and potential magnitudes of effect, the benefits of modest fish consumption (1-2 servings/wk) outweigh the risks among adults and, excepting a few selected fish species, among women of childbearing age. Avoidance of modest fish consumption due to confusion regarding risks and benefits could result in thousands of excess CHD deaths annually and suboptimal neurodevelopment in children.

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Study concept and design; acquisition of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content: Mozaffarian, Rimm.
Analysis and interpretation of data; statistical analysis; obtained funding: Mozaffarian.
Administrative, technical, or material support; study supervision: Rimm.
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prevented the development of protective immunity. In another murine model, protective immunity was also inhibited by azithromycin.[9] Brunham et al[10] observed that while chlamydial sexually transmitted infections in Vancouver decreased substantially over a few years after an azithromycin treatment program began, they estimated that annual risk of re-infection increased by 4.6% thereafter.

Personal hygiene and environmental improvements have already eliminated blinding trachoma in developed and some developing countries. Emphasis should be placed on all SAFE components with further evaluation of the antibiotic component, longitudinal assessments of efficacy, and vaccine development for sustainability.

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CORRECTIONS

Citation Error: In the Original Contribution entitled "Impact of Annual Targeted Treatment on Infectious Trachoma and Susceptibility to Reinfection" published in the September 27, 2006, issue of *JAMA* (2006;296:1488-1497) page 1493 contained an error in the use of a citation. The sentence "Since the immune response to *C trachomatis* is usually sustained for only 1 to 4 months,[24] we reasoned that individuals with resolved infection (conversion of PCR-positive result to negative at a subsequent time point) would be susceptible to infection at the next time point, 6 months later" should read "Since the duration of *C trachomatis* infection is reduced in older age groups, presumably as a result of acquired immunity,[24] we reasoned that if the immune response is usually sustained for only 1 to 4 months, individuals with resolved infection (conversion of PCR-positive result to negative at a subsequent time point) would be susceptible to infection at the next time point, 6 months later."

Omitted Financial Disclosure Information: In the Clinical Review entitled "Fish Intake, Contaminants, and Human Health" published in the October 18, 2006 issue of *JAMA* (2006;296:1885-1899), financial disclosure information was omitted. The disclosure for Dr Mozaffarian should have read: Dr Mozaffarian reported that he has received honoraria for presentations or articles about fish or *trans* fat consumption & cardiovascular health from the Institute of Food Technologists, the Danish Nutrition Council, the American Oil Chemists' Society, Project Syndicate, and several academic medical centers.

How Might Selenium Moderate the Toxic Effects of Mercury in Stream Fish of the Western US?

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Selenium and Mercury Interactions with Emphasis on Fish Tissue

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This review addresses the effects of mercury (Hg) in fish as it relates to the health of the fish themselves as well as potential risks of toxicity in wildlife and humans that consume fish. In particular, it addresses selenium (Se) as a bioindicator of susceptibility to harmful effects of Hg exposures and evaluates how Se moderates the toxic effects of Hg in a variety of test animals, emphasizing the importance of these potential effects in fish. A major conclusion of this review is that Hg toxicity risks to animal life cannot be accurately assessed without considering the moderating effects of Se. Therefore, Se:Hg molar ratios and their mathematical inverse are important factors that need to be considered when assessing risks from Hg exposures because exposures are related directly to toxicity outcome. In addition, actual measurement of both beneficial nutrients (e.g., Se, omega-3 fatty acids) and contaminants (e.g., Hg, polychlorinated biphenyls [PCB]) in fish tissue, rather than gross associations between the amounts of fish tissue consumed and changes in child IQ, motor skills, and verbal skill scores, has been recommended by human health effects researchers. This integrated approach will improve accuracy and reliability of environmental risk assessments for fish and fish consumers.

Keywords mercury, selenium, toxicity, Se–Hg interaction, fish, humans

Introduction

Mercury (Hg) is a well-known environmental toxicant that produces adverse effects in highly exposed animals (Ganther et al. 1972; Chen et al. 1973; Ohi et al. 1976; Watanabe et al. 1999) and humans (Tsubaki and Irukayama 1977; Grandjean et al. 1997). However, it appears that environmental and dietary availability of selenium (Se) must also be considered as a bioindicator of susceptibility to adverse effects of Hg

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exposures. Selenium's ability to moderate Hg toxicity was first demonstrated in rats by Pařízek and Oštádalová in 1967. Since that time, Se's moderating effects have been demonstrated in a wide variety of animal species (Cuvin-Aralar and Furness 1991; Yang et al. 2008); perhaps because all higher animal life forms require Se-dependent enzymes to protect their brains against oxidative damage. There is some evidence that Se might not always produce beneficial effects against Hg toxicity (Whanger 1985), but such evidence is limited. Whanger (1985) cites extensive research studies that demonstrate Se alleviates the toxicity of both inorganic and organic Hg in animal models and that a 1:1 Se:Hg molar ratio plays an important role. Thus the ratio of Se:Hg in animal tissues serves as an excellent bioindicator of susceptibility to Hg exposure. Since Se-dependent enzymes tend to be highly conserved in all vertebrate species, the moderating effect of Hg toxicity by Se in animal models suggests that similar protections occur in humans. Because selenoenzyme activities are so highly conserved, human vulnerabilities to Hg exposures may differ in degree from animal models but are unlikely to differ mechanistically.

The primary purpose of this review is to describe findings of studies that address interactions between Se and Hg as bioindicators of susceptibility to methylmercury (MeHg) toxicity. We draw from theoretical studies because they describe molecular mechanisms and from laboratory animal toxicity studies because they are numerous and applicable. Further, we cite aquatic field studies because they are environmentally relevant and several recent human epidemiological studies because they define actual risks of toxicity associated with human environmental exposures. The focus of this review is on fish and fish consumption as they relate to MeHg toxicity, but with sufficient examples from other toxicity studies to provide a background for the aquatic studies. Also, because aquatic organisms bioaccummulate MeHg, Se moderates MeHg toxicity effects, and fish consumption is the primary exposure route for both wildlife and humans, the review examines Se as a bioindicator of risks associated with MeHg exposure from fish and seafood.

Mercury

There is no known physiological requirement for Hg in animal metabolism, and high Hg or MeHg exposures can result in toxicity. Perhaps the most infamous incident of MeHg poisoning to animals and humans took place at Minamata Bay, Japan, in the mid-1950s, where very high concentrations of inorganic Hg were discharged to the bay from chemical plants (Tsubaki and Irukayama 1977). Bacterial methylation of the Hg resulted in severe MeHg poisoning (Minamata Disease) to both animals and humans that consumed fish and other seafood from the bay.

MeHg, one of the organic forms of Hg that bioaccumulates and comprises 95%–97% of the Hg in fish muscle tissue (Bloom 1992), is one of the most readily absorbed and toxic Hg forms encountered in nature. Because total Hg concentration usually approximates that of MeHg in fish filet tissue (Bloom 1992) and total Hg is much easier to measure, total Hg analyses are recommended for fish tissue surveys (U.S. Environmental Protection Agency 1997). Yeardley et al. (1998) developed a whole-fish tissue-based threshold of 0.1 μg MeHg $\cdot$ g^{-1} (wet weight) for protection of small piscivorous mammals (mink and otter). In 2001, the U.S. Environmental Protection Agency (EPA) established a fish tissue-based water quality criterion of 0.3 μg MeHg $\cdot$ g^{-1} wet weight for eatable fish tissue (usually filet) as a protection to human consumers against MeHg toxicity (U.S. Environmental Protection Agency 2001).

Selenium

At high exposures, Se can be an environmental toxicant to wildlife and humans, but unlike Hg, Se is required for the activity of enzymes that are normally present in all cells of all vertebrate forms of animal life (Behne et al. 2000). Dietary Se is required for synthesis of Se-dependent proteins (selenoproteins) and enzymes (selenoenzymes) that are essential for normal metabolic processes (Schwarz and Foltz 1957; Whanger 1981; Behne et al. 2000), especially in the brain and related tissues (Chen and Berry 2003; Schweizer et al. 2004). Selenoenzymes regulate intracellular redox status, protect against and reverse oxidative damage in brain and related tissues, and regulate thyroid metabolism (Kohrle 1999; Behne et al. 2000). Changes in dietary Se intakes result in Se concentration changes in somatic tissues such as muscle, liver, and kidney but have very little effect on Se concentrations in the central nervous and neuroendocrine tissues (Behne et al. 2000). Homeostatic control mechanisms activate when Se deficiency occurs in the brain and related tissues. The result is that somatic tissues selectively release their Se reserves, thereby maintaining uninterrupted supplies of Se to the otherwise deficient brain tissues (Kohrle 1999; Behne et al. 2000). Selenoenzyme activities that prevent oxidative damage decline rapidly in Hg-impaired tissues lacking sufficient Se to replace that lost to Hg binding (Dyrssen and Wedborg 1991). Because brain and related tissues are able to draw Se reserves from somatic cells during times of need (Kohrle 1999; Behne et al. 2000), most dietary manipulations cause only slight changes in selenoenzyme activities in adult rat brain tissues. However, in fetal and developing offspring with high maternal MeHg exposure, there are no tissue Se reserves to supply the developing brain with Se when MeHg selectively impairs Se delivery to the fetus (Parizek et al. 1971). Under these circumstances, the fetal brain can become Se-deficient, resulting in failure to protect against oxidative damage. Since impairment of these protective enzymes will naturally increase oxidative damage, it is not surprising that symptoms of Hg toxicity such as impaired walking ability are inversely related to brain Se in the exposed offspring (Watanabe et al. 1999).

While low-to-moderate Se intakes are required to support life, chronically excessive intakes can produce toxicity. However, this is characteristic of all essential nutrients and is hardly unique to Se. The nutritionally relevant range of dietary Se concentrations span two log orders, but there is a common perception that a relatively fine line exists between benefits and toxic effects. This is because the absolute concentrations of Se in the environment and its nutritional requirements are lower than for other essential elements. Despite this perception, the levels of chronic Se intakes associated with toxicity are ~20 times higher than the amounts required to optimize selenoenzyme levels in somatic cells. Differences in metabolic pathways employed by various animal types and distinctions in the ways various molecular forms of Se are processed influence the range of Se intakes that maintain health and produce toxic effect thresholds. Thus Se-dependent moderation of Hg toxicity would be similarly unequal for these various molecular forms. Ralston et al. (2007) state that growing mammals maintained on diets containing less than 0.1 μmol Se · kg^{-1} (~0.008 μg Se · g^{-1}) are unable to maintain normal Se selenoenzyme activities in their somatic tissues. Diets containing ~1.0 μmol Se · kg^{-1} (~0.08 μg Se · g^{-1}) are adequate to support normal selenoenzyme activities. Diets containing 10 μmol Se · kg^{-1} (~0.80 μg Se · g^{-1}) support an enhanced level of selenoenzyme activity that protects against free radical damage and fully charges somatic tissue Se reserves. However, as dietary Se concentrations rise above 25 μmol Se · kg^{-1} (~2 μg Se · g^{-1}), sustained consumption eventually saturates Se excretory pathways and initial signs of Se toxicity (selenosis) become increasingly apparent (Ralston et al. 2007).

The potential for aquatic Se toxicity and the difficulty in predicting tissue concentrations and/or effects from water concentrations prompted EPA to draft an edible portion fish tissue-based total Se water quality criterion of 7.9 μg Se · g^{-1} dry wt (approximately 2.0 μg Se · g^{-1} wet wt) for the protection of aquatic life (U.S. Environmental Protection Agency 2004). There has been much discussion concerning the final criterion since toxic effects vary with fish species, temperature, and other environmental variables. Thus the Se criterion has remained in draft form since 2004 but is scheduled to be finalized in 2009. The draft Se criteria document cites many studies concerning Se effects on fish, but there are few generalizations relative to threshold-level effects to organisms that consume those fish. However, the draft criterion (U.S. Environmental Protection Agency 2004) cites 17 papers by Dennis Lemly, several of which address Se toxicity thresholds for fish consumption. These studies found that in fish with whole body Se concentrations ≥4 μg Se · g^{-1} dry wt (~1.0 μg Se · g^{-1} wet wt), reproduction was adversely affected and deaths in juvenile fish increased (Lemly 2002).

Selenium–Mercury Interactions

While high Se or Hg exposures can each individually induce toxicity, co-occurrence of moderately high concentrations of these elements does not produce additive effects but, rather, antagonistic effects. That is, their co-occurrence can mutually reduce the toxic effect of each element. This phenomenon was first reported by Pařízek and Ošt'ádalová (1967). Several researchers picked up on this finding, and a considerable literature developed indicating that supplemental dietary Se moderates or counteracts Hg toxicity (Ganther et al. 1972; Chen et al. 1973; Ohi et al. 1976; Luten et al. 1980; Ohi et al. 1980; Whanger 1985). A recent renewal of interest in Se as a bioindicator of susceptibility to Hg bioaccumulation and toxicity has resulted in compelling reasons to consider the moderating effects of Se on Hg toxicity (Raymond and Ralston 2004; Belzile et al. 2006; Ralston et al. 2006, 2007, 2008; Ralston 2008; Mergler et al. 2007; Scheuhammer et al. 2007; Yang et al. 2008), particularly as it relates to effects on fish and fish consumers.

Selenium Physiology

Studies showing that supplemental Se counteracts Hg toxicity have employed several molecular forms of Se (Ganther et al. 1972; Chen et al. 1973; Ohi et al. 1976). In soils, Se occurs primarily as inorganic selenite and selenate, which enter the biological food chain through plant uptake and incorporation into proteins as selenomethionine and related forms. When the plants are eaten by animals, the selenomethionine is absorbed and incorporated into tissues via the same pathways that regulate methionine metabolism. In animal cells, selenomethionine eventually releases its Se for subsequent incorporation into selenocysteine that enters tightly regulated selenoprotein metabolic cycles. Regardless of whether Se is consumed as the inorganic, selenomethionine, selenocysteine, or other organic forms, once incorporated into an animal cell, all Se that eventually is incorporated into selenocysteine must first be converted into selenide: the precursor to selenocysteine that forms de novo during each cycle of cellular protein synthesis in the absence of divalent Hg (Hg^{2+}) or MeHg (Ralston et al. 2006).

If either form of Hg accumulates excessively in the cell, the normal selenocysteine cycle will be disrupted. Previously it was thought that these forms of Hg caused oxidative damage directly. However, Watanabe et al. (1999) pointed out, "the metabolism of neurotransmitters in adult rats was altered by dietary Se deficiency that lasted as short as two

weeks." Following this, Seppanen et al. (2004) showed that Hg toxicity most likely results from Hg inhibiting the activity of Se-dependent enzymes that normally prevent oxidative damage. This is termed the "selenium sequestration mechanism of mercury toxicity" (Ralston et al. 2006) wherein Hg-dependent inhibition of selenoenzymes appears to be the proximate cause of the oxidative damage that occurs as a result of Hg intoxication. That is, intracellular Hg sequesters Se, forming organic (most likely MeHg([Cys]) or inorganic HgSe complexes in the brain and other body tissues, thereby tying up both elements as highly insoluble compounds. While alternative theoretical explanations for the Se-protective mechanism have been proposed, the selenium sequestration mechanism described above is the most complete. Seppanen et al. (2004) provided convincing evidence in support of this mechanism. Additional support for the Se sequestration mechanism of mercury toxicity is the black, granular material identified as HgSe that accumulates in the brains and livers of higher organisms such as cormorants, sea lions, seals, and whales (Nigro and Leonzio 1996; Arai et al. 2004; Huggins et al. 2009). Similar evidence for Se-dependent protections to organisms are derived from the reverse application when otherwise toxic concentrations of Se are counteracted by feeding increased amounts of dietary MeHg (Ganther and Sunde 1974). The earliest evidence for this was based on adding mercuric chloride to the diets of chicks containing otherwise toxic concentrations of Se dioxide (Hill 1974). As mercury chloride was increased in the diet, the effects of Se toxicity gradually decreased until a Se:Hg molar ratio of 1:1 was reached. More recent evidence for mutual detoxification responses in crickets (Ralston et al. 2006), mice (Watanabe et al. 1999), and rats (Raymond and Ralston 2004; Ralston et al. 2006, 2007, 2008) have been observed.

Because selenide has an extremely high affinity constant with Hg^{2+} (10^{45} M), which is a million times greater than sulfide's affinity constant with Hg^{2+} (10^{39} M) (Dyrssen and Wedborg 1991), the combined effect of thermodynamic driving forces and biochemical distinctions between sulfur and Se metabolism results in the preferential formation of HgSe. So long as intracellular molar concentrations of Hg remain sufficiently low in comparison to Se in the brain and central nervous system, selenoenzyme activities in these tissues remain active. However, as increasing intracellular Hg exceeds Se, portions of the cellular Se essential for selenoenzyme production become sequestered and symptoms of Hg toxicity develop (Hirota 1986; Raymond and Ralston 2004). Therefore, it appears that it is not the concentration of Hg^{2+} or MeHg present in an organism that is critical, but rather the moles of Hg relative to the moles of Se in the tissues. Likewise, it appears that Se:Hg molar ratios that are < 1:1 increase Hg toxicity potentials, while Se:Hg molar ratios that approach or exceed 1:1 increasingly protect against Hg toxicity (Kasuya 1976). Provided cellular selenoenzyme activities are not diminished or interrupted by Hg toxicity, their protection against oxidative damage in vulnerable tissues such as brain is reduced or prevented. From this perspective, mass action effects explain the benefits of providing supplemental dietary Se in overcoming MeHg-dependent inhibition of selenoenzymes. We assume this protective mechanism is fully functional in fish since certain marine species contain Hg concentrations that would be expected to produce toxic effects, yet while they could harbor some neurological effects not readily observable, they show no outward sign of Hg toxicity (Kaneko and Ralston 2007). What these fish have in addition to high Hg concentrations is a molar concentration of Se greater than that of Hg (Se:Hg >1). The average molar ratio of Hg:Se in marine and freshwater fish muscle has been reported to be 0.65 and 0.99, respectively (Cappon and Smith 1981).

Ganther and Sunde (1974) fed high-Hg-content (0.7 – 1.0 μg Hg · g^{-1}) lyophilized canned tuna supplemented with MeHgOH and corn meal to five generations of Japanese

quail. The food mixture contained 17% tuna, and the final MeHg content of the food was 1, 10, and 20 μg Hg · g^{-1}. They compared the results of this feeding with controls containing the same amount of MeHgOH and corn meal, but no tuna Hg. Their primary findings were as follows: 1) tuna reduced the toxicity of MeHg, 2) Se was probably the substance in tuna that reduced the MeHg toxicity, and 3) Se and Hg in the tuna fed to quail had a Se:Hg molar ratio of ~1:1. In addition, Ganther and Sunde (1974) stated that by choosing appropriate levels of Hg and Se, it was possible for Se to reduce the toxic effects of Hg and also for Hg to reduce the toxic effects of Se. Therefore, by extension of the presumed protective mechanism described above, by virtue of apparently healthy marine fish having high whole-body MeHg concentrations but also having Se:Hg molar ratios ≥ 1 (Kaneko and Ralston, 2007), and since organisms draw Se from somatic tissue to supply the needs of the brain and central nervous system during times of Se depletion (Kohrle 1999; Behne et al. 2000; Seppanen et al. 2004), we assume that fish (marine or freshwater) having a molar ratio of Se:Hg >1 generally will be protected against Hg toxicity. If these fish themselves are protected from Hg toxicity by the Se, it seems reasonable to assume that consumers of the fish most likely will not suffer MeHg toxicity effects from eating these fish (Harris et al. 2003; Cabañero et al. 2007; see the "Mercury Forms and Selenium in Fish Tissue" section of this paper).

Laboratory Animal Models

The brains and neuroendocrine systems of all higher life forms are protected against oxidative damage by selenoenzymes as well as other antioxidants (Kohrle 1999; Behne et al. 2000). Since selenoenzyme systems throughout most of the animal kingdom are remarkably similar, rat and mouse models frequently are used as surrogates to study human selenoenzyme metabolism. Mouse studies support the conclusion that a small molar surplus of Se (Se:Hg >1) is sufficient to maintain uninterrupted selenoenzyme activity, thereby preventing Hg toxicity effects (Watanabe et al. 1999). Ralston et al. (2008) found that rat dietary Se intakes in the nutritionally relevant range from 0.1 to 10 μmol Se · kg^{-1} had no effect on growth in the presence of low MeHg (0.5 μmol MeHg · kg^{-1}). However, toxic effects of high MeHg (50 μmol MeHg · kg^{-1}; ~10 μg Hg · g^{-1}) exposures were inversely related to dietary Se as Se concentrations increased from 0.1–10 μmol Se · kg^{-1}. As the Se:Hg molar ratio in diets increased from 0.002 to 0.2, growth inhibition decreased to nonexistent at 0.2, and growth would have remained optimal as Se:Hg molar ratios entered into the normal healthy range. Thus growth impairment and neurotoxic effects were not dependent on MeHg exposure alone, but were inversely related to dietary Se and directly related to dietary Hg:Se molar ratios.

Environmental Selenium

A second mechanism of Se protection against Hg toxicity derives from the apparent ability of environmental Se to diminish Hg bioaccumulation in organisms. Björnberg et al. (1988) developed a theory regarding the mechanisms regulating bioavailability of Hg in an aquatic environment that focused on equilibrium reactions and their causal relationships. They concluded that the activity of Hg^{2+} was regulated primarily by the activity of S^{2-}, which in turn, is strongly affected by pH and redox conditions. In addition, they stated that equilibrium between Hg^{2+} and HgS is governed by the solubility product ($K_{sp} = 10^{-52}$). Finally, they concluded that in the presence of sulfide (reducing conditions) essentially all Hg will be in the form of HgS. It is important to note that sulfur and Se have very similar

chemical characteristics but that the S in HgS (binding affinity 10^{39} M) can be displaced in the chemical replacement series by Se to form HgSe (binding affinity 10^{45} M), which has an even lower solubility product ($K_{sp} = 10^{-59}$) than HgS. Björnberg et al. (1988) postulated that in areas where S^{2-} or Se^{2-} is abundant in soil and rocks, Hg concentrations in fish would remain low. They suggested that the introduction of Se into an aquatic environment containing high concentrations of Hg would reduce Hg bioaccumulation in fish tissue. While bioaccumulation differs from toxicity, the latter cannot occur without the former, thus reductions in MeHg bioaccumulation should lead to reductions in MeHg toxicity.

The theory of Björnberg et al. (1988) was field-tested in Sweden where several lakes had been black-listed because of high Hg concentrations in fish. Sodium selenite (Na_2SeO_3) added to Lake Oltertjärn increased the Se concentration in the water from 0.4 to ~3-5 $\mu g \cdot L^{-1}$, where it was maintained for 3 years (Paulsson and Lundbergh 1989). As a result, Hg concentrations in 17- to 25-cm-long (Year Class 1) perch (*Perca fluviatalis*) declined, on average, by 77%. At the end of 2 years, the Hg reduction averaged 75%, and by the end of Year 3, it averaged 84%. However, fish toxicity (selenosis) occurred in four of 11 lakes treated with Se. This led Lindqvist et al. (1991) to recommend against treating with inorganic forms of Se in deference to approaches that accomplish a slower Se release. Further evaluation of the technique in the English–Wabigoon River system in Ontario, Canada, led researchers to conclude that, although functional, the technique needed to be used with caution and Se additions should not exceed 1 $\mu g \cdot L^{-1}$ (Rudd et al. 1980, 1983).

More recent and compelling evidence that Se is protective against Hg bioaccumulation by aquatic organisms in the environment comes from Belzile et al. (2006). Their study examined the bioaccumulation of Hg by various trophic compartments of the aquatic food web in several lakes downgradient from the Se source at the Sudbury, Ontario, smelters. This study focused on concentrations of total and MeHg relative to Se concentrations in lake water and in zooplankton, mayflies (*Stenonema femoratum*), amphipods (*Hyalella azteca*), and young-of-the-year perch (*Perca flavesens*). They found that bioaccumulation of Hg in all of these organisms increased with decreasing Se in the water of lakes downwind from the Se source at the Sudbury smelters; a factor directly dependent on distance from that source. Peterson et al. (2007) described Hg in fish tissue from a probability-based sampling of 625 stream sites across 12 western states of the United States. This area is characterized by soil Se concentrations ranging from 0.17 to 0.74 μg/g (Gustavsson et al. 2001; Oldfield 2002). Thus it was anticipated that Se:Hg molar ratios in fish from streams of the western United States might be highly variable, with Se exceeding Hg in some locations and Hg exceeding Se in others. Therefore, Peterson et al. (2009) reanalyzed archived fish tissue samples from the 2000–2004 survey for Se. They found that nearly all fish (97.5%) from this area, with widely varying Se concentrations in the soil, had molar Se concentrations in excess of Hg molar concentrations. Further, they found that all fish with Se:Hg molar ratios <1 were of the genus *Ptychocheilus spp.* = pikeminnow, a large piscivorous member of the minnow family (*Cyprinidae*). Thus, according to the Se:Hg 1:1 molar ratios associated with protection as highlighted above, 97.5% of fish analyzed from the western U.S. streams would be expected to be minimally affected or unaffected by Hg toxicity. By extension, consumers of those fish might also be protected as evidenced by the finding of Cabañero et al. (2007) that the primary MeHg form found in fish tissue (MeHg[Cys]) stays intact and does not dissociate into toxic MeHg forms upon passing through an artificial digestive system. Kehrig et al. (2009) have reported a large Se molar excess in relation to Hg (total Hg) in plankton and fish from a tropical estuary food web. Peterson et al. (in preparation) have

found that fish from lakes in Idaho and from the northeastern United States have similar molar Se excesses over Hg. It appears the excess of Se over Hg in both marine and freshwater fish might be more widespread than previously expected. Thus it seems that the calculation of Hg toxicity potentials in fish tissue would benefit from further definition of Se protective effects against MeHg toxicity in fish and their consumers and that factoring that information into the protective assessment equation would be useful.

Mercury Forms and Selenium in Fish Tissue

Since wildlife (fish, birds, mammals) typically consume a whole fish carcass and the Se:Hg molar ratios in studies by Peterson et al. (2009) were based on whole fish analyses, those Se:Hg ratios are directly relatable to potential wildlife toxicity. Humans consume primarily fish muscle tissue (filets), and the human health Hg criterion is based on eatable tissue (usually filet) Hg concentrations. While we can calculate filet Hg concentrations from whole fish tissue Hg analyses (Peterson et al. 2007) and can thus relate whole fish Hg concentrations to the human health Hg criterion, no similar relationship has been developed for Se in freshwater fish. However, if we assume that Se:Hg molar ratios in whole fish directly influence fish toxicity potential, whole fish Se:Hg molar ratios can be used to estimate Hg toxicity potentials to the fish and, possibly, to wildlife that consume those fish.

MeHg exposure to wildlife and humans through fish consumption has driven concern for aquatic Hg toxicity. However, the MeHg present in fish tissue might not be as toxic as has been suspected. Recent structural analysis determined that fish tissue (filet) MeHg most closely resembles MeHg cysteine (MeHg[Cys]) (or chemically related species) which contains linear two-coordinate Hg with methyl and cysteinyl sulfur donors (Harris et al. 2003). The same authors point out that MeHg[Cys] is far less toxic to organisms than the MeHgCl that is commonly used in Hg toxicity studies. For example, day-old zebrafish (*Danio rerio*) larvae tolerate 20 times the concentration of MeHg[Cys] as they do MeHgCl. In addition, Ralston (2008), in discussing the metabolic cycles of selenomethionine (SeMet), selenocysteine (Sec), and inorganic Se, points out that protein synthesis cycles do not differentiate between SeMet and methionine (Met). Therefore, SeMet tends to be nonspecifically incorporated into proteins, and the rate of SeMet degradation is linked to rates of Met degradation. Thus the SeMet may engage in many cycles of protein synthesis as a methionine equivalent before eventually degrading to release Se, which is essential for Sec synthesis.

Since MeHg[Cys] in fish tissue appears to also participate in metabolism as a molecular mimic of Met, this may explain why it is 20 times less toxic than its MeHgCl equivalent. Since Cl^- has lower affinity for Hg than the sulfur of Cys, MeHgCl would release MeHg much more quickly than MeHg[Cys], increasing the rate at which it sequesters Se and SeCys. This is also supported by the finding that MeHg[Cys] does not dissociate into toxic MeHg forms upon passing through an artificial digestive system (Cabañero et al.2007). Beyond this, Korbas et al. (2008) suggest that, at least in some cases in nature, there might be a three-way antagonism involving Hg, Se, and arsenic (As) in association with glutathione (GSH) working in fish tissue to form ($[GS]_2$ $AsSeHgCH_3$). This MeHg-associated fish tissue protein molecule might provide yet another mechanism of protection against discrete hazards of elements that are generally perceived to be environmentally hazardous. All of these biochemical interactions indicate Se's metabolic relationship with MeHg needs to be considered in environmental assessments of potential fish tissue MeHg toxicity.

Selenium–Mercury Interactions and Humans

In the case of human beings, the protection of Se against Hg is less clear and somewhat conflicting. For example, Myers et al. (2003) observed no consistent pattern of adverse associations with prenatal MeHg exposure in children of the Seychelles Islands through age 9 despite the fact that average cord blood Hg concentrations were higher in children from the Seychelles than in children from the Faroe Islands (Grandjean et al. 1997). Meyers et al. (2007) reported that mean fish consumption by mothers in the Seychelles was 12 times/week, and their hair Hg concentrations averaged 6.9 $\mu g \cdot g^{-1}$. These researchers found further that adverse associations with MeHg appeared only when the statistical models were adjusted for nutrient status, whereas the positive associations of developmental tests with long-chain polyunsaturated acids (LCPUFA) became much stronger when the models were adjusted for MeHg. They stated that this suggests beneficial nutrients and the adverse effects of maternal exposure to MeHg from fish consumption during pregnancy may modify each other's effects on developmental outcomes in the children.

Hamada and Igata (1976) studied the effects of MeHg exposure on residents of the Tohoku Islands Japan. Like the Seychelles, these islands are mostly isolated from outside contaminant sources, and ocean fish is the primary food source. Since this population consumes copious amounts of marine fish, the average Hg concentration in hair of the Tohoku residents was greater than that found in Nigata, where symptoms of Hg poisoning had been observed. Despite the high MeHg exposures and high Hg concentrations found in their hair, Hamada and Igata (1976) found no symptoms of Minamata disease in the Tohoku Islanders. Thus the Seychelle Islands and the Tohoku Islands studies are similar in many ways, including the reported lack of adverse effects from relatively high MeHg exposures.

In the Faroe Island seafood consumption study conducted by Grandjean et al. (1997) cord blood MeHg levels varied considerably and ranged up to 350 $\mu g \cdot L^{-1}$. Their study detected adverse neurological effects on children at age 7. However, while this level of MeHg in cord blood might have been expected to produce profound effects, in reality, the effects were statistically weak and inconsistent across tests. The authors pointed out that the major source of MeHg in the Faroese children came from whale meat consumption by their mothers during pregnancy. Pilot whale meat contains high levels of Hg (mean 3.3 $\mu g\ Hg \cdot g^{-1}$) as well as PCBs and other organic contaminants (Weihe et al. 1996). Another source of MeHg was from the consumption of marine fish, but the marine fish, unlike whale meat, contained Se in molar excess of Hg. Budtz-Jorgenson et al. (2007) recognized that beneficial effects from consumption of ocean fish had a protective effect against MeHg. Therefore, the beneficial effects of Se from ocean fish might well have been responsible for the statistically weak and inconsistent effects observed by Grandjean et al. (1997). It is also possible that whale meat MeHg might be more bioavailable than that from fish tissue. The molar concentrations of Hg in whale meat average 4–5 times higher than Se, indicating only a small fraction of the total Hg could be in association with Se. Bioavailability of MeHg from whale meat has never been assessed in comparison to MeHg from ocean fish meat. However, MeHg from ocean fish meat that has passed through an artificial digestive system does not readily dissociate into toxic forms as previously had been suspected (Cabañero et al. 2007). If the toxicity of whale meat MeHg differs from that of ocean fish, it would be inappropriate to use the effects of MeHg exposure from whale meat consumption to predict risks associated with fish consumption.

Still another possibility is that effects on children observed by Grandjean et al. (1997) could have resulted from exposure to unknown substances in addition to MeHg from maternal consumption of whale meat during the gestation period. Since effects of these additional exposures would have occurred concomitantly with MeHg and the adverse effects of these exposures on child development might have occurred at any time during the pregnancy, it would be impossible to distinguish their discrete effects. Since pilot whale meat contains some of the highest levels of PCBs known to occur in a food source (Weihe et al. 1996) and other organic contaminants, high whale meat consumption results in extremely high PCB exposures in the Faroe Islands. For this reason, researchers explored effects of PCB exposures and ruled them out, but exposures to other organotoxins and the transient influences of high-level exposures to MeHg well before the cord samples were taken cannot be ruled out. The cord blood sample does not necessarily represent a time-integrated sample over the duration of the pregnancy. Therefore, it is entirely possible that high transient exposures to organotoxins in addition to MeHg temporarily impaired Se availability to the fetus. Watanabe et al. (1999) demonstrated that a small shortage of Se for as little as two weeks had adverse effects on adult rats. Effects to a fetus would likely occur much quicker. Exposures to these pollutant effects are not unique to pilot whale meats, but because they are concomitant with the high MeHg content of the whale meats, may have been attributed to MeHg alone. Grandjean (2003) raised some of these possibilities himself in discussing concerns about confounding and why the Hg effect might have been overestimated in the Faroes study: a) association of mercury intake with exposure to other neurotoxic pollutant(s), b) other types of residual confounding, and c) inadequate adjustment for multiple comparisons.

Both Hg and Se were measured in cord whole blood for all children participating in the Faroes study. Using this database, Choi et al. (2007) attempted to evaluate the effect of Se on the toxic effects observed by Grandjean et al. (1997). Neurodevelopmental outcomes were evaluated in two separate cohorts of 7-year-old children in their study. Each outcome was modeled as a function of Hg and Se interactions (with adjustments for potential risk factors) by expressing the effects of $\log_{10}$ (Hg) with the lowest 25%, the middle 50%, and highest 25% of the Se distribution. The study measured 17 neurodevelopmental outcomes in each of the three groups. The low Se group produced three statistically significant outcomes out of 17, the medium Se group one out of 17, and the high Se group zero out of 17. The confidence intervals (CIs) of all other outcomes (n = 51) included zero and thus were statistically insignificant. Choi et al. (2007) concluded from this that, "regression analyses failed to show consistent effects of Se, or statistically significant interaction terms between Se and MeHg." While this conclusion is technically correct based on the statistics, it is highly unlikely that the study could have turned out any other way because all of the study groups were replete with Se. Based on the molecular mechanism of methylmercury toxicity and the knowledge that Se moderates the effects of MeHg, evidence of that moderation appears to have presented itself in the Faroes study. Although the children with the highest Hg exposures and greatest adverse effects had Hg:Se molar ratios that approached 1:1, these discrete effects would be lost by considering study groups discriminated on the basis of their blood Se levels instead of their blood Hg:Se molar ratios. Since all of the groups were replete with Se at the time of delivery, any Se-Hg interaction that might have occurred had already taken place and no additional interaction would be expected. Therefore, the Grandjean et al. (1997) results indicate that MeHg toxicity may have taken place in the Faroe Islands, even with excess Se present However, it also suggests that if the effects were manifested by MeHg, they most likely occurred during a temporary spike in the mothers' MeHg intake and that the

adverse effects might have been considerably worse if the mother's dietary Se intakes had been lower.

The Choi et al. (2007) data report remarkably high, statistically significant correlations between cord blood Hg concentrations and Hg:Se molar ratios ($r^2 > 0.98$, $p < 0.001$) in the children studied in the Faroes. Therefore, any effects currently attributed to increasing MeHg exposures most likely could also be attributed to an increasing Hg:Se molar ratio. If that is the case, the Faroes data, rather than indicating no interaction between Hg and Se, would suggest that Hg sequestration of Se likely is an important factor in moderating MeHg toxicity. As described above, there might be several reasons for the neurodevelopmental effects observed by Grandjean et al. (1997). However, it is most likely that nutrients in fish contributed to the moderating effect against Hg toxicity that has been recognized in association with increasing fish consumption (Budtz-Jorgenson et al. 2007). Meyers et al. (2007) stated that, "the benefits of nutrients and the adverse effects of maternal exposure to MeHg from fish consumption during pregnancy may modify each other's effects on developmental outcomes in children." They stated further that, "these results suggest that it is critical to assess dietary nutrients as well as neurotoxic exposures in determining the risks and benefits of fish consumption."

The Grandjean et al. (1997) and Choi et al. (2007) papers suggest that neurodevelopmental effects of MeHg exposure might be detected even when the Se:Hg molar ratios approach or exceed 1:1. Their data indicate that mean Se was far more abundant than mean Hg but also that the cord blood Hg of several children approached a 1:1 molar stoichiometry with Se. These children would have been the most susceptible to declines in Se availability required for normal brain development and the most likely to exhibit adverse neurodevelopmental symptoms. However, it should also be noted that cord blood samples taken at birth represent only the last ~120–150 days prior to birth based on the life expectancy of red blood cells. Therefore, they are not indicative of conditions over an entire pregnancy and might not detect temporary Se shortages or other adverse effects that could have occurred during the first trimester. A short-term spike in MeHg concentration due to a few large whale meat meals (whale meat averaged 3.3 $\mu g\ Hg \cdot g^{-1}$) during the first trimester might produce a temporary Se deficiency accompanied by MeHg-induced brain damage (see Watanabe et al. 1999) Since the brain damage is irreversible, it would be detected in child test outcomes.

A recent reevaluation of the Faroe Island data by Budtz-Jorgensen et al. (2007) reported that maternal fish intake during pregnancy was associated with higher performance on all seven outcomes studied at child ages 7–14 years. They also reported that the effects of fish and Hg were each strengthened with mutual adjustment. This mutual adjustment appears to support the finding of Grandjean et al. (1997) that Hg caused adverse effects in the Faroe Islands while, at the same time, demonstrating the benefits of fish consumption. Both are plausible given the complexity of issues discussed above. It is precisely this complexity that sometimes leads to potentially conflicting conclusions in large-scale observational studies. As Dr. Grandjean stated, "While no scientific process can provide absolute proof, observational studies, in particular, will lead to conclusions that are likely to be refined as the depth of understanding improves" (Grandjean 2003).

Oken et al. (2005) studied 135 mother-child pairs in the United States to determine the effects of increasing maternal fish consumption on their children. They reported higher fish intake was associated with higher infant cognition (Oken et al. 2005). For each additional weekly fish serving, offspring visual recognition memory (VRM) score was 4.0 points higher (95% CI, 1.3 to 6.7). However, a 1.0-$\mu g \cdot g^{-1}$ increase in Hg was associated with a decrement in VRM score of 7.5 (95% CI, −13.7 to −1.2) points. Oken et al. (2005)

concluded that pregnant women should eat fish often but that the fish consumed should be those with low Hg concentrations, which is consistent with current EPA and U.S. Food and Drug Administration advice.

Hibbeln et al. (2007) used the Avon Longitudinal Study of Parents and Children (ALSPAC) involving 11,875 mother-child pairs to assess the possible benefits and hazards to children's development as a result of mothers consuming fish during pregnancy. They found that children of mothers who consumed less than 340 g of seafood per week scored among the lowest quartile for verbal intelligence quotient (IQ). Low maternal seafood intake was also associated with increased risk of suboptimum outcomes for prosocial behavior, fine motor, communication, and social development scores. These authors suggested that the benefits of seafood consumption due to omega-3 fatty acids outweigh the risks of consuming potential toxicants. Both the Oken et al. (2005) and the Hibbeln et al. (2007) studies report influences of seafood intake on child development. However, neither study has reported the amounts of Hg and Se in maternal or cord blood samples.

A survey by Oken et al. (2008a) examined 341 mother–child pairs in Massachusetts. They studied the neurodevelopment of 3-year-old children relative to the mother's second-trimester fish intake and erythrocyte Hg levels. They cite limitations of their finding by indicating that it is possible that unmeasured confounding may account for at least part of the observed findings. Also, they advise that they did not measure other contaminants that may be found in fish, such as PCBs. However, they go on to state that, "our finding that the benefit of fish intake is strengthened with adjustment for mercury levels suggests that if mercury contamination were not present, the cognitive benefits of fish intake would be greater."

The Danish National Birth Cohort Study involving 25,446 mother-child pairs was used to examine the associations of maternal fish intake during pregnancy, breast feeding duration, and developmental milestones in early childhood (Oken et al. 2008b). The Hg levels of fish consumed by women in this study were relatively low (0.034 to 0.049 $\mu g\ Hg \cdot g^{-1}$). The investigators used multivariate cumulative ordinal logistic regression to evaluate the odds of higher developmental scores associated with maternal fish intake and breastfeeding, after adjustment for child age, sex, and growth; maternal size and pregnancy characteristics; and parental education and social status. Because of the large sample number, the statistical strength of observed outcomes is better than in their previous study. Again, these authors reported improved child development scores at 18 months being associated with higher intakes of seafood by the mothers (odds ratio: 1.29 [95% CI: 1.20, 1.38] for the highest versus the lowest quintile of fish intake, and 1.28 [1.18, 1.38] for breast feeding for ≥ 10 months compared with breast feeding for ≤ 1 month). They concluded that higher fish intake was associated with improved developmental scores and that association of fish intake with child development scores did not differ by breast feeding duration. They further concluded that fish intake during pregnancy and the duration of breast feeding are independently associated with better early child development. They recommended that future research and consumption guidelines, incorporating nutritional benefits as well as contaminant risks, should consider the overall effect of prenatal fish consumption on child development. While this is an excellent recommendation, until those studies are completed for a cohort that includes a range of Se:Hg molar ratios spanning 1:1 and not totally replete with Se or Hg, there will remain some question about the interaction of Se and Hg in humans. Only when a more complete profile of contaminants and beneficial nutrients has been developed in a study cohort can an improved assessment of proportional effects be performed.

Rayman et al. (2008) and Ralston (2008) recommend that Se speciation in foods should be assessed so that more accurate conclusions concerning benefits and risks to consumers relative to Se intakes can be ensured. The speciation approach holds promise for greater understanding of the complex issues surrounding the effects of Se and Hg independently and also of their interactions. However, the assessment of Se:Hg molar ratios in fish or seafood consumed incorporated with total Se and Hg molar concentrations might be a useful interim assessment tool. For instance, the Se-HBV suggested by Kaneko and Ralston (2007) incorporates Se into the Hg toxicity risk assessment and is, therefore, a more robust predictor of potential Hg toxicity associated with Hg exposures (Ralston et al. 2008) than is the measurement of MeHg per se in fish tissue (Ralston 2008).

In another example, Falnoga et al. (2000) found remarkable relationships between Se and Hg (airborne elemental Hg) levels in various human tissues collected at autopsy from mercury miners and residents of Idrija, Slovenia. Some were control subjects with low Hg exposures (n = 22), some were occupationally unexposed but living in a Hg-contaminated environment (n = 9), and some were retired Idrija Hg mine workers (n = 4). Their ages at death ranged from 33 to 99 yr (mean 62 yr). The retired miners' ages ranged from 61 to 68 (mean 64). The cause of death was not listed, but it was noted that none of the miners showed any overt signs of Hg toxicity. As expected, the retired mine workers had the highest tissue concentrations of Hg with the thyroid, pituitary, kidney cortex, and dentate nucleus of the cerebellum averaging 26, 10, 7, and 3 $\mu g\ Hg \cdot g^{-1}$, respectively. While there were also some increased tissue Hg concentrations in the control population living in the Hg-contaminated environment, the most revealing information was associated with the retired mine worker group when the Se concentrations and the Hg:Se molar ratios were considered. While this was a very small sample, it was found that in addition to the elevated Hg levels in the tissues, the miners group also had elevated Se levels. The most revealing piece of information was that while tissue level concentrations of Hg and Se were indicative of Hg and Se exposure, the most precise information on this association was obtained from homogenization/centrifugation of tissue samples, in other words, from the cellular level. When examined at the cellular level, the thyroid, hippocampus, dentate nucleus of the cerebellum, and kidney cortex displayed Hg:Se molar ratios of 1.19, 0.59, 0.92, and 0.96, respectively. That is, regardless of the Hg concentration in the cells of these tissues, the Hg:Se molar ratios were always close to 1. However, other than in thyroid where complexation with iodine may have been occurring, the amount of Se in excess of Hg in all of these tissues was uniformly present at levels approximating the amount of Se present in tissues of people with low Hg exposures, i.e., Se was present in sufficient excess of Hg to have supported uninterrupted selenoenzyme activities.

Bioaccumulation of Hg in tissues often results in increased retention or coaccumulation of Se that counters or moderates the toxic effects of the Hg. Speciation of molecular forms of both elements before and after formation of HgSe complexes would be useful in assessing aquatic toxicity. However, until more sophisticated Se and Hg speciation tools and evaluation approaches are developed, simple Se:Hg or Hg:Se molar ratio assessments in relation to absolute intakes might be a useful interim bioindicator for assessing susceptibility to Hg toxicity (Ralston 2008).

Summary

The subject of Hg toxicity in fish, and to the consumers of fish, is quite complex. Selenium diminishes Hg accumulation and toxicity in multiple ways that function not only within tissues, but in the aquatic environment as well (Belzile et al. 2006; Yang et al. 2008).

While several questions remain to be answered, it is clear that Se has the ability to moderate both Hg bioaccumulation in the environment and Hg toxicity. The intake of Se is of paramount importance when the Hg:Se molar ratio in the animal's diet or in the animal's tissues approach or exceed 1:1 (Cuvin-Aralar and Furness 1991).

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1200 6th Avenue
Suite 900 M/S OWW-130
Seattle, WA 98101

Revised Fact Sheet

Public Comment Start Date: July 18, 2013
Public Comment Expiration Date: September 3, 2013

Technical Contact: Brian Nickel
206-553-6251
800-424-4372, ext. 6251 (within Alaska, Idaho, Oregon and Washington)
Nickel.Brian@epa.gov

Proposed Reissuance of a National Pollutant Discharge Elimination System (NPDES) Permit to Discharge Pollutants Pursuant to the Provisions of the Clean Water Act (CWA)

City of Coeur d'Alene
Wastewater Treatment Plant

EPA Proposes To Reissue NPDES Permit
The EPA proposes to reissue an NPDES permit to the facility referenced above. The draft permit places conditions on the discharge of pollutants from the wastewater treatment plant to waters of the United States. In order to ensure protection of water quality and human health, the permit places limits on the types and amounts of pollutants that can be discharged from the facility.

This Fact Sheet includes:
- information on public comment, public hearing, and appeal procedures
- a listing of proposed effluent limitations and other conditions for the facility
- a map and description of the discharge location
- technical material supporting the conditions in the permit

401 Certification
The EPA is requesting that the Idaho Department of Environmental Quality certify the NPDES permit for this facility, under section 401 of the Clean Water Act. Comments regarding the certification should be directed to:

Regional Administrator
Idaho Department of Environmental Quality
2110 Ironwood Pkwy
Coeur d'Alene, ID 83814

Public Comment
Pursuant to 40 CFR 124.14(c), at this time, the EPA is only accepting comments on aspects of the draft permit that are different from those in the draft permit that was issued for public comment on February 16, 2007. These are as follows:

- The final effluent limitations for total phosphorus, five day carbonaceous biochemical oxygen demand ($CBOD_5$), total suspended solids (TSS), ammonia, silver, and zinc have been revised (see the revised draft permit at Table 1, Part I.B).
- The draft permit now includes effluent limits for cadmium and lead.
- The schedules of compliance for new water quality-based effluent limits for phosphorus and $CBOD_5$, including the interim milestones and the effluent limitations (which apply during the term of the compliance schedule) have been revised (see the revised draft permit at Parts I.C and I.D).
- Surface water monitoring requirements have been changed (see the revised draft permit at Part I.F).
- The compliance evaluation level for total residual chlorine effluent limits has been changed from 100 µg/L to 50 µg/L.
- The draft permit now requires more frequent effluent monitoring for whole effluent toxicity and total residual chlorine relative to the 2007 draft permit (see the revised draft permit at Parts I.B and I.E).
- In addition to more frequent monitoring, the draft permit includes additional requirements for whole effluent toxicity testing (e.g. accelerated testing, toxicity reduction evaluation) to ensure consistency with EPA guidance (see the revised draft permit at Part I.E).
- The permit now includes influent and effluent monitoring requirements for 2,3,7,8 tetrachlorodibenzo-p-dioxin (2,3,7,8 TCDD) (see the revised draft permit at Parts I.B and II.I).
- The phosphorus management plan requirements have been changed (see the revised draft permit at Part II.B).
- The permit now includes best management practices requirements intended to reduce the discharge of polychlorinated biphenyls (PCBs) and 2,3,7,8 TCDD (see the revised draft permit at Part II.I).
- The permit now requires the permittee to participate in the Spokane River Regional Toxics Task Force (see the revised draft permit at Part II.H).

Persons wishing to comment on the tentative determinations contained in the draft permit may do so in writing to the above address or by e-mail to "Nickel.Brian@epa.gov" within 45 days of the date of this public notice. Comments must be received within the 45 day period to be considered in the formulation of final determinations regarding the applications. All comments should include the name, address and telephone number of the commenter and a concise statement of the exact basis of any comment and the relevant facts upon which it is based. All written comments and requests should be submitted to the EPA at the above address to the attention of the Director, Office of Water and Watersheds.

Workshop and Public Hearing
A workshop and public hearing will be held.

Date: August 28, 2013
Time: Workshop from 2:00 PM to 4:00 PM
Public hearing from 5:00 PM to 7:30 PM
Place: Coeur d'Alene Public Library
Lower Level, Community Room
702 East Front Avenue
Coeur d'Alene, ID 83814

Comments made on the draft permits at the public hearing will become part of the administrative record for the permits, along with any written comments received.

After the Public Notice expires, and all comments have been considered, the EPA's regional Director for the Office of Water will make a final decision regarding permit issuance. If no substantive comments are received, the proposed conditions in the draft permit will become final, and the permit will become effective upon issuance. If comments are received, the EPA will address the comments and issue the permit. The permit will become effective 30 days after the issuance date, unless an appeal is submitted to the Environmental Appeals Board within 30 days of the service of notice of the final permit decision.

Documents are Available for Review
The draft NPDES permit and related documents can be reviewed or obtained by visiting or contacting the EPA's Regional Office in Seattle between 8:30 a.m. and 4:00 p.m., Monday through Friday at the address below. The draft permits, fact sheet, and other information can also be found by visiting the Region 10 NPDES website at "http://epa.gov/r10earth/waterpermits.htm."

United States Environmental Protection Agency
Region 10
1200 Sixth Avenue
Suite 900 M/S OWW-130
Seattle, Washington 98101
(206) 553-6251 or
Toll Free 1-800-424-4372 (within Alaska, Idaho, Oregon and Washington)

The fact sheet and draft permits are also available at:

U.S. Environmental Protection Agency
Coeur d'Alene Field Office
1910 Northwest Blvd., Suite 208
Coeur d'Alene, ID 83814
208-665-0458

Idaho Department of Environmental Quality
Coeur d'Alene Regional Office
2110 Ironwood Parkway

Coeur d'Alene, ID 83814
(208) 769-1422
(877) 370-0017

Post Falls Public Library
821 North Spokane Street
Post Falls, ID 83854
(208) 773-1506

Rathdrum Public Library
16780 West Hwy 41
Rathdrum, ID 83858
(208) 687-1029

Hayden Public Library
8385 North Government Way
Hayden, ID 83835
(208) 772-5612

Washington State Department of Ecology
Eastern Regional Office
4601 North Monroe Street, Suite 202
Spokane, WA 99205-1295
509-329-3400

and

EPA Idaho Operations Office
950 West Bannock Street
Boise, Idaho 83702
208-378-5746

Table of Contents

Acronyms

1Q10	1 day, 10 year low flow
7Q10	7 day, 10 year low flow
30B3	Biologically-based design flow intended to ensure an excursion frequency of less than once every three years, for a 30-day average flow.
AML	Average Monthly Limit
BOD_5	Biochemical oxygen demand, five-day
°C	Degrees Celsius
CFR	Code of Federal Regulations
CV	Coefficient of Variation
CWA	Clean Water Act
DMR	Discharge Monitoring Report
DO	Dissolved oxygen
EFH	Essential Fish Habitat
EPA	U.S. Environmental Protection Agency
ESA	Endangered Species Act
FR	Federal Register
IDEQ	Idaho Department of Environmental Quality
lbs/day	Pounds per day
LTA	Long Term Average
mg/L	Milligrams per liter
ml	milliliters
ML	Minimum Level
µg/L	Micrograms per liter
mgd	Million gallons per day
MDL	Maximum Daily Limit
N	Nitrogen
NOAA	National Oceanic and Atmospheric Administration
NPDES	National Pollutant Discharge Elimination System
OW	Office of Water
O&M	Operations and maintenance
POTW	Publicly owned treatment works

QAP	Quality assurance plan
RP	Reasonable Potential
RPM	Reasonable Potential Multiplier
RWC	Receiving Water Concentration
SRRTTF	Spokane River Regional Toxics Task Force
s.u.	Standard Units
TMDL	Total Maximum Daily Load
TSD	Technical Support Document for Water Quality-based Toxics Control (EPA/505/2-90-001)
TSS	Total suspended solids
USFWS	U.S. Fish and Wildlife Service
USGS	United States Geological Survey
WLA	Wasteload allocation
WQBEL	Water quality-based effluent limit
WWTP	Wastewater treatment plant

I. Applicant

This fact sheet provides information on the draft NPDES permit for the following entity:

City of Coeur d'Alene
NPDES Permit # ID0022853

Mailing Address:
710 East Mullan Avenue
Coeur d'Alene, ID 83814

Physical Address:
915 Hubbard Avenue
Coeur d'Alene, ID 83814

Contact:
Sid Fredrickson, Superintendent

II. Scope of Reopened Public Comment Period

Federal regulations state that comments filed during a reopened comment period shall be limited to the substantial new questions that caused its reopening, and that the public notice under 40 CFR 124.10 shall define the scope of the reopening (40 CFR 124.14). As stated in the public notice, the EPA is only accepting comments on permit conditions that are different from those proposed in the draft permit that was issued for public review and comment on February 16, 2007.

The EPA is making significant changes to the draft permit as it was proposed in February 2007. These changes result from comments made during the initial public comment period, the availability of the final *Spokane River and Lake Spokane Dissolved Oxygen Total Maximum Daily Load: Water Quality Improvement Report*, hereinafter referred to as the "Spokane DO TMDL" (Ecology 2010), more recent effluent and receiving water quality and quantity data, updated computer modeling of the impact of the discharge, a revised draft Clean Water Act (CWA) Section 401 certification prepared by the Idaho Department of Environmental Quality (IDEQ), and EPA guidance documents. To allow the public an opportunity to comment on all of these changes, the EPA has decided to reopen the public comment period to accept comments on these specific changes. The changed conditions are as follows:

- The final effluent limitations for total phosphorus (TP), five day carbonaceous biochemical oxygen demand ($CBOD_5$), total suspended solids (TSS), ammonia, silver, and zinc have been revised (see the revised draft permit at Table 1, Part I.B).
- The draft permit now includes effluent limits for cadmium and lead.
- The schedules of compliance for new water quality-based effluent limits for phosphorus and $CBOD_5$, including the interim milestones and the effluent limitations (which apply during the term of the compliance schedule) have been revised (see the revised draft permit at Parts I.C and I.D).
- Surface water monitoring requirements have been changed (see the revised draft permit at Part I.F).

- The compliance evaluation level for total residual chlorine effluent limits has been changed from 100 µg/L to 50 µg/L.
- The draft permit now requires more frequent effluent monitoring for whole effluent toxicity and total residual chlorine relative to the 2007 draft permit (see the revised draft permit at Parts I.B and I.E).
- In addition to more frequent monitoring, the draft permit includes additional requirements for whole effluent toxicity testing (e.g. accelerated testing, toxicity reduction evaluation) to ensure consistency with EPA guidance (see the revised draft permit at Part I.E).
- The permit now includes influent and effluent monitoring requirements for dioxin[1] (see the revised draft permit at Parts I.B and II.I).
- The phosphorus management plan requirements have been changed (see the revised draft permit at Part II.B).
- The permit now includes best management practices requirements intended to reduce the discharge of polychlorinated biphenyls (PCBs) and dioxin (see the revised draft permit at Part II.I).
- The permit now requires the permittee to participate in the Spokane River Regional Toxics Task Force (see the revised draft permit at Part II.H).

III. Facility Information

In general, facility information is provided in the fact sheet for the initial public comment period dated February 16, 2007. A map of the treatment plant and discharge location is provided in Appendix A.

IV. Receiving Water

This facility discharges to the Spokane River in Kootenai County, Idaho. The outfall location is between the outlet of Lake Coeur d'Alene and the Post Falls Dam, about one-half mile upstream of the US Highway 95 bridge at river mile 110.2.

A. Low Flow Conditions

The *Technical Support Document for Water Quality-Based Toxics Control* (hereinafter referred to as the TSD) (EPA 1991) and the Idaho Water Quality Standards (WQS) recommend the flow conditions for use in calculating water quality-based effluent limits (WQBELs) using steady-state modeling. The TSD and the Idaho WQS state that WQBELs intended to protect aquatic life uses should be based on the lowest seven-day average flow rate expected to occur once every ten years (7Q10) for chronic criteria and the lowest one-day average flow rate expected to occur once every ten years (1Q10) for acute criteria. However, because the chronic criterion for ammonia is a 30-day average concentration not to be exceeded more than once every three years, the EPA has used the 30Q10 for the chronic ammonia criterion instead of the 7Q10. In the 2007 draft permit, the 30B3 flow rate was generally paired with the chronic ammonia criterion. However, later versions of the software used to calculate low flow conditions do not allow the calculation of the 30B3 flow rate on a seasonal basis, so the 30Q10 flow rate has been used instead of the 30B3. The 30Q10 is as protective as the 30B3 and may be used instead of the 30B3 (64 FR 71976).

[1] For the purposes of this fact sheet, "dioxin" refers to 2,3,7,8 tetrachlorodibenzo-p-dioxin (2,3,7,8 TCDD).

The EPA has re-calculated the low flow values, using more recent river flow data, since the close of the 2007 public comment period. The values in Table 1 were calculated using data from the Post Falls gauge (USGS station # 12419000), using a period of record of 1978-2008.

The seasons used to calculate the critical low flows have also been changed relative to the 2007 draft permit and fact sheet in order to match the seasonal calculations used to develop the 1999 permit. This allows a direct comparison to determine if the effluent limits in the 1999 permit remain adequate to protect water quality in the Spokane River.

From July – September, the critical low flow rates based on historical data are less than the minimum flow rates specified in the Federal Energy Regulatory Commission (FERC) license for the Post Falls Dam. The EPA has used the FERC minimum flows for effluent limit calculations, in lieu of the historical low flows.

Table 1: Seasonal Low Flows in the Spokane River

Season	1Q10 (CFS)	7Q10 (CFS)	30Q10 (CFS)
October – June	890	1030	1270
July – Sep. (based on historical data)	248	292	363
July – Sep. (FERC license)	500		

B. Water Quality Standards

Section 301(b)(1)(C) of the Clean Water Act (Act) requires that NPDES permits contain effluent limits more stringent than technology-based limits when necessary to meet water quality standards. A State's water quality standards are composed of use classifications, numeric and/or narrative water quality criteria, and an anti-degradation policy. The use classification system designates the beneficial uses (such as cold water aquatic life, contact recreation, etc.) that each water body is expected to achieve. The numeric and/or narrative water quality criteria are the criteria deemed necessary by the State to support the beneficial use classification of each water body. The anti-degradation policy represents a three-tiered approach to maintain and protect various levels of water quality and uses.

Idaho Water Quality Standards

At the point of discharge, the Spokane River is protected for the following designated uses (IDAPA 58.01.02.110.12):

- cold water aquatic life habitat
- salmonid spawning
- primary contact recreation
- domestic water supply

In addition, the Idaho Water Quality Standards state that all waters of the State of Idaho are protected for industrial and agricultural water supply (Section 100.03.b and c.), wildlife habitats (100.04) and aesthetics (100.05).

Primary contact recreation is defined by the Idaho Water Quality Standards as "water quality appropriate for prolonged and intimate contact by humans or for recreational activities when the ingestion of small quantities of water is likely to occur. Such activities include, but are not restricted to swimming, water skiing, or skin diving."

The Spokane River also has site-specific criteria for ammonia (IDAPA 58.01.02.283). The site-specific ammonia criteria are identical to the statewide ammonia criteria for waters designated for cold water aquatic life when early life stages of fish are present (IDAPA 58.01.02.250.02.d.).

Idaho's Antidegradation Policy

The EPA is required under Section 301(b)(1)(C) of the Clean Water Act (CWA) and implementing regulations (40 CFR 122.4(d) and 122.44(d)) to establish conditions in NPDES permits that ensure compliance with State water quality standards, including antidegradation requirements. The antidegradation analysis is conducted as part of the State's CWA Section 401 certification (see Appendix H).

Washington Water Quality Standards

The City of Coeur d'Alene wastewater treatment plant outfall is located approximately 14 river miles upstream from the Washington border. Federal regulations require that NPDES permits include conditions necessary to ensure compliance with the water quality requirements of all affected States (40 CFR 122.4(d), 40 CFR 122.44(d)(4), see also CWA Section 401(a)(2)). Therefore it is necessary to determine if the discharge has the reasonable potential to cause or contribute to excursions above Washington's water quality standards, in addition to Idaho's water quality standards. If the discharge has the reasonable potential to cause or contribute to excursions above Washington's water quality standards, effluent limits must be established, which ensure compliance with Washington's water quality standards, in addition to Idaho's water quality standards. The EPA has determined that the discharge has the reasonable potential to cause or contribute to excursions above Washington's water quality standards for dissolved oxygen, and has established effluent limits for total phosphorus (TP), total ammonia as nitrogen (N), and $CBOD_5$ which ensure compliance with both Idaho's and Washington's water quality standards for nutrients and dissolved oxygen. See Appendix B for a complete discussion of the effluent limits based upon Washington's water quality standards.

C. Water Quality Limited Segment

A water quality limited segment is any waterbody, or definable portion of a waterbody, where it is known that water quality does not meet applicable water quality standards, and/or is not expected to meet applicable water quality standards. In accordance with section 303(d) of the Clean Water Act, States must identify waters not achieving water quality standards in spite of the application of technology-based controls in National Pollutant Discharge Elimination System (NPDES) permits for point sources. Such waterbodies are known as water quality limited segments (WQLSs), and the list of such waterbodies is called the "303(d) list." Once a water body is identified as a WQLS, the States are required under the Clean Water Act to develop a total maximum daily load (TMDL). A TMDL is a determination of the amount of a pollutant, or property of a pollutant, from point, nonpoint, and natural background sources (including a margin of safety) that may be discharged to a water body without causing the water body to exceed the water quality criterion for that pollutant. The Spokane River flows through Idaho and Washington, and various segments of the river are water quality limited in both States.

Total Phosphorus (Idaho)

The Spokane River is listed in Idaho's 2010 303(d)/305(b) integrated report as not attaining or not being expected to attain water quality standards for total phosphorus. As explained in Appendix B, the water quality-based effluent limits for total phosphorus in the draft permit will ensure compliance with Idaho's narrative water quality criterion for nutrients (IDAPA 58.01.02.200.06).

Cadmium, Lead and Zinc (Idaho)

The segment of the Spokane River to which the City of Coeur d'Alene discharges was listed in Idaho's 1998 303(d) list as not attaining or not expected to meet State water quality standards for cadmium, lead, and zinc. In August of 2000, the EPA approved a TMDL submitted by the State of Idaho for metals in the Coeur d'Alene River Basin, which included this segment of the Spokane River. However, in 2003, the Idaho Supreme Court determined that the TMDL was invalid. Therefore, the Spokane River remains listed in the 2010 303(d)/305(b) integrated report as being impaired for cadmium, lead, and zinc.

Even though the Idaho Supreme Court invalidated the Coeur d'Alene River Basin TMDL under State law, the EPA must nonetheless evaluate whether water quality-based effluent limits are necessary for cadmium, lead, and zinc under CWA regulations at 40 CFR 122.44(d)(1)(i – iii), and assure that any such effluent limits are derived from and comply with applicable water quality standards (40 CFR 122.44(d)(1)(vii)(A)). Furthermore, NPDES permits issued by the EPA must incorporate the requirements specified in a CWA Section 401 certification (40 CFR 122.44(d)(3), 124.53(e), 124.55(a)(2)).

The 1999 permit (as modified in 2004) included effluent limits for zinc. The EPA has determined that the concentration effluent limits for zinc in the 1999 permit (as modified in 2004) are not stringent enough to ensure compliance with Idaho's water quality criteria. Therefore, the EPA has proposed more-stringent effluent limits for zinc.

In its draft CWA Section 401 certification, the State of Idaho specified effluent limits for cadmium and lead. The certification states that these limits are necessary to ensure compliance with IDAPA 58.01.02.055.04. Because the State of Idaho's 2010 integrated report lists the Spokane River as a high priority for TMDL development, IDAPA 58.01.02.055.04 requires that the loading of pollutants causing water quality impairments remains constant or decreases within the watershed. The limits specified by the State of Idaho will ensure that the City of Coeur d'Alene's loading of cadmium and lead remains constant or decreases. NPDES permits issued by the EPA must incorporate the requirements specified in a CWA Section 401 certification (40 CFR 122.44(d)(3), 124.53(e), 124.55(a)(2)). Therefore, the draft permit includes the cadmium and lead limits specified in the draft CWA Section 401 certification.

The EPA is specifically requesting comments on the effluent limits for cadmium, lead, and zinc. A more detailed discussion of the effluent limits for cadmium, lead, and zinc is provided in Appendix C.

Temperature (Idaho)

The fact sheet dated February 16, 2007 stated that the Spokane River was listed in Idaho's 2002/2004 303(d)/305(b) integrated report as being impaired for temperature. The Spokane

River is not listed for temperature in Idaho's 2010 integrated report. The 1999 permit did not include effluent limits for temperature. When developing the 2007 draft permit, the EPA determined that the discharge did not have the reasonable potential to cause or contribute to excursions above water quality standards for temperature, and no temperature effluent limits were proposed in the 2007 draft permit. In developing the revised draft permit, the EPA re-evaluated the need for effluent limits for temperature and has once again determined that the discharge does not have the reasonable potential to cause or contribute to excursions above water quality standards for temperature; therefore, no effluent limits are proposed for temperature in the revised draft permit.

The finding that the discharge does not have the reasonable potential to cause or contribute to excursions above Idaho's water quality standards for temperature has not changed since the 2007 draft permit was issued for public review and is not one of the substantial new questions that caused the reopening of the comment period.

Dissolved Oxygen (Washington)

In the fact sheets dated February 16, 2007 for the Cities of Coeur d'Alene and Post Falls and the Hayden Area Regional Sewer Board (HARSB), the EPA made a finding that the discharges of oxygen-demanding pollution from those sources have the reasonable potential to cause or contribute to excursions below Washington's water quality criterion for dissolved oxygen in Lake Spokane. The draft permits issued for public review and comment in February 2007 therefore included water quality-based effluent limits for phosphorus, $CBOD_5$, and ammonia, which were intended to ensure compliance with Washington's water quality criterion for dissolved oxygen in lakes and reservoirs, as required by federal regulations (40 CFR 122.4(d), 122.44(d)(4), see also CWA Section 401(a)(2)). The "reasonable potential" finding (which determines whether or not water quality-based effluent limits based upon Washington water quality standards are necessary for oxygen-demanding pollutants, see 40 CFR 122.44(d)(1)(i – iii)) remains valid.

However, comments received during the 2007 public comment period regarding the calculation of phosphorus, ammonia, and $CBOD_5$ limits led the EPA to re-evaluate the effluent limits for these parameters. Commenters stated that the effluent limits should be calculated based on the cumulative dissolved oxygen impact of all human actions. Furthermore, in February 2008, after the close of the initial public comment period, the EPA approved revisions to Washington's water quality standards, which made those revised standards effective for Clean Water Act purposes, including NPDES permits (40 CFR 131.21). Among the changes to Washington's water quality standards was a change to the water quality criterion for dissolved oxygen (DO) in lakes and reservoirs. At the time of the initial public comment period in 2007, the water quality criterion for DO in lakes and reservoirs that was in effect for Clean Water Act purposes read "no measurable decrease from natural conditions" (WAC 173-201A-030(5)(c)(ii), 1997). The revised standard reads "for lakes, human actions considered cumulatively may not decrease the dissolved oxygen concentration more than 0.2 mg/L below natural conditions" (WAC 173-201A-200(1)(d)(ii), 2006). The significant differences between the old and current criteria are that the allowable amount of DO decrease relative to the natural condition is now numeric (0.2 mg/L) instead of a narrative statement ("no measurable decrease"), and the current criterion states that this allowable DO decrease is based on the cumulative impact of human actions.

In addition, the State of Washington has prepared and the EPA has approved the *Spokane River and Lake Spokane Dissolved Oxygen Total Maximum Daily Load: Water Quality Improvement Report*, dated February 2010 and hereinafter referred to as the Spokane DO TMDL. In the Spokane DO TMDL, the State of Washington made specific assumptions about the amounts of oxygen-demanding pollution that will be discharged by sources in Idaho. In 2011, the State of Washington issued NPDES permits to point sources discharging to the Spokane River in Washington, which include effluent limits for phosphorus, ammonia and $CBOD_5$ that are consistent with the wasteload allocations in the Spokane DO TMDL.

In light of the comments received during the initial comment period, the changes to the Washington water quality standards, and the availability of the Spokane DO TMDL, the EPA has determined that the effluent limits for phosphorus, ammonia and $CBOD_5$ proposed in the 2007 draft permit should be changed in order to ensure compliance with Washington's dissolved oxygen criterion for lakes and reservoirs.

Therefore, the EPA has proposed revised water quality-based effluent limitations for phosphorus, ammonia, and five-day carbonaceous biochemical oxygen demand in the City of Coeur d'Alene draft permit. These effluent limits ensure that the level of water quality to be achieved by limits on point sources is derived from and complies with all applicable water quality standards (40 CFR 122.44(d)(1)(vii)(A)). The effluent limits are based on the cumulative impact of all human actions that affect dissolved oxygen concentrations in Lake Spokane. See Appendix B for a complete explanation of the water quality-based phosphorus, ammonia, and $CBOD_5$ effluent limits in the draft permit, that are based on Washington water quality standards for dissolved oxygen. The EPA is specifically requesting public comments on the revised water quality-based effluent limits in the draft permit for total phosphorus, $CBOD_5$ and ammonia, which are derived from Washington's water quality standards.

Metals (Washington)

The segment of the Spokane River immediately downstream from the State line is listed in Washington's 2008 303(d)/305(b) integrated report for cadmium, lead, and zinc. The listing category for these metals is 4A, which means that a TMDL has been prepared for these pollutants. The *Spokane River Dissolved Metals Total Maximum Daily Load* (Butkus and Merrill, 1999) was approved by the EPA on August 25, 1999.

As stated in the fact sheet dated February 16, 2007, the EPA has determined that the City's discharge does not have the reasonable potential to cause or contribute to excursions above Washington's water quality standards for cadmium, lead or zinc. The finding that the discharge does not have the reasonable potential to cause or contribute to excursions above Washington's water quality standards for cadmium, lead, or zinc has not changed since the 2007 draft permit was issued for public review and is not one of the substantial new questions that caused the reopening of the comment period.

Temperature (Washington)

The segment of the Spokane River immediately downstream from the State line is listed in Washington's 2008 303(d)/305(b) integrated report as not attaining or not being expected to attain water quality standards for temperature. As explained in Appendix B, the EPA has determined that the discharges from Idaho point sources do not have the reasonable potential to

cause or contribute to excursions above Washington's water quality standards for temperature in the Spokane River.

The finding that the discharge does not have the reasonable potential to cause or contribute to excursions above Washington's water quality standards for temperature has not changed since the 2007 draft permit was issued for public review and is not one of the substantial new questions that caused the reopening of the comment period.

Total Polychlorinated Biphenyls and Dioxin (Washington)

The Spokane River is listed in Washington's 2008 303(d)/305(b) integrated report as not attaining or not being expected to attain water quality standards for total polychlorinated biphenyls (PCBs), due to elevated concentrations in fish tissue. The Spokane Tribe of Indians has EPA-approved water quality standards for its waters, which are downstream of the Long Lake Dam, and data from lower Lake Spokane indicate that the Tribe's water quality criterion for PCBs (in the water column) is not being attained (Serdar et al. 2011). The Spokane River is also listed in Washington's 2008 303(d)/305(b) integrated report as not attaining or not being expected to attain water quality standards for dioxin, due to elevated concentrations in fish tissue.

Currently, there are insufficient data to determine if the discharges from point sources to the Spokane River in Idaho have the reasonable potential to cause or contribute to excursions above water quality standards for PCBs or dioxin in waters of the State of Washington or the Spokane Tribe of Indians. Therefore, no numeric water quality-based effluent limits are proposed for PCBs or dioxin in the draft permit.

The draft permits for the Cities of Post Falls and Coeur d'Alene and HARSB propose influent, effluent and surface water column monitoring for PCBs. These data will be used to determine if the discharges have the reasonable potential to cause or contribute to excursions above water quality standards for PCBs in waters of the State of Idaho, the State of Washington or the Spokane Tribe of Indians. Monitoring requirements for PCBs are discussed in more detail in Section VI.D below.

The permits propose quarterly influent and effluent monitoring for dioxin. The permits do not propose surface water monitoring for dioxin because the detection limit of EPA Method 1613B (4.4 picograms per liter) is much greater than the water quality criterion for dioxin that is currently in effect for Clean Water Act purposes in Idaho (0.013 picograms per liter) (EPA 1994). Thus, surface water monitoring for dioxin using Method 1613B would be unlikely to yield meaningful data.

The NPDES permits for municipal separate storm sewer systems that discharge pollutants to the Spokane River in Idaho also include monitoring requirements for PCBs.

The average total PCB concentration at the Washington – Idaho border is 106 picograms per liter (pg/L) (Serdar et al. 2011). This concentration is 38% less than Washington's and Idaho's water quality criteria for total PCBs (170 pg/L) that are in effect under the CWA.[2] The Spokane Tribe's water quality criterion for PCBs is 3.37 pg/L. Furthermore, in 1999, the USGS performed sampling of fish tissue in Idaho at station #12419000 (Spokane River near Post Falls, Idaho). The concentration of PCBs measured in fish collected from this station was 270 µg/kg

[2] Idaho's PCB water quality criterion that is in effect under State law is 64 pg/L. However, the EPA has disapproved this criterion and therefore it is not in effect for Clean Water Act purposes. (See 40 CFR 131.21(c)(2))

(USGS 2003). The 170 pg/L Clean Water Act effective water column criterion for PCBs in Idaho and Washington corresponds to a fish tissue concentration of 5.3 µg/kg.[3,4] Since the measured fish tissue concentration is greater than the fish tissue concentration that corresponds to the water column criterion, the measured fish tissue concentration indicates elevated levels of PCBs.

PCBs have been detected in effluent from POTWs discharging to the Spokane River in the State of Washington (i.e., the City of Spokane and the Liberty Lake Sewer and Water District) as well as other POTWs in Washington State operated by the Cities of Medical Lake, Okanogan, College Place, Walla Walla, Pullman, Colfax, Albion, Bremerton, Tacoma, and Everett, and King and Pierce counties. Effluent concentrations of total PCBs at these 14 facilities (a total of 34 samples) ranged from 46.6 to 39,785 pg/L with a median concentration of 810 pg/L, and 82% of the results (28 out of 34) were greater than Idaho's and Washington's Clean Water Act effective water quality criterion of 170 pg/L (Coots and Deligeannis 2010; Ecology 2010; Johnson et al. 2004; Serdar 2003; Serdar et al. 2011; personal communication with Richard Koch, Ecology, September 8, 2011). Design flows of these POTWs range from 0.54 mgd (Okanogan) to 215 mgd (King County West Point). PCBs were also detected in 96% of samples (69 out of 72) of effluents collected from 18 POTWs discharging to the Yakima River in central Washington State in 2007 and 2008. The median effluent concentration of total PCBs at these 18 POTWs was 370 pg/L and the maximum concentration was 7,400 pg/L; 82% of the samples (59 out of 72) exceeded Washington's water quality criterion of 170 pg/L (Johnson et al. 2010).

The fact that the average concentration of PCBs at the State line is more than half the value of the water quality criterion that is in effect under the Clean Water Act in Washington and Idaho and that high concentrations of PCBs have been measured in fish tissue in the Spokane River in Idaho, in addition to the frequent detection of PCBs at concentrations above water quality criteria in other POTWs as described above, suggests that pollution sources in Idaho may be contributing to exceedances of water quality criteria for PCBs.

Moreover, dioxin has been detected in the effluent from the City of Medical Lake wastewater treatment plant (1.85 mgd design flow) in Washington State at a concentration of 0.56 pg/L, which is 43 times the criterion that is in effect for Clean Water Act purposes in both Idaho and Washington, which is 0.013 pg/L (Coots and Deligeannis 2010).[5] According to data obtained from EPA's Envirofacts database, dioxin has also been detected in the effluents from seven POTWs in Arizona, California and Florida. The median concentration of dioxin among 36 samples from those seven POTWs was 1.05 pg/L, which is 81 times the criterion (Nickel 2011). Design flows of the Arizona, California, and Florida POTWs with dioxin effluent data range from 2.2 to 37 mgd.

[3] The PCB water quality criterion that is in effect under State law in Idaho is equivalent to a fish tissue concentration of 2.0 µg/kg.

[4] The bioconcentration factor (BCF) is the ratio of a substance's concentration in tissue versus its concentration in water, in situations where the food chain is not exposed or contaminated. For non-metabolized substances, it represents equilibrium partitioning between water and organisms. The BCF for PCBs is 31,200 L/kg (EPA 2002). Multiplying the BCF by the water column criterion yields the equivalent fish tissue concentration.

[5] Idaho's 2,3,7,8 TCDD water quality criterion that is in effect under State law is 0.005 pg/L. However, the EPA has disapproved this criterion and therefore it is not in effect for Clean Water Act purposes. (See 40 CFR 131.21(c)(2))

Studies in the 1990s found mixtures of dioxins and furans in POTW effluents of 0.27 to 0.81 toxicity equivalents (TEQ)[6] (EPA 2006). Potential sources of dioxins and furans in POTW discharges include laundry wastewater, particularly from clothing dyes and pigments containing dioxins and furans and from cotton treated with pentachlorophenol (which is used in some developing countries), runoff from streets with high traffic density, and industrial sources such as metal manufacturing (EPA 2006). This information suggests that point sources in Idaho may also be contributing to excursions above water quality standards for dioxin in waters of the State of Washington.

Therefore, although it is not known at this time which specific sources contribute PCBs or dioxin to the Spokane River in Idaho, the EPA believes that, similar to POTWs in the State of Washington and elsewhere, the Idaho POTWs may be discharging PCBs and dioxin, and that best management practices (BMP) requirements to control or abate the discharge of PCBs and dioxin are reasonably necessary to carry out the purposes and intent of the Clean Water Act. Due to the lack of data, it is infeasible to calculate numeric water quality-based effluent limits for PCBs and dioxin at this time. Therefore, the draft permit includes BMP requirements for PCBs and dioxin, consistent with 40 CFR 122.44(k)(3) and (4). The BMP requirements are in Part II.I of the draft permit.

The draft permit also requires the permittee to participate in the Spokane River Regional Toxics Task Force (SRRTTF). See the draft permit at Part II.H.

The EPA is specifically requesting comments on the monitoring and BMP requirements for PCBs and dioxin and the requirement to participate in the SRRTTF.

V. Effluent Limitations

A. Basis for Effluent Limitations

In general, the Clean Water Act (Act) requires that the effluent limits for a particular pollutant be the more stringent of either technology-based limits or water quality-based limits. Technology-based limits are set according to the level of treatment that is achievable using available technology. A water quality-based effluent limit is designed to ensure that the water quality standards of a waterbody are being met and may be more stringent than technology-based effluent limits. The bases for the proposed effluent limits in the draft permit are provided in Appendices B, C, D, E, F, and G.

B. Proposed Effluent Limitations

Below are the proposed effluent limits that are in the draft permit (see Part I.B).

1. Removal Requirements for $CBOD_5$ and TSS: The monthly average effluent concentration must not exceed 15 percent of the monthly average influent concentration. Percent removal of $CBOD_5$ and TSS must be reported on the Discharge Monitoring Reports (DMRs). For each parameter, the monthly average percent removal must be calculated from the arithmetic mean of the influent values

[6] The TEQ procedure translates the complex mixture of dioxins and furans characteristic of environmental releases into an equivalent toxicity concentration of 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD), the most toxic member of this class of compounds.

and the arithmetic mean of the effluent values for that month. Influent and effluent samples must be taken over approximately the same time period.

2. The permittee must not discharge floating, suspended or submerged matter of any kind in concentrations causing nuisance or objectionable conditions or that may impair designated beneficial uses.

Table 2 (below) presents the proposed final seasonal average, average monthly, average weekly, maximum daily, and instantaneous maximum effluent limits. Limits that are different from those in the 2007 draft permit are shown in italic type. The EPA is specifically requesting public comments on all of these revised effluent limits.

C. Schedules of Compliance

Schedules of compliance are authorized by federal NPDES regulations at 40 CFR 122.47 and by Section 400.03 of the Idaho Water Quality Standards. The Idaho water quality standards allow for compliance schedules "when new limitations are in the permit for the first time." The federal regulation allows schedules of compliance "when appropriate," and requires that such schedules require compliance as soon as possible. When the compliance schedule is longer than 1 year, federal regulations require that the schedule shall set forth interim requirements and the dates for their achievement. The time between the interim dates shall generally not exceed 1 year, and when the time necessary to complete any interim requirement is more than one year, the schedule shall require reports on progress toward completion of these interim requirements. Federal regulations also generally require that interim effluent limits be at least as stringent as the final limits in the previous permit (40 CFR 122.44(l)(1)).

Table 2: Proposed Final Effluent Limits

Parameter	Units	Effluent Limits		
		Average Monthly Limit	**Average Weekly Limit**	**Maximum Daily Limit**
Five-Day Carbonaceous Biochemical Oxygen Demand ($CBOD_5$) *November – January*	mg/L	25	40	—
	lb/day	1251	2002	—
	% removal	85% (minimum)	—	—
$CBOD_5$ [2] *February – March*	mg/L	*25*	*40*	—
	lb/day	*Seasonal Average Limit: 226 lb/day*		
	% removal	85% (minimum)	—	—
$CBOD_5$ [2] *April - October*	mg/L	*25*	*40*	—
	lb/day	*Seasonal Average Limit: 203 lb/day*		
	% removal	85% (minimum)	—	—
Total Suspended Solids (TSS)	mg/L	30	45	—
	lb/day	1501	2252	—
	% removal	85% (minimum)	—	—
pH October – June	s.u.	*6.3 – 9.0*		
pH July – September	s.u.	*6.5 – 9.0*		
Total Phosphorus as P[2] (Feb. – Oct.)	lb/day	*Seasonal Average Limit: 3.17 lb/day*		

Table 2: Proposed Final Effluent Limits				
Parameter	**Units**	**Effluent Limits**		
		Average Monthly Limit	**Average Weekly Limit**	**Maximum Daily Limit**
E. Coli Bacteria	#/100 ml	126 (geometric mean)	—	406 (single sample maximum)
Total Residual Chlorine July – September	µg/L	39	—	102
	lb/day	2.0	—	5.1
Total Residual Chlorine October – June	µg/L	150	—	390
	lb/day	7.5	—	20
Total Ammonia as N[2] March – June	lb/day	*649*	—	*1547*
Total Ammonia as N[2] July – September	mg/L	*6.59*	—	*15.7*
	lb/day	*330*	—	*786*
Total Ammonia as N[2] March – October	lb/day	*272 seasonal average*		
Silver October – June, effluent flow > 4.2 mgd	µg/L	*8.01*	—	*22.5*
	lb/day	*0.401*	—	*1.13*
Cadmium (Based on the State of Idaho's draft CWA Section 401 certification.)	µg/L	*0.149*	*0.187*	—
Lead (Based on the State of Idaho's draft CWA Section 401 certification.)	µg/L	*2.5*	—	*5.8*
Zinc	µg/L	*135*	—	168
	lb/day	*6.76*	—	8.42

Notes:
1. No single sample may exceed 406 organisms per 100 ml (instantaneous maximum limit).
2. These effluent limits are subject to a compliance schedule. Until the final effluent limits become effective, the permittee must comply with interim effluent limitations (see Table 3, below).
3. The monthly geometric mean concentration of E. coli must not exceed 126 organisms per 100 ml.

EPA policy states that, in order to grant a compliance schedule, a permitting authority must make a reasonable finding that the permittee cannot comply with the effluent limit immediately upon the effective date of the final permit (see the *US EPA NPDES Permit Writers' Manual* at Section 9.1.3). Some of the proposed effluent limits for phosphorus, $CBOD_5$, ammonia, cadmium, lead, zinc, and silver are new limits that are in the permit for the first time. However, the EPA has determined that the permittee can, in fact, comply with all of these effluent limits, except phosphorus, $CBOD_5$, and ammonia, immediately upon the effective date of the final permit, as explained in Appendix G.

Therefore, compliance schedules are proposed only for phosphorus, $CBOD_5$ and ammonia. The compliance schedules include interim effluent limitations, as shown in Table 3, below. The interim phosphorus limits retain the average monthly 1 mg/L effluent limit from the 1999 permit, in order to ensure compliance with 40 CFR 122.44(l)(1). In order to ensure compliance with 40 CFR 122.45(f), which requires that effluent limits are expressed in terms of mass, the EPA has calculated interim mass effluent limits for phosphorus, which apply in addition to the concentration limits. The interim monthly average mass limit is equal to the mass loading of phosphorus that the permittee could have discharged, at the POTW's design flow rate, while maintaining compliance with the concentration effluent limit in the 1999 permit. Federal regulations require that effluent limits for POTWs be calculated based on the design flow of the POTW (40 CFR 122.45(b)(1)). In order to ensure compliance with 40 CFR 122.45(d), which requires that effluent limits for POTWs shall generally be expressed as average weekly and

average monthly discharge limitations, the EPA has included an interim average weekly mass limit for phosphorus, which is equal to the average monthly limit multiplied by 1.6, which is the same ratio as the technology-based effluent limits for $CBOD_5$. This accounts for effluent variability within a month.

The interim ammonia and $CBOD_5$ limits are identical to the ammonia limits in the 1999 final permit, in compliance with 40 CFR 122.44(l)(1).

The compliance schedules are based on the draft Clean Water Act Section 401 certification provided to the EPA by the Idaho Department of Environmental Quality. The final permit will contain compliance schedules consistent with the State of Idaho's final Clean Water Act Section 401 certification, which may differ from the draft certification. The EPA believes that the compliance schedule proposed for phosphorus complies with the regulatory requirement that compliance be achieved "as soon as possible" (40 CFR 122.47(a)(1)), as explained in Appendix G.

Table 3: Interim Effluent Limits

Parameter	Units	Effluent Limits		
		Average Monthly Limit	Average Weekly Limit	Maximum Daily Limit
$CBOD_5$	mg/L	25	40	—
	lb/day	1250	2000	—
	% removal	85% (min.)	—	—
Total Ammonia as N July – September Effluent flow ≤ 4.2 mgd	mg/L	10	—	29
	lb/day	350	—	1000
Total Ammonia as N July – September Effluent flow > 4.2 mgd	mg/L	7.4	—	21
	lb/day	370	—	1100
Total Phosphorus as P February – October	mg/L	1.0	1.6	—
	lb/day	50	80	—

Because the compliance schedules are authorized by the State of Idaho in the Section 401 certification, comments on the compliance schedules should be directed to the Idaho Department of Environmental Quality at the address listed on the front page of this Fact Sheet and in the public notice of the availability of this draft permit, in addition to the EPA.

D. Total Residual Chlorine Compliance Evaluation Level

The 2007 draft permit contained a compliance evaluation level of 100 µg/L (0.1 mg/L) for total residual chlorine. This compliance evaluation level was based on the minimum level (ML) of chlorine analytical methods that are no longer approved for use in NPDES permitting (see 40 CFR 136).

Currently approved methods can quantify chlorine at a concentration of 50 µg/L. With the exception of the average monthly chlorine limit in effect from July – September, the proposed effluent limits for total residual chlorine are greater than the concentrations that can be quantified using approved analytical methods for chlorine. Thus, the compliance evaluation level for the

July – September total residual chlorine average monthly limit has been changed to 50 µg/L from 100 µg/L.

The EPA is specifically requesting comments on the change to the total residual chlorine compliance evaluation level.

E. Basis for Substitution of E. coli Limits for Fecal Coliform Limits

The draft permit proposes effluent limits for E. coli in lieu of the 1999 permit's fecal coliform limits. The basis for this change is explained in the fact sheet dated February 16, 2007. The proposed substitution of E. coli for the 1999 permit's fecal coliform limits is unchanged from the draft permit issued for public review in 2007 and is not one of the substantial new questions that caused the EPA to reopen the public comment period and is included here for the purpose of providing background context. Therefore, the EPA is not requesting comments on the E. coli limits at this time.

VI. Monitoring Requirements

A. Basis for Effluent and Surface Water Monitoring

Section 308 of the CWA and the federal regulation 40 CFR 122.44(i) require monitoring in permits to determine compliance with effluent limitations. Monitoring may also be required to gather effluent and surface water data to determine if additional effluent limitations are required and/or to monitor effluent impacts on receiving water quality. The permittee is responsible for conducting the monitoring and for reporting results on Discharge Monitoring Reports (DMRs) or on the application for renewal, as appropriate, to the EPA.

B. Effluent Monitoring

In general, the basis for the effluent monitoring requirements in the draft permit was explained in the fact sheet dated February 16, 2007. Some changes to the effluent monitoring requirements are proposed, as explained below. The proposed effluent monitoring requirements are shown in Table 4, below.

Whole Effluent Toxicity

The whole effluent toxicity (WET) testing requirements have been expanded to include a requirement to prepare an initial investigation toxicity reduction evaluation (TRE) workplan, a requirement to conduct accelerated testing in the event of an excursion above a trigger value (which is based on the dilution of the effluent in the receiving water at the edge of the authorized mixing zone) and a requirement to conduct a TRE if an additional excursion above the trigger occurs during accelerated testing. These requirements are consistent with the recommendations of the EPA *Regions 9 and 10 Guidance for Implementing Whole Effluent Toxicity Testing Programs* (EPA 1996b). These requirements were included in the 1999 permit, but were omitted from the 2007 draft permit.

In addition, the revised draft permit proposes a semi-annual (twice per year) monitoring frequency for WET, which is the same as the 1999 permit. The 2007 draft permit had proposed annual (once per year) monitoring for WET, however, there is no basis to reduce the WET

monitoring frequency relative to the 1999 permit. Finally, in the draft permit, the EPA is proposing to require the permittee to use three organisms for toxicity testing (a fish, an invertebrate, and a plant), consistent with the recommendations of the *Regions 9 and 10 Guidance for Implementing Whole Effluent Toxicity Testing Programs* (Page 2-18) and the *Technical Support Document for Water Quality-based Toxics Control* (Section 3.3.3). The 2007 draft permit only required testing of a fish and an invertebrate.

The EPA is specifically requesting public comment on the revised WET testing requirements.

Total Residual Chlorine

In the 2007 draft permit, the EPA had proposed to reduce the monitoring frequency for total residual chlorine from three times per day in the 1999 permit to five times per week from July – October and once per week from October - June. However, the EPA has determined that reducing the total residual chlorine monitoring frequency to this extent would not be consistent with the EPA's *Interim Guidance for Performance - Based Reductions of NPDES Permit Monitoring Frequencies* (EPA 1996a).

The average effluent concentration of total residual chlorine is 28 µg/L, which is 18% of the proposed average monthly effluent limit for October – June and 69% of the average monthly effluent limit for July – September. The *Interim Guidance for Performance - Based Reductions of NPDES Permit Monitoring Frequencies* does not discuss monitoring reduction for a baseline frequency of three samples per day, so the EPA has applied the recommendations of the guidance for three times per week sampling to the three samples per day sampling frequency that was required in the 1999 permit. This results in a reduction in sampling frequency for October – June to once per day, and no reduction in sampling frequency for July – September.

Permit Application Monitoring

The draft permit proposes to require all of the monitoring that would be necessary to produce a complete application for renewal of this permit. Effluent monitoring required by Part B.6 of application form 2A (which is required of all facilities with a design flow greater than or equal to 0.1 mgd) is required at a frequency of quarterly for oil and grease and total dissolved solids, and monthly for dissolved oxygen and for forms of nitrogen and phosphorus that are not subject to effluent limits. More frequent monitoring is required for nitrogen and phosphorus species because these are nutrients, and nutrients are known to contribute to water quality impairments in this watershed (i.e., for dissolved oxygen in the State of Washington and total phosphorus in the State of Idaho).

Effluent monitoring required by Part D of application form 2A, which is not required by other provisions of this permit, is required at the minimum frequency required by the application (three samples over the term of the permit).

Table 4: Effluent Monitoring Requirements				
Parameter	**Unit**	**Sample Location**	**Sample Frequency**	**Sample Type**
Flow	mgd	Effluent	Continuous	Recording
$CBOD_5$ November – January	mg/L	Influent and Effluent	1/week	24-hour composite
	lbs/day	Influent and Effluent		calculation[1]
	% Removal	--	1/month	calculation[2]
$CBOD_5$ February – October	mg/L	Influent and Effluent	3/week	24-hour composite
	lbs/day	Influent and Effluent		calculation[1]
	% Removal	--	1/month	calculation[2]
TSS	mg/L	Influent and Effluent	1/week	24-hour composite
	lbs/day	Influent and Effluent		calculation[1]
	% Removal	--	1/month	calculation[2]
pH	standard units	Effluent	5/week	grab
E. Coli Bacteria	#/100 ml	Effluent	5/month	grab
Total Residual Chlorine (July – September)	µg/L	Effluent	3/day	grab
	lb/day			calculation
Total Residual Chlorine (October – June)	µg/L	Effluent	1/day	grab
	lb/day			calculation
Total Ammonia as N (Mar. – Oct.)	mg/L	Effluent	3/week	24-hour composite
	lb/day			calculation
Total Ammonia as N (Nov. – Feb.)	mg/L	Effluent	1/month	24-hour composite
Total Phosphorus February – October	µg/L	Effluent	3/week	24-hour composite
	lb/day			calculation
Total Phosphorus November – January	µg/L	Effluent	1/week	24-hour composite
Cadmium	µg/L	Effluent	1/month	24-hour composite
	lb/day			calculation
Lead	µg/L	Effluent	1/month	24-hour composite
	lb/day			calculation
Zinc	µg/L	Effluent	1/month	24-hour composite
	lb/day			calculation
Temperature	ºC	Effluent	5/week	grab
Copper	µg/L	Effluent	1/month	24-hour composite
Silver	µg/L	Effluent	1/month	24-hour composite
Alkalinity	mg/L as $CaCO_3$	Effluent	1/month	24-hour composite
Hardness	mg/L as $CaCO_3$	Effluent	1/month	24-hour composite
Oil and Grease	mg/L	Effluent	1/quarter	grab
Total Dissolved Solids	mg/L	Effluent	1/quarter	24-hour composite
Polychlorinated Biphenyl (PCB) Congeners	pg/L	Influent	1/2 months	24-hour composite
PCB Congeners	pg/L	Effluent	1/quarter	24-hour composite
2,3,7,8 Tetrachlorodibenzo-p-dioxin	pg/L	Influent and Effluent	1/quarter	24-hour composite
Orthophosphate as P	mg/L	Effluent	1/month	24-hour composite
Total Kjeldahl Nitrogen	mg/L	Effluent	1/month	24-hour composite
Nitrate plus Nitrite Nitrogen	mg/L	Effluent	1/month	24-hour composite
Dissolved Oxygen	mg/L	Effluent	1/month	grab

Table 4: Effluent Monitoring Requirements				
Parameter	**Unit**	**Sample Location**	**Sample Frequency**	**Sample Type**
NPDES Application Form 2A Expanded Effluent Testing	---	Effluent	3x/5years	---
Whole Effluent Toxicity	TU_c	Effluent	2/year	24-hour composite

Notes:
1. Maximum daily loading is calculated by multiplying the concentration in mg/L by the average daily flow in mgd and a conversion factor of 8.34.
2. Percent removal is calculated using the following equation:
(average monthly influent - effluent) ÷ average monthly influent.

C. Surface Water Monitoring

The EPA received comments during the 2007 public comment period regarding the surface water monitoring requirements. Commenters stated that the 2007 draft permit proposed to require surface water monitoring at locations that are outside the influence or control of the dischargers performing the sampling, and that sampling should instead be required exclusively upstream and downstream of each discharger's outfall.

The EPA agrees that surface water monitoring upstream and downstream of each discharger's outfall would adequately characterize the dischargers' effect on water quality in the Spokane River. The EPA therefore proposes to change the surface water monitoring requirements such that the permit requires surface water monitoring upstream and downstream of each discharger's outfall.

Commenters also stated that the permit should not require surface water monitoring in Skalan Creek. Commenters stated that access to the mouth of the creek (the proposed required sampling point in the 2007 draft permit) required access to private property that could not be assured, and that the creek does not flow for much of the year. Given the lack of reliable access to the mouth of Skalan Creek, the fact that the creek does not flow for much of the year, and the fact that the Spokane River discharges have no influence upon water quality in Skalan Creek, the EPA has deleted the surface water monitoring requirements for Skalan Creek from the draft permit. The EPA is specifically requesting public comment on the revised surface water monitoring requirements in the draft permit.

Table 5: Surface Water Monitoring Requirements				
Parameter (units)	**Sample Locations**	**Sample Frequency**	**Sample Type**	**Maximum ML**
$CBOD_5$	Upstream and Downstream	8/year[1]	Grab	—
Total Ammonia as N (mg/L)	Upstream and Downstream	8/year[1]	Grab	0.05 mg/L
pH (standard units)	Upstream and Downstream	8/year[1]	Grab	—
Total Nitrogen (mg/L)	Upstream and Downstream	8/year[1]	Grab	0.05 mg/L
Total Phosphorus as P (µg/L)	Upstream and Downstream	8/year[1]	Grab	5 µg/L
Orthophosphate as P (µg/L)	Upstream and Downstream	8/year[1]	Grab	5 µg/L

Table 5: Surface Water Monitoring Requirements				
Parameter (units)	**Sample Locations**	**Sample Frequency**	**Sample Type**	**Maximum ML**
Dissolved Oxygen (mg/L)	Upstream and Downstream	8/year[1]	Grab	—
Chlorophyll a	Upstream and Downstream	8/year[1]	Grab	—
PCB Congeners	Upstream and Downstream	2/year[2]	Grab	See Note 3.

Notes:
1. The permittee must sample the receiving water at least twice per month during the months of July, August, September, and October.
2. The permittee must sample the receiving water at least once during the season of April 1 – June 30 and at least once during the season of July 1 – September 30.
3. The permittee must use EPA Method 1668 for analysis of receiving water samples for PCBs, must target an MDL no greater than 10 pg/L per congener, and must analyze for each of the 209 individual congeners.

D. Monitoring Requirements for PCBs

The draft permits for the Cities of Post Falls and Coeur d'Alene and HARSB propose bi-monthly influent and quarterly effluent monitoring for PCB congeners. These monitoring frequencies are the same as required in the State of Washington's permit for the Liberty Lake Sewer and Water District.

The draft permits also propose twice yearly surface water column monitoring upstream and downstream of the outfall for PCB congeners. The surface water column monitoring is required because there are very little data available for PCB concentrations in the Spokane River in Idaho. To reduce duplication of effort, the permit allows surface water monitoring performed by or for the SRRTTF to be used to fulfill permit requirements, if such monitoring would otherwise meet the requirements of the permit.

These data will be used to determine if the discharges have the reasonable potential to cause or contribute to excursions above water quality standards for PCBs in waters of the State of Idaho, the State of Washington or the Spokane Tribe of Indians and to evaluate the effectiveness of the toxics management plan.

The permit specifies the analytical methods and maximum detection limits that must be used for analysis of PCB congeners and dioxin. In general, the draft permit requires the use of EPA Method 1668 for PCB monitoring because it is the most sensitive method available, and it analyzes for all 209 of the individual PCB congeners. However, EPA method 8082 may be used for influent and effluent monitoring (but not receiving water monitoring), if initial screening with method 1668 shows that influent and/or effluent PCB concentrations are high enough that method 8082 could accurately quantify the PCB concentrations at those location(s).

Federal regulations require that, to assure compliance with permit limitations, permits must include requirements to monitor "according to procedures approved under 40 CFR Part 136," unless another method is required by 40 CFR Parts 400 – 471, 501, or 503 (i.e. pretreatment requirements, effluent limit guidelines, or sewage sludge requirements). See 40 CFR 122.44(i)(1)(iv).

EPA methods 1668 and 8082 are not approved methods under 40 CFR Part 136, thus, if effluent limits for total PCBs are established in the future, methods 1668 or 8082 could not be used to determine compliance with such effluent limits unless those methods are approved under 40 CFR 136 for either nationwide or limited use at the time such limits are established. The EPA proposed to approve Method 1668 Revision C on September 23, 2010 (75 FR 58027). On May 18, 2012, the EPA chose to defer approval of Method 1668C while it considers the large number of public comments received on the proposed approval. However, the EPA noted that "this decision does not negate the merits of this method for the determination of PCB congeners in regulatory programs or for other purposes when analyses are performed by an experienced laboratory" (77 FR 29763).

The EPA may require the use of methods 1668 or 8082 in this case because the permit requires analysis of PCB congeners, and the methods approved under 40 CFR 136 are not capable of analysis for individual PCB congeners. While method 8082 cannot measure for all 209 PCB congeners, it can measure for some individual congeners. Congener analysis is appropriate in this case because it will aid in source identification, which is one of the goals of the toxics management plan requirements. For pollutants for which there are no approved methods under 40 CFR Part 136 (such as PCB congeners), monitoring must be conducted according to a test procedure specified in the permit (40 CFR 122.44(i)(1)(iv)). Therefore, the EPA has specified the use of EPA method 1668, or, if it would be adequately sensitive, 8082. Furthermore, the monitoring is being required for effluent and receiving water characterization as opposed to determining compliance with effluent limits.

VII. Sludge (Biosolids) Requirements

EPA Region 10 separates wastewater and sludge permitting. Under the CWA, the EPA has the authority to issue separate sludge-only permits for the purposes of regulating biosolids. The EPA may issue a sludge-only permit to each facility at a later date, as appropriate.

Until future issuance of a sludge-only permit, sludge management and disposal activities at each facility continue to be subject to the national sewage sludge standards at 40 CFR Part 503 and any requirements of the State's biosolids program. The Part 503 regulations are self-implementing, which means that facilities must comply with them whether or not a permit has been issued.

The absence of specific biosolids requirements in the draft permit is unchanged from the 2007 draft permit. This information is included here for the purpose of providing background context and is not one of the substantial new questions that caused the EPA to reopen the public comment period. Therefore the EPA is not requesting comments on the absence of specific biosolids requirements in the draft permit at this time.

VIII. Other Permit Conditions

A. Quality Assurance Plan

The quality assurance plan requirements (see the revised draft permit at Part II.C) are identical to those in the 2007 draft permit and are explained in the fact sheet dated February 16, 2007. The quality assurance plan requirements are not among the substantial new questions that caused the EPA to reopen the public comment period. The requirements are discussed here for the purpose

of providing background context. Therefore the EPA is not requesting comments on the quality assurance plan requirements at this time.

B. Phosphorus Management Plan

In general, the phosphorus management plan requirements (see the revised draft permit at Part II.B) are similar to those in the 2007 draft permit. However, unlike the 2007 draft permit, the revised draft permit requires that the phosphorus management plan and implementation plan be submitted to the EPA and IDEQ, and requires annual reporting of reductions achieved through the phosphorus management plan. The phosphorus management plan requirements are effective year-round, including November – January when no numeric phosphorus limits are in place. The EPA is specifically requesting public comments on the phosphorus management plan requirements.

C. Pretreatment

The proposed permit contains requirements that the City control industrial dischargers, pursuant to 40 CFR 403. Indirect dischargers to the treatment plant must comply with the applicable requirements of 40 CFR 403, any categorical pretreatment standards promulgated by the EPA, and any additional or more stringent requirements imposed by the City of Coeur d'Alene as part of its approved pretreatment program or sewer use ordinance (e.g., local limits).

The pretreatment requirements are not among the substantial new questions that caused the EPA to reopen the public comment period and are discussed here for the purpose of providing background context. Therefore, the EPA is not requesting comments on the pretreatment requirements at this time.

D. Sanitary Sewer Overflows and Proper Operation and Maintenance of the Collection System

Untreated or partially treated discharges from separate sanitary sewer systems are referred to as sanitary sewer overflows (SSOs). SSOs may present serious risks of human exposure when released to certain areas, such as streets, private property, basements, and receiving waters used for drinking water, fishing and shellfishing, or contact recreation. Untreated sewage contains pathogens and other pollutants, which are toxic. SSOs are not authorized under this permit. Pursuant to the NPDES regulations, discharges from separate sanitary sewer systems authorized by NPDES permits must meet effluent limitations that are based upon secondary treatment. Further, discharges must meet any more stringent effluent limitations that are established to meet State or Tribal water quality standards.

The permit contains language to address SSO reporting and public notice and operation and maintenance of the collection system. The permit requires that the permittee identify SSO occurrences and their causes. In addition, the permit establishes reporting, record keeping and third party notification of SSOs. Finally, the permit requires proper operation and maintenance of the collection system. The following specific permit conditions apply:

Immediate Reporting – The permittee is required to notify the EPA of an SSO within 24 hours of the time the permittee becomes aware of the overflow. (See 40 CFR 122.41(l)(6)).

Written Reports – The permittee is required to provide the EPA a written report within five days of the time it became aware of any overflow that is subject to the immediate reporting provision. (See 40 CFR 122.41(l)(6)(i)).

Third Party Notice – The permit requires that the permittee establish a process to notify specified third parties of SSOs that may endanger health due to a likelihood of human exposure; or unanticipated bypass and upset that exceeds any effluent limitation in the permit or that may endanger health due to a likelihood of human exposure. The permittee is required to develop, in consultation with appropriate authorities at the local, county, tribal and/or state level, a plan that describes how, under various overflow (and unanticipated bypass and upset) scenarios, the public, as well as other entities, would be notified of overflows that may endanger health. The plan should identify all overflows that would be reported and to whom, and the specific information that would be reported. The plan should include a description of lines of communication and the identities of responsible officials. (See 40 CFR 122.41(l)(6)).

Record Keeping – The permittee is required to keep records of SSOs. The permittee must retain the reports submitted to the EPA and other appropriate reports that could include work orders associated with investigation of system problems related to a SSO, that describes the steps taken or planned to reduce, eliminate, and prevent reoccurrence of the SSO. (See 40 CFR 122.41(j)).

Proper Operation and Maintenance – The permit requires proper operation and maintenance of the collection system. (See 40 CFR 122.41(d) and (e)). SSOs may be indicative of improper operation and maintenance of the collection system. The permittee may consider the development and implementation of a capacity, management, operation and maintenance (CMOM) program.

The permittee may refer to the Guide for Evaluating Capacity, Management, Operation, and Maintenance (CMOM) Programs at Sanitary Sewer Collection Systems (EPA 305-B-05-002). This guide identifies some of the criteria used by EPA inspectors to evaluate a collection system's management, operation and maintenance program activities. Owners/operators can review their own systems against the checklist (Chapter 3) to reduce the occurrence of sewer overflows and improve or maintain compliance.

E. Additional Permit Provisions

Sections III, IV, and V of the draft permit contain standard regulatory language that must be included in all NPDES permits. Because they are regulations, they cannot be challenged in the context of an NPDES permit action. The standard regulatory language covers requirements such as monitoring, recording, and reporting requirements, compliance responsibilities, and other general requirements.

IX. Other Legal Requirements

A. Endangered Species Act and Essential Fish Habitat

As explained in the fact sheet dated February 16, 2007, the EPA has determined that the discharge is not likely to adversely affect bull trout, and will have no effect on other threatened and endangered species (EPA 2007). In a letter dated April 5, 2007, USFWS concurred with EPA's effects determination of "not likely to adversely to affect," for bull trout.

In general, the effluent limitations in the revised draft permit are as stringent as or more stringent than those in the 2007 draft permit. Furthermore, on August 9, 2007, the bald eagle was removed from the list of threatened and endangered species. Therefore, further consultation under the Endangered Species Act is not necessary.

Essential fish habitat (EFH) is the waters and substrate (sediments, etc.) necessary for fish to spawn, breed, feed, or grow to maturity. The Magnuson-Stevens Fishery Conservation and Management Act (January 21, 1999) requires the EPA to consult with NOAA Fisheries when a proposed discharge has the potential to adversely affect EFH (i.e., reduce quality and/or quantity of EFH).

The EFH regulations define an adverse effect as any impact which reduces quality and/or quantity of EFH and may include direct (e.g. contamination or physical disruption), indirect (e.g. loss of prey, reduction in species' fecundity), site specific, or habitat-wide impacts, including individual, cumulative, or synergistic consequences of actions.

The EPA has determined that issuance of this permit is not likely to adversely affect EFH in the vicinity of the discharge. The Spokane River is not designated as EFH. The EPA has provided NOAA Fisheries with copies of the draft permit and fact sheet during the public notice period. Any comments received from NOAA Fisheries regarding EFH will be considered prior to reissuance of this permit.

B. State/Tribal Certification

Section 401 of the CWA requires the EPA to seek State or Tribal certification before issuing a final permit. As a result of the certification, the State may require more stringent permit conditions or additional monitoring requirements to ensure that the permit complies with water quality standards.

C. Permit Expiration

The permit will expire five years from the effective date.

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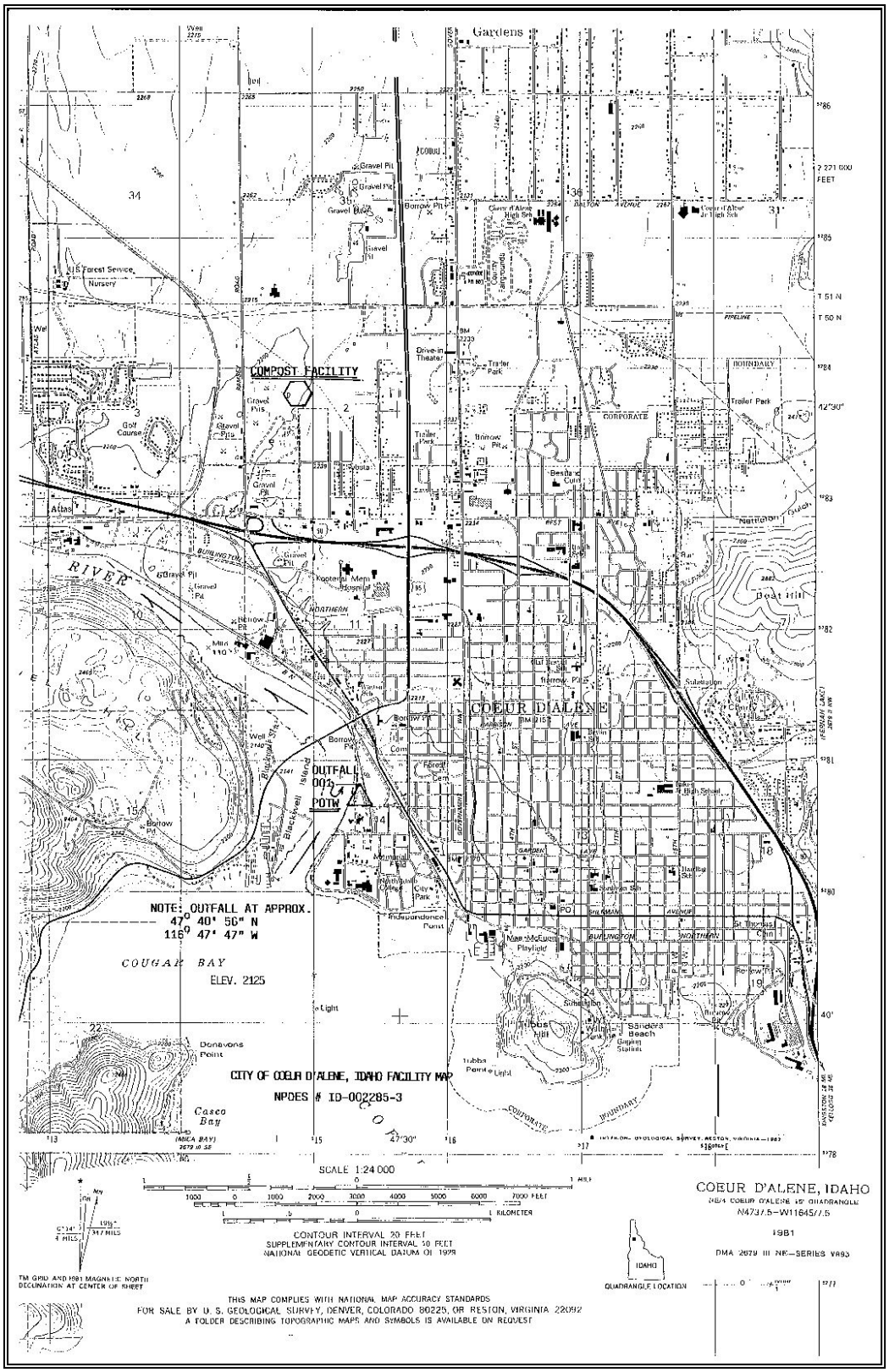
Appendix A: Facility Map



Appendix B: Water Quality-based Effluent Limits for Phosphorus, Ammonia and Carbonaceous Biochemical Oxygen Demand Necessary to Meet Water Quality Criteria for Dissolved Oxygen in Washington and Nutrients in Idaho

A. Overview

Federal regulations require NPDES permits to be conditioned to ensure compliance with the water quality requirements of all affected States (40 CFR 122.4(d), 122.44(d)(4), see also Clean Water Act Section 401(a)(2)). The EPA has determined that waters of the State of Washington are affected by discharges of nutrient and oxygen-demanding pollution, specifically total phosphorus (TP), five-day carbonaceous biochemical oxygen demand ($CBOD_5$), and total ammonia as nitrogen (ammonia), from point sources in Idaho. These three pollutants can decrease dissolved oxygen concentrations in the Spokane River and in Lake Spokane, in the State of Washington. Thus, the EPA must establish water quality-based effluent limits for these parameters, which ensure that the level of water quality to be achieved by limits on point sources is derived from and complies with all applicable water quality standards, including Washington water quality standards (40 CFR 122.44(d)(1)(vii)(A)). Some of the applicable water quality standards for the State of Washington explicitly require that the cumulative impact of all human actions be considered. Therefore, the effluent limits are set at a level that will assure that these discharges, considered cumulatively with all other human sources of pollution, including those in the State of Washington, will achieve the Washington DO standard in Lake Spokane.

B. Requirement to Meet Washington's Water Quality Standards

The federal regulation 40 CFR 122.4(d) states that "no permit may be issued…when the imposition of conditions cannot ensure compliance with the applicable water quality requirements of all affected States." In the reasonable potential analysis described below, the EPA determined that discharges of TP, $CBOD_5$, and ammonia from the City of Coeur d'Alene, the City of Post Falls and the Hayden Area Regional Sewer Board (HARSB) affect water quality in waters of the State of Washington, because they have the reasonable potential to cause or contribute to excursions below Washington's water quality criteria for DO. Therefore, the State of Washington is an "affected State" under 40 CFR 122.4(d).

Furthermore, 40 CFR 122.44(d)(4) requires that NPDES permits must include any requirements necessary to "conform to applicable water quality requirements under section 401(a)(2) of CWA when the discharge affects a State other than the certifying State." Therefore, the EPA must establish conditions in the permits for these facilities, which ensure compliance with the applicable water quality requirements of the State of Washington.

Reasonable Potential Analysis

The federal regulation 40 CFR 122.44(d)(1)(i), which implements Section 301(b)(1)(C) of the Clean Water Act, requires that NPDES permits contain water quality-based effluent limitations for all pollutants or pollutant parameters that the EPA determines are or may be discharged at a level that will cause, have the reasonable potential to cause, or contribute to an excursion above any State water quality standard, including narrative criteria for water quality.

In the fact sheets for the 2007 draft permits for the Cities of Coeur d'Alene and Post Falls and HARSB, the EPA found that the discharges of oxygen-demanding pollution from those sources have the reasonable potential to cause or contribute to excursions below Washington's water quality criterion for dissolved oxygen in Lake Spokane. Specifically, the modeling conducted in support of the 2007 draft Idaho permits showed that the levels of discharge allowed by the 1999 permits, from the Idaho wastewater treatment plants alone, could decrease dissolved oxygen concentrations in Lake Spokane by 0.57 mg/L as an average over depth below 8 meters, at the time and location of maximum impact.[1] Washington's water quality standard only allows a DO decrease of 0.2 mg/L below the natural condition for all human sources considered cumulatively (see "Applicable Water Quality Standards and Status of Waters," below). Therefore, a decrease of 0.57 mg/L would cause an excursion above Washington's water quality criterion for DO in lakes and reservoirs (because it is a greater decrease than allowed by the standards). In addition, the modeling conducted in support of the 2007 draft Idaho permits showed that currently permitted levels of discharge could increase pH at the state line to more than 9.0 standard units, which is an excursion above both Idaho and Washington water quality standards (Cope 2006).

Reasonable potential determinations must account for existing controls on point and nonpoint sources of pollution (40 CFR 122.44(d)(1)(ii)). Additional anthropogenic nutrients and oxygen demand discharged by municipal separate storm sewer systems in Idaho further contribute to excursions below dissolved oxygen standards, which serves as additional evidence for the reasonable potential finding.

Therefore, the discharges of TP, ammonia, and $CBOD_5$ from the three WWTPs discharging to the Spokane River in Idaho affect water quality in waters of the State of Washington and have the reasonable potential to cause or contribute to excursions above water quality standards for dissolved oxygen and pH in waters of the State of Washington. The EPA has therefore established water quality-based effluent limits for TP, ammonia and $CBOD_5$ for the Idaho dischargers to the Spokane River that ensure a level of water quality that is derived from and complies with both Washington's and Idaho's water quality standards (40 CFR 122.44(d)(1)(vii)(A)).

C. Applicable Water Quality Standards and Status of Waters

Lake Spokane (also called "Long Lake"), a reservoir located in the State of Washington, and the segments of the Spokane River between the Idaho-Washington border and Lake Spokane, are listed as impaired for DO in Washington's 2008 303(d)/305(b) integrated report. The Spokane River is also listed as a "water of concern" (category 2) for pH in Washington.

The Spokane River is not impaired for dissolved oxygen or pH in the State of Idaho. However, the entire length of the Spokane River that is in Idaho (i.e., both above and below the Post Falls Dam) is listed in Idaho's 2010 303(d)/305(b) integrated report as being impaired for TP. See

[1] The fact sheets for the 2007 draft permits for the City of Coeur d'Alene, the City of Post Falls, and HARSB stated the maximum DO decrease in Lake Spokane resulting from currently permitted Idaho discharges as 1.1 mg/L. This was the 95th percentile DO decrease, over the depth of the lake, at the time and location of maximum impact, predicted under the "Permit" modeling scenario (Cope 2006). The Spokane DO TMDL quantifies the DO decrease as the average DO decrease, over the depth of the lake, below 8 meters (see the Spokane DO TMDL at page 36). When this metric is applied to the "Permit" scenario described in the 2006 Cope report and the 2007 fact sheets, the Idaho wastewater treatment plants' potential impact on DO, based on currently-permitted levels of discharge, is 0.57 mg/L.

Table 1, below, for a summary of the applicable water quality criteria for DO, pH, and nutrients or aesthetics for the Spokane River and Lake Spokane in the States of Idaho and Washington.

Table 1: Dissolved Oxygen and pH Criteria for the Spokane River and Lake Spokane

Spokane River		
Parameter	**Idaho Standards**	**Washington Standards**
Dissolved Oxygen	**Numeric Criteria:** Below Post Falls Dam, except during August and September: One (1) day minimum of not less than six point zero (6.0) mg/l or ninety percent (90%) of saturation, whichever is greater. Other times and locations: Dissolved Oxygen Concentrations exceeding six (6) mg/l at all times. (IDAPA 58.01.02, Sections 110.12 and 250) **Natural condition provision:** When natural background conditions exceed any applicable water quality criteria set forth in Sections 210, 250, 251, 252, or 253, the applicable water quality criteria shall not apply; instead, there shall be no lowering of water quality from natural background conditions. (IDAPA 58.01.02.200.09.)	**Numeric Criteria:** From Nine Mile Bridge (river mile 58.0) to the Idaho border (river mile 96.5): 1-day minimum of 8.0 mg/L. From Long Lake Dam (river mile 33.9) to Nine Mile Bridge: 1-day minimum of 9.5 mg/L. (WAC 173-201A, Tables 200(1)(d) and 602) **Natural condition provision:** When a waterbody's D.O. is lower than the criteria in Table 200 (1)(d) (or within 0.2 mg/L of the criteria) and that condition is due to natural conditions, then human actions considered cumulatively may not cause the D.O. of that water body to decrease more than 0.2 mg/L. (WAC 173-201A-200(1)(d)(i))
pH	Within the range of six point five (6.5) to nine point zero (9.0). (IDAPA 58.01.02.250.01.a).	From Nine Mile Bridge (river mile 58.0) to the Idaho border (river mile 96.5): pH shall be within the range of 6.5 to 8.5 with a human-caused variation within the above range of less than 0.5 units. From Long Lake Dam (river mile 33.9) to Nine Mile Bridge: pH shall be within the range of 6.5 to 8.5, with a human-caused variation within the above range of less than 0.2 units. (WAC 173-201A, Tables 200(1)(g) and 602)
Natural Conditions Definition	The physical, chemical, biological, or radiological conditions existing in a water body without human sources of pollution within the watershed. Natural disturbances including, but not limited to, wildfire, geologic disturbance, diseased vegetation, or flow extremes that affect the physical, chemical, and biological integrity of the water are part of natural background conditions. Natural background conditions should be described and evaluated taking into account this inherent variability with time and place. (IDAPA 58.01.02.010.56)	"Natural conditions" or "natural background levels" means surface water quality that was present before any human-caused pollution. When estimating natural conditions in the headwaters of a disturbed watershed it may be necessary to use the less disturbed conditions of a neighboring or similar watershed as a reference condition. (WAC 173-201A-020)
Nutrients / Aesthetics	Surface waters of the state shall be free from excess nutrients that can cause visible slime growths or other nuisance aquatic growths impairing designated beneficial uses. (IDAPA 58.01.02.200.06)	Aesthetic values must not be impaired by the presence of materials or their effects, excluding those of natural origin, which offend the senses of sight, smell, touch, or taste (see WAC 173-201A-230 for guidance on establishing lake nutrient standards to protect aesthetics). (WAC 173-201A-260(2)(b))
Lake Spokane (Washington Water Quality Standards)		
Dissolved Oxygen	For lakes, human actions considered cumulatively may not decrease the dissolved oxygen concentration more than 0.2 mg/L below natural conditions. (WAC 173-201A-200(1)(d)(ii))	

Requirement for Cumulative Analysis of Human Actions

Washington's water quality criterion for dissolved oxygen in lakes and reservoirs requires that "*human actions considered cumulatively* may not decrease the dissolved oxygen concentration more than 0.2 mg/L below natural conditions" (emphasis added). In order to assure that the Idaho sources meet Washington State standards, the dissolved oxygen impact of discharges from Idaho sources must be considered cumulatively with the impact of the Washington sources.

D. Modeling Supporting the Permit Limits

The Clean Water Act's primary mechanism for addressing water quality impairments on a cumulative basis is the total maximum daily load (TMDL) process. However, TMDLs are generally prepared by the States, and a TMDL prepared by a State cannot establish load and wasteload allocations for pollution sources located outside the boundaries of that State. However, when a State prepares a TMDL, the State may reasonably assume that NPDES permits for point sources in upstream States, which have an effect on water quality in the downstream State that is preparing the TMDL, will include effluent limits that ensure compliance with the downstream State's water quality requirements, including water quality standards, because this is required by federal regulations (40 CFR 122.4(d), 40 CFR 122.44(d)(4)). Furthermore, if the EPA is the NPDES permitting authority for the point source discharges in the upstream State (as it is in this case) the downstream State may object to the issuance of the permits in the upstream state if the federal permits in the upstream State will affect the quality of its waters so as to violate any water quality requirements in the downstream State (CWA Section 401(a)(2)). Thus, when the Washington State Department of Ecology (Ecology) prepared the *Spokane River and Lake Spokane Dissolved Oxygen Total Maximum Daily Load* (TMDL) Ecology assumed that the NPDES permits for point sources discharging to the Spokane River in Idaho would include limits that would ensure compliance with Washington's water quality standards.

The DO TMDL's Modeling Assumptions for Idaho Point Sources

To ensure that the TMDL's load and wasteload allocations, Avista's DO responsibility, and the loadings from Idaho would cumulatively meet DO WQS in Lake Spokane, when developing the TMDL, Ecology modeled the cumulative impact of both Idaho and Washington pollution sources upon the lake.

The TMDL states: "The dissolved oxygen depletion predicted to result from these assumed Idaho pollutant loads is shown in Tables 14 and 15 of PSU (2010) (the Idaho only source assessment scenario results). The EPA will incorporate permit limits into the NPDES permits for Idaho point source dischargers that ensure that the total dissolved oxygen depletion resulting from those dischargers is no greater than that shown in Tables 14 and 15 of (the Spokane River Modeling Final Scenarios Report 2010, the "2010 modeling report," by Portland State University)." Id. at 35.

Thus, when developing the TMDL, Ecology assumed certain loadings of oxygen-demanding pollution would be discharged in Idaho (shown in the 2010 modeling report at Table 2, the "prior modeling assumptions"), and the modeling supporting the TMDL thereby accounts for any dissolved oxygen decrease resulting from sources in Idaho. However, the TMDL does not apply to the Idaho permits, and the prior modeling assumptions are not binding on the EPA when it drafts the Idaho permits. The prior modeling assumptions are not wasteload allocations with

which the effluent limits in the Idaho permits must be consistent (40 CFR 122.44(d)(1)(vii)(B)). The EPA is free to establish any limits in the Idaho permits for $CBOD_5$, ammonia and TP so long as those limits ensure compliance with both Idaho and Washington WQS, when considered cumulatively with other sources of pollution (40 CFR 122.4(d), 122.44(d)(4)).

The language on Page 35 of the TMDL assumed that, in order to determine if the effluent limits in the Idaho permits would meet Washington's DO criteria, the EPA would isolate the impact of the Idaho point sources and then evaluate those results against the DO impact of the Idaho sources as assumed in the TMDL modeling. The limits would then be set to ensure that the DO depletion from Idaho sources, specifically, was no greater than assumed in the TMDL. This approach would ensure compliance with Washington water quality standards for DO on a cumulative basis by ensuring that the DO impact from *both* Idaho and Washington sources (and therefore the cumulative DO impact from sources in both States) was the same or less than predicted by the TMDL modeling.

However, the EPA believes it is more realistic to conduct the modeling supporting effluent limits for Idaho point sources to reflect the cumulative effect of all human actions that influence DO and to then evaluate the modeling results against Washington's water quality standards. This approach more directly ensures compliance with Washington's water quality standards on a cumulative basis. Thus, the effluent limits are based on modeling of all known human sources of nutrient and oxygen-demanding pollution (i.e. point and non-point sources in Washington and Idaho).

Summary of Model Results

The effluent limits in the draft permits are not the same as the loadings that were assumed in the modeling supporting the TMDL, for Idaho point sources. However, as explained below, the effluent limits for Idaho point sources ensure compliance with Washington's water quality standards for dissolved oxygen, when considered cumulatively with the Washington NPDES permits' effluent limits, the TMDL's load allocations for oxygen-demanding pollution from non-point sources, and Avista's dissolved oxygen responsibility (LimnoTech 2011, PSU 2011).

The effluent limits meet Washington's DO criteria (WAC 173-201A-200(1)(d)) when the precision of the water quality model is considered (as explained in detail below). The effluent limits in the Washington and Idaho NPDES permits do not decrease the cumulative average dissolved oxygen in the shaded cells in Table 7 of the final TMDL (i.e., when and where Avista has a DO responsibility) relative to the prior modeling assumptions. In fact, the effluent limits *improve* the dissolved oxygen by 0.006 mg/l relative to the prior modeling assumptions and Washington wasteload allocations when averaged over all reservoir segments and all times of Avista responsibility.

Model Precision

With three exceptions, each individual model output result ensures compliance with Washington's DO criteria (WAC 173-201A-200(1)(d)), when considered cumulatively with the load allocations in Table 6 of the TMDL and Avista's DO responsibility as reported in Table 7 of the TMDL, after results are rounded to the nearest 0.1 mg/l. Each of the three exceptions is characterized by a markedly low arithmetic tolerance for any decrease in DO relative to the TMDL modeling. That is to say, in each of these instances, the DO sag resulting from point and non-point controls under the TMDL scenario, after considering Avista's responsibility, was just

slightly less than 0.25 mg/L. Thus, in those instances, a very small additional DO sag (e.g., 0.002 mg/L) would cause the difference, rounded to the nearest 0.1 mg/L, to change from 0.2 mg/L to 0.3 mg/L. The actual DO decreases in the three exceptions, relative to the TMDL, were 0.002 – 0.003 mg/L (see Table 2, below).

Table 2: Increases in Rounded DO Sag to 0.3 mg/L

Segment	Time Period	Tolerance (mg/L)	Modeled DO Change Relative to TMDL (mg/L)
188	July 1-15	0.0008	-0.003
188	September 1-15	0.0001	-0.002
186	September 16-30	0.0014	-0.003

The EPA believes these deviations are within the precision of the CE-QUAL-W2 model. In a memo dated December 28, 2010, LimnoTech described some issues encountered when performing a sensitivity analysis for the Idaho point sources. As stated on Page 2 of the memo, a reduction in Post Falls' $CBOD_5$ discharge (with all other model inputs held constant) actually effected a 0.002 mg/L *decrease* in the average DO in the reservoir, in times and locations where Avista has a DO responsibility. Other inputs being equal, the DO should have *increased* in response to decreased CBOD discharges. Even if the change in $CBOD_5$ loading was too small to have any discernible impact, the DO should have, at a minimum, been unchanged. Thus, it is reasonable to consider the difference between these two results (0.002 mg/L) to be within the precision of the model for the average DO in times and locations where Avista has a DO responsibility.

Because this average DO is computed from 106 individual results, the model is less precise than 0.002 mg/L for any individual result. Therefore, the EPA believes that the 0.002 – 0.003 mg/L deviations from the TMDL scenario, which resulted in a 0.3 mg/L rounded DO sag in three instances, are within the precision of the CE-QUAL-W2 model. Two results that vary by less than the precision of the model are functionally the same result.

Improvements in DO Relative to the TMDL

Under the proposed effluent limits for Idaho and Washington point sources, the cumulative DO sag, rounded to the nearest tenth of a milligram per liter, would actually decrease to 0.1 mg/L from 0.2 mg/L in five instances, as shown in Table 3, below. Also, as stated above, the alternative improves the dissolved oxygen by 0.006 mg/l (relative to the TMDL) when averaged over all segments and times of Avista responsibility. This means that any decreases in DO concentrations relative to the TDML scenario, at specific times and locations, are balanced by DO improvements at other times and in other locations.

Table 3: Decreases in Rounded DO Sag to 0.1 mg/L		
Segment	**Time Period**	**Modeled Change Relative to TMDL (mg/L)**
172	August 1-15	+0.007
177	September 1-15	+0.018
185	September 1-15	+0.001
175	September 16-30	+0.025
180	September 16-30	+0.018

The Exceptions are Very Infrequent

The three instances where the cumulative DO sag increased to 0.3 mg/L, when rounded to the tenths place, comprise less than 3% of the times and locations where Avista has a DO responsibility (106 total), and 0.7% of all of the times and locations that were evaluated in Table 7 of the TMDL (448 total). Since Table 7 of the Spokane River DO TMDL only provides DO results for June 1st - December 31st, and modeling indicates no violations of DO WQS prior to June 1st, this percentage would be even smaller than 0.7% on a year-round basis.

The TMDL's Margin of Safety

The TMDL has an implicit margin of safety comprised of several conservative assumptions (see the TMDL at Page 51). Some of these will tend to exaggerate the impact of nutrients and oxygen demand discharged by point sources. Specifically:

- Low flows (year 2001) were used as the baseline hydrologic condition.
- All TP is assumed to be bioavailable.[2]
- The top eight meters of the reservoir are not included in the vertical averaging because of amplified algal activity which increases daytime dissolved oxygen levels.

Therefore, the actual DO impact of the point source discharges may be somewhat less than that predicted by the model.

Conclusion

Because the effluent limits in the Idaho and Washington NPDES permits are equivalent to the scenario used to develop the Spokane River TMDL for the reasons described above, the EPA believes that these effluent limits will ensure compliance with Washington's water quality standards for DO, when considered cumulatively with other actions taking place under the TMDL.

Effluent Flow Rates used in the Model Inputs

In 2009, the EPA asked the City of Coeur d'Alene, the City of Post Falls, and HARSB to provide effluent flow rate projections for the year 2027, for use in developing the Spokane River TMDL and those facilities' NPDES permits. The flow projections provided by the utilities at that time were between 6.4 and 7.9 mgd for the City of Coeur d'Alene, 5.0 mgd for the City of Post Falls, and 3.2 mgd for HARSB. After further discussion between the EPA, the City of Coeur d'Alene and IDEQ, a flow projection of 7.6 mgd was established for the City of Coeur d'Alene.

[2] The model partitions point source phosphorus into two fractions: One which is immediately bioavailable and another that is not immediately bioavailable but becomes bioavailable over time according to first-order kinetics.

These flows are similar to projections made in 2005 (for the year 2028) as part of the Spokane River TMDL collaboration process. The 2005 flow projections were 7.0 mgd for the City of Coeur d'Alene, 5.7 mgd for the City of Post Falls, and 3.2 mgd for HARSB (Spokane River DO TMDL Collaboration Flows and Loadings Workgroup 2005). For Idaho point sources, the modeling supporting the TMDL was based on the effluent flow rates projected in 2009 and effluent concentrations described in the 2010 modeling report at Table 2 (PSU 2010). For the City of Coeur d'Alene and HARSB, these flow projections were also used to determine calculate the effluent limits in the draft permits, as described below.

In March 2010, JUB Engineers completed a revised flow projection for the City of Post Falls, which was 7.65 mgd (JUB 2010). The projection considered projected population growth within the service area, and a 25% addition for wastewater from non-municipal uses. For the City of Post Falls, the increased pollutant loads resulting from this increased flow rate (relative to the 2005 and 2009 projections) were represented in the model using proportionally increased effluent concentrations, instead of an increased effluent flow (see Table 4 below).

Basis for Loads

The model input effluent concentrations of TP, $CBOD_5$, and ammonia for each of the Idaho point sources are summarized in Table 4, below. The seasonal average loads of TP, ammonia, and $CBOD_5$ that are necessary to meet Washington's water quality criterion for DO in Lake Spokane, based on the modeling, are calculated by multiplying the projected flow rates for each facility, which were used in the modeling, by the modeled concentrations and the density of water (8.34 lb/gallon). The resulting seasonal average loads are shown in Table 4, below.

Table 4: Idaho Loads used in Modeling Supporting the Permit Limits

Point Source Discharge	Modeled Flow Rate (mgd)	Seasonal Average Modeled Concentrations, February – October Unless Otherwise Noted (mg/L)			Seasonal Average Modeled Loads, February – October Unless Otherwise Noted (lb/day)		
		Ammonia	TP	$CBOD_5$	Ammonia	TP	$CBOD_5$
City of Coeur d'Alene WWTP	7.6	4.29 (Mar. – Oct.)	0.05	3.56 (Feb. – Mar.)	**272 (Mar. – Oct.)**	**3.17**	**226 (Feb. – Mar.)**
				3.2 (Apr. – Oct.)			**203 (Apr. – Oct.)**
HARSB WWTP	3.2	2.9	0.05	2.9	**77.4**	**1.33**	**77.4**
City of Post Falls WRF[1]	5.0	6.1	0.0765	6.1	**255**	**3.19**	**255**

Notes:
1. Effluent loads for the City of Post Falls are equivalent to a discharge of 0.05 mg/L TP, 4.0 mg/L $CBOD_5$, and 4.0 mg/L ammonia at a flow rate of 7.65 mgd.

E. Translating the Modeled Loads to Effluent Limits

The modeled loads in Table 4 are seasonal average values. However, 40 CFR 122.45(d)(2) states that "(f)or continuous discharges all permit effluent limitations, standards, and prohibitions, including those necessary to achieve water quality standards, shall unless impracticable be stated as…(a)verage weekly and average monthly discharge limitations for POTWs."

In some cases, it is impracticable to express effluent limits as average monthly limits and average weekly limits. In the draft permits for the City of Coeur d'Alene, City of Post Falls, and

HARSB, the effluent limits for E. coli, chlorine, metals, ammonia, TP, and, in some cases, CBOD are not expressed as average monthly limits and average weekly limits. The basis for expressing effluent limits for E. coli, chlorine and metals using averaging periods other than monthly and weekly is explained in Appendices C and E.

The EPA has determined that it is impracticable to express the water quality-based effluent limits for TP, ammonia, and CBOD that are necessary to meet Washington's water quality criteria for dissolved oxygen as monthly average and weekly average limits, in this case, for the reasons discussed below. The water quality-based effluent limits for TP, ammonia and CBOD are expressed as seasonal average loading limits that are identical to the loads of TP simulated in the modeling.

Basis for Expressing Effluent Limits for TP, ammonia and CBOD as Seasonal Average Limits

In a memorandum dated March 3, 2004 (the Chesapeake Bay Memo), James A. Hanlon, the director of the EPA's Office of Wastewater Management, stated that, for the protection of Chesapeake Bay and its tidal tributaries from excess nutrient loading, it was impracticable to express permit effluent limitations for nutrients (total nitrogen and TP) as daily maximum, weekly average, or monthly average effluent limitations.

The Chesapeake Bay Memo states that:

> *"Establishing appropriate permit limits (for nitrogen and TP) for Chesapeake Bay and its tidal tributaries is different from setting limits for other parameters such as toxic pollutants because: the exposure period of concern for nutrients loading to Chesapeake Bay and its tidal tributaries is very long; the area of concern is far-field (as opposed to the immediate vicinity of the discharge); and the average pollutant load rather than the maximum pollutant load is of concern"* (Page 2).

The Chesapeake Bay Memo further states that:

> *"The nutrient dynamics of (Chesapeake) Bay may not be unique. The establishment of an annual limit with a similar finding of 'impracticability' pursuant to 40 CFR 122.45(d) may be appropriate for the implementation of nutrient criteria in other watersheds when: attainment of the criteria is dependent on long-term average loadings rather than short-term maximum loadings; the circumstances match those outlined in this memo for Chesapeake Bay and its tidal tributaries; annual limits are technically supportable with robust data and modeling as they are in the Chesapeake Bay context; and appropriate safeguards to protect all other applicable water quality standards are employed"* (Pages 2-3).

Similar to Chesapeake Bay, the EPA believes that a finding of impracticability is appropriate in this case as well, under 40 CFR 122.45(d).

Modeling and Hydrology Supports the use of Seasonal Average Limits

As stated in the TMDL (Page 33), the wasteload allocations for Washington point sources and the loading assumptions for the Idaho point sources are seasonal average values. Thus, attainment of dissolved oxygen criteria in Lake Spokane is based on long-term average loadings rather than short-term maximum loadings.

Modeling has shown that highly variable TP discharges from Spokane River point sources, which have an average of 50 µg/L TP, have a very similar impact upon DO in Lake Spokane relative to constant discharges from those sources of exactly 50 µg/L TP each day (HDR 2009). At times and in locations where Avista had a dissolved oxygen responsibility in the TMDL (see TMDL at Table 7, Pages 49-50), on average, the variable discharge scenario resulted in a 0.003 mg/L *improvement* in DO relative to constant discharges. The variable TP discharges increased DO by as much as 0.09 mg/L relative to constant discharges in some segments, and the maximum decrease in DO in any reservoir segment at any time was only 0.05 mg/L. Therefore, dissolved oxygen in Lake Spokane is insensitive to short-term increases in TP loading, as long as the seasonal average TP load remains unchanged.

In addition, the retention time of Lake Spokane, in a low-flow year, ranges from about 20 days to more than 100 days during the critical summer period (Cusimano 2004). The water quality in Lake Spokane during the critical summer period would therefore be affected by average pollutant loading from upstream sources as opposed to short-term maximum loading.

Because of the long residence time of Lake Spokane, the EPA expects that dissolved oxygen in Lake Spokane would be insensitive to short-term increases in CBOD or ammonia loading, as long as the seasonal average load remains unchanged, similar to the effects of TP.

The TP, Ammonia and CBOD Limits are intended to Control Far Field Effects

Similar to Chesapeake Bay, the TP, ammonia and CBOD effluent limits are intended to control far-field effects. Lake Spokane is a 24-mile-long reservoir, the upstream end of which is 42.5 miles downstream from the closest Idaho POTW (the City of Post Falls).

The Permits Include Additional Requirements to Ensure Water Quality Standards are Met with the use of Seasonal Limits

The draft permits include additional requirements to ensure that water quality standards are met. These requirements include required reporting of monthly average TP, ammonia, and CBOD loadings. In addition, if, at the end of any month from February through September, the average TP, ammonia and CBOD discharge measured to date is greater than the seasonal average loading limit, the permittee must submit a report explaining how it will lower the loading of the relevant pollutant(s)in order to comply with the seasonal average effluent limitations.

As explained below, the EPA has established average monthly and maximum daily limits for ammonia, whenever this was necessary to ensure compliance with Idaho's water quality criteria for ammonia or with the anti-backsliding provisions of the Clean Water Act.

The Future Effluent Variability is Unknown

In order to calculate average monthly and average weekly limits that are consistent with a seasonal average load, the effluent variability must be known. Effluent variability may be quantified by the coefficient of variation (CV), which is the ratio of the standard deviation to the mean of the effluent data (also called the relative standard deviation).

Because the TP effluent limits require levels of discharge much lower than current levels, the treatment systems must be upgraded in order to achieve compliance with the TP limits. In some cases, upgrades will be necessary to meet new water quality-based effluent limits for ammonia as well. The variability of the effluent CBOD loads for the upgraded facilities may also be different from the historical variability.

While historical monitoring data are available, which could be used to quantify the variability of TP, ammonia and CBOD in the effluents of the *existing* treatment facilities, the variability of these parameters in the effluent, after these upgrades are completed, is unknown.

On Page E-3, the TSD states that "typical values for the CV range from 0.2 to 1.2." Because the loading levels in the TMDL and modeling are long-term (e.g., February – October or March – October) average values, the value of the CV can have a significant impact on the value of the average monthly limit. For example, according to Table 5-2 of the TSD, if a facility that sampled 10 times per month had a CV of 0.2 for a given pollutant, its 95th percentile probability basis average monthly limit should be set at 1.12 times the long-term average. If that facility's CV were equal to 1.2, that facility's average monthly limit should be set at 1.80 times the long-term average. This means that the facility with a CV of 1.2 would have an average monthly limit 60% greater than a facility with a CV of 0.2. If the limits are set at the 99th percentile probability basis, the difference between limits based on a CV of 1.2 as opposed to a CV of 0.2 becomes even larger.

In some cases, if the CV is not known, an estimate can be made. In fact, it is common practice in the calculation of effluent limits for toxic parameters to assume that the CV is equal to 0.6, if the actual CV is unknown (see the TSD at Pages 53 and E-3). However, in the context of calculating average monthly and average weekly limits from a fixed long-term average, if the estimated CV is less than the actual CV, the effluent limits will be artificially stringent. Conversely, if the estimated CV is greater than the actual CV, the permittee may be able to consistently discharge at levels greater than those modeled, yet maintain compliance with the average monthly effluent limits. This possibility is recognized in the Chesapeake Bay Memo (see Page 4). The Chesapeake Bay Memo also points out that "the effluent loading of nutrients is not constant due to seasonal temperature fluctuations in northern climates" because biological nutrient removal is less effective at lower temperatures (Page 5). The TSD does not provide a means to account for this additional variability in the effectiveness of biological nutrient removal due to temperature.

In contrast, as stated on Page E-3 of the TSD, when calculating effluent limits for toxic parameters, "in many cases, changes in the CV will have little impact on the final permit limit." This is because the averaging periods for water quality criteria for toxic parameters are very short (generally 4 days for chronic aquatic life criteria and 1 hour for acute aquatic life criteria, see IDAPA 58.01.02.010). Effluent limits for toxic parameters must therefore control short-term peak concentrations. This constrains the effluent limit calculations, making the final effluent limits relatively insensitive to effluent variability.

In addition to the CV, it is unknown whether individual measurements of TP, CBOD or ammonia will be independent, or whether they will be correlated to one another (i.e. autocorrelated). Autocorrelation can be important in the derivation of average monthly permit limits (see TSD at Page E-15).

Seasonal Average Limit Summary

In summary, modeling and the hydrology of Lake Spokane show that, similar to Chesapeake Bay, DO concentrations in Lake Spokane are related not to maximum TP, ammonia and CBOD loading but to the seasonal average loadings of these pollutants. That is to say, Lake Spokane is insensitive to short-term increases in loading of oxygen-demanding pollutants from Idaho point sources, as long as the seasonal average loadings are less than or equal to the modeled loads. The effluent limits for TP, ammonia and CBOD, in this case, are based on far-field, as opposed to near-field, water quality concerns. Because the future variability of TP, ammonia and CBOD concentrations and loadings in these effluents is unknown, the EPA cannot calculate appropriate monthly average and weekly average effluent limits for these pollutants with any degree of certainty. If the EPA were to assume a CV, this could result in effluent limits for TP, ammonia, and CBOD that are artificially stringent, or which could allow the loading of TP, ammonia and/or CBOD to exceed that simulated in the modeling supporting the permits and the TMDL.

For these reasons, the EPA believes that it is impracticable to calculate appropriate average monthly and average weekly limits for TP, ammonia, and CBOD, in this case. The effluent limits for TP, ammonia, and CBOD that are necessary to meet Washington's water quality standards are therefore stated as seasonal average effluent limits. The seasonal average TP, CBOD, and ammonia effluent limits are identical to the seasonal average loads simulated in the modeling supporting the permits and the TMDL (see Table 4, above).

Reporting Requirements for Seasonal Average Limits

The permits include additional reporting requirements to ensure that water quality standards are attained. These include reporting the monthly average and maximum weekly or daily loads and concentrations on the monthly DMR, reporting the partial seasonal average loads through the last day of the monitoring month, and, if the partial seasonal average load of a given pollutant is greater than the seasonal average effluent limit, the permittee must submit a written report with the DMR, explaining the steps that the permittee will take to reduce its discharge of the relevant pollutant(s) in order to achieve compliance with the seasonal average effluent limit by the end of the season (October 31st in most cases).

If the permittee ceases discharge to the river for at least three days during the season(s) during which seasonal average limits apply, the permittee may include zero pounds per day values in the calculation of the seasonal average loads (and the partial seasonal average loads) as specified in Attachment A of the draft permit. The purpose of Attachment A is to ensure that periods of zero discharge are given the same weight as the periods of time when the permittee is discharging, in the calculation of the seasonal average discharge. The number of zeros allowed for averaging is equal to the required sampling frequency of three times per week (0.429 samples per day), multiplied by the number of days of zero discharge, and rounded down to the nearest whole number.

Ammonia Toxicity

In addition to exhibiting an oxygen demand, ammonia can be directly toxic to aquatic life at high concentrations. In order to prevent acute toxicity to aquatic life, the *Technical Support Document for Water Quality-Based Toxics Control* (EPA/505/2-90-001) or TSD recommends that effluent limits for pollutants which may be toxic to aquatic life be expressed as average

monthly and maximum daily limits, because even an average weekly limit has an averaging period that is too long to ensure that acute toxicity is prevented (see TSD at section 5.2.3).

Maximum daily limits are not necessary for HARSB because, as described in Appendix D, the EPA has determined, based on effluent data, that HARSB does not have the reasonable potential to cause or contribute to excursions above Idaho's water quality criteria for ammonia, for toxicity (IDAPA 58.01.02.283). Therefore the new water quality-based effluent limits for ammonia, for HARSB, have been established exclusively for the purpose of ensuring compliance with Washington's water quality criteria for DO, as opposed to preventing toxicity near the outfall, in waters of the State of Idaho. Therefore, the effluent limits for ammonia, for HARSB are expressed exclusively as seasonal average limits.

Effluent limits for ammonia, for the City of Coeur d'Alene and the City of Post Falls, are expressed as a combination of seasonal average, average monthly, and maximum daily effluent limits. The seasonal average limit is based on meeting water quality standards for dissolved oxygen in the State of Washington, downstream from the point of discharge and is identical to the seasonal average modeled loading of ammonia in Table 4, above.

For Coeur d'Alene, the average monthly and maximum daily limits are based on Idaho water quality standards that are intended to prevent acute and chronic toxicity from ammonia, near the point of discharge. The use of average monthly limits in combination with maximum daily limits, when effluent limits are based on preventing toxicity to aquatic life, is consistent with the recommendations of the TSD (Section 5.2.3). It is impracticable to prevent acute toxicity using an average weekly limit. Therefore, the structure of City of Coeur d'Alene's effluent limits for ammonia is consistent with 40 CFR 122.45(d)(2) and with EPA guidance. The calculation of the toxicity-based ammonia limits for the City of Coeur d'Alene is explained in the City of Coeur d'Alene's fact sheet.

For Post Falls, average monthly and maximum daily limits for ammonia are necessary for July - September in order to ensure compliance with the anti-backsliding provisions of the Clean Water Act. These effluent limits will also ensure compliance with Idaho's water quality criteria for ammonia.

Basis for Mass Limits

The federal regulation 40 CFR 122.45(f)(1) requires that effluent limits be expressed in terms of mass, except for pollutants that cannot be properly expressed as mass (e.g. pH and temperature). Effluent limits for TP, ammonia, and $CBOD_5$ can be properly expressed as mass. Therefore, effluent limits for these parameters are, at a minimum, expressed in terms of mass.

Effluent limits for TP are expressed exclusively in terms of mass because there are no applicable technology-based standards or numeric in-stream water quality standards for TP, the effluent limitations for TP are intended to meet Washington water quality standards, which apply several miles downstream from the discharges after complete mixing has occurred, and phosphate phosphorus is neither directly toxic to aquatic life nor directly hazardous to human health. Therefore, there is no basis to express the water quality-based TP limits in units other than mass.

As explained below, $CBOD_5$ and, in some cases, ammonia, are additionally limited in terms of other units of measurement.

Basis for Concentration and Removal Rate Limits for $CBOD_5$ and Ammonia

Pollutants which are limited in terms of mass may be additionally limited in terms of other units of measurement, and the permit shall require the permittee to comply with both limitations (40 CFR 122.45(f)(2)).

Applicable technology-based standards for $CBOD_5$ are expressed in terms of concentration and removal rate (40 CFR 133.102(a)(4)). Therefore, in addition to the water quality-based mass limits described above, the permits include additional technology-based effluent limits for $CBOD_5$, which are expressed in terms of concentration (25 mg/L monthly average and 40 mg/L weekly average, 40 CFR 133.102(a)(4)(i – ii)) and a minimum removal rate of 85% (40 CFR 133.102(a)(4)(iii)).

The proposed concentration and removal rate limits for $CBOD_5$ are technology-based limits. The $CBOD_5$ mass limits for November – January are also technology-based limits. The proposed final mass limits for $CBOD_5$, for February – October, are water quality-based limits.

For parameters which may be directly toxic to aquatic life, the TSD recommends that effluent limitations be expressed in terms of both concentration and mass for effluents discharging to waters with less than 100-fold dilution (see TSD at Section 5.7.1).

The average monthly and maximum daily limits for ammonia, for the City of Coeur d'Alene, are based on Idaho's water quality criteria, for toxicity. From July – September, the complete-mix dilution ratio, based on the FERC-mandated minimum river flow rate and the current treatment plant design flow rate, is less than 100:1. Therefore, the average monthly and maximum daily limits for ammonia, for Coeur d'Alene, for July – September, are expressed in terms of both mass and concentration.

In addition, for HARSB and Post Falls, concentration limits are included in the draft reissued permits from November – January, to ensure compliance with the anti-backsliding provisions of the Clean Water Act. For Post Falls, concentration limits are also necessary to ensure compliance with the anti-backsliding provisions of the Clean Water Act from July – September.

Proposed Effluent Limits Summary

The effluent limits for TP, $CBOD_5$, and ammonia that are derived from and comply with the applicable water quality standards of Idaho and Washington are as follows:

Table 5: Proposed Effluent Limits for TP, $CBOD_5$ and ammonia				
Parameter	**Units**	**Effluent Limits**		
		Average Monthly Limit	**Average Weekly Limit**	**Maximum Daily Limit**
Proposed Effluent Limits for the City of Coeur d'Alene				
TP as P (Feb. – Oct.)	lb/day	3.17 seasonal average		
TP as P (Nov. – Jan.)	lb/day	Phosphorus management plan. See permit at Part II.C.		
$CBOD_5$ (November – January)	mg/L	25	40	—
	lb/day	1251	2002	—
	% removal	85% min.	—	—
$CBOD_5$ (February – March)	mg/L	25	40	—
	lb/day	226 seasonal average		
	% removal	85% min.	—	—
$CBOD_5$ (April – October)	mg/L	25	40	—
	lb/day	203 seasonal average		
	% removal	85% min.	—	—
Ammonia (March – June)	lb/day	649	—	1547
Ammonia (July – September)	mg/L	6.59	—	15.7
	lb/day	330	—	786
Ammonia (March - October)	lb/day	272 seasonal average		
Ammonia (November – February)	No limits. Monitor and report only.			
Proposed Effluent Limits for the City of Post Falls				
TP as P (Feb – Oct.)	lb/day	3.19 seasonal average		
TP as P (Nov. – Jan.)	lb/day	Phosphorus management plan. See permit at Part II.C.		
$CBOD_5$ (November – January)	mg/L	25	40	—
	lb/day	1043	1668	—
	% removal	85% min.	—	—
$CBOD_5$ (February – October)	mg/L	25	40	—
	lb/day	255 seasonal average		
	% removal	85% min.	—	—
Ammonia (February –October)	lb/day	255 seasonal average		
Ammonia (July – September)	mg/L	8.2	—	29.5
	lb/day	342	—	1230
Ammonia (November – January)	mg/L	25.4	—	91.7
	lb/day	1059	—	3824
Proposed Effluent Limits for the HARSB				
TP as P (Feb. – Oct.)	lb/day	1.33 seasonal average		
TP as P (Nov. – Jan.)	lb/day	Phosphorus management plan. See permit at Part II.C.		
$CBOD_5$ (November – January)	mg/L	25	40	—
	lb/day	500	801	—
	% removal	85% min.	—	—
$CBOD_5$ (February – October)	mg/L	25	40	—
	lb/day	77.4 seasonal average		

Table 5: Proposed Effluent Limits for TP, $CBOD_5$ and ammonia				
Parameter	**Units**	**Effluent Limits**		
		Average Monthly Limit	**Average Weekly Limit**	**Maximum Daily Limit**
	% removal	85% min.	—	—
Ammonia (February – October)	lb/day	77.4 seasonal average		
Ammonia (November – January)	mg/L	78.7	—	250
	lb/day	1575	—	5004

Comparison of Proposed Effluent Limits to the Corresponding Limits in the 2007 Draft Permits

The following nine figures provide a comparison of the phosphorus, ammonia, and $CBOD_5$ limits in the current draft permits to the corresponding effluent limits in the 2007 draft permits. Note that the 2007 draft permits did not propose effluent limits for TP in February, whereas the current draft permits do propose such limits.

Figure 1

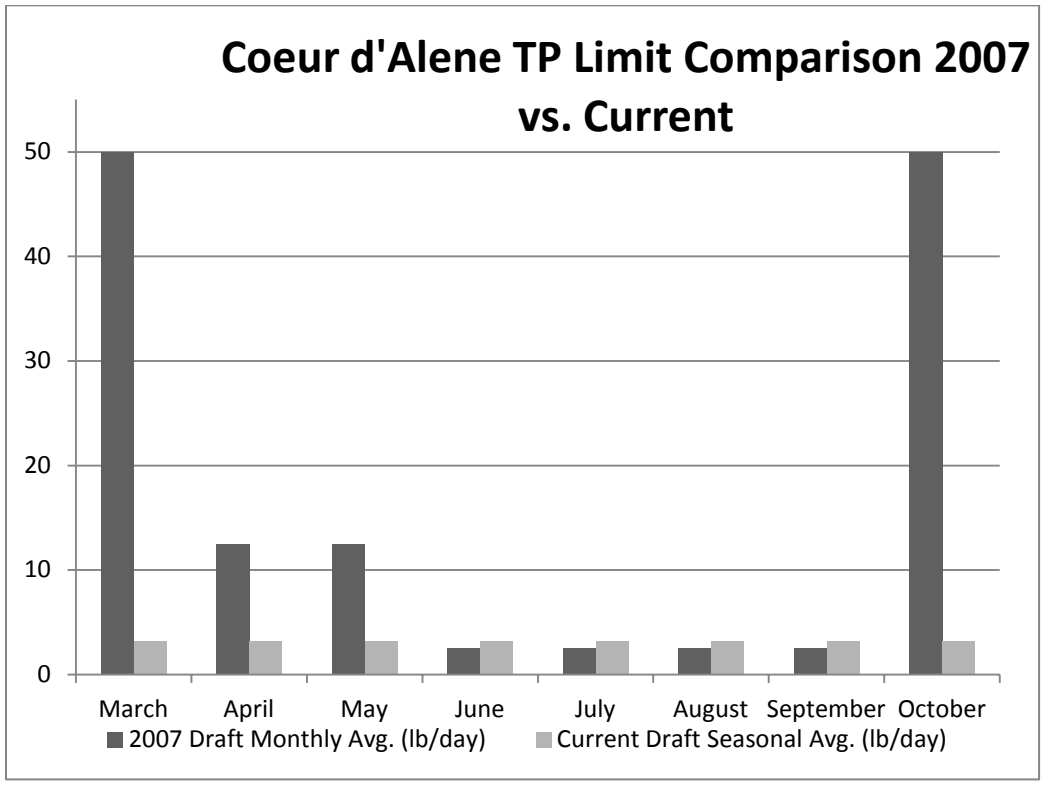


Figure 2

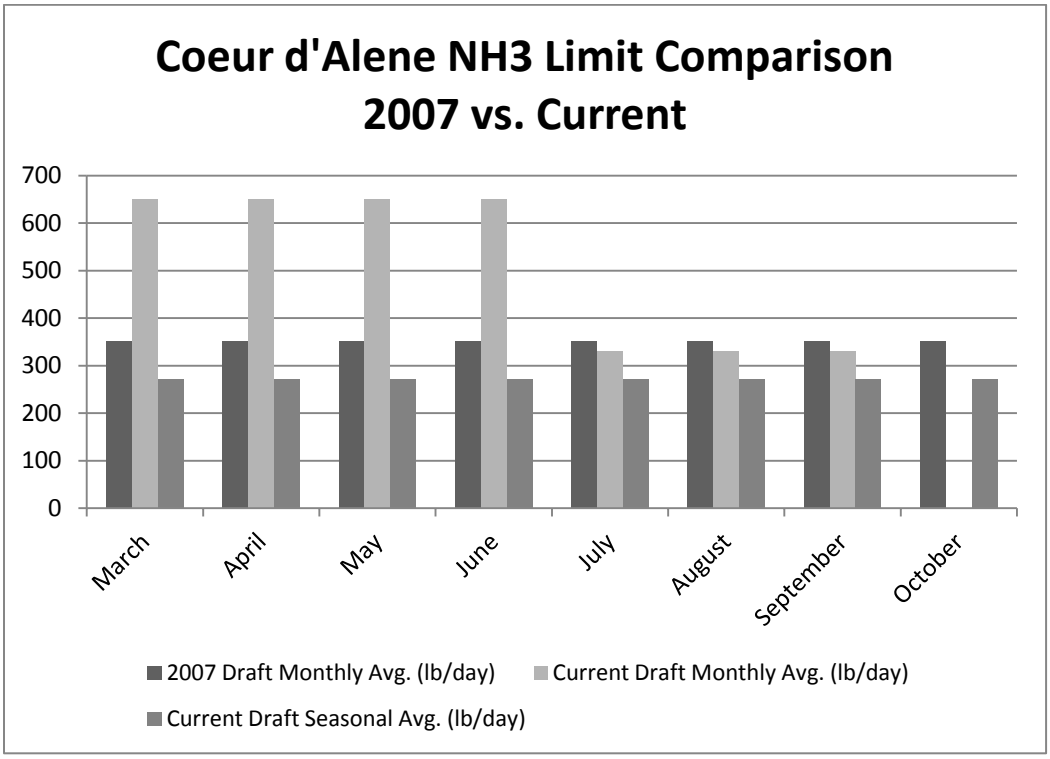


Figure 3

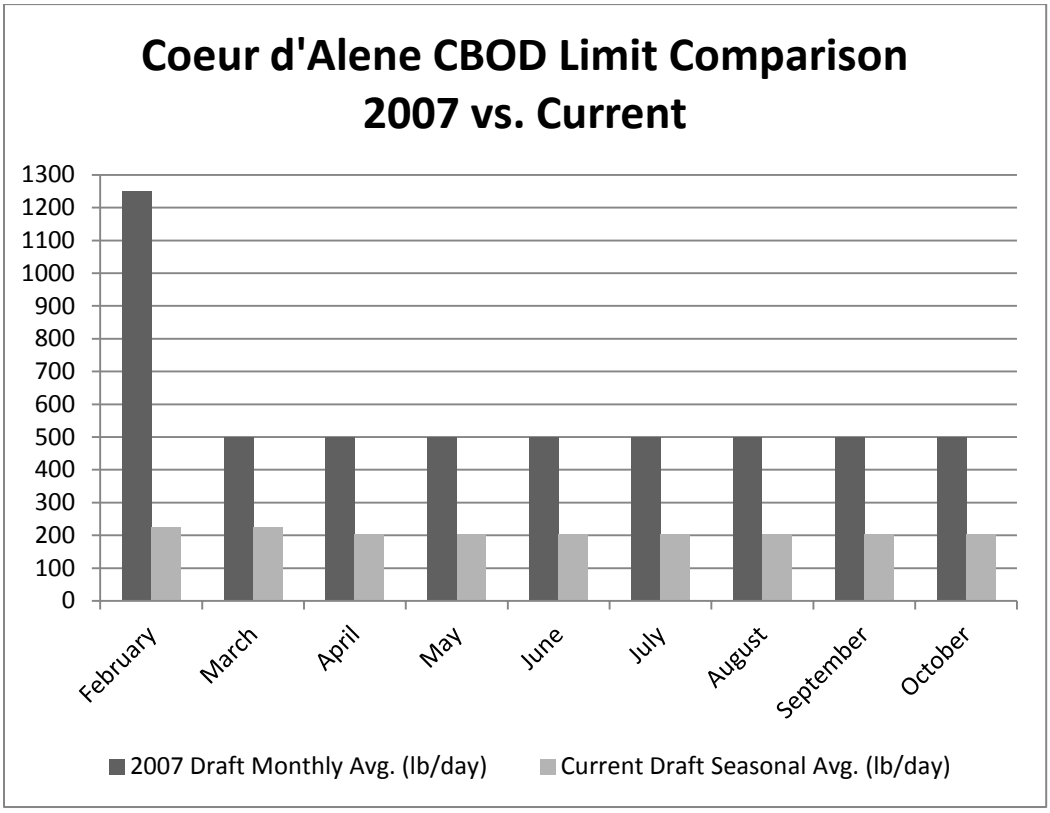
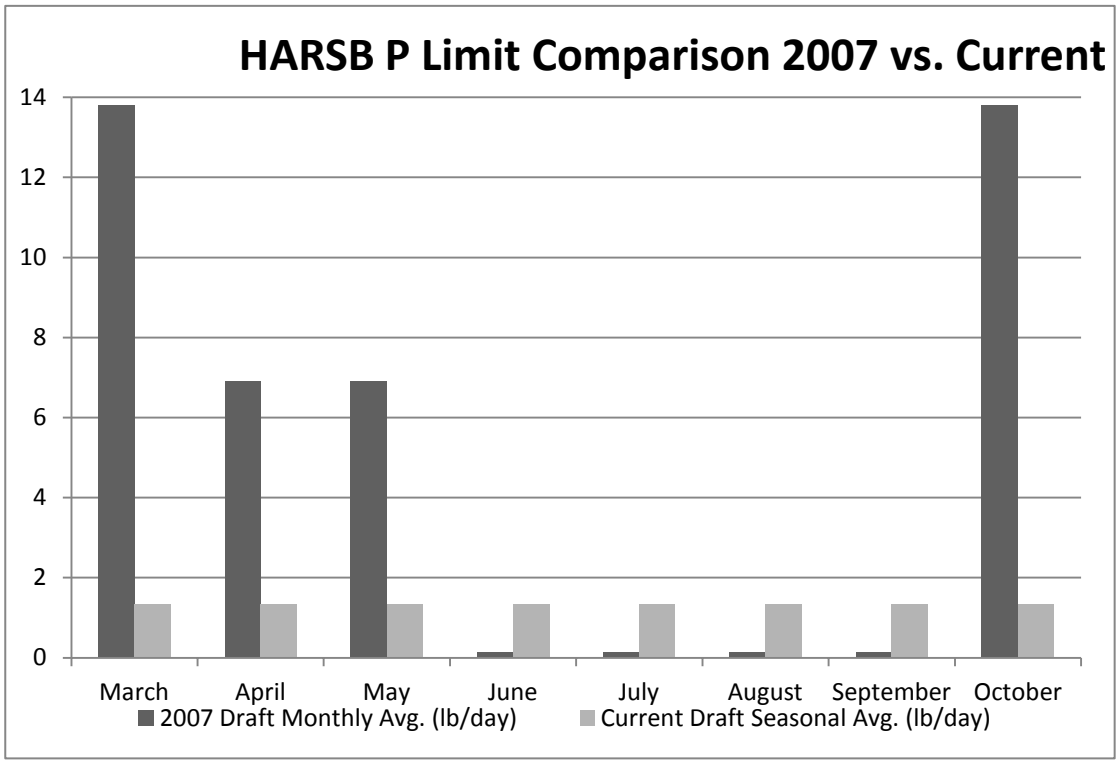


Figure 4



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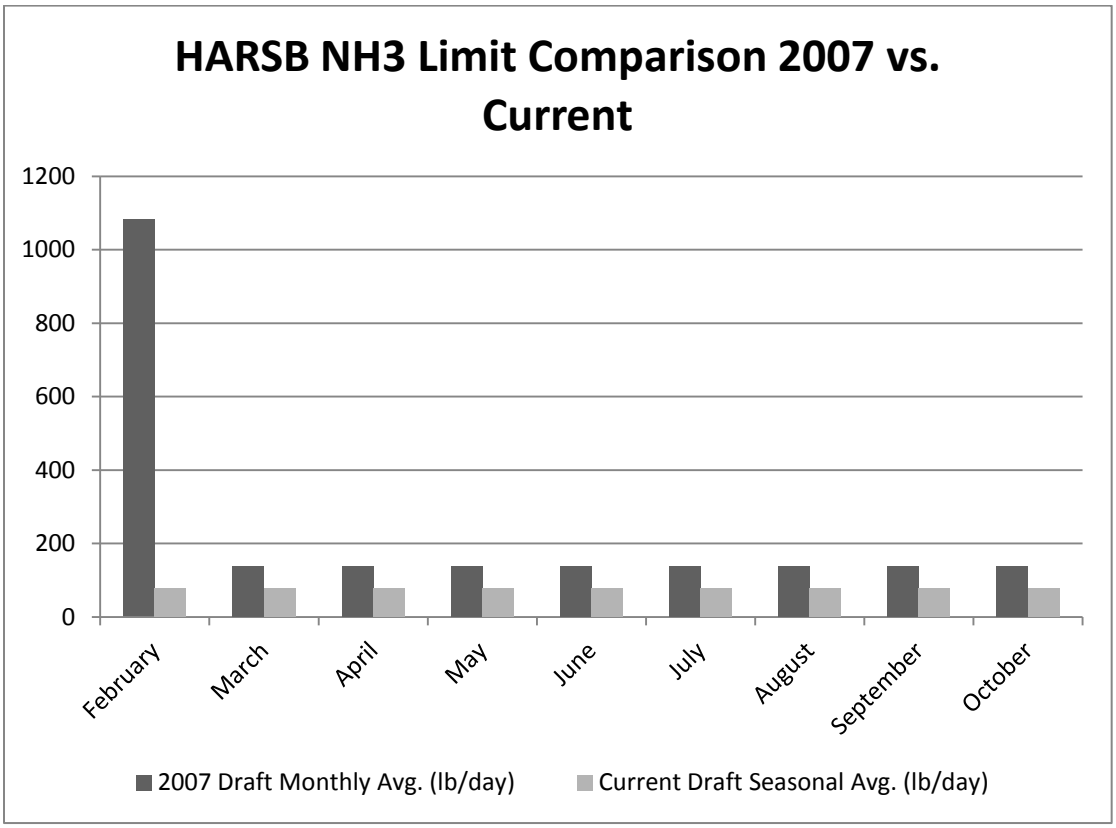
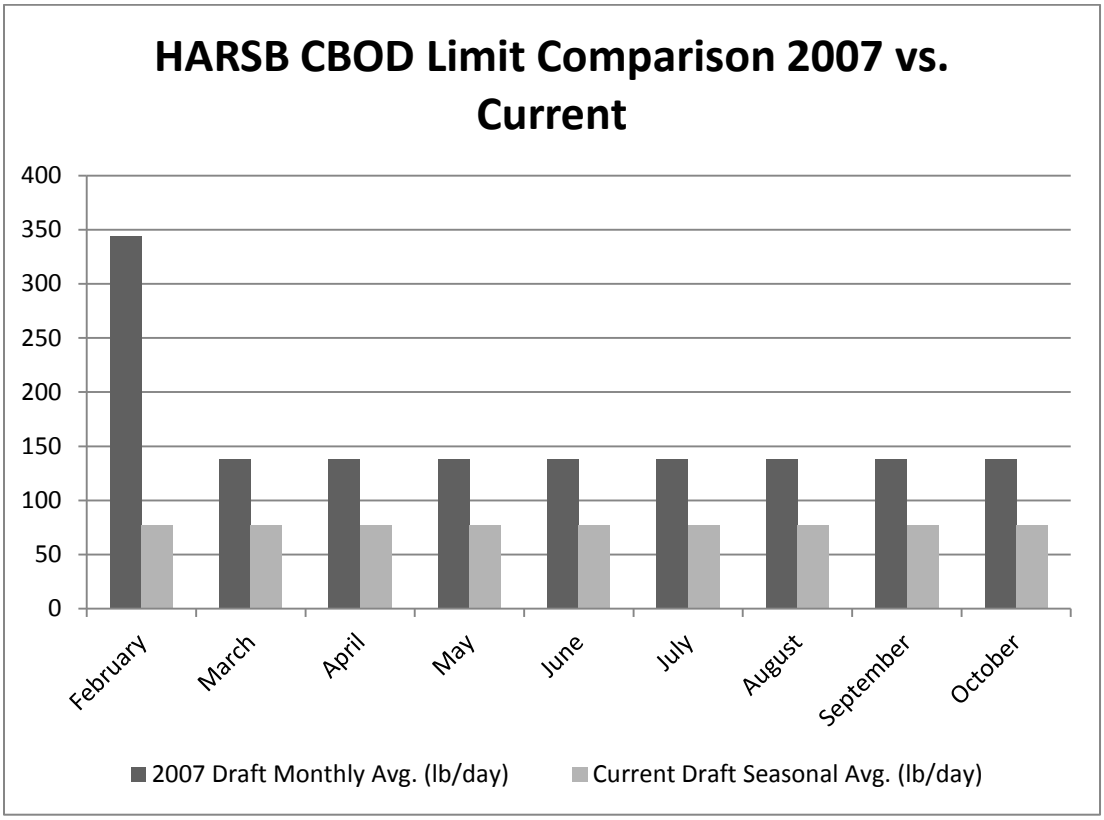


Figure 6



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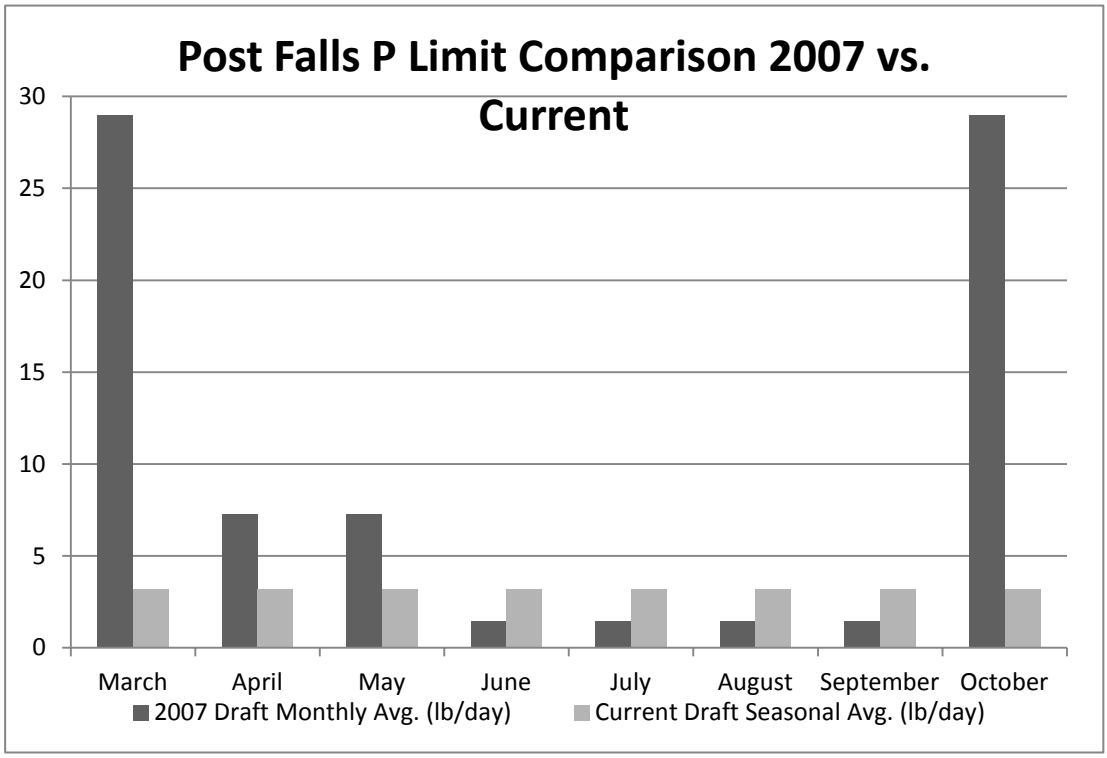


Figure 8

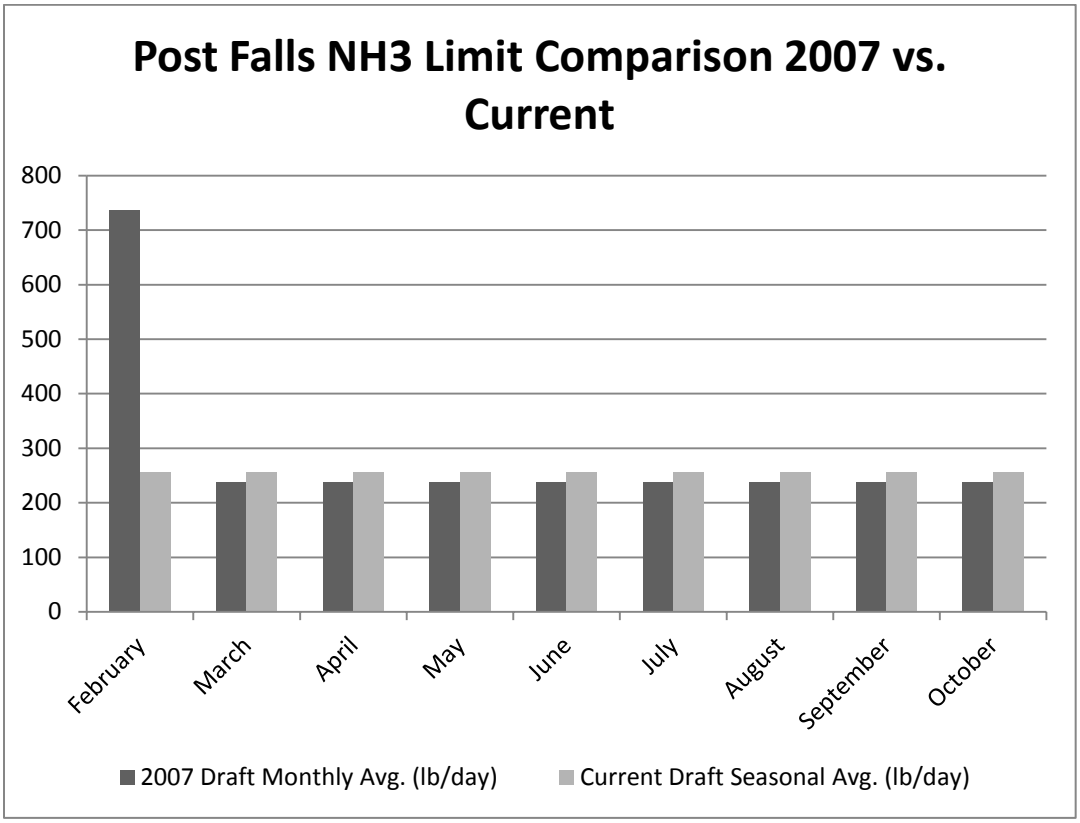
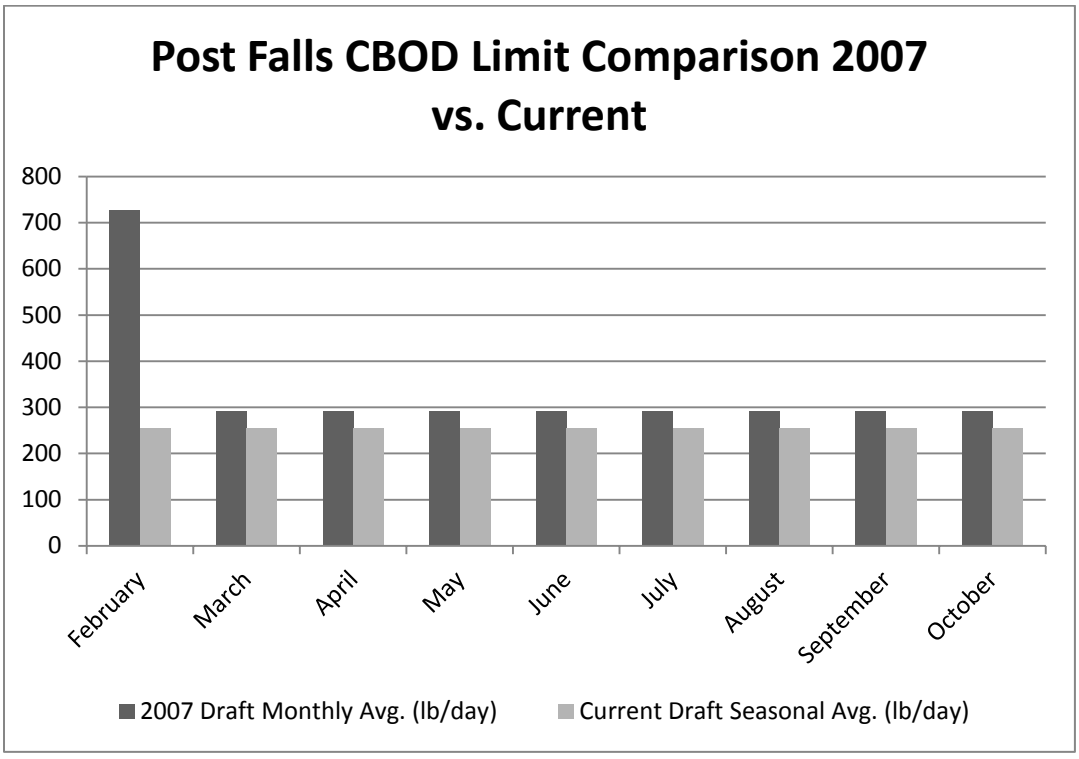


Figure 9



F. Effect of the Proposed Effluent Limits

Lake Spokane

As explained above, modeling shows that the proposed effluent limits for TP, $CBOD_5$ and ammonia, considered cumulatively with the effluent limits for Washington point sources in their NPDES permits and the load allocations for Washington non-point sources and the DO improvements required of Avista in the DO TMDL, will ensure compliance with Washington's water quality criterion for DO in Lake Spokane.

State Line

The memoranda from Portland State University and LimnoTech do not specifically analyze the effect of the proposed effluent limits at the state line. Therefore, as explained below, the EPA has analyzed the model output and determined that, in compliance with 40 CFR 122.4(d) and 40 CFR 122.44(d)(4), the proposed effluent limits for the Idaho point sources will ensure that Washington's and Idaho's water quality standards are met at the state line.

Dissolved Oxygen

Even with zero discharge of human-caused pollution in Idaho, Washington's numeric criterion for dissolved oxygen (8.0 mg/L) would only be attained at the state line about 96% of the time. That is to say, the remaining 4% of the time, the natural background DO concentration at the state line is less than 8.0 mg/L. However, this does not mean that Washington's water quality standards would not be attained. Washington's water quality standards state that, "when a water body's DO is lower than the (numeric) criteria…(or within 0.2 mg/L of the criteria) and that condition is due to natural conditions, then human actions considered cumulatively may not cause the DO of that water body to decrease more than 0.2 mg/L" (WAC 173-201A-200(1)(d)(i)).

At times when the model predicts that DO is less than 8.2 mg/L (i.e., within 0.2 mg/L of the numeric criterion), with zero discharge of human-caused pollution in Idaho, the maximum DO decrease attributable to the Idaho dischargers, including stormwater discharges, at the state line, is 0.13 mg/L below natural conditions, which is less than the decrease allowed by the standards (0.2 mg/L). Therefore, the effluent limits will ensure compliance with Washington's water quality standards for dissolved oxygen at the state line.

In Idaho, in waters designated for salmonid spawning, the applicable numeric dissolved oxygen criterion is 6.0 mg/L or 90% of saturation, whichever is greater. Modeling predicts that, under the proposed effluent limits, the DO concentration at the state line will be greater than 6.0 mg/L at all times (the minimum DO is 7.65 mg/L). The dissolved oxygen concentration will be greater than 90% of saturation, 99.96% of the time, under both the no source (i.e., zero discharge) and effluent limit scenarios. Therefore, the effluent limits will ensure compliance with Idaho's numeric DO criteria 99.96% of the time, and the very infrequent excursions below the numeric criteria (0.04% of the time) occur due to natural background conditions and do not violate Idaho's water quality standards (see IDAPA 58.01.02.200.09).

pH

The Washington pH criterion for the Spokane River at the state line is "pH shall be within the range of 6.5 to 8.5 with a human-caused variation within the above range of less than 0.5 units"

(WAC 173-201A, Table 200(1)(g)). Idaho's water quality standard is "within the range of six point five (6.5) to nine point zero (9.0)" (IDAPA 58.01.02.250.01.a).

Under the proposed effluent limits, the predicted minimum and maximum pH at the state line are 7.12 and 7.96 standard units, respectively, which complies with the criteria for pH range for both Idaho and Washington. The maximum human-caused pH changes are an increase of 0.21 standard units, and a decrease of 0.26 standard units, which are less than the 0.5 unit human-caused variation allowed by the Washington standards. Therefore, the proposed effluent limits ensure compliance with both Washington's and Idaho's water quality standards for pH, at the state line.

Phosphorus

Neither Idaho nor Washington has statewide numeric water quality criteria for TP. However, Idaho does have a narrative criterion for nutrients (IDAPA 58.01.02.200.06), and the Spokane River is 303(d) listed for TP in Idaho. The EPA has a Clean Water Act Section 304(a) recommended water quality criterion for TP, for the western forested mountains ecoregion, which is 10 µg/L (EPA 822-B-00-015, Table 2). The criteria document recommends that nutrient criteria be applied using a seasonal or annual averaging period (Page 6).

The model predicts that, with the proposed effluent limits in place, the median TP concentration at the state line, from February through October, will be 9.1 µg/L. This is less than the EPA-recommended criterion for TP, for this ecoregion, which is 10.0 µg/L (EPA 2000). The model predicts that the proposed effluent limits will result in only a 0.8 µg/L increase relative to the February – October median TP concentration predicted under the "no source" scenario (i.e., with no discharge from any Idaho point sources, including storm water). The concentration of TP at the State line, from February through October, will be less than 10 µg/L 55% of the time, with the proposed effluent limits in place. Therefore, the effluent limits proposed in the draft permits will ensure compliance with Idaho's and Washington's narrative criteria for nutrients and aesthetics (IDAPA 58.01.02.200.06, WAC 173-201A-260(2)(b)).

Temperature

The Washington water quality standard for temperature in the Spokane River at the state line is: "Temperature shall not exceed a 1-DMax of 20.0°C due to human activities. When natural conditions exceed a 1-DMax of 20.0°C no temperature increase will be allowed which will raise the receiving water temperature by greater than 0.3°C; nor shall such temperature increases, at any time exceed t=34/(T+9)" (WAC 173-201A-602).

The capital "T" represents the background temperature as measured at a point or points unaffected by the discharge and representative of the highest ambient water temperature in the vicinity of the discharge (WAC 173-201A-200(1)(c)(ii)(A)). Modeling predicts that the maximum temperature with no discharge from any Idaho point sources at the state line is 26.4 ºC; the value of 34/(T + 9) therefore equals 0.96 ºC. The maximum temperature increase attributable to the Idaho dischargers, at any time, is 0.27 °C, which is much less than the allowable increase (0.96 °C). At times when the predicted temperature, with no discharge from Idaho point sources, is greater than or equal to 20 ºC, the maximum temperature increase attributable to the Idaho point sources is 0.13 ºC, less than half the increase allowed by the criterion (0.3 °C).

Therefore, the Idaho dischargers do not have the reasonable potential to cause or contribute to excursions above water quality standards for temperature in the State of Washington, and it is not necessary to include effluent limits for temperature in these permits, in order to ensure compliance with Washington's water quality criteria for temperature.

Furthermore, the EPA has determined that the Idaho dischargers do not have the reasonable potential to cause or contribute to excursions above water quality standards for temperature, in waters of the State of Idaho (Nickel 2007, 2012). Therefore, the permits do not require water quality-based effluent limits for temperature.

Ammonia

The model predicts that, under the proposed ammonia effluent limits, the maximum instantaneous concentration of ammonia at the state line will be 0.42 mg/L, which is less than either State's chronic numeric water quality criteria for ammonia, under critical conditions for temperature and pH. Thus, the effluent limits in the draft permits will ensure compliance with both States' numeric water quality criteria for ammonia, at the state line.

The State of Washington's Antidegradation Policy

In addition to ensuring compliance with the State of Washington's water quality criteria, the draft permits for the City of Coeur d'Alene, City of Post Falls, and HARSB ensure compliance with the State of Washington's antidegradation requirements (WAC 173-201A-300 – 330).

In the State of Washington, the Spokane River is currently 303(d) listed for dissolved oxygen, lead, temperature, total dissolved gas, dioxin, and PCBs. The Spokane River is therefore not of higher quality than the applicable water quality criteria for these parameters. Therefore, the affected waters of the State of Washington are not afforded "Tier II" antidegradation protection under WAC 173-201A-320, for these parameters.

The Spokane River and Lake Spokane are 303(d)-listed for DO in the State of Washington. Washington's antidegradation policy states that "for waters that do not meet assigned criteria, or protect existing or designated uses, the department will take appropriate and definitive steps to bring the water quality back into compliance with the water quality standards." As explained above, the effluent limits for TP, $CBOD_5$, and ammonia ensure compliance with Washington's water quality criteria for dissolved oxygen. The permits contain effluent limits that ensure compliance with Idaho's water quality criteria for lead (which are more stringent than Washington's criteria) at the end-of-pipe. Thus, the lead limits are also stringent enough to ensure compliance with Washington's water quality criteria for lead. Furthermore, as explained above, these discharges do not have the reasonable potential to cause or contribute to excursions above Washington's water quality criteria for temperature. Washington's EPA-approved water quality criteria for these parameters ensure that existing and designated uses are maintained and protected, thereby ensuring compliance with Washington's Tier I antidegradation requirements (WAC 173-201A-310).

No antidegradation analysis is necessary for PCBs or dioxin because the Idaho permits do not contain effluent limits for these parameters and there is no information demonstrating that the Idaho permittees discharge these parameters. Therefore the discharges do not allow lower water quality due to these pollutants. The permits include monitoring requirements for PCBs and dioxin. The monitoring data will be used to determine if the discharges have the reasonable

potential to cause or contribute to excursions above water quality standards for PCBs or dioxin. Available data indicate that the Spokane River does not exceed either State's Clean Water Act effective PCB criterion at the State line (Serdar et al. 2011).[3]

For other parameters, in general, the effluent limits in the draft permits are as stringent as or more stringent than the corresponding effluent limits in the previous permits. In those cases, the permits are not new or expanded relative to the 1999 permits, thus they will not cause a lowering of water quality under Washington's Tier II antidegradation provisions (WAC 173-201A-320).

The Spokane River has not been designated an outstanding resource water. Therefore, the Tier III antidegradation protections of WAC 173-201A-330 do not apply to the Spokane River.

Summary

The effluent limits that the EPA is proposing for TP, ammonia and $CBOD_5$ ensure a level of water quality that is derived from and complies with the applicable water quality standards of the States of Idaho and Washington, for dissolved oxygen, pH, ammonia, and nutrients, based on the cumulative impact of all human actions. Therefore, the level of water quality to be achieved by these effluent limits is derived from and complies with the applicable water quality standards of the States of Washington and Idaho, in compliance with federal regulations (40 CFR 122.4(d), 122.44(d)(1)(vii)(A), 122.44(d)(4)).

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[3] Washington's PCB criterion is identical to the criterion that is in effect for Clean Water Act purposes in Idaho.

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Appendix C: General Basis for Effluent Limits

The following discussion explains in more detail the statutory and regulatory bases for the technology and water quality-based effluent limits in the draft permit. Part A discusses technology-based effluent limits, Part B discusses water quality-based effluent limits in general, and Part C discusses facility specific effluent limits.

A. Technology-Based Effluent Limits

Federal Secondary Treatment Effluent Limits

In sections 301(b)(1)(B) and 304(d)(1), the CWA established a performance level, referred to as "secondary treatment," which all POTWs are required to meet. The EPA developed and promulgated "secondary treatment" regulations that are found in 40 CFR 133.102. These technology-based limits identify the minimum level of effluent quality attainable by secondary treatment in terms of five-day biochemical oxygen demand (BOD_5) or five-day carbonaceous biochemical oxygen demand ($CBOD_5$), total suspended solids (TSS), and pH.

The regulations allow effluent limits for oxygen demanding material to be expressed as either BOD_5 or $CBOD_5$, at the option of the permitting authority. The EPA has chosen to express the effluent limits in terms of $CBOD_5$ in this case. The federally promulgated secondary treatment effluent limits are listed in Table C-1.

Table C-1: Secondary Treatment Effluent Limits
(40 CFR 133.102)

Parameter	Average Monthly Limit	Average Weekly Limit	Range
$CBOD_5$	25 mg/L	40 mg/L	—
TSS	30 mg/L	45 mg/L	—
Removal Rates for $CBOD_5$ and TSS	85% (minimum)	—	—
pH	—	—	6.0 – 9.0 s.u.

The EPA has determined that the secondary treatment $CBOD_5$ effluent limits are adequately stringent to protect water quality in the States of Idaho and Washington from November through January. From February through October, more stringent water quality-based $CBOD_5$ effluent limits apply (see Appendix B).

The EPA has determined that the secondary treatment TSS limits are adequately stringent to protect water quality in the Spokane River at all times, therefore, the TSS limits in the draft permit are the secondary treatment limits.

The EPA has determined that the secondary treatment pH effluent limits are not stringent enough to protect water quality in the Spokane River. Therefore, more stringent water quality-based pH effluent limits apply.

Chlorine

Chlorine is often used to disinfect municipal wastewater prior to discharge. The Coeur d'Alene facility uses chlorine disinfection.

A 0.5 mg/L average monthly limit for chlorine is derived from standard operating practices. The Water Pollution Control Federation's *Chlorination of Wastewater* (1976) states that a properly designed and maintained wastewater treatment plant can achieve adequate disinfection if a 0.5 mg/L chlorine residual is maintained after 15 minutes of contact time. Therefore, a wastewater treatment plant that provides adequate chlorine contact time can meet a 0.5 mg/L total residual chlorine limit on a monthly average basis. In addition to average monthly limits (AMLs), NPDES regulations require effluent limits for POTWs to be expressed as average weekly limits (AWLs) unless impracticable. The AWL is calculated to be 1.5 times the AML, consistent with the "secondary treatment" limits for BOD_5 and TSS. This results in an AWL for chlorine of 0.75 mg/L.

The EPA has determined that the technology-based effluent limits for chlorine are not stringent enough to ensure compliance with water quality standards. Therefore, the draft permit proposes more stringent water quality-based effluent limits for chlorine.

Mass-Based Limits

Effluent limits are generally calculated on a concentration basis. The federal regulation at 40 CFR 122.45(f) generally requires that effluent limits be expressed in terms of mass. The regulation at 40 CFR 122.45(b)(1) requires that effluent limitations for POTWs be calculated based on the design flow of the facility. The mass based limits are expressed in pounds per day and are generally calculated from the corresponding concentration limits as follows:

Mass based limit (lb/day) = concentration limit (mg/L or ppm) × design flow (mgd) × 8.34[1]

For example, the technology-based mass limits for $CBOD_5$ are as follows:

Average Monthly Limit:

25 mg/L × 6 mgd × 8.34 lb/gallon = 1251 lb/day

Average Weekly limit:

40 mg/L × 6 mgd × 8.34 lb/gallon = 2002 lb/day

From February – October, the mass limits for CBOD are calculated independently of the concentration limits. The concentration limits are technology-based at all times. The mass limits are water quality-based from February – October and technology-based from November – January.

B. Water Quality-based Effluent Limits

Statutory and Regulatory Basis

Section 301(b)(1)(C) of the CWA requires the development of limitations in permits necessary to meet water quality standards. Discharges to State or Tribal waters must also comply with limitations imposed by the State or Tribe as part of its certification of NPDES permits under section 401 of the CWA. The NPDES regulation 40 CFR 122.44(d)(1) implementing Section 301(b)(1)(C) of the CWA requires that permits include limits for all pollutants or parameters which are or may be discharged at a level which will cause, have the reasonable potential to

[1] 8.34 is the density of water, in units of pounds per gallon.

cause, or contribute to an excursion above any State or Tribal water quality standard, including narrative criteria for water quality. Effluent limits must also meet the applicable water quality requirements of affected States other than the State in which the discharge originates, which may include downstream States (40 CFR 122.4(d), 122.44(d)(4), see also CWA Section 401(a)(2)).

The regulations require the permitting authority to make this evaluation using procedures which account for existing controls on point and nonpoint sources of pollution, the variability of the pollutant in the effluent, species sensitivity (for toxicity), and where appropriate, dilution in the receiving water. The limits must be stringent enough to ensure that water quality standards are met, and must be consistent with any available wasteload allocation for the discharge in an approved TMDL. There are no approved TMDLs that specify wasteload allocations for this discharge; all of the water quality-based effluent limits are calculated directly from the applicable water quality standards.

Reasonable Potential Analysis

When evaluating the effluent to determine if water quality-based effluent limits are needed based on numeric criteria, the EPA projects the receiving water concentration for each pollutant of concern. The EPA uses the concentration of the pollutant in the effluent and receiving water and, if appropriate, the dilution available from the receiving water, to project the receiving water concentration. Dilution is considered in the reasonable potential analysis if and only if the State authorizes a mixing zone in its draft CWA Section 401 certification. If the projected concentration of the pollutant in the receiving water exceeds the numeric criterion for that specific chemical, then the discharge has the reasonable potential to cause or contribute to an excursion above the applicable water quality standard, and a water quality-based effluent limit is required.

Mixing Zones

Sometimes it is appropriate to allow a small area of the receiving water to provide dilution of the effluent. These areas are called mixing zones. Mixing zone allowances will increase the mass loadings of the pollutant to the water body, and decrease treatment requirements. Mixing zones can be used only when there is adequate receiving water flow volume and the receiving water meets the criteria necessary to protect the designated uses of the water body. Mixing zones are authorized by the Idaho Department of Environmental Quality (IDEQ). Based on IDEQ's draft Clean Water Act Section 401 certification, some of the water quality-based effluent limits in this permit have been calculated using a mixing zone. Effluent limit and reasonable potential calculations for cadmium, lead, and zinc did not use mixing zones because the receiving water does not meet water quality standards for those pollutants. If IDEQ does not authorize mixing zones in the final Clean Water Act Section 401 certification for certain parameters, the water quality-based effluent limits for those parameters will be recalculated such that the criteria are met before the effluent is discharged to the receiving water.

Procedure for Deriving Water Quality-based Effluent Limits

The first step in developing a water quality-based effluent limit is to develop a wasteload allocation (WLA) for the pollutant. A wasteload allocation is the concentration or loading of a

pollutant that the permittee may discharge without causing or contributing to an excursion above water quality standards in the receiving water.

In cases where a mixing zone is not authorized (e.g., for zinc, in this case), either because the receiving water already exceeds the criterion, the receiving water flow is too low to provide dilution, or the State does not authorize one, the criterion becomes the WLA. Establishing the criterion as the wasteload allocation ensures that the permittee will not cause or contribute to an excursion above the criterion. The following discussion details the specific water quality-based effluent limits in the draft permit.

Once a WLA is developed, the EPA calculates effluent limits which are protective of the WLA using statistical procedures described in Appendix F.

C. Facility-Specific Limits

pH

The most stringent water quality criteria for pH are for the protection of aquatic life uses. The "aquatic life" pH criteria state that the pH must be no less than 6.5 and no greater than 9.0 standard units.

The permittee has collected pH and alkalinity data for the effluent. The EPA obtained pH and alkalinity data for the receiving water from the USGS monitoring station at the outlet from Lake Coeur d'Alene into the Spokane River. The EPA has used these data to determine the discharge's effects on the pH of the receiving water. The EPA believes that a mixing zone for pH is appropriate from October through June. From July through September a pH mixing zone cannot be authorized because the Spokane River pH can be close to 6.5, and because there is relatively little dilution available.

The proposed pH limits are 6.3 to 9.0 from October through June and 6.5 to 9.0 (criteria end-of-pipe) from July through September. If IDEQ does not grant a mixing zone for pH in its final CWA Section 401 certification, the EPA will change the pH limits to a range of 6.5 to 9.0 standard units year round, thus requiring that the pH criteria are met before the effluent is discharged to the receiving water. See Appendix F for effluent limit calculations for pH.

Total Phosphorus

The EPA has determined that the phosphorus in the permitted discharge, together with the discharges of phosphorus from the HARSB and the City of Post Falls as well as municipal stormwater discharged to the Spokane River in Idaho, has the reasonable potential to cause or contribute to excursions above water quality criteria dissolved oxygen in the State of Washington, downstream of the discharge. The EPA has calculated water quality-based effluent limits for total phosphorus which ensure a level of water quality that is derived from and complies with the applicable water quality requirements of both Washington and Idaho. See Appendix B for a complete discussion of the calculation of water quality-based effluent limits for total phosphorus.

Ammonia

As explained in Appendix B, the EPA has determined that, independent of any concerns about the Coeur d'Alene facility's discharge of ammonia causing or contributing to excursions above water quality standards for ammonia in waters of the State of Idaho, the Coeur d'Alene facility's discharge of ammonia, in combination with other sources of oxygen-demanding pollution, has the reasonable potential cause or contribute to nonattainment of Washington's water quality standards for dissolved oxygen (DO), from March – October. Therefore effluent limits are necessary for ammonia, from March – October, in order to ensure compliance with Washington's water quality standards for DO.

The ammonia effluent limit that is based on Washington's water quality standards is a seasonal average limit of 272 lb/day, which is applicable from March – October. Because this seasonal average limit does not control the short-term (e.g., monthly or daily) maximum loads or concentrations of ammonia in the discharge, it may not, by itself, ensure compliance with Idaho's numeric water quality criteria for ammonia, which are expressed as maximum allowable 1-hour, 4-day, and 30-day averages (IDAPA 58.01.02.283).

EPA has determined that the Coeur d'Alene facility has the reasonable potential to cause or contribute to excursions above Idaho's water quality criteria for ammonia from March – September. Therefore, in addition to the seasonal average mass limit for ammonia, the draft permit proposes average monthly and maximum daily effluent limits for ammonia, during March – September.

During November – February, the EPA has determined that the City's discharge of does not have the reasonable potential to cause or contribute to excursions above water quality standards in Idaho or Washington. Therefore, no effluent limits are proposed for ammonia from November – February.

Five-Day Carbonaceous Biochemical Oxygen Demand

As stated above, the EPA has promulgated technology-based effluent limits for $CBOD_5$. The technology-based limits apply from November through January.

However, the EPA has determined that, from February through October, more stringent mass effluent limits are necessary for $CBOD_5$, in order to ensure compliance with water quality criteria for dissolved oxygen in the State of Washington. The concentration and removal rate limits remain technology-based, year-round. See Appendix B for a complete discussion of the basis for the water quality-based mass effluent limits for $CBOD_5$ for February – October.

Metals

In the 1999 permit, the EPA established "criteria end-of-pipe" water quality-based effluent limits for lead and zinc. Since the Spokane River is 303(d) listed for cadmium, lead, and zinc, the river has no assimilative capacity to dilute these metals in an effluent. Therefore, no mixing zone may be authorized for cadmium, lead, or zinc.

In 2004, the EPA modified the metals limits in the City of Coeur d'Alene's permit. The lead limits were deleted and the zinc limits were made less stringent than those in the unmodified 1999 permit.

The numeric values of the acute and chronic water quality criteria for cadmium, lead, zinc, and certain other metals are dependent upon the hardness of the water. For the criteria end-of-pipe reasonable potential and effluent limit calculations for cadmium, lead and zinc, the effluent hardness was used to calculate the water quality criteria. As long as the concentrations of cadmium, lead, and zinc in the effluent are below the water quality criteria (calculated at the effluent hardness) the effluent will not cause or contribute to an in-stream excursion above water quality standards as it mixes with the receiving water.[2]

Zinc

The EPA has determined that the concentration (i.e., µg/L) effluent limits for zinc in the 1999 permit, as modified in 2004, are not stringent enough to ensure compliance with water quality criteria, with no mixing zone. Therefore, the EPA has recalculated the concentration effluent limits for zinc, and has proposed more-stringent concentration limits for zinc (see Appendix E).

Cadmium and Lead

A reasonable potential analysis, which did not consider the dilution of the effluent in the receiving water, showed that the discharge does not have the reasonable potential to cause or contribute to excursions above water quality criteria for cadmium or lead. However, IDAPA 58.01.02.055.04 requires that the total load of pollutants causing water quality limited listings must remain constant or decrease within the watershed until a TMDL or equivalent process is completed. Even though the 1999 permit (as modified in 2004) did not include effluent limits for cadmium or lead and the discharge does not have the reasonable potential to cause or contribute to excursions above water quality criteria for cadmium or lead, the facility does discharge cadmium and lead. To ensure that the total loading of cadmium and lead does not increase, the State of Idaho specified effluent limits for cadmium and lead in its CWA Section 401 certification. These effluent limits must be incorporated into the permit (40 CFR 122.44(d)(3), 124.53(e), 124.55(a)(2)).

The EPA is specifically requesting public comments on the effluent limits for cadmium, lead and zinc.

Copper and Silver

The EPA has determined that the discharge does not have the reasonable potential to cause or contribute to excursions above water quality standards for copper. Therefore the draft permit does not propose any effluent limits for copper.

The EPA has also determined that the discharge does not have the reasonable potential to excursions above water quality standards for silver from July – September and from October – June when the effluent flow is less than or equal to 4.2 mgd. Therefore, the draft permit does not propose effluent limits for silver under these circumstances.

However, the EPA has determined that the prior permit's effluent limits for silver, for October – June, when effluent flows are greater than 4.2 mgd, are not stringent enough to ensure

[2] Because the shape of the lead criteria curves, when plotted against hardness, are "concave up," (i.e., the second derivative is always positive), calculating criteria end-of-pipe water quality-based effluent limits for lead, using the hardness of the effluent, can contribute to excursions above water quality criteria as the discharge mixes with a receiving water that is softer than the effluent. This was addressed in this case by calculating a tangent line to the water quality criteria at the State of Idaho's hardness "floor" of 25 mg/L as CaCO3 and calculating water quality-based effluent limits based on the tangent line.

compliance with water quality criteria. Therefore, the EPA has calculated more-stringent water quality-based effluent limits for silver, for October – June, when effluent flows are greater than 4.2 mgd.

E. Coli

The Idaho water quality standards state that waters of the State of Idaho that are designated for recreation are not to contain E. coli bacteria in concentrations exceeding a geometric mean of 126 organisms per 100 ml based on a minimum of five samples taken every three to seven days over a thirty day period. Therefore, the draft permit contains a monthly geometric mean effluent limit for E. coli of 126 organisms per 100 ml, and a minimum sampling frequency of five grab samples per month (IDAPA 58.01.02.251.01.a.).

The Idaho water quality standards also state that a water sample that exceeds certain "single sample maximum" values indicates a likely exceedance of the geometric mean criterion, although it is not, in and of itself, a violation of water quality standards. For waters designated for primary contact recreation, the "single sample maximum" value is 406 organisms per 100 ml (IDAPA 58.01.02.251.01.b.ii.).

The goal of a water quality-based effluent limit is to ensure a low probability that water quality standards will be exceeded in the receiving water as a result of a discharge, while considering the variability of the pollutant in the effluent (see TSD at Section 5.3.1). Because a single sample value exceeding 406 organisms per 100 ml indicates a likely exceedance of the geometric mean criterion, the EPA has imposed an instantaneous (single grab sample) maximum effluent limit for E. coli of 406 organisms per 100 ml, in addition to a monthly geometric mean limit of 126 organisms per 100 ml, which directly implements the water quality criterion for E. coli. This will ensure that the discharge will have a low probability of exceeding water quality standards for E. coli.

Regulations at 40 CFR 122.45(d)(2) require that effluent limitations for continuous discharges from POTWs be expressed as average monthly and average weekly limits, unless impracticable. The terms "average monthly limit" and "average weekly limit" are defined in 40 CFR 122.2 as arithmetic (as opposed to geometric) averages.

It is impracticable to properly implement a 30-day geometric mean criterion in a permit using monthly and weekly arithmetic average limits. The geometric mean of a given data set is equal to the arithmetic mean of that data set if and only if all of the values in that data set are equal. Otherwise, the geometric mean is always less than the arithmetic mean. In order to ensure that the effluent limits are "derived from and comply with" the geometric mean water quality criterion, as required by 40 CFR 122.44(d)(1)(vii)(A), it is necessary to express the effluent limits as a monthly geometric mean and an instantaneous maximum limit.

D. Summary of Limits and Bases

The following table summarizes the general statutory and regulatory bases for the limits in the draft permit.

Table C-3 Summary of Bases for Effluent Limits and BMP Requirements	
Limited Parameter	**Basis for Limit**
Ammonia (March – Septemer monthly average and maximum daily)	CWA Section 301(b)(1)(C), 40 CFR 122.4(d), 40 CFR 122.44(d), IDAPA 58.01.02.283, IDAPA 58.01.02.060 (water quality-based, with mixing zone)
Ammonia (March – October seasonal average)	CWA Section 301(b)(1)(C), 40 CFR 122.4(d), 40 CFR 122.44(d), WAC 173-201A-200(1)(d)(ii) (water quality-based, all affected States)
$CBOD_5$ (concentration & removal rate)	Clean Water Act (CWA) Section 301(b)(1)(B), 40 CFR 133 (technology-based)
$CBOD_5$ (mass, February – October)	CWA Section 301(b)(1)(C), 40 CFR 122.4(d), 40 CFR 122.44(d), WAC 173-201A-200(1)(d)(ii) (water quality-based, all affected States)
$CBOD_5$ (mass, November – January)	Clean Water Act (CWA) Section 301(b)(1)(B), 40 CFR 133, 40 CFR 122.45(b)(1), 122.45(f) (technology-based, mass limits)
Chlorine	CWA Sections 402(o), 301(b)(1)(C), 40 CFR 122.44(d), IDAPA 58.01.02.051 (anti-backsliding, antidegradation)
E. Coli	CWA Section 301(b)(1)(C), 40 CFR 122.44(d), IDAPA 58.01.02.251.01 (water quality-based)
Floating, Suspended or Submerged Matter	CWA Section 301(b)(1)(C), 40 CFR 122.44(d), IDAPA 58.01.02.200.05 (water quality-based)
pH (July – September)	CWA Section 301(b)(1)(C), 40 CFR 122.44(d), IDAPA 58.01.02.250.01.a. (water quality-based)
pH (October – June)	CWA Section 301(b)(1)(C), 40 CFR 122.44(d), IDAPA 58.01.02.250.01.a, IDAPA 58.01.02.060 (water quality-based, with mixing zone)
Phosphorus (February – October)	CWA Section 301(b)(1)(C), 40 CFR 122.4(d), 40 CFR 122.44(d), WAC 173-201A-200(1)(d)(ii) (water quality-based, all affected States)
Phosphorus Management Plan	40 CFR 122.44(k) (best management practices)
Silver (October – June, effluent flow > 4.2 mgd)	CWA Section 301(b)(1)(C), 40 CFR 122.4(d), 40 CFR 122.44(d), IDAPA 58.01.02.210, IDAPA 58.01.02.060 (water quality-based, with mixing zone)
Toxics Management Plan	40 CFR 122.44(k) (best management practices)
TSS	CWA Section 301(b)(1)(B), 40 CFR 133 , 40 CFR 122.45(b)(1), 122.45(f) (technology-based, mass limits)
Cadmium and Lead	40 CFR 122.44(d)(3), 124.53(e), 124.55(a)(2) (conforming to the conditions of a CWA Section 401 certification)
Zinc	CWA Section 301(b)(1)(C), 40 CFR 122.4(d), 40 CFR 122.44(d), IDAPA 58.01.02.210 (water quality-based)

Appendix D: Reasonable Potential Calculations

The following describes the process the EPA has used to determine if the discharge authorized in the draft permit has the reasonable potential to cause or contribute to an excursion above Idaho's federally approved water quality standards for certain pollutants. The EPA generally uses the process described in Section 3.3 of the *Technical Support Document for Water Quality-based Toxics Control* (EPA 1991) to determine reasonable potential.

To determine if there is reasonable potential for the discharge to cause or contribute to an excursion above water quality criteria for a given pollutant, the EPA compares the maximum projected receiving water concentration to the criteria for that pollutant. If the projected receiving water concentration exceeds the criteria, then the discharge has the reasonable potential to cause or contribute to excursions above water quality standards, and a water quality-based effluent limit must be included in the permit. This section discusses how the maximum projected receiving water concentration is determined.

A. Mass Balance

For discharges to flowing water bodies, the maximum projected receiving water concentration is determined using the following mass balance equation:

$$C_dQ_d = C_eQ_e + C_uQ_u \quad \text{(Equation D-1)}$$

where,

C_d = Receiving water concentration downstream of the effluent discharge (that is, the concentration at the edge of the mixing zone)
C_e = Maximum projected effluent concentration
C_u = 95th percentile measured receiving water upstream concentration
Q_d = Receiving water flow rate downstream of the effluent discharge = $Q_e + Q_u$
Q_e = Effluent flow rate (generally set equal to the design flow of the treatment plant per 40 CFR 122.45(b)(1)).
Q_u = Receiving water low flow rate upstream of the discharge (e.g. 1Q10, 7Q10)

When the mass balance equation is solved for C_d, it becomes:

$$C_d = \frac{C_eQ_e + C_uQ_u}{Q_e + Q_u} \quad \text{(Equation D-2)}$$

The above form of the equation is based on the assumption that the discharge is rapidly and completely mixed with the receiving stream and that 100% of the stream flow is available for mixing. However, the Idaho water quality standards generally restrict the percentage of the stream flow that may be allowed for dilution of the effluent. When the mixing zone uses less than 100% of the stream flow, the equation becomes:

$$C_d = \frac{C_eQ_e + C_u(Q_u \times MZ)}{Q_e + (Q_u \times MZ)} \quad \text{(Equation D-3)}$$

In the above equation, MZ is the fraction of the receiving water flow available for dilution. The Idaho water quality standards generally limit mixing zones to 25% of the volume of the stream flow (IDAPA 58.01.02.060). The MZ was generally set equal to 0.25 (25%) for the reasonable

potential analysis. Exceptions include cadmium, lead, and zinc (because the receiving water is impaired for those parameters and cannot provide dilution of the effluent, therefore no mixing zone may be authorized for those parameters).

If a mixing zone is not allowed, dilution is not considered when projecting the receiving water concentration and,

$$C_d = C_e \qquad \text{(Equation D-4)}$$

The criteria for the metals of concern are expressed as dissolved metal. However, effluent limits for metals in NPDES permits must be expressed as total recoverable metal. The dissolved criterion must be converted to an equivalent total recoverable concentration by using a conversion factor, as shown in Equation D-5:

$$C_d = CF \times C_e \qquad \text{(Equation D-5)}$$

Equation D-3 can be simplified by introducing a "dilution factor,"

$$D = \frac{Q_e + 0.25 \times Q_u}{Q_e} \qquad \text{(Equation D-6)}$$

The dilution factors for the various seasons, for the reasonable potential analysis are shown in Table D-1, below:

Table D-1: Dilution Factors

Season	**Mixing Zone** (% of critical flow)	**Acute Dilution Factor** (1Q10)	**Chronic Dilution Factor** (7Q10)	**Chronic Ammonia Criterion Dilution Factor** (30Q10)	**Human Health Non-Carcinogen Dilution Factor** (30Q5)	**Human Health Carcinogen Dilution Factor** (Harmonic Mean)
Full Year	25%	N/A	N/A	N/A	14.5	56.2
July – September ≤ 4.2 mgd	25%	20.2	20.2	N/A	N/A	N/A
July – September > 4.2 mgd	25%	14.5	14.5	N/A	N/A	N/A
October – June	25%	25.0	28.7	N/A	N/A	N/A
November – February for ammonia	25%	29.8	N/A	38.2	N/A	N/A
Cadmium, lead, and zinc	No mixing zone (receiving water is impaired).					

After the dilution factor simplification, Equation D-2 becomes:

$$C_d = \frac{C_e - C_u}{D} + C_u \qquad \text{(Equation D-7)}$$

If the criterion is expressed as dissolved metal, the effluent concentrations are measured in total recoverable metal and must be converted to dissolved metal as shown in Equation D-8, which applies when a mixing zone may be granted for a metal with criteria expressed as dissolved metal.

$$C_d = \left[\frac{CF \times C_e - C_u}{D} \right] + C_u \qquad \text{(Equation D-8)}$$

In equation D-8, C_e is expressed as total recoverable metal and C_d and C_u are expressed as dissolved metal. Equations D-5, D-7, and D-8 are the forms of the mass balance equation which were used to determine reasonable potential and calculate wasteload allocations.

B. Maximum Projected Effluent Concentration

Parameters with Water Quality-based Effluent Limits in the 1999 Permit

For parameters that were subject to water quality-based effluent limits in the 1999 permit and for which effluent are not necessary to meet Washington's water quality standards (chlorine, silver, and zinc) the EPA has used the maximum daily effluent limits in the 1999 permit as the maximum projected effluent concentrations. This allows the EPA to determine if the effluent limits in the 1999 permit are stringent enough to prevent the discharge from causing or contributing to excursions above water quality standards for these pollutants. If a discharge at the maximum daily limits in the 1999 permit did not have the reasonable potential to cause or contribute to excursions above water quality standards, the EPA retained the 1999 effluent limits under the anti-backsliding provisions of the Act (Section 402(o)).

Ammonia Limits Necessary to Meet Washington's Water Quality Standards

As explained in Appendix B, the EPA has determined that, independent of any concerns about the Coeur d'Alene facility's discharge of ammonia causing or contributing to excursions above water quality standards for ammonia in waters of the State of Idaho, the Coeur d'Alene facility's discharge of ammonia, in combination with other sources of oxygen-demanding pollution, has the reasonable potential cause or contribute to nonattainment of Washington's water quality standards for dissolved oxygen, from March – October. Therefore effluent limits are necessary for ammonia, from March – October.

The ammonia limit that is derived from Washington's water quality standards is expressed as a seasonal average mass limit. Because compliance with this limit is evaluated based on the average discharge over an 8-month period, this limit may not, by itself, prevent acute, near-field toxicity as required by the Idaho water quality standards.

Therefore, instead of using the seasonal average effluent limit to calculate the maximum projected effluent ammonia concentration, the EPA has used the procedure described in section 3.3 of the TSD and under "Other Parameters," below, to determine if short-term effluent limits were necessary to ensure compliance with Idaho's water quality criteria for ammonia, based on the historical effluent data.

Other Parameters

To calculate the maximum projected effluent concentration for parameters not specifically discussed above, the EPA has used the procedure described in section 3.3 of the TSD, "Determining the Need for Permit Limits with Effluent Monitoring Data." In this procedure, the 99th percentile of the effluent data is the maximum projected effluent concentration in the mass balance equation.

Since there are a limited number of data points available in most cases, the 99th percentile is calculated by multiplying the maximum reported effluent concentration by a "reasonable potential multiplier" (RPM). The RPM is the ratio of the 99th percentile concentration to the maximum reported effluent concentration. The RPM is calculated from the coefficient of variation (CV) of the data and the number of data points. The CV is defined as the ratio of the standard deviation of the data set to the mean, but when fewer than 10 data points are available, the TSD recommends making the assumption that the CV is equal to 0.6.

In addition to Section 3.3 of the TSD, the procedures for calculating a maximum projected effluent concentration from effluent data are described in detail in Appendix D of the fact sheet dated February 16, 2007. The results of the reasonable potential analysis are described below.

C. Results

Table 2 on the following page, summarizes the reasonable potential calculations.

Table 2: Reasonable Potential Calculations

Effluent Percentile value	99%																
				State Water Quality Standard		Max concentration at edge of...											
Parameter	Metal Criteria Translator as decimal Acute	Metal Criteria Translator as decimal Chronic	Ambient Concentration (metals as dissolved) ug/L	Acute ug/L	Chronic ug/L	Acute Mixing Zone ug/L	Chronic Mixing Zone ug/L	LIMIT REQ'D?	Pn	Max effluent conc. measured (metals as total recoverable) ug/L	Coeff Variation CV	s	# of samples n	Multiplier	Acute Dil'n Factor	Chronic Dil'n Factor	COMMENTS
Ammonia Jul - Sep Prev. Lim.	1.00	1.00	0.1000	6.75	1.43	9.01	1.54	YES	N/A	21.00	N/A	N/A	N/A	1.00	2.35	14.5	2.5% MZ Acute 25% MZ Chronic
Ammonia March - June Effluent	1.00	1.00	0.1000	6.75	2.17	7.05	0.52	YES	0.984	30.50	0.31	0.31	281	1.06	4.64	77.5	2.5% MZ Acute 25% MZ Chronic
Ammonia Nov. - Feb. Effluent	1.00	1.00	0.1000	6.75	2.80	1.34	1.07	NO	0.980	34.0	0.32	0.31	228	1.09	29.8	38.2	25% MZ
Ammonia Oct Effluent	1.00	1.00		6.7484	2.5724	5.62	0.51	NO	0.926	16.15	0.31	0.30	60.00	1.30	3.75	41.4	2.5% MZ Acute 25% MZ Chronic
Cadmium (EOP)	0.93	0.90		1.69	0.67	0.25	0.24	NO	0.955	0.21	0.43	0.41	101	1.29	1	1	RW Impaired; no MZ
Chlorine (Oct - June Prev. Lim.)	1.00	1.00		11.0	19.0	15.62	13.57	YES	N/A	390	N/A	N/A	N/A	1.00	25.0	28.7	25% MZ
Chlorline (July - Sept. Prev. Lim.)	1.00	1.00		11.0	19.0	7.05	7.05	NO	N/A	102	N/A	N/A	N/A	1.00	14.5	14.5	25% MZ
Copper (July - Sept)	0.86	0.88		4.61	3.47	0.94	0.96	NO	0.958	12.90	0.35	0.34	107	1.23	14.5	14.5	25% MZ
Copper (Oct - June)	0.86	0.88		4.61	3.47	0.54	0.48	NO	0.958	12.90	0.35	0.34	107	1.23	25.0	28.7	25% MZ
Lead (EOP)	0.15	0.15		80.8	3.1	0.58	0.58	NO	0.958	2.73	0.70	0.63	107	1.46	1	1	RW Impaired; no MZ
NO2 + NO3	1.00	1.00	0.0915		10.0		4.90	NO	0.215	12.4	0.60	0.55	3	5.62		14.5	25% MZ
Silver (July - Sept)	0.35	N/A		0.318	N/A	0.15	N/A	NO	0.958	3.30	1.43	1.06	107	1.88	14.5	N/A	25% MZ, No chronic criterion for Ag
Silver (October - June)	0.35	N/A		0.318	N/A	0.09	N/A	NO	0.958	3.30	1.43	1.06	107	1.88	25.0	N/A	25% MZ, No chronic criterion for Ag
Silver, Prev. Lim. (Oct - June)	0.35	N/A		0.318	N/A	0.45	N/A	YES	0.958	31.90	1.43	1.06	107	1.00	25.0	N/A	25% MZ, No chronic criterion for Ag
Zinc (EOP, prev. lim.)	0.88	0.88		148	149	177	177	YES	N/A	201	N/A	N/A	N/A	1.00	1	1	RW Impaired; no MZ

D. References

EPA. 1991. *Technical Support Document for Water Quality-based Toxics Control.* US Environmental Protection Agency, Office of Water, EPA/505/2-90-001. http://www.epa.gov/npdes/pubs/owm0264.pdf

Appendix E: WQBEL Calculations – Acute and Chronic Numeric Aquatic Life Criteria

The discussion explains how water quality-based effluent limits (WQBELs) in the draft permit were calculated based on Idaho's numeric water quality criteria for aquatic life uses. The calculations for all WQBELs based on aquatic life criteria are summarized in Tables 2 and 3, below.

A. Calculate the Wasteload Allocations (WLAs)

Wasteload allocations (WLAs) are calculated using the same mass balance equations used to calculate the concentration of the pollutant at the edge of the mixing zone in the reasonable potential analysis. These equations are explained in Appendix D. To calculate the wasteload allocations, the downstream concentration (C_d) is set equal to the acute or chronic water quality criterion and the equation is solved for the effluent concentration (C_e). The calculated C_e is the acute or chronic WLA. Equation D-6 is rearranged to solve for the WLA, becoming:

$$C_e = WLA = D \times (C_d - C_u) + C_u \qquad \text{(Equation E-1)}$$

Idaho's water quality criteria for some metals are expressed as the dissolved fraction, but the Federal regulation at 40 CFR 122.45(c) requires that effluent limits be expressed as total recoverable metal. Therefore, the EPA must calculate a wasteload allocation in total recoverable metal that will be protective of the dissolved criterion. This is accomplished by dividing the WLA expressed as dissolved by the criteria translator (CT), as shown in equation E-2.

$$C_e = WLA = \frac{D \times (C_d - C_u) + C_u}{CT} \qquad \text{(Equation E-2)}$$

Or, if no mixing zone is allowed, for metals with criteria expressed as the dissolved fraction:

$$C_e = WLA = C_d \div CT \qquad \text{(Equation E-3)}$$

Mixing Zones for Ammonia for March - September

In general, mixing zones for effluent limit calculations are the same as those used for the reasonable potential analysis and described in Appendix D.

A smaller mixing zone was used for acute criteria for ammonia, from March – September. Section 5.1.1 of EPA's *Water Quality Standards Handbook Second Edition* ("Handbook") states that mixing zones must be limited to an area or volume as small as practicable (EPA 1994). The City of Coeur d'Alene must reduce its effluent ammonia loads from current levels on a seasonal average basis, from March – October, in order to ensure compliance with water quality standards for dissolved oxygen (DO) in the State of Washington (see Appendix B). This reduction will also allow Coeur d'Alene to meet Idaho's water quality criteria for ammonia using a smaller mixing zone than would otherwise be necessary. The Handbook also states that the acute water quality criterion "should be met within 10 percent of the distance from the edge of the outfall structure to the edge of the mixing zone in any spatial direction." Based on the Handbook's recommendations, and given the fact that ammonia discharges must be reduced from current levels in order to meet Washington's water quality standards (as explained in Appendix B) the

effluent limit calculations for ammonia use a mixing zone for the acute ammonia criterion that uses 2.5% of the 1Q10 flow of the Spokane River. The chronic mixing zone for ammonia continues to be based on 25% of the 30Q10 flow of the Spokane River. This will ensure that the acute water quality criterion for ammonia is roughly 10% of the size of the chronic mixing zone, as recommended by the Handbook. The dilution factors for the ammonia mixing zones, for March – October, are shown in Table 1, below.

Table 1: Dilution Factors for Ammonia Effluent Limits based on Idaho WQS for March – October

Season	1Q10 River Flow	30Q10 River Flow	Acute Mixing Zone (% of critical flow)	Chronic Mixing Zone (% of critical flow)	Acute Dilution Factor (1Q10)	Chronic Dilution Factor (30Q10)
March – June	1350	2840	2.5%	25%	4.64	77.5
July – September	500	500	2.5%	25%	2.35	14.5

B. Basis for Expressing Effluent Limits for Toxic Parameters as Average Monthly and Maximum Daily Limits

In general, effluent limits for POTWs must be expressed as average monthly and average weekly limits (40 CFR 122.45(d)(2)). In order to prevent acute toxicity to aquatic life, the *Technical Support Document for Water Quality-based Toxics Control* ("TSD") recommends that effluent limits for pollutants which may be toxic to aquatic life be expressed as average monthly and maximum daily limits, because an average weekly limit has an averaging period that is too long to ensure that acute toxicity is prevented (see TSD at section 5.2.3). Similarly, the 272 lb/day seasonal average ammonia effluent limit that is required to meet Washington's water quality standards (see Appendix B) would not prevent short-term discharges of high loadings or concentrations of ammonia which could cause acute toxicity. Therefore, effluent limits for total residual chlorine, ammonia, silver, and zinc are expressed as average monthly and maximum daily limits, based on the recommendations of Section 5.2.3 of the TSD.

C. Calculating the Average Monthly and Maximum Daily Effluent Limits

The statistical procedures for calculating of average monthly and maximum daily effluent limits from the wasteload allocations are described in Section 5.4 of the TSD and in Appendix G of the fact sheet dated February 16, 2007.

Although the reasonable potential analysis in Appendix D showed that a discharge at the 1999 permit's maximum daily limits for total residual chlorine for October – June could cause or contribute to excursions above water quality standards for chlorine, when the EPA re-calculated the effluent limits for chlorine using the procedure described below, the re-calculated effluent limits were less stringent than those in the 1999 permit (see Table 1, below). Therefore, the October – June chlorine effluent limits in the 1999 permit have been continued forward in accordance with the anti-backsliding provisions of the Clean Water Act (Section 402(o)).

D. Results

The results of the effluent limit calculations are summarized in Tables 2 and 3, on the following page.

Table 2: Effluent Limit Calculations for Chlorine, Zinc, and Silver

Permit Limit Calculation Summary											Waste Load Allocation (WLA) and Long Term Average (LTA) Calculations						
	Acute Dil'n Factor	Chronic Dil'n Factor	Metal Criteria Translator	Metal Criteria Translator	Ambient Concentration	Water Quality Standard Acute	Water Quality Standard Chronic	Average Monthly Limit (AML)	Maximum Daily Limit (MDL)	Comments	WLA Acute	WLA Chronic	LTA Acute	LTA Chronic	Limiting LTA	Coeff. Var. (CV)	# of Samples per Month
PARAMETER			Acute	Chronic	*ug/L*	*ug/L*	*ug/L*	ug/L	ug/L		*ug/L*	*ug/L*	*ug/L*	*ug/L*	*ug/L*	*decimal*	*n*
Chlorine (Oct - June)	24.97	28.74	1.00	1.00		19.00	11.00	**175**	**474**	**25% Mixing Zone**	474	316	146.0	162.0	146.0	0.63	30.00
Zinc	1.00	1.00	0.88	0.88		148	149	**135**	**168**	**EOP**	168	170	119.0	142.2	119.0	0.15	4.00
Silver (Oct - June > 4.2 mgd)	24.97	N/A	0.35	N/A		0.32		**8.01**	**22.5**	**25% Mixing Zone**	22	N/A	3.5	N/A	3.5	1.36	4.00

Table 3: Calculations for Ammonia Effluent Limits based on Idaho WQS

Permit Limit Calculation Summary													Waste Load Allocation (WLA) and Long Term Average (LTA) Calculations						
	Acute Dil'n Factor	Chronic Dil'n Factor	Metal Criteria Translator	Metal Criteria Translator	Ambient Concentration	Water Quality Standard Acute	Water Quality Standard Chronic	Average Monthly Limit (AML)	Maximum Daily Limit (MDL)	Average Monthly Limit (AML)	Maximum Daily Limit (MDL)	Comments	WLA Acute	WLA Chronic	LTA Acute	LTA Chronic	Limiting LTA	Coeff. Var. (CV)	# of Samples per Month
PARAMETER			Acute	Chronic	*mg/L*	*mg/L*	*mg/L*	mg/L	mg/L	lb/day	lb/day		*mg/L*	*mg/L*	*mg/L*	*mg/L*	*mg/L*	*decimal*	*n*
Ammonia March - June	4.64	77.48	1.00	1.00	0.10	6.75	2.17	**13.0**	**30.9**	**649**	**1547**	**2.5% MZ Acute 25% MZ Chronic**	30.9	161	9.9	125.4	9.9	0.60	12.00
Ammonia July - Sep	2.35	14.46	1.00	1.00	0.10	6.75	1.43	**6.59**	**15.7**	**330**	**786**	**2.5% MZ Acute 25% MZ Chronic**	15.7	19	5.0	15.0	5.0	0.60	12.00

E. References

EPA. 1991. *Technical Support Document for Water Quality-based Toxics Control*. US Environmental Protection Agency. Office of Water. Washington, DC. March 1991. The EPA/505/2-90-001. http://www.epa.gov/npdes/pubs/owm0264.pdf

EPA. 1994. *Water Quality Standards Handbook: Second Edition*. Environmental Protection Agency. Office of Water. Washington, DC. August 1994. EPA 823-B-94-005a. http://water.epa.gov/scitech/swguidance/standards/handbook/index.cfm

Appendix F: Effluent Limit Calculations for pH

The following table demonstrates how appropriate effluent limitations were determined for pH.

Table F-1: Effluent Limit Calculations for the Low pH Critical Condition

INPUT	Oct. – June	July – Sept.
DILUTION FACTOR AT MIXING ZONE BOUNDARY	25.0	14.5
UPSTREAM/BACKGROUND CHARACTERISTICS		
Temperature (deg C):	18.4	25.0
pH:	6.60	6.60
Alkalinity (mg CaCO3/L):	19.2	19.2
EFFLUENT CHARACTERISTICS		
Temperature (deg C):	17.2	17.2
pH:	**6.3**	**6.5**
Alkalinity (mg CaCO3/L):	150	150
OUTPUT		
1. IONIZATION CONSTANTS		
Upstream/Background pKa:	6.39	6.35
Effluent pKa:	6.40	6.40
2. IONIZATION FRACTIONS		
Upstream/Background Ionization Fraction:	0.62	0.64
Effluent Ionization Fraction:	0.44	0.56
3. TOTAL INORGANIC CARBON		
Upstream/Background Total Inorganic Carbon (mg CaCO3/L):	31.13	30.00
Effluent Total Inorganic Carbon (mg CaCO3/L):	339.95	269.85
CONDITIONS AT MIXING ZONE BOUNDARY		
Temperature (deg C):	18.35	24.46
Alkalinity (mg CaCO3/L):	24.44	28.24
Total Inorganic Carbon (mg CaCO3/L):	43.50	46.58
pKa:	6.39	6.35
pH at Mixing Zone Boundary:	**6.50**	**6.54**

Appendix G: Compliance Schedules and Interim Limits for New Water Quality-based Effluent Limits

A. Overview

In order to establish a compliance schedule in an NPDES permit, the permitting authority must make a reasonable finding that the permittee cannot comply with the new water quality-based effluent limit immediately upon the effective date of the final permit (see the *US EPA NPDES Permit Writers' Manual* at Section 9.1.3). Compliance schedules may only be allowed if the State's water quality standards or implementing regulations allow for compliance schedules (see *In The Matter of Star-Kist Caribe, Inc*., 3 E.A.D. 172, 175, 177 (1990)). The State of Idaho has a compliance schedule authorizing provision which reads, "discharge permits for point sources may incorporate compliance schedules which allow a discharger to phase in, over time, compliance with water quality-based effluent limitations when new limitations are in the permit for the first time" (IDAPA 58.01.02.400.03). The State of Idaho has authorized compliance schedules for some of the new water quality-based effluent limits in the City of Coeur d'Alene permit in its draft Clean Water Act Section 401 certification of this permit.

The EPA has evaluated the historic performance of the Coeur d'Alene wastewater treatment plant to determine if the City could immediately comply with the new water quality-based effluent limits proposed in the draft permit. For those effluent limits that cannot be achieved immediately on the effective date of the final permit, the compliance schedule must comply with the regulatory requirement that compliance be achieved as soon as possible (40 CFR 122.47(a)(1)). The EPA has determined that the compliance schedules proposed in the draft permit require compliance as soon as possible, as explained below.

B. Immediate Achievability

In general, for each parameter for which a new water quality-based effluent limit is proposed, the EPA quantified the facility's current performance. The current performance was compared to the proposed new water quality-based effluent limits to determine if the facility could comply with the new water quality-based effluent limits immediately upon the effective date of the final permit. The methods used to evaluate the facility's current performance are described below.

In general, if the facility's current performance, as quantified by the methods described below, showed that the facility could comply with the new water quality-based effluent limits immediately upon the effective date of the final permit, then no compliance schedule has been proposed in the draft permit. In addition to the facility's current performance, the EPA has also considered the treatment plant's design characteristics and the performance of other facilities of similar design. If the Coeur d'Alene facility's treatment processes would allow for immediate compliance with new water quality-based effluent limits, then no compliance schedule has been proposed in the draft permit, even if historical effluent data do not indicate immediate achievability.

If effluent data and the facility's current design both demonstrate that the facility cannot comply with the effluent limits immediately upon the effective date of the final permit, then a schedule of compliance is appropriate and has been proposed in the draft permit.

Average Monthly and Average Weekly or Maximum Daily Limits

Performance-based Effluent Limit Spreadsheet Method

This spreadsheet calculates performance-based effluent limits based on historical effluent data and the required sampling frequency. The spreadsheet is based upon the procedures of Appendix E of the *Technical Support Document for Water Quality-based Toxics Control* (EPA 1991).

Percentile Method

When individual sample results are available, the expected maximum monthly, weekly, and daily loadings or concentrations can be represented by percentiles. The expected maximum monthly average concentration or loading is that which can be achieved 11/12ths (92%) of the time, and the expected maximum weekly average and maximum daily concentration or loading is that which can be achieved 51/52nds (98%) and 364/365ths (99.7%) of the time, respectively. The EPA used this method of quantifying treatment plant performance in the *Municipal Nutrient Removal Technologies Reference Document* (EPA 2008). If less than 365 data points were available, the maximum individual sample was used for comparison with a proposed water quality-based maximum daily limit.

Seasonal Average Limits

For effluent limits expressed as seasonal averages, the EPA evaluated the performance of the WWTP to determine if the permittee could comply with the new water quality-based effluent limits immediately.

Results of Effluent Data Analysis

The results of the analysis are summarized in Table 1, below.

Discussion of Results

$CBOD_5$

The $CBOD_5$ mass effluent limits are expressed as a seasonal average limit in lieu of average monthly and average weekly limits (see Appendix B). The seasonal average effluent limits are 226 lb/day from February 1st – March 31st and 203 lb/day from April 1 – October 31st.

At the facility's design flow of 6.0 mgd, the seasonal average $CBOD_5$ effluent limits correspond to concentrations of 4.52 and 4.06 mg/L, for February – March and April – October, respectively. The median of the monthly average effluent concentrations of $CBOD_5$ measured between January 2008 and February 2013 is 4.55 mg/L. The monthly average effluent concentrations of $CBOD_5$ measured during that span of time have been greater than the concentrations corresponding to the proposed seasonal average effluent limits 53% of the time and 80% of the time, for February – March and April – October, respectively.

Therefore, the City cannot comply with the new water quality-based effluent limits for $CBOD_5$ immediately upon the effective date of the final permit.

Table 1: Comparison of New Water Quality-based Effluent Limits to Historic Performance

New Water Quality-based Effluent Limit Parameter, Season, and Units	Proposed Limits		Current Performance				Limits Achievable Immediately?
	Avg. Monthly Limit	Max. Daily or Avg. Weekly Limit	PERFORMLIM Spreadsheet		Percentiles		
			Max. Month	Max. Day/ Week	Max. Month	Max. Day/Week	
Ammonia, March - June (lb/day)	649	1547	532	928	685	938	**NO**
Ammonia, July - September (mg/L)	6.59	15.7	14.9	20.9	10.6	18.3	**NO**
Ammonia, July - September (lb/day)	330	786	315	546	430	605	**NO**
Silver, October – June, Effluent Flow > 4.2 mgd (µg/L)	8.01	22.5	1.0	1.8	0.71	3.3	**YES**
Lead (µg/L)	2.5	5.8	0.86	1.16	0.85	2.73	**YES**
Zinc (µg/L)	135	168	59	67	55.0	60.5	**YES**

Notes:
1. Year-round effluent data were used for comparison with the proposed $CBOD_5$ effluent limits. The $CBOD_5$ effluent load is relatively stable over time (coefficient of variation = 0.31).

Ammonia

As shown in Table 1, above, in general, the percentile and performance-based spreadsheet calculations indicate that the Coeur d'Alene facility cannot comply with the new water quality-based average monthly and maximum daily limits for ammonia that are proposed in the draft permit immediately upon the effective date of the final permit. The performance-based limit spreadsheet indicates that the facility may be able to comply with the new water quality-based load limits for ammonia, but the percentile method indicates that it cannot. Furthermore, neither the performance-based limit spreadsheet nor the percentile method indicates that the facility can comply with the new water quality-based concentration limits for ammonia that apply from July – September. Therefore, the City cannot comply with these new water quality-based effluent limits for ammonia and, a compliance schedule is appropriate for the new water quality-based average monthly and maximum daily limits for ammonia.

With respect to the new water quality-based seasonal average limit for ammonia, which is 272 lb/day from March – October, the City's average ammonia load from March – October is 365 lb/day, which is greater than the effluent limit. Therefore the City cannot comply with the new water quality-based seasonal average effluent limit for ammonia immediately upon the effective date of the final permit and a compliance schedule is appropriate for this effluent limit.

Lead, Silver and Zinc

As shown in Table 1, effluent data indicate that the Coeur d'Alene facility can comply with the new water quality-based effluent limits for lead, silver and zinc immediately upon the effective date of the final permit. Therefore, no compliance schedule may be authorized for the new water quality-based lead, silver and zinc effluent limits.

Cadmium

The cadmium effluent limits that were specified in the State of Idaho's draft CWA Section 401 certification are performance-based effluent limits and thus are achievable immediately upon the effective date of the final permit. Therefore no compliance schedule is proposed for the Coeur d'Alene facility's new cadmium limits.

Phosphorus

The effluent limit for total phosphorus is a seasonal average of 3.17 lb/day. The current average phosphorus loading is 36.5 lb/day. Therefore the City cannot comply with the new water quality-based seasonal average effluent limit for total phosphorus immediately upon the effective date of the final permit and a compliance schedule is appropriate for this effluent limit.

Summary

The permittee can comply with all of the new water quality-based effluent limits in the draft permit, except for the new phosphorus limits and some of the new ammonia limits. Therefore, a compliance schedule is proposed for the new water quality-based phosphorus limits and the new water quality-based ammonia limits except for the average monthly and maximum daily ammonia loading limits for the month of October.

Interim Limits

Basis for Interim Limits

The federal regulation 40 CFR 122.47 states that "…if a permit establishes a schedule of compliance which exceeds 1 year from the date of permit issuance, the schedule shall set forth interim requirements and the dates for their achievement." The federal regulation 40 CFR 122.44(l)(1) states that "…when a permit is renewed or reissued, interim effluent limitations, standards or conditions must be at least as stringent as the final effluent limitations, standards, or conditions in the previous permit."

Therefore, the EPA has proposed interim effluent limits in the draft permit, which apply during the term of the compliance schedule, in order to ensure that the reissued permit does not authorize the discharge of ammonia or phosphorus in greater amounts than authorized by the previous permit, during the term of the compliance schedule.

Total Phosphorus

The previous permit states, "the average monthly effluent phosphorus loading (measured as total P) shall not exceed 15 percent of the average monthly influent loading (measured as total P) or 1 mg/l, whichever is greater." Thus, the prior permit has average monthly limits expressed in terms of concentration or removal rate (whichever is less stringent or results in a greater effluent load) but it lacks average weekly limits and limits expressed in terms of mass, both of which are required by federal regulations (40 CFR 122.45(d)(2), 122.45(f). Thus, the EPA has established mass limits and average weekly limits in order to comply with federal regulations.

The interim average monthly TP limit is 1 mg/L, which is the same as the final phosphorus concentration effluent limit in the previous permit. The EPA has calculated an average monthly mass limit for TP based on the design flow of the POTW (which is 6 mgd), based on 40 CFR 122.45(b)(1). The interim average monthly TP mass limit is 50 lb/day.

In order to ensure compliance with federal regulations requiring that, in general, effluent limits for POTWs are stated as average monthly and average weekly limits, the EPA has also established interim average weekly TP limits based on the average monthly limits, and a ratio that accounts for effluent variability within a month. The EPA has used the same ratio as the ratio between the technology-based average monthly and average weekly $CBOD_5$ limits (1.6:1). The EPA believes this ratio is representative of typical effluent variability for POTWs. Thus, the average weekly TP limits are 1.6 mg/L and 80 lb/day.

The draft permit proposes to delete the option for removal rate effluent limits that are less stringent than the concentration limits. The EPA believes that the 1 mg/L average monthly effluent limit is achievable by the facility.

The prior permit's phosphorus limits generally applied from March 1st through October 31st each year. The interim effluent limits for total phosphorus apply from February 1st through October 31st each year, which is the same season during which the final TP effluent limits will apply. Modeling has shown that discharges of TP at any time during this season can affect dissolved oxygen concentrations in Lake Spokane.

Ammonia

The interim effluent limits for ammonia, for July – September, are identical to the ammonia effluent limits in the prior permit, consistent with 40 CFR 122.41(l)(1). The EPA has determined that these limits will ensure compliance with Idaho's water quality criteria for ammonia after mixing with less than 25% of the critical low flows of the receiving water.

No interim ammonia effluent limits are proposed for March – June or during October. The prior permit did not include any effluent limits for ammonia during these months.

$CBOD_5$

The interim effluent limits for $CBOD_5$, for February – October, are identical to the $CBOD_5$ effluent limits in the prior permit, consistent with 40 CFR 122.41(l)(1).

C. As Soon as Possible

In its draft CWA Section 401 certification, the State of Idaho authorized a schedule of compliance which requires compliance with the draft permit's new total phosphorus limits and the new total ammonia as N effluent limits (except for the average monthly and maximum daily limits in effect during October) not later than 10 years after the effective date of the final permit.

Federal regulations require that compliance schedules in NPDES permits "shall require compliance as soon as possible." The draft certification states that the authorized compliance schedule "provides the permittee a reasonable amount of time to achieve the final effluent limitations as specified in the permit. At the same time, the schedule ensures that compliance with the final effluent limits is accomplished as soon as possible."

The EPA agrees with the State of Idaho's finding that the 10-year schedule of compliance requires compliance with the new water quality-based effluent limits for total phosphorus and ammonia as soon as possible. The City's planned schedule for completion of the necessary plant upgrades to ensure compliance with effluent limits is provided in the City's *Phase 5 Program Schedule*, updated on December 30, 2011. The *Phase 5 Program Schedule* explains that the City

must undertake several subtasks before it is able to comply with the new water quality-based phosphorus and ammonia limits in the draft permit, including:

- Funding (either a bond election or a judicial confirmation).
- Property acquisition and land use adjustments.
- Sewer rate study and financing plan.
- Phased construction and optimization of advanced treatment facilities:
    - Completion of tankage and 1 mgd of tertiary membrane filtration (TMF) capacity by late 2013 (Phase 5C.1)
    - 1 year of assessment of the performance of the 1 mgd TMF system
    - Design and construction of an additional 3 mgd of TMF capacity (4 mgd total TMF capacity), to be completed by early 2019 (Phase 5C.2).
    - Two years of optimization of the 4 mgd TMF system, to be completed by early 2021.
    - Design and construct an additional 2 mgd of TMF capacity (6 mgd total, phase 5C.3) in parallel with phase 5C.2). Construction will be completed in 2021; full compliance will be achieved after two years of optimization, in 2023, or 10 years after the effective date of the final permit.

The *Phase 5 Program Schedule* explains that, since current wastewater flows are less than 4 mgd, incremental implementation of the TMF improvements is appropriate. The incremental implementation will reduce the City's costs and allow the City to evaluate the performance of the improvements before committing to further and more costly improvements.

D. References

City of Coeur d'Alene Wastewater Department. *Phase 5 Program Schedule.* February 26, 2008. Updated December 30, 2011.

EPA. 1991. *Technical Support Document for Water Quality-based Toxics Control*. US Environmental Protection Agency, Office of Water, EPA/505/2-90-001. March 1991. http://www.epa.gov/npdes/pubs/owm0264.pdf

EPA. 2008. *Municipal Nutrient Removal Technologies Reference Document*. US Environmental Protection Agency. Office of Wastewater Management, Municipal Support Division, Municipal Technology Branch. The EPA 832-R-08-006. September 2008. http://water.epa.gov/scitech/wastetech/upload/mnrt-volume1.pdf

Appendix H: Draft Clean Water Act Section 401 Certification

STATE OF IDAHO
DEPARTMENT OF
ENVIRONMENTAL QUALITY

2110 Ironwood Parkway • Coeur d'Alene, Idaho 83814 • (208) 769-1422

C.L. "Butch" Otter, Governor
Toni Hardesty, Director

June 25, 2013

Mr. Michael Lidgard
US Environmental Protection Agency, Region 10
1200 6th Avenue, OW-130
Seattle, WA 98101

RE: Third Revision Draft §401 Water Quality Certification for the Draft NPDES Permit No. ID-0022853 for the City of Coeur d'Alene Wastewater Facility (Coeur d'Alene)

Dear Mr. Lidgard:

On May 21, 2013, the State of Idaho Department of Environmental Quality (DEQ) Director Curt Fransen sent a letter to Representatives Eskridge and Anderson clarifying the agency's interpretation of IDAPA 58.01.02.055.04. This interpretation necessitated some changes to our draft 401 certifications for the three Spokane River dischargers. We have made the necessary revisions and are resubmitting the draft certification for Coeur d'Alene to you in its entirety.

To recap the Coeur d'Alene certification process, on August 28, 2012 DEQ submitted our first draft certification. On September 18, 2012 DEQ revised the draft certification due to an error in the mixing zone section. We submitted another revised draft certification on April 26, 2013 in response to a revised draft permit.

Please direct any questions to June Bergquist at 208.666.4605 or june.bergquist@deq.idaho.gov .

Sincerely,

Daniel Redline
Regional Administrator
Coeur d'Alene Regional Office

Enclosure

C: Miranda Adams, DEQ Boise
Brian Nickel, EPA Region 10, Seattle
Sid Fredrickson, City of Coeur d'Alene

Idaho Department of Environmental Quality

Revised Draft 401 Water Quality Certification

June 25, 2013

NPDES Permit Number(s): ID-002285-3 City of Coeur d'Alene Wastewater Facility

Receiving Water Body: Spokane River

Pursuant to the provisions of Section 401(a)(1) of the Federal Water Pollution Control Act (Clean Water Act), as amended; 33 U.S.C. Section 1341(a)(1); and Idaho Code §§ 39-101 et seq. and 39-3601 et seq., the Idaho Department of Environmental Quality (DEQ) has authority to review National Pollutant Discharge Elimination System (NPDES) permits and issue water quality certification decisions.

Based upon its review of the above-referenced permit and associated fact sheet, DEQ certifies that if the permittee complies with the terms and conditions imposed by the permit along with the conditions set forth in this water quality certification, then there is reasonable assurance the discharge will comply with the applicable requirements of Sections 301, 302, 303, 306, and 307 of the Clean Water Act, the Idaho Water Quality Standards (WQS) (IDAPA 58.01.02), and other appropriate water quality requirements of state law.

This certification does not constitute authorization of the permitted activities by any other state or federal agency or private person or entity. This certification does not excuse the permit holder from the obligation to obtain any other necessary approvals, authorizations, or permits.

Antidegradation Review

In March 2011, Idaho incorporated new provisions in Idaho Code § 39-3603 addressing antidegradation implementation. At the same time, Idaho adopted antidegradation implementation procedures in the Idaho WQS. DEQ submitted the antidegradation implementation procedures to the US Environmental Protection Agency (EPA) for approval on April 15, 2011. On August 18, 2011, EPA approved the implementation procedures.

The WQS contain an antidegradation policy providing three levels of protection to water bodies in Idaho (IDAPA 58.01.02.051).

- Tier 1 Protection. The first level of protection applies to all water bodies subject to Clean Water Act jurisdiction and ensures that existing uses of a water body and the level of water quality necessary to protect those existing uses will be maintained and protected (IDAPA 58.01.02.051.01; 58.01.02.052.01). Additionally, a Tier 1 review is performed for all new or reissued permits or licenses (IDAPA 58.01.02.052.05).
- Tier 2 Protection. The second level of protection applies to those water bodies considered high quality and ensures that no lowering of water quality will be allowed unless deemed

necessary to accommodate important economic or social development (IDAPA 58.01.02.051.02; 58.01.02.052.06).

- Tier 3 Protection. The third level of protection applies to water bodies that have been designated outstanding resource waters and requires that activities not cause a lowering of water quality (IDAPA 58.01.02.051.03; 58.01.02.052.07).

DEQ is employing a water body by water body approach to implementing Idaho's antidegradation policy. This approach means that any water body fully supporting its beneficial uses will be considered high quality (Idaho Code § 39-3603(2)(b)(i)). Any water body not fully supporting its beneficial uses will be provided Tier 1 protection for that use, unless specific circumstances warranting Tier 2 protection are met (Idaho Code § 39-3603(2)(b)(iii)). The most recent federally approved Integrated Report and supporting data are used to determine support status and the tier of protection (Idaho Code § 39-3603(2)(b)).

Pollutants of Concern

The City of Coeur d'Alene discharges the following pollutants of concern: carbonaceous biochemical oxygen demand ($CBOD_5$), total suspended solids (TSS), pH, E. coli, chlorine, ammonia, phosphorus, silver and zinc. Effluent limits have been developed for these pollutants of concern. Copper, lead, cadmium and nitrate + nitrite are additional pollutants of concern for which a reasonable potential analysis was performed. No effluent limits were established for these pollutants because results of the analysis indicated they had no reasonable potential to exceed water quality standards. However, this 401 certification includes effluent limits for cadmium and lead to meet requirements of the Idaho Water Quality Standards.

Receiving Water Body Level of Protection

The City of Coeur d'Alene discharges to the Spokane River assessment unit (AU) ID17010305PN004_04 (Coeur d'Alene Lake to Post Falls Dam). This AU has the following designated beneficial uses: cold water aquatic life, salmonid spawning, primary contact recreation, domestic, agricultural and industrial water supply, wildlife habitat, and aesthetics. There is no available information indicating the presence of any existing beneficial aside from those that are already designated.

The cold water aquatic life use in the Spokane River AU is not fully supported due to excess cadmium, lead, zinc and phosphorus (2010 Integrated Report). The primary contact recreation beneficial use has not been assessed; however, E. coli data collected in 2007 indicate that recreation uses are fully supported. As such, DEQ will provide Tier 1 protection only for the aquatic life use and Tier 2 protection, in addition to Tier 1, for the recreation beneficial use (Idaho Code § 39-3603(2)(b)).

Protection and Maintenance of Existing Uses (Tier 1 Protection)

As noted above, a Tier 1 review is performed for all new or reissued permits or licenses, applies to all waters subject to the jurisdiction of the Clean Water Act, and requires demonstration that existing uses and the level of water quality necessary to protect existing uses shall be maintained and protected. In order to protect and maintain designated and existing beneficial uses, a permitted discharge must comply with narrative and numeric criteria of the Idaho WQS, as well

as other provisions of the WQS such as Section 055, which addresses water quality limited waters. The numeric and narrative criteria in the WQS are set at levels that ensure protection of designated beneficial uses. The effluent limitations and associated requirements contained in the City of Coeur d'Alene permit are set at levels that ensure compliance with the narrative and numeric criteria in the WQS.

Water bodies not supporting existing or designated beneficial uses must be identified as water quality limited, and a total maximum daily load (TMDL) must be prepared for those pollutants causing impairment. A central purpose of TMDLs is to establish wasteload allocations for point source discharges, which are set at levels designed to help restore the water body to a condition that supports existing and designated beneficial uses. Discharge permits must contain limitations that are consistent with wasteload allocations in the approved TMDL.

The WQS provide that until a TMDL or equivalent process is completed for a high priority water quality limited waterbody, the total load of the impairing pollutant must remain constant or decrease within the watershed. (IDAPA58.01.02.055.04). The cold water aquatic life use in the Spokane River AU is not fully supported due to excess cadmium, lead, zinc and phosphorus (2010 Integrated Report). In addition, the 2010 Integrated Report lists the Spokane River as high priority for TMDL development. Therefore, section 055.04 is applicable to the discharges of phosphorus, lead, zinc and cadmium.

Phosphorus

The restrictions on loading set forth in 055.04 are only applicable until a TMDL or equivalent process is completed. DEQ believes a process equivalent to a TMDL has been completed for phosphorus. In order to meet Washington and Idaho WQS, EPA modeled the cumulative impact of all sources of nutrients and oxygen-demanding pollutants, both point and non-point sources, in Idaho and Washington for the Spokane River. The limits EPA has set in the draft permits for the point sources in Idaho, including the CDA permit, are based upon this modeling analysis. The proposed effluent limits will result in a concentration of approximately 9.1 µg/L of TP in the Idaho portion of the Spokane River. This level meets or exceeds Idaho's narrative criteria for excess nutrients. (See IDAPA 58.01.02.200.06). In summary, equivalent to a TMDL, EPA has calculated the loading from point and non-point sources, and set limits that will attain WQS for phosphorus in Idaho. Therefore, the effluent limits in the draft permit are consistent with section 055.04.

Cadmium, Zinc and Lead

In August 2000, EPA approved a TMDL prepared by DEQ for cadmium, lead and zinc in the CDA River Basin, which included the Spokane River. The TMDL included allocations for the point source dischargers to the Spokane River, including CDA. However, this TMDL was invalidated by the Idaho Supreme Court in 2003. There has been no more recent effort by DEQ to develop a TMDL for metals in the Spokane River, and therefore, the river is still on the state's 303d list for metals and is identified as a high priority water body for TMDL development. Thus, the load restrictions in section 055.04 apply to the metals discharged to the Spokane River.

The intent of section 055.04 is to ensure that water quality for designated uses is at least maintained at current levels, until DEQ can make a determination, through a TMDL or equivalent process, regarding reductions necessary to attain WQS. To achieve this goal, section

055.04 requires that the "load" of the impairing pollutant remain constant or decrease in the watershed. "Load" is not defined in the Idaho WQS. In the context of a TMDL, however, load is defined as an amount of matter, and is expressed in terms of mass per time, toxicity or other appropriate measure (see 40 CFR 130.2(e) (definition of "load") and 40 CFR 130.2(i) (definition of "TMDL")). The water quality criteria for lead, zinc and cadmium is expressed as dissolved metal concentrations. For these pollutants, it is the concentration, rather than the mass, that is critical for the protection of the designated aquatic life uses. Therefore, in this instance, ensuring the load remains constant in the watershed means ensuring that the concentration of lead, zinc and cadmium in the City of Coeur d'Alene effluent does not increase.

In the draft NPDES permit for CDA, EPA has included effluent limits for zinc that ensure the effluent meets the water quality criteria at the end of pipe. These limits are more stringent than the 1999 permit based upon the results of the reasonable potential analyses. These limits ensure compliance with Section 055.04. However, the draft permit does not contain cadmium or lead limits. In order to ensure compliance with section 055.04, DEQ has included in the draft certification cadmium limits that reflect the current concentration of cadmium in CDA's effluent using the 99th percentile value from the 2006-2011 DMR data. Lead effluent limits from the 1999 permit which were removed by the 2004 modification have been reinstated by the 401 certification to meet requirements of section 055.04. Table 1 provides a summary of the existing permit limits and the proposed reissued permit limits, including effluent limitations for cadmium and lead specified in the draft 401 certification. The City of Coeur d'Alene is not requesting a design flow increase.

Section 055.04 provides that once a TMDL or equivalent process is completed, the discharge of causative pollutants must be consistent with the TMDL or equivalent process. Therefore, once a TMDL for metals is completed by DEQ for the Spokane River and approved by EPA, the limits for metals in the permit, including the limits discussed herein, should be adjusted to reflect the approved TMDL.

In summary, the effluent limitations and associated requirements contained in the CDA permit are set at levels that ensure compliance with the narrative and numeric criteria in the WQS. Therefore, DEQ has determined the permit will protect and maintain existing and designated beneficial uses in the Spokane River.

Table 1. Comparison of current and proposed permit limits.

		Proposed Permit			Current Permit			Change[1]
Parameter	Units	AML	AWL	Max Daily	AML	AWL	Max Daily	
Pollutants with limits in both the current and proposed permit								
$CBOD_5$ November-January	mg/L	25	40	-	25	40	-	I[2]
	lb/day	1251	2002	-	1250	2000	-	
	% removal	85%	-	-	85%	-	-	
$CBOD_5$ February-March	mg/L	25	40	-	25	40	-	D
	lb/day	seasonal average 226 lb/day		-	1250	2000	-	
	% removal	85%	-	-	85%	-	-	
$CBOD_5$ April-October	mg/L	25	40	-	25	40	-	D
	lb/day	seasonal average 203 lb/day		-	1250	2000	-	
	% removal	85%	-	-	85%	-	-	
$CBOD_5$ year around interim limit	mg/L	25	40	-	25	40	-	nc
	lb/day	1250	2000	-	1250	2000	-	
	% removal	85%	-	-	85%	-	-	
TSS	mg/L	30	45	-	30	45	-	I[2]
	lb/day	1501	2252	-	1,500	2,250	-	
	% removal	85%	-	-	85%	-	-	
pH Oct-June	s.u.	6.3 – 9.0 all times			6.2 – 9.0 all times			D
pH July-Sept	s.u.	6.5 – 9.0 all times			6.3 – 9.0 all times			D
E. coli	#/100 mL	126	-	406	-	-	-	nc[3]
Fecal coliform[3] May-Sept	#/100 mL	-	-	-	50	200	500	nc[3]
Fecal coliform[3] October-April	#/100 mL	-	-	-	-	200	800	nc[3]
Chlorine October-June	µg/L	150	-	390	36	-	161	I[2]
	lb/day	7.5	-	20	1.04	-	4.67	
Chlorine July-Sept	µg/L	39	-	102	147	-	662	I[2]
	lb/day	2.0	-	5.1	4.27	-	19.2	
Ammonia (July-Sept)	mg/L	-	-	-	10	-	29	D
	lb/day		≤4mgd	-	350		1,000	D
Ammonia (July-Sept)	mg/L	-		-	7.4	-	21	D
	lb/day	-	>4.2mgd		370	-	1,100	D
Ammonia July-Sept interim limits	mg/L	10	-	29				nc
	lb/day	350	≤4mgd	1,000		-		nc
Ammonia July-Sept interim limits	mg/L	7.4	-	21				nc
	lb/day	370	>4.2mgd	1,100				nc
Ammonia (March-June)	mg/L	-	-	-	-	-	-	-
	lb/day	649	-	1547	-	-	-	D
Ammonia (July-Sept)	mg/L	6.59	-	15.7	-	-	-	D
	lb/day	330	-	786	-	-	-	D
Ammonia (October)	mg/L	-	-	-	-	-	-	nc
	lb/day	-	-	-	-	-	-	
Ammonia (March-Oct)	mg/L	-	-	-	-	-	-	-
	lb/day	Seasonal Average Limit 272lb/day			-	-	-	D

Table 1 Continued…

		Proposed Permit			Current Permit		Change[1]	
Parameter	Units	Average Monthly Limit	Average Weekly Limit	Maximum Daily Limit	Average Monthly Limit	Average Weekly Limit	Maximum Daily Limit	
Pollutants with limits in both the current and proposed permit (continued)								
Phosphorus (March-Oct)	percent removal	-	-	-	85%	-	-	D
Phosphorus Feb-Oct[4] interim limits	µg/L	1,000	1,600	-	1,000	-	-	nc[4]
	lb/day	50	80		85% removal	-	-	
Phosphorus February-October	µg/L	-	-	-	-	-	-	D
	lb/day	3.17 seasonal	average	-	-	-	-	D
Silver (Oct-June>4.2 mgd	µg/L	8.01	-	22.5	16.0	-	31.9	D
	lb/day	0.401	-	1.13	0.80	-	1.60	D
Zinc	µg/L	135	-	168	136.2	-	200.8	D
	lb/day	6.76	-	8.42	6.8	-	10.0	D
Pollutants with limits only in the proposed permit								
Cadmium[5]	µg/L	0.149	0.187	-			-	nc[5]
Lead[5]	µg/L	2.5	-	5.8			-	nc[5]

Table 1 Continued...		***Proposed Permit***			***Current Permit***			***Change***[1]
Parameter	*Units*	*Average Monthly Limit*	*Average Weekly Limit*	*Maximum Daily Limit*	*Average Monthly Limit*	*Average Weekly Limit*	*Maximum Daily Limit*	
Pollutants with no limits in either the current and proposed permit								
Temperature	***°C***	***Report***	-	***Report***	-	-	***Report***	***nc***
PCB	***pg/L***	***Report***		***Report***	-	-	-	***nc***
Mercury	***ng/L***	-	-	-	-	-	-	***nc***
TCDD	***pg/L***	***Report***	-	***Report***	-	-	-	***nc***
Silver	***µg/L***	***Report***	-	***Report***	-	-	-	***nc***
	lb/day	-	-	-	-	-	-	
Alkalinity	***mg/L as $CaCO_3$***	***Report***	-	***Report***	-	-	-	***nc***
Hardness	***mg/L as $CaCO_3$***	***Report***	-	***Report***	-	-	-	***nc***
Oil and Grease	***mg/L***	***Report***	-	***Report***	-	-	-	***nc***
TDS	***mg/L***	***Report***	-	***Report***	-	-	-	***nc***
Ortho-phosphate	***µg/L***	***Report***	-	***Report***	-	-	-	***nc***
Kjeldahl Nitrogen	***mg/L***	***Report***	-	***Report***	-	-	-	***nc***
Nitrate-Nitrite	***mg/L***	***Report***	-	***Report***	-	-	-	***nc***
Dissolved Oxygen	***mg/L***	***Report minimum and average***			-	-	-	***nc***

[1] ***nc*** = no change in effluent limit from current permit; ***I*** = increase of pollutants from current permit; ***D*** = decrease of pollutants from current permit;

[2]The increased loads of these pollutants in the draft permit do not exceed narrative or numeric criteria in the Idaho WQS and meets the requirements for Tier 1 protection.

[3] DEQ requested EPA replace the fecal coliform limits with *E. coli* effluent limits. See discussion under High Quality Waters section (below).

[4]Interim effluent limits for phosphorus were established based on Coeur d'Alene's current design flow and treatment levels authorized by their current permit. See discussion on page 3 regarding the use of an equivalent process.

[5]Effluent limits for cadmium and lead have been added by the 401 certification to ensure that the concentration of these metals remain constant to meet the requirements of IDAPA 58.01.02.055.04. The cadmium limit was based on the actual concentration of cadmium currently discharged, using the 2006-2011 DMR data. Similarly, the lead effluent limits in the 1999 permit have been reinstated by the 401 certification to comply with section 055.04.

High-Quality Waters (Tier 2 Protection)

The Spokane River is not assessed for recreation use. Monitoring data for E. coli collected in 2007 within the subject assessment unit, indicates that the Spokane River is high quality for the primary contact recreation beneficial use. As such, the water quality relevant to recreational uses of the Spokane River must be maintained and protected, unless a lowering of water quality is deemed necessary to accommodate important social or economic development.

To determine whether degradation will occur, DEQ must evaluate how the permit issuance will affect water quality for each pollutant that is relevant to recreational uses of the Spokane River (IDAPA 58.01.02.052.04). These include the following: E. coli bacteria, phosphorus and mercury. Effluent limits are set in the proposed and existing permit for all these pollutants except mercury.

For a reissued permit or license, the effect on water quality is determined by looking at the difference in water quality that would result from the activity or discharge as authorized in the current permit and the water quality that would result from the activity or discharge as proposed in the reissued permit or license (IDAPA 58.01.02.052.04.a). For a new permit or license, the effect on water quality is determined by reviewing the difference between the existing receiving water quality and the water quality that would result from the activity or discharge as proposed in the new permit or license (IDAPA 58.01.02.052.04.a).

Pollutants with Limits in the Current and Proposed Permit: E. coli, phosphorus

For Tier 2 related pollutants that are currently limited (have effluent limits) and will have limits under the reissued permit, the current discharge quality is based on the limits in the current permit or license (IDAPA 58.01.02.052.04.a.i), and the future discharge quality is based on the proposed permit limits (IDAPA 58.01.02.052.04.a.ii). For the City of Coeur d'Alene permit, this means determining the permit's effect on water quality based upon the limits for E. coli and phosphorus in the current and proposed permits. Table 1 provides a summary of the current permit limits and the proposed or reissued permit limits.

E. coli

The existing permit for the City of Coeur d'Alene contains effluent limits for fecal coliform and *E. coli*. In 1986, EPA updated its criteria to protect recreational use of water by recommending an *E. coli* criterion as a better indicator than fecal coliform of bacteria levels that may cause gastrointestinal distress in swimmers. In 2000, DEQ changed its bacteria criterion from fecal coliform to *E. coli*. The *E. coli* limits are in the existing permit to reflect the bacteria criterion that DEQ adopted to protect the contact recreation beneficial use (IDAPA 58.01.02.251.01). The fecal coliform limits are in the current permit because at the time the permit was issued, IDAPA 58.01.02.420.05 established a disinfection requirement for sewage wastewater treatment plant effluent. This requirement specified that fecal coliform concentrations not exceed a geometric mean of 200/100 mL based on a minimum of five samples in one week. This section of the Idaho WQS was revised in 2002 to reflect the change in the bacteria criterion from fecal coliform to *E. coli*. The *E. coli* limits are as or more protective of water quality than the old fecal coliform limits. The proposed final permit contains both fecal coliform and *E. coli* effluent limits that comply with previous and current numeric "end-of-pipe" criteria.

Because the fecal coliform criterion has been replaced with an *E. coli* criterion, DEQ is requesting that EPA remove the fecal coliform effluent limits, consistent with how EPA has handled other NPDES permits for wastewater treatment plants in Idaho. Retaining the *E. coli* limits will ensure that the receiving water quality will not be degraded even when the fecal coliform limits are removed. Even with the omission of fecal coliform limits, DEQ believes the discharge will not cause or contribute to a violation of the bacteria criteria because the permit incorporates "end-of-pipe" limits for *E. coli*. Thus, removal of the fecal coliform limits complies with both the Tier 1 and Tier 2 components of Idaho's antidegradation policy.

Phosphorus

The proposed permit for Coeur d'Alene includes a new final effluent limit for phosphorus (draft permit Table 1). Tier 2 waters are waters in which the quality of the water is better than necessary to support beneficial uses. The tier 2 antidegradation policy provides that pollutants relevant to recreational uses may be significantly increased only if socially or economically justified. However, while the Spokane River is tier 2 for recreational uses, it is also impaired for aquatic life uses due to excess total phosphorous (TP). Because TP is relevant to both uses, and the water quality standards require both uses be protected, the use with the more stringent requirement limits the TP levels. Thus, the phosphorus levels must be reduced to get the River back into compliance with criteria for support of aquatic life uses. This needed reduction is reflected in the proposed permit limits. Because the River is impaired for phosphorus in Idaho, and because the CDA permit must ensure compliance with Washington WQS, the limits in the permit require a significant reduction in phosphorus. Specifically, the draft permit final effluent limits for the three Idaho dischargers will reduce phosphorus concentrations in the Idaho portion of the Spokane River to approximately 9.1 µg/L at the state line. These limits meet the Tier 2 requirement under the antidegradation policy because there will be no degradation in water quality, but rather an improvement in TP levels.

Pollutants with No Limits: Mercury

Mercury is a pollutant relevant to Tier 2 protection of recreation that currently is not limited and for which the proposed permit also contains no limit (Table 1). For such pollutants, a change in water quality is determined by reviewing whether changes in production, treatment, or operation that will increase the discharge of these pollutants are likely (IDAPA 58.01.02.052.04.a.ii). With respect to mercury, there is no reason to believe this pollutant will be discharged in quantities greater than those discharged under the current permit. This conclusion is based upon the fact that there have been no changes in the design flow, influent quality or treatment processes that would likely result in an increased discharge of this pollutant. Additionally, whole effluent toxicity testing using three different organisms will be required twice per year to detect toxics in toxic amounts. A toxicity reduction evaluation is required in the event of an excursion above a trigger value. Mercury monitoring will be required three times over a five year period as part of the expanded effluent testing requirements in Part D of the NPDES application Form 2A (EPA Form 3510-2A, revised 1-99). Because of these provisions, the proposed permit does not allow for any increased water quality impact from this pollutant, DEQ concludes that the proposed permit should not cause a lowering of water quality for mercury. As such, the proposed permit should maintain the existing high water quality in the Spokane River.

Conditions Necessary to Ensure Compliance with Water Quality Standards or Other Appropriate Water Quality Requirements of State Law

The 2010 Integrated Report lists the Spokane River as high priority for TMDL development. Pursuant to IDAPA 58.01.02.055.04, DEQ must ensure that discharges of pollutants of concern remain constant or decrease within the watershed. Pollutants of concerns for which a TMDL is to be developed are cadmium, lead, zinc and total phosphorus. The draft permit reduces the previously permitted effluent limit for zinc, but lacks effluent limits for cadmium and lead because the discharge didn't have reasonable potential to exceed WQS criteria for these pollutants. Therefore, to meet Section 055.04 requirements, this 401 certification adds effluent limits as specified in Table 2, below.

Table 2: Final Effluent Limit Requirements for Outfall 001 at Design Flow of 6 MGD

Parameter	Units	Average Monthly Limit	Average Weekly Limit	Maximum Daily Limit
Lead	µg/L	2.5	-	5.8
Cadmium	µg/L	0.149	0.187	-

Once a TMDL for metals is approved by EPA, the wasteload allocations specified in the TMDL shall replace the above Table 2 effluent limit requirements.

Compliance Schedule

Pursuant to IDAPA 58.01.02.400.03, DEQ may authorize compliance schedules for water quality-based effluent limits issued in a permit for the first time. City of Coeur d'Alene cannot immediately achieve compliance with the effluent limits for ammonia, $CBOD_5$ and phosphorus; therefore, DEQ authorizes a compliance schedule and interim requirements as set forth below.

Table 3. Interim Limits

Parameter	Units	Average Monthly Limit	Average Weekly Limit
Ammonia (March-June)	mg/L	report	report
Ammonia July-Sept	mg/L	10	29
≤4.2 mgd	lb/day	350	1000
Ammonia July-Sept	mg/L	7.4	21
>4.2 mgd	lb/day	370	1100
$CBOD_5$ (February-October)	mg/L	25	40
	lb/day	1250	2000
	% removal	85% (min)	-
Phosphorus (February-October)	mg/L	1.0	1.6
	lb/day	50	80

The proposed compliance schedule allows Coeur d'Alene time to upgrade their facility to tertiary treatment, which will reduce effluent loads and concentrations of ammonia, phosphorus and $CBOD_5$ to levels necessary to meet the final effluent limits. In addition, Coeur d'Alene will have to make certain modifications to their existing treatment plant to accomplish the upgrade (Appendix A). During this time, final $CBOD_5$ limits will not be achievable. The $CBOD_5$ interim limits identified in Table 3 maintain the currently permitted load and concentration (Table 1). A compliance schedule provides the permittee a reasonable amount of time to achieve the final effluent limitations as specified in the permit. At the same time, the schedule ensures that compliance with the final effluent limits is accomplished as soon as possible.

1. The permittee must comply with all effluent limitations and monitoring requirements in Part I.B and I.C beginning on the effective date of the permit, except those for which a compliance schedule is specified in Part I.D.

2. The permittee must achieve compliance with the final effluent limitations for phosphorus, ammonia and $CBOD_5$ as set forth in Part I.B of the permit, not later than ten (10) years after the effective date of the final permit.

3. While the schedules of compliance specified in Part I.D are in effect, the permittee must complete interim requirements and meet interim effluent limits and monitoring requirements as specified in Part I.E of the permit.

4. All other provisions of the permit, except the final effluent limits for phosphorus, $CBOD_5$ and ammonia as described in Table 3 of this certification, must be met after the effective date of the final permit.

Interim Requirements for Compliance Schedules

1. By one (1) year after the effective date of the final permit, the permittee must provide a preliminary engineering report to EPA and IDEQ outlining estimated costs and schedules for completing capacity expansion and implementation of technologies to achieve final effluent limitations. This schedule must include a timeline for full scale pilot testing and results of any testing conducted to date.

2. By three (3) years after the effective date of the final permit, the permittee must provide written notice to EPA and IDEQ that full scale pilot testing of the technology that will be employed to achieve the final limits has been completed and must submit a summary report of results and plan for implementation.

3. By five years after the effective date of the final permit, the permittee must provide EPA and IDEQ with written notice that design has been completed and bids have been awarded to begin construction to achieve final effluent limitations.

4. By eight (8) years after the effective date of the final permit, the permittee must provide EPA and DEQ with written notice that construction has been completed on the facilities to achieve final effluent limitations.

5. By ten (10) years after the effective date of the final permit, the permittee must provide EPA and DEQ with a written report providing details of a completed start up and optimization phase of the new treatment system and must achieve compliance with the final effluent limitations of Part I.B. The report shall include two years of effluent data demonstrating that final effluent limits can be achieved (the two years of data do not have to consistently meet final effluent limits but demonstrate that at the end of this period final limits can be met).

6. By year six (6), seven (7), and eight (8) after the effective date of the final permit, the permittee must submit to EPA and IDEQ progress reports, which outline the progress made toward achieving compliance with the phosphorus, $CBOD_5$ and ammonia effluent limitations. At a minimum, the reports must include:
   a) An assessment of the previous year of effluent data and comparison to the interim effluent limitations.
   b) A report on progress made toward meeting the final effluent limits.
   c) Further actions and milestones targeted for the upcoming year.

7. When the schedules of compliance specified in Part I.D are in effect, the permittee must comply with interim effluent limitations and monitoring requirements as specified in Part I.E of the permit.

Mixing Zones

Pursuant to IDAPA 58.01.02.060, DEQ authorizes the use of mixing zones as described in Table 3 of the critical flow volumes of the Spokane River for the following pollutants: pH, TSS, silver, copper, chlorine, nitrate + nitrite and ammonia.

Table 4: Mixing Zones

Pollutant	Mixing Zone (%)
pH	25
TSS	25
silver	25
copper (October – June)	25
copper (July – September)	25
chlorine	25
nitrate + nitrite	25
ammonia acute (March – October)	2.5
ammonia chronic	25

Pollutant Trading

Pursuant to IDAPA 58.01.02.055.06, DEQ authorizes pollutant trading for phosphorus and other oxygen demanding pollutants. Trading must be conducted in a manner that is consistent with the most recent version of DEQ's *Water Quality Pollutant Trading Guidance*, available at: http://www.deq.idaho.gov/media/488798-water_quality_pollutant_trading_guidance_0710.pdf.

The use of pollutant offsets is authorized for purposes of compliance with antidegradation rules and IDAPA 58.01.02.055.

Other Conditions

This certification is conditioned upon the requirement that any material modification of the permit or the permitted activities—including without limitation, any modifications of the permit to reflect new or modified TMDLs, wasteload allocations, site-specific criteria, variances, or other new information—shall first be provided to DEQ for review to determine compliance with Idaho WQS and to provide additional certification pursuant to Section 401.

Right to Appeal Final Certification

The final Section 401 Water Quality Certification may be appealed by submitting a petition to initiate a contested case, pursuant to Idaho Code § 39-107(5) and the "Rules of Administrative Procedure before the Board of Environmental Quality" (IDAPA 58.01.23), within 35 days of the date of the final certification.

Questions regarding the actions taken in this certification should be directed to June Bergquist, Coeur d'Alene Regional Office at 208.666.4605 or via email at june.bergquist@deq.idaho.gov .

DRAFT

Daniel Redline
Regional Administrator
Coeur d'Alene Regional Office

Appendix A

Compliance Schedule Justification Letters
dated
April 3, 2013 and April 22, 2013
from
City of Coeur d'Alene Wastewater Facility

CITY OF COEUR D'ALENE
WASTEWATER UTILITY DEPARTMENT
CITY HALL, 710 E. MULLAN
COEUR D'ALENE, IDAHO 83814-3958
208/769-2277– FAX 208/769-2338
E-mail: stdf@cdaid.org

April 3, 2013

Sent via E-mail to: Daniel.Redline@deq.idaho.gov

Daniel Redline
Regional Administrator
Coeur d'Alene Regional Office
Department of Environmental Quality
State of Idaho
2110 Ironwood Parkway
Coeur d'Alene, ID 83814

Re: Revised Draft §401 Water Quality Certification for City of Coeur d'Alene WTP
NPDES Permit Number ID-002285-3 – CBOD Compliance Schedule Request

Dear Mr. Redline.

The City of Coeur d'Alene requests that the section 401 water quality certification for its NPDES permit include a compliance schedule for meeting new CBOD5 effluent limits. As an existing discharger, the City of Coeur d'Alene is entitled to a compliance schedule to meet new effluent requirements for CBOD, ammonia, and phosphorus that result from the Washington Ecology dissolved oxygen TMDL. Washington dischargers have been afforded compliance schedules and interim discharge permit limits for CBOD, ammonia, and phosphorus in order to provide adequate time to make facility improvements necessary to ensure compliance with new effluent limitations. For example, the City of Spokane NPDES permit maintains existing limits at 30 mg/L BOD in the interim and requires new treatment process facilities to be installed by March 1, 2018 and compliance with the TMDL limits for BOD to begin March 1, 2021.

Although historical effluent CBOD performance at the Coeur d'Alene treatment plant have been excellent, it should be recognized that this has been the result of utilizing the existing infrastructure at the treatment plant to comply with both CBOD and ammonia effluent limits, when the original design was intended only to meet secondary treatment requirements and effluent BOD of 30 mg/L.

The new facilities intended for compliance with the TMDL based limits have yet to be constructed and until they are completed, the City runs the risk of being unable to sustain very low levels of CBOD in a plant designed for effluent BOD of 30 mg/L. This has been recognized for ammonia and phosphorus and interim limits have been provided for these parameters.

Transition to Tertiary Treatment

The City plans extensive improvements to the liquid stream treatment processes for compliance with the new limits for CBOD, ammonia, and phosphorus. These improvements will be

designed and constructed in phases over a number of years to take advantage of the important treatment technology developments resulting from the City's pilot testing program. In order to prove out findings from the pilot program at full-scale, initial improvements will be constructed at less than full plant capacity and operated to confirm final design and sizing criteria for the tertiary facility. This progression of implementation steps is provided for in the compliance schedule for phosphorous and ammonia.

The City will endeavor to maintain excellent effluent CBOD performance in the interim, however full compliance with the new effluent limits will not be assured until the transition to tertiary treatment is completed.

Interim Compliance Risk

The City will carry an unreasonable risk of non-compliance absent a compliance schedule and interim limits for CBOD. The City will need sufficient time to implement improvements to meet the new TMDL requirements. During that time the City should not be required to meet the final CBOD limits that are beyond the design capacity of the existing facility.

This will not result in additional water quality protection for the Spokane River, only the risk of noncompliance if the City is unable to maintain treatment performance in the interim until the required improvements are constructed. On average at design flow, the effluent CBOD concentration associated with the TMDL driven seasonal mass load limit of 203 pounds per day would fall to 4.06 mg/L compared to the current permit limits of 25 mg/L. This is an 84% reduction in the allowable effluent CBOD effective the date of issuance of the NPDES permit without an opportunity to implement the required treatment improvements.

This is inconsistent with the much larger loading from the City of Spokane which will be allowed to continue to discharge BOD at 30 mg/L until 2021 at a flow rate an order of magnitude larger than the City of Coeur d'Alene at a location much closer to Lake Spokane, which is the water body intended to be protected by the TMDL driving the new BOD limits.

I appreciate your consideration of this letter.

Sincerely,

H. Sid Fredrickson
Wastewater Superintendent

cc: June Bergquist, Idaho DEQ (june.bergquist@deq.idaho.gov)

4825-5215-8179, v. 1

CITY OF COEUR D'ALENE

WASTEWATER UTILITY DEPARTMENT

CITY HALL, 710 E. MULLAN
COEUR D'ALENE, IDAHO 83814-3958
208/769-2277– FAX 208/769-2338
E-mail: sidf@cdaid.org

April 22, 2013

Mr. John Tindall, PE
Idaho DEQ
2110 Ironwood Parkway
Coeur d'Alene, ID 83814

Dear John,

In further enhancement of our justification for a $CBOD_5$ compliance schedule, our engineers and us have looked at the proposed construction schedule for the various 5C sub-phases. We note that there will be disruptions to the existing secondary treatment process that will have a negative effect on the $CBOD_5$ removal rates. The following outlines the process disruptions that will lower CBOD removal rates:

Phase 5C.1

- Tie-in to secondary effluent line for transfer pumping station.
  - Impact: Requires stopping plant flow at trickling filters.
  - Potential Upset: potential loss of some biomass in trickling filters resulting in reduced CBOD removal.
- Tie-in to secondary effluent line for permeate return.
  - Impact: Requires stopping plant flow at trickling filters.
  - Potential Upset: potential loss of some biomass in trickling filters resulting in reduced CBOD removal.
- Tie-in to trickling filter effluent line for trickling filter effluent transfer pumping.
  - Impact: Requires stopping plant flow at trickling filters.
  - Potential Upset: potential loss of some biomass in trickling filters resulting in reduced CBOD removal.
- Tie-in to existing return tertiary sludge line for return tertiary sludge pumping to expanded solids contact tank.
  - Impact: Require existing return secondary sludge system for both clarifiers to be taken offline.
  - Potential Upset: potential anoxic conditions in secondary clarifiers resulting in floating sludge and increased TSS when brought back online.
- Tie-in to existing solids contact tank for expanded solids contact tank drain return.
  - Impact: Requires solids contact tank to be taken offline.
  - Potential Upset: reduced solids contact volume potentially resulting in increased effluent BOD and ammonia.
- Connection to and modification of existing tank drain and secondary scum piping.

- Impact: Will require secondary clarifiers to be taken offline (one at a time).
- Potential Upset: Increased hydraulic and solids loading to on-line clarifier potentially resulting in increased effluent TSS and BOD.

- Replacement of secondar aeration blowers with turbine blowers of higher capacity
  - Impact: Requires shutting down aeration tankage
  - Potential Upset: Reduced nitrification and CBOD removal
- Upsizing of scour air supply for IFAS nitrification modules
  - Impact: Requires shutting down aeration tankage
  - Potential Upset: Reduced nitrification and CBOD removal

Phase 5C.2

- Construction of third primary clarifier split structure and primary clarifier.
  - Impact: Requires several shut downs for process tie-ins, possibly diverting flow around existing split structure.
  - Potential impact: Potential decrease in TSS and BOD removal.
- Reconstruction of existing secondary clarifier splitter box.
  - Impact: Requires stopping plant flow at trickling filters for piping modifications.
  - Potential Upset: potential loss of biomass in trickling filters (see above).
- Construction of third secondary clarifier.
  - Impact: Requires several shut downs of plant flow at trickling filters for multiple tie-ins to secondary influent and effluent lines and return secondary sludge line.
  - Potential Upset: potential loss of biomass in trickling filters (see above).

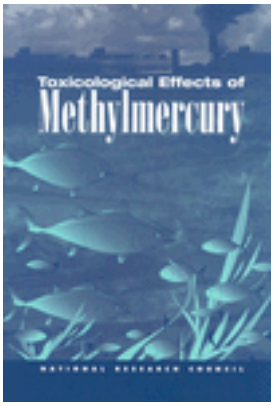
We hope you will take these issues under consideration for issuing the city a $CBOD_5$ compliance schedule. Feel free to contact me if you have additional questions.

Sincerely.

H. Sid Fredrickson
Wastewater Superintendent

C: June Bergquist. DEQ
Dave Clark. PE. HDR Engineering
Don Keil. Asst. Wastewater Supt.
James Tupper
Kris Holm

2



Toxicological Effects of Methylmercury

Committee on the Toxicological Effects of Methylmercury, Board on Environmental Studies and Toxicology, National Research Council
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Toxicological Effects of Methylmercury

Committee on the Toxicological Effects of Methylmercury
Board on Environmental Studies and Toxicology
Commission on Life Sciences
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PREFACE

In 1997, the U.S. Environmental Protection Agency (EPA) issued two reports to the U.S. Congress on mercury (Hg) and its effects on public health. The first of these reports, the *Mercury Study Report to Congress,* assessed the source and amount of Hg emissions in the United States, the detrimental effects of Hg on humans and wildlife, and the feasibility of control technologies. The second report, the *Utility Hazardous Air Pollutant Report to Congress,* looked specifically at emissions from utility companies and cited Hg as a major contaminant, especially in emissions from coal-fired power plants. Once in the environment, Hg can be converted to methylmercury (MeHg), which bioaccumulates up the food chain. Such bioaccummulation can lead to high concentrations of MeHg in predatory fish. Because of concerns about MeHg exposure levels in the United States from the consumption of contaminated fish, particularly among sensitive populations, questions have arisen among federal agencies over what is an acceptable level of exposure to MeHg. Because of gaps in the scientific data regarding Hg toxicity, particularly MeHg, the potentially widespread implications for human health, and the high financial costs and feasibility problems associated with further regulating Hg emissions, Congress directed EPA in the House Appropriations Report for EPA's Fiscal 1999 funding to contract with the National Research Council (NRC) to prepare recommendations on the appropriate reference dose for Hg exposure.

In this report, the Committee on the Toxicological Effects of Methylmercury of the NRC independently reviewed the reference dose

for MeHg. The committee reviewed the available toxicological, epidemiological, and exposure data (from food and water) and determined the appropriateness of the critical study, end points of toxicity, and uncertainty factors used by EPA in the derivation of the reference dose for MeHg. The committee was also asked to identify data gaps and make recommendations for future research.

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise in accordance with procedures approved by the NRC's Report Review Committee for reviewing NRC and Institute of Medicine reports. The purpose of this independent review is to provide candid and critical comments that will assist the NRC in making the published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscripts remain confidential to protect the integrity of the deliberative process. The committee wishes to thank the following individuals, who are neither officials nor employees of the NRC, for their participation in the review of this report: Melvin Andersen, Colorado State University; Michael Aschner, Wake Forest University; Kenny Crump, ICF Consulting; Kim Dietrich, University of Cincinnati; Johanna Dwyer, New England Medical Center; John Emmerson, Eli Lilly (retired); Susan Miller, University of California at San Francisco; Charles Poole, University of North Carolina; Jonathan Samet, Johns Hopkins University; Ellen Silbergeld, University of Maryland; Christopher Whipple, Environ International Corporation; James Woods, University of Washington.

The individuals listed above have provided many constructive comments and suggestions. It must be emphasized, however, that responsibility for the final content of this report rests entirely with the authoring committee and the NRC.

The committee gratefully acknowledges the following individuals for providing background information and for making presentations to the committee: Richard Duffy of the office of Senator Patrick Leahy (Vermont); Lee Alman of the office of Congressman Alan Mollohan (West Virginia); George Lucier, National Institute of Environmental Health Sciences; William Farland, EPA; Michael Bolger, Food and Drug Administration; Christopher DeRosa, Agency for Toxic Substances and Disease Registry; E. Spencer Garrett, National Oceanic and Atmospheric Administration, Fran Sharples, Office of Science and Technology; Michael Bender, Mercury Policy Project; Jane Williams, California

Communities Against Toxics; Eric Uram, Sierra Club-Great Lakes Program; Greg Schaefer, Arch Coal, Inc.; Leonard Levin, Electric Power Research Institute; and David Michaud, Wisconsin Electric Power Company. The committee also heard from a number of researchers actively investigating issues related to MeHg exposure. Those researchers are Tord Kjellstrom, University of Auckland, New Zealand; Donna Mergler, University of Quebec at Montreal; Kenny Crump, ICF Kaiser; Ellen Silbergeld, University of Maryland; Philippe Grandjean, University of Southern Denmark; Neils Keiding and Esben Budtz-Jøergensen, both from the University of Copenhagen; and Thomas Clarkson, Christopher Cox, Gary Myers, Philip Davidson, and Mark Moss, all from the University of Rochester. In addition, the committee wants to give special thanks to individuals and groups who provided further analyses and information at the request of the committee. Those are Wayne Rosamond, University of North Carolina; Philippe Grandjean; Neils Keiding; Esben Budtz-Jørgensen; Thomas Clarkson; Christopher Cox; Tord Kjellstrom; Harvey Clewell III; Jeffrey Swartout; Cynthia Van Landingham; and Kenny Crump. The committee also gratefully acknowledges input from individuals representing the Environmental Working Group, the Dental Amalgam Mercury Syndrome (DAMS) organization and the Mercury Free Press.

The committee is grateful for the assistance of the NRC staff in preparing the report. Staff members who contributed to this effort are Carol A. Maczka, senior program director for the Toxicology and Risk Assessment Program; Michelle Catlin, research associate; Ruth E. Crossgrove, editor; Laura Holliday and Judy Estep, senior project assistants; and Mirsada Karalic-Loncarevic, information specialist.

Finally, I would like to thank all the members of the committee for their dedicated efforts throughout the development of this report.

Robert A. Goyer
Chair, Committee on the Toxicological
Effects of Methylmercury

CONTENTS

Toxicological Effects of Methylmercury

EXECUTIVE SUMMARY

MERCURY (Hg) is widespread and persistent in the environment. Its use in many products and its emission from combustion processes have resulted in well-documented instances of population poisonings, high-level exposures of occupational groups, and worldwide chronic, low-level environmental exposures. In the environment, Hg is found in its elemental form and in various organic compounds and complexes. Methylmercury (MeHg), one organic form of Hg, can accumulate up the food chain in aquatic systems and lead to high concentrations of MeHg in predatory fish,[1] which, when consumed by humans, can result in an increased risk of adverse effects in highly exposed or sensitive populations. Consumption of contaminated fish is the major source of human exposure to MeHg in the United States.

In recent years, the U.S. Environmental Protection Agency (EPA) has issued two major reports on Hg to the U.S. Congress on Hg — the *Mercury Study Report to Congress* (issued in December 1997) and the *Utility Hazardous Air Pollutant Report to Congress* (issued in March 1998). In those reports, fossil-fuel power plants, especially coal-fired utility boilers, were identified as the source category that generates the greatest Hg emissions, releasing approximately 40 tons annually in the United States. EPA is currently considering rule-making for supplemental controls on Hg emissions from utilities. However, because of gaps in the

[1]In this report, the term fish includes shellfish and marine mammals, such as pilot whales, that are consumed by certain populations.

scientific data regarding Hg toxicity, Congress directed EPA, in the appropriations report for EPA's fiscal 1999 funding, to request the National Academy of Sciences to perform an independent study on the toxicological effects of MeHg and to prepare recommendations on the establishment of a scientifically appropriate MeHg exposure reference dose (RfD).[2]

THE CHARGE TO THE COMMITTEE

In response to the request, the National Research Council (NRC) of the National Academies of Sciences and Engineering convened the Committee on Toxicological Effects of Methylmercury, whose members have expertise in the fields of toxicology, pharmacology, medicine, epidemiology, neurophysiology, developmental psychology, public health, nutrition, statistics, exposure assessment, and risk assessment. Specifically, the committee was assigned the following tasks:

1. Evaluate the body of evidence that led to EPA's current RfD for MeHg. On the basis of available human epidemiological and animal toxicity data, determine whether the critical study, end point of toxicity, and uncertainty factors used by EPA in the derivation of the RfD for MeHg are scientifically appropriate. Sensitive subpopulations should be considered.
2. Evaluate any new data not considered in the 1997 *Mercury Study Report to Congress* that could affect the adequacy of EPA's MeHg RfD for protecting human health.
3. Consider exposures in the environment relevant to evaluation of likely human exposures (especially to sensitive subpopulations and especially from consumption of fish that contain MeHg). The evaluation should focus on those elements of exposure relevant to the establishment of an appropriate RfD.
4. Identify data gaps and make recommendations for future research.

[2]A reference dose is defined as an estimate of a daily exposure to the human population (including sensitive subpopulations) that is likely to be without a risk of adverse effects when experienced over a lifetime.

THE COMMITTEE'S APPROACH TO ITS CHARGE

To gather background information relevant to MeHg toxicity, the committee heard presentations from various government agencies, trade organizations, public interest groups, and concerned citizens. Representatives from the offices of Congressman Alan Mollohan (West Virginia) and Senator Patrick Leahy (Vermont) also addressed the committee.

The committee evaluated the body of evidence that provided the scientific basis for the risk assessments conducted by EPA and other regulatory and health agencies. The committee also evaluated new findings that have emerged since the development of EPA's current RfD and met with the investigators of major ongoing epidemiological studies to examine and compare the methods and results.

The committee was not charged to calculate an RfD for MeHg. Instead, in its report, the committee provides scientific guidance to EPA on the development of an RfD. To develop such guidance, the committee reviewed the health effects of MeHg to determine the target organ, critical study, end point of toxicity, and dose on which to base the RfD. Because various biomarkers of exposure (i.e., concentrations of Hg in hair and umbilical-cord blood) have been used to estimate the dose of MeHg ingested by individuals, the committee evaluated the appropriateness of those biomarkers for estimating dose and the extent to which individual differences can influence the estimates. Other sources of uncertainty in the MeHg data base that should be considered when deriving an RfD were also evaluated. To estimate the appropriate point of departure[3] to use in calculating an RfD, the committee statistically analyzed available dose-response data. A margin-of-exposure[4] analysis was also performed to assess the public-health implications of MeHg.

[3]The point of departure represents an estimate or observed level of exposure or dose which is associated with an increase in adverse effect(s) in the study population. Examples of points of departure include NOAELs, LOAELs, BMDs, and BMDLs.

[4]A margin-of-exposure analysis compares the levels of MeHg to which the U.S. population is exposed with the point of departure to characterize the risk to the U.S. population. The larger the ratio, the greater degree of assumed safety for the population.

THE COMMITTEE'S EVALUATION

Health Effects of Methylmercury

MeHg is rapidly absorbed from the gastrointestinal tract and readily enters the adult and fetal brain, where it accumulates and is slowly converted to inorganic Hg. The exact mechanism by which MeHg causes neurotoxic effects is not known, and data are not available on how exposure to other forms of Hg affects MeHg toxicity.

MeHg is highly toxic. Exposure to MeHg can result in adverse effects in several organ systems throughout the life span of humans and animals. There are extensive data on the effects of MeHg on the development of the brain (neurodevelopmental effects) in humans and animals. The most severe effects reported in humans were seen following high-dose poisoning episodes in Japan and Iraq. Effects included mental retardation, cerebral palsy, deafness, blindness, and dysarthria in individuals who were exposed in utero and sensory and motor impairment in exposed adults. Chronic, low-dose prenatal MeHg exposure from maternal consumption of fish has been associated with more subtle end points of neurotoxicity in children. Those end points include poor performance on neurobehavioral tests, particularly on tests of attention, fine-motor function, language, visual-spatial abilities (e.g., drawing), and verbal memory. Of three large epidemiological studies, two studies — one conducted in the Faroe Islands and one in New Zealand — found such associations, but those effects were not seen in a major study conducted in the Seychelles islands.

Overall, data from animal studies, including studies on nonhuman primates, indicate that the developing nervous system is a sensitive target organ for low-dose MeHg exposure. Results from animal studies have reported effects on cognitive, motor, and sensory functions.

There is also evidence in humans and animals that exposure to MeHg can have adverse effects on the developing and adult cardiovascular system (blood-pressure regulation, heart-rate variability, and heart disease). Some research demonstrated adverse cardiovascular effects at or below MeHg exposure levels associated with neurodevelopmental effects. Some studies demonstrated an association between MeHg and cancer, but, overall, the evidence for MeHg being carcinogenic is incon

clusive. There is also evidence in animals that the immune and reproductive systems are sensitive targets for MeHg.

On the basis of the body of evidence from human and animal studies, the committee concludes that neurodevelopmental deficits are the most sensitive, well-documented effects and currently the most appropriate for the derivation of the RfD.

Determination of the Critical Study for the RfD

The standard approach for developing an RfD involves selecting a critical study that is well conducted and identifies the most sensitive end point of toxicity. The current EPA RfD is based on data from a poisoning episode in Iraq. However, MeHg exposures in that study population were not comparable to low-level, chronic exposures seen in the North American population, and there are a number of uncertainties associated with the Iraqi data. In light of those considerations and more recent epidemiological studies, the committee concludes that the Iraqi study should no longer be considered the critical study for the derivation of the RfD.

Results from the three large epidemiological studies — the Seychelles, Faroe Islands, and New Zealand studies — have added substantially to the body of knowledge on brain development following long-term exposure to small amounts of MeHg. Each of the studies was well designed and carefully conducted, and each examined prenatal MeHg exposures within the range of the general U.S. population exposures. In the Faroe Islands and New Zealand studies, MeHg exposure was associated with poor neurodevelopmental outcomes, but no relation with outcome was seen in the Seychelles study.

Differences in the study designs and in the characteristics of the study populations might explain the differences in findings between the Faroe and the Seychelles studies. Differences include the ways MeHg exposure was measured (i.e., in umbilical-cord blood versus maternal hair), the types of neurological and psychological tests administered, the age of testing (7 years versus 5.5 years of age), and the patterns of MeHg exposure. When taking the New Zealand study into account, however, those differences in study characteristics do not appear to explain the

differences in the findings. The New Zealand study used a research design and entailed a pattern of exposure similar to the Seychelles study, but it reported associations with Hg that were similar to those found in the Faroe Islands.

The committee concludes that there do not appear to be any serious flaws in the design and conduct of the Seychelles, Faroe Islands, and New Zealand studies that would preclude their use in a risk assessment. However, because there is a large body of scientific evidence showing adverse neurodevelopmental effects, including well-designed epidemiological studies, the committee concludes that an RfD should not be derived from a study, such as the Seychelles study, that did not observe any associations with MeHg.

In comparing the studies that observed effects, the strengths of the New Zealand study include an ethnically mixed population and the use of end points that are more valid for predicting school performance. The advantages of the Faroe Islands study over the New Zealand study include a larger study population, the use of two measures of exposure (i.e., hair and umbilical-cord blood), extensive peer review in the epidemiological literature, and re-analysis in response to questions raised by panelists at a 1998 NIEHS workshop and by this committee in the course of its deliberations.

The Faroe Islands population was also exposed to relatively high levels of polychlorinated biphenyls (PCBs). However, on the basis of an analysis of the data, the committee concluded that the adverse effects found in the Faroe Islands study, including those seen in the Boston Naming Test,[5] were not attributable to PCB exposure and that PCB exposure did not invalidate the use of the Faroe Islands study as the basis of risk assessment for MeHg.

The committee concludes that, given the strengths of the Faroe Islands study, it is the most appropriate study for deriving an RfD.

Estimation of Dose and Biological Variability

In epidemiological studies, uncertainties and limitations in estimating

[5]The Boston Naming Test is a neuropsychological test that assesses an individual's ability to retrieve a word that appropriately expresses a particular concept. **07596**

exposures can make it difficult to quantify dose-response associations and can thereby lead to inaccuracies when deriving an RfD. An individual's exposure to MeHg can be estimated from dietary records or by measuring a biomarker of exposure (i.e., concentration of Hg in the blood or hair).

Dietary records, umbilical-cord-blood Hg concentrations, and maternal-hair Hg concentrations all provide different kinds of exposure information. Dietary records can provide information on Hg intake but depend on accurate knowledge of Hg concentrations in fish. The records also might be subject to problems with estimating portion size and capturing intermittent eating patterns. Umbilical-cord-blood Hg concentrations would be expected to correlate most closely with fetal-brain Hg concentrations during late gestation and correlate less well with Hg intake than do the other measures (e.g., dietary records and maternal-hair Hg concentration). Maternal-hair Hg concentrations can provide data on Hg exposure over time, but they might not provide as close a correlation with fetal-brain Hg concentrations as umbilical-cord-blood Hg concentrations, at least during the latter period of gestation. Use of data from two or more of these measurement methods increases the likelihood of uncovering true dose-response relationships. The use of either umbilical-cord-blood or maternal-hair Hg concentrations as biomarkers of exposure is adequate for estimating a dose received by an individual.

Individual responses to MeHg exposure are variable and a key source of uncertainty. Factors that might influence the responses include genetics, age, sex, health status, nutritional supplements, nutritional influences, including dietary interactions, and linking the time and intensity of MeHg exposure to the critical periods of brain development. In addition, people exposed to the same amount of MeHg can have different concentrations of Hg at the target organ because of individual variability in the way the body handles MeHg. Individual differences that affect the estimation of dose can be addressed in the derivation of the RfD by applying an uncertainty factor to the estimated dose. If an RfD is based on a Fig concentration in maternal-hair or umbilical-cord blood, adjusting by an uncertainty factor of 2-3 would account for individual differences in the estimation of dose in 95% to 99% of the general population.

Modeling the Dose-Response Relationships

An important step in deriving an RfD is choosing an appropriate dose to be used as the "point of departure" (i.e., the dose to which uncertainty factors will be applied to estimate the RfD). The best available data for assessing the risk of adverse effects for MeHg are from the Faroe Islands study. Because those data are epidemiological, and exposure is measured on a continuous scale, there is no generally accepted procedure for determining a dose at which no adverse effects occur. The committee concludes, therefore, that a statistical approach (i.e., calculation of a benchmark dose level, BMDL[6]) should be used to determine the point of departure for MeHg instead of identifying the dose at which no adverse effects occur or the lowest dose at which adverse effects occur. The committee cautions, however, that the type of statistical analysis conducted (i.e., the model choice — K power, logarithmic, or square root) can have a substantial effect on the estimated BMDL. The committee recommends the use of the K-power model with the constraint of $K \geq 1$, because it is the most plausible model from a biological perspective and also because it tends to yield the most consistent results for the Faroe Islands data. It should be noted that, for the data from the Faroe Islands study, the results of the K-power model with the constraint of $K \geq 1$ are equivalent to the results of the linear model.

The adverse effects observed in the Faroe Islands study were most sensitively detected when using cord blood as the biomarker. Based on cord-blood analyses from the Faroe Islands study, the lowest BMD for a neurobehavioral end point the committee considered to be sufficiently reliable is for the Boston Naming Test. Thus, on the basis of that study and that test, the committee's preferred estimate of the BMDL is 58 parts per billion (ppb)[7] of Hg in cord blood. To estimate this BMDL, the

[6]A benchmark dose level is the lowest dose, estimated from the modeled data, that is expected to be associated with a small increase in the incidence of adverse outcome (typically in the range of 1% to 10%).

[7]The BMDL of 58 ppb is calculated statistically and represents the lower 95% confidence limit on the dose (or biomarker concentration) that is estimated to result in a 5% increase in the incidence of abnormal scores on the Boston Naming Tes**07598**

committee's calculations involved a series of steps, each involving one or more assumptions and related uncertainties. Alternative assumptions could have an impact on the estimated BMDL value. In selecting a single point of departure, the committee followed established public-health practice of using the lowest value for the most sensitive, relevant end point.

In addition to deriving a BMDL based on the Faroe Islands study, the committee performed an integrative analysis of the data from all three studies to evaluate the full range of effects of MeHg exposure. The values obtained by the committee using that approach are consistent with the results of the benchmark analysis of the Boston Naming Test from the Faroe Islands study. Because an integrative analysis is not a standard approach at present, the committee does not recommend that it be used as the basis for an RfD.

Public-Health Implications

The committee's margin-of-exposure analysis based on estimates of MeHg exposures in U.S. populations indicates that the risk of adverse effects from current MeHg exposures in the majority of the population is low. However, individuals with high MeHg exposures from frequent fish consumption might have little or no margin of safety (i.e., exposures of high-end consumers are close to those with observable adverse effects). The population at highest risk is the children of women who consumed large amounts of fish and seafood during pregnancy. The committee concludes that the risk to that population is likely to be sufficient to result in an increase in the number of children who have to struggle to keep up in school and who might require remedial classes or special education. Because of the beneficial effects of fish consumption, the long-term goal needs to be a reduction in the concentrations of MeHg in fish rather than a replacement of fish in the diet by other foods. In the interim, the best method of maintaining fish consumption and minimizing Hg exposure is the consumption of fish known to have lower MeHg concentrations.

In the derivation of an RfD, the benchmark dose is divided by uncertainty factors. The committee identified two major categories of uncertainty, based on the body of scientific literature, that should be consid

ered when revising the RfD: (1) biological variability when estimating dose and (2) data-base insufficiencies. On the basis of the available scientific data, the committee concludes that a safety factor of 2-3 will account for biological variability in dose estimation. The choice of an uncertainty factor for data-base insufficiencies is, in part, a policy decision. However, given the data indicating possible long-term neurological effects not evident at childhood, immununotoxicity, and cardiovascular effects, the committee supports an overall composite uncertainty factor of no less than 10.

RESEARCH NEEDS

To better characterize the health effects of MeHg, the committee recommends further investigation of the following:

- The impacts of MeHg on the prevalence of hypertension and cardiovascular disease in the United States. Such data should be considered in a re-evaluation of the RfD as they become available.
- The relationships between low-dose exposure to MeHg throughout the life span of humans and animals and carcinogenic, reproductive, neurological, and immunological effects.
- The potential for delayed neurological effects resulting from Hg remaining in the brain years after exposure.
- The emergence of neurological effects later in life following low-dose prenatal MeHg exposure.
- The mechanisms underlying MeHg toxicity.

To improve estimates of dose and to clarify the impact of biological variability and other factors on MeHg dose-response relationships, the committee recommends the following:

- The analysis of hair samples to evaluate the variability in short-term exposures, including peak exposures. Hair that has been stored from the Seychelles and the Faroe Islands studies should be analyzed to determine variability in exposures over time.
- The collection of information on what species of fish are eaten at

specific meals to improve estimates of dietary intakes and temporal variability in MeHg intake.

- The assessment of factors that can influence individual responses to MeHg exposures in humans and animals. Such factors include age, sex, genetics, health status, nutritional supplement use, and diet. Food components considered to be protective against MeHg toxicity in humans also deserve closer study (e.g., wheat bran and vitamin E).

To determine the most appropriate methods for handling model uncertainty in benchmark analysis, the committee recommends that further statistical research be conducted.

To better characterize the risk to the U.S. population from current MeHg exposures, the committee recommends obtaining data on the following:

- Regional differences in MeHg exposure, populations with high consumptions of fish, and trends in MeHg exposure. Characterization should include improved nutritional and dietary exposure assessments and improved biomonitoring of subpopulations.
- Exposure to all chemical forms of Hg, including exposure to elemental Hg from dental amalgams.

RECOMMENDATIONS

On the basis of its evaluation, the committee's consensus is that the value of EPA's current RfD for MeHg, 0.1 µg/kg per day, is a scientifically justifiable level for the protection of public health. However, the committee recommends that the Iraqi study no longer be used as the scientific basis of the RfD. The RfD should still be based on the developmental neurotoxic effects of MeHg, but the Faroe Islands study should be used as the critical study for the derivation of the RfD. Based on cord-blood analyses from the Faroe Islands study, the lowest BMD for a neurobehavioral end point the committee considered to be sufficiently reliable is for the Boston Naming Test. For that end point, dose-response data based on Hg concentrations in cord blood should be modeled using

the K-power model ($K \geq 1$). That approach estimates a BMDL of 58 ppb of Hg in cord blood (corresponding to a BMDL of 12 ppm of Hg in hair) as a reasonable point of departure for deriving the RfD. To calculate the RfD, the BMDL should be divided by uncertainty factors that take into consideration biological variability when estimating dose and MeHg data-base insufficiencies. As stated earlier, given those considerations, an uncertainty factor of at least 10 is supported by the committee.

The committee further concludes that the case of MeHg presents a strong illustration of the need for harmonization of efforts to establish a common scientific basis for exposure guidance and to reduce current differences among agencies, recognizing that risk-management efforts reflect the differing mandates and responsibilities of the agencies.

1

INTRODUCTION

MERCURY (Hg) is a persistent substance that comes from natural and anthropogenic sources. Hg that enters our oceans, lakes, and rivers is converted to methylmercury (MeHg) by aquatic biota and bioaccumulates in aquatic food webs including fish and shellfish. Humans and wildlife are exposed to MeHg primarily through the consumption of contaminated fish,[1] particularly large predatory fish species such as tuna, swordfish, shark, and whale. In humans, MeHg is known to be neurotoxic. The fetus is more sensitive to those effects than the adult (EPA 1997a).

In 1997, the U.S. Environmental Protection Agency (EPA) issued two reports on Hg and its effects on public health to the U.S. Congress. The first of these reports, the *Mercury Study Report to Congress* (EPA 1997a,b,c), assessed the source and amount of Hg emissions in the United States, the detrimental effects of Hg on humans and wildlife, and the feasibility of control technologies. The second report, the *Study of Hazardous Air Pollutant Emissions from Electric Utility Steam Generating Units. Final Report to Congress* (EPA 1998), looked specifically at emissions from utility companies and cited Hg as a major contaminant,

[1]In this report, the term fish includes shellfish and marine mammals, such as the pilot whale, that are consumed by certain populations.

especially in emissions from coal-fired power plants. Because concerns have been raised about Hg exposure levels in the United States, particularly among sensitive populations, questions have arisen among federal agencies over what is an acceptable level of exposure to MeHg.

Due to disagreement over the appropriate level of concern for MeHg exposure, the potentially widespread implications for human health, and the challenges associated with further regulating Hg emissions, Congress directed EPA in the House Appropriations Report for EPA's Fiscal 1999 funding to contract with the National Research Council (NRC) to prepare recommendations on the appropriate value for a Hg exposure reference dose (RfD). In response, the NRC convened the Committee on the Toxicological Effects of Mercury, whose membership includes experts in toxicology, pharmacology, medicine, epidemiology, developmental psychology, neurophysiology, neuropsychology, public health, nutrition, statistics, exposure assessment, and risk assessment. The committee was charged with the following specific tasks:

1. Evaluate the body of evidence that led to the EPA-derived MeHg RfD. Human epidemiological and animal toxicity data should be the basis of the evaluation. The evaluation should determine the appropriateness of the critical study, end point of toxicity, and uncertainty factors used by EPA in deriving the RfD for MeHg. Sensitive populations should be considered.
2. Evaluate any new data (e.g., mechanistic data) that were not considered in EPA's 1997 Hg report that are relevant to EPA's MeHg RfD for protecting human health.
3. Consider exposure pathways (especially from the consumption of MeHg in fish) in evaluating likely human exposures, especially exposures of sensitive subpopulations. The evaluation should focus on those elements of exposure relevant to the establishment of an appropriate RfD.
4. Identify data gaps and make recommendations for future research.

Although the committee name, the Committee on the Toxicological Effects of Mercury, does not limit the scope of this report to MeHg, the committee focused on the health effects of this organic form of Hg because the toxicity due to this form is of greatest concern. In addition,

the committee did not attempt to establish an RfD for MeHg. Instead, the committee provides guidance to EPA on the data sets, exposure-assessment approaches, modeling techniques, and statistical analysis that should be considered in deriving an appropriate Hg RfD.

SOURCES OF HG

In the environment, Hg comes from natural and anthropogenic sources. Mercuric sulfide, or Hg in cinnabar, is the natural form of Hg. The concentration of cinnabar varies greatly with the location of deposits. Hg can be released into the air through weathering of rock containing Hg ore or through human activities, principally incineration and burning of fossil fuels. Hg is a global pollutant, that once released to the air can travel long distances and impact distant sites. Water contamination can occur from run-off water, contaminated by either natural or anthropogenic sources, or from air deposition. Potential sources of general population exposure to Hg include inhalation of Hg vapors in ambient air, ingestion of drinking water and foodstuffs contaminated with Hg, and exposure to Hg from dental amalgams and medical treatments. Dietary intake is one of the most important sources of non-occupational exposure to Hg, fish and other seafood products being the dominant source of Hg in the diet. Most of the Hg consumed in fish or other seafood is the highly absorbable MeHg form. The substantial variation in human MeHg exposure is based on the differences in frequency and amount of fish consumed and Hg concentration in the fish. MeHg exposure is a major problem in some populations, especially subsistence fish eaters who consume large amounts of fish (EPA 1997a). Intake of elemental Hg from dental analgams is another major contributing source to the total Hg body burden in humans in the general population (IPCS 1990, 1991).

The World Health Organization (WHO) has estimated that anthropogenic sources, mainly the combustion of fossil fuels, contribute 25% of the overall (natural and anthropogenic) Hg emissions to the atmosphere (ATSDR 1999). EPA has estimated that those sources account for 50% to 75% of the total yearly input of Hg into the atmosphere (EPA 1997a). In the United States, the majority of Hg emissions are from

combustion sources. Medical and municipal waste incinerators and coal-fired utility boilers account for greater than 80% of the Hg emitted from point sources (EPA 1997b; ATSDR 1999).

FATE AND TRANSPORT

Hg has three valence states (Hg^0, Hg^{1+}, Hg^{2+}) and is found in the environment in the metallic form and in various inorganic and organic complexes. The natural global bio-geochemical cycling of Hg is characterized by degassing of the element from soils and surface waters, atmospheric transport, deposition of Hg back to land and surface water, sorption of the compound onto soil or sediment particles, and revolatilization from land and surface water (see Figure 1-1). This emission, deposition, and revolatilization creates difficulties in tracing the movement of Hg to its sources (ATSDR 1999). Once in the environment, interconversion between the different forms of Hg can occur. Particulate-bound Hg can be converted to insoluble Hg sulfide and precipitated or bioconverted into more volatile or soluble forms that re-enter the atmosphere or are bioaccumulated in aquatic and terrestrial food chains. Conversion of inorganic Hg to MeHg occurs primarily in microorganisms especially in aquatic systems. Once in its methylated form, Hg bioaccumulates up the food chain; the microorganisms are consumed by fish, and the smaller fish are consumed by larger fish. Such bioaccumulation can result in very high concentrations of MeHg in some fish, which are one of the main sources of human and piscivorus wildlife exposure to MeHg.

HEALTH EFFECTS

Human exposure to MeHg from contaminated fish and seafood can pose a variety of health risks. A spectrum of adverse health effects has been observed following MeHg exposure, with the severity depending largely on the magnitude of the dose. Fatalities and devastating neurological damage were observed in association with the extremely high exposures that occurred during the Minamata and Iraqi poisoning

episodes. The fetus is considered much more sensitive than the adult. Prenatal exposures interfere with the growth and migration of neurons and have the potential to cause irreversible damage to the developing central nervous system (EPA 1997a). Infants exposed in utero to MeHg during the Minamata and Iraqi episodes were born with severe disabilities, such as mental retardation, seizure disorders, cerebral palsy, blindness, and deafness. At much lower doses that result from chronic maternal fish consumption, infants might appear normal during the first few months of life but might later display deficits in subtle neurological end points (e.g., IQ deficits, abnormal muscle tone, decrements in motor function, attention, and visuospatial performance).

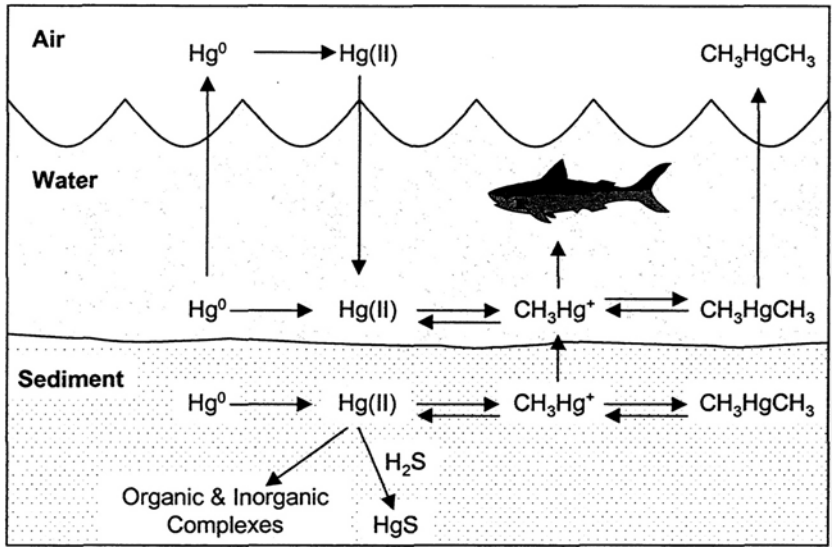

FIGURE 1-1 Cycling of Hg in aquatic system. CH_3Hg^+, methylmercury ion; CH3HgCH3, dimethylmercury; Hg(ll), mercuric mercury; Hg^0, elemental mercury; H_2S, hydrogen sulfide; HgS, cinnabar. Source: Adapted from EPA 1997b.

Exposures that occur during childhood and adulthood can also cause damage to the central nervous system, as evidenced by human poison

ing incidents in Japan, Iraq, and the United States, in which the first signs of toxicity often appear several months after exposure has ended (EPA 1997b, Davis et al. 1994).

There is evidence that MeHg also effects other systems. In 1995, researchers in Finland found a correlation between consumption of MeHg-contaminated fish and the risk of acute myocardial infarction (Salonen et al., 1995). This prospective study of 1,833 fishermen was intended to confirm previous studies in which fish consumption was associated with a reduced risk of heart disease. Instead, they discovered that hair Hg levels above 2 parts per million (ppm), or daily ingestion of more than 30 grams (g) of fish, increased the risk of acute myocardial infarction (AMI) or cardiovascular death 2- to 3-fold. The estimated daily dietary Hg intake ranged from 1.1 µg to 95.3 µg (mean, 7.6 µg). The investigators theorized that the cardiovascular effects of MeHg might be caused, at least in part, by the ability of Hg to enhance lipid peroxidation via a Fenton-type reaction.

Inorganic and organic forms of Hg are also well-known renal toxicants. Human case investigations and animal feeding studies have repeatedly confirmed that effect. Human exposures to organic Hg have resulted in symptoms of polyuria and albuminuria (Jalili and Abbasi 1961; Cinca et al. 1979). Autopsies of patients who died following ingestion of alkyl Hg revealed nephritis and tubular degeneration (Al Saleem 1976; Cinca et al. 1979). Animal studies have shown that MeHg damages the proximal tubules in the kidney (Mitsumori et al. 1990).

During the past decade, researchers have studied the effects of MeHg on immune function and blood-pressure regulation. After administering MeHg to mice for 12 weeks, IIbäck (1991) noted changes in the thymus and natural killer-cell activity. Sørensen et al. (1999) found an association between prenatal exposure to MeHg and childhood blood pressure. Diastolic and systolic blood pressures, measured at age 7, increased 13.9 millimeters (mm) and 14.6 mm, respectively, as cord-blood Hg concentrations rose from 1 to 10 micrograms per liter (µg/L).

EXPOSURE EVENTS AND STUDIES

Between 1950 and 1975, several MeHg poisoning incidents occurred in Japan and Iraq. Scientists who investigated those events identified

developmental neurotoxicity as the health effect of greatest concern following high-level episodic exposures. Individuals poisoned by MeHg through consumption of contaminated fish in Japan exhibited paresthesia, ataxia, sensory disturbances, tremors, impairment of hearing, and difficulty walking (Harada 1995). In Iraq, exposure was due to the consumption of home-made bread that was made with grain treated with MeHg as a fungicide. In that outbreak, the most common symptom in adults was paresthesia; the most severely affected individuals exhibited ataxia, blurred vision, slurred speech, hearing difficulties, blindness, deafness, and death (Marsh et al. 1987). In both Iraq and Japan, the effects in offspring who were exposed to MeHg in utero were more serious, and in some cases seen at lower doses, than in adults. Both exposure episodes have been studied to determine the doses and the effects resulting from exposure to MeHg. Although the doses that produced those effects in the Japanese and Iraqi populations were undoubtedly quite high, precise dose-response relationships have not been established, and the exposure scenarios are not comparable to the low-dose chronic exposure that the general population in North America might experience.

In an attempt to establish dose-response relationships, three large prospective epidemiological studies have evaluated subtle end points of neurotoxicity. One study was conducted in the Republic of the Seychelles, a nation of islands located in the Indian Ocean off the coast of East Africa (Davidson et al. 1995, 1998). Another major study was conducted in the Faroe Islands (part of Denmark), which are located in the North Sea between Scotland and Iceland (Grandjean et al. 1997, 1998, 1999). The other major study was conducted in New Zealand (Kjellström et al. 1986, 1989). The populations of the Seychelles, Faroe Islands, and New Zealand were chosen for study, because their dietary dependence on fish and marine mammals provides an ongoing source of exposure to MeHg. Prenatal MeHg exposures in those populations were within the range of at least some U.S. population exposures. All three studies evaluated large numbers of subjects.

The 66-month study of 711 children in the Seychelles islands assessed the effects of prenatal MeHg in tests of global intelligence and developmental milestones. No adverse effects were seen that could be attributed to MeHg. Maternal hair samples collected at birth contained Hg concentrations that ranged from 0.5 to 27 ppm (mean, 6.8 ppm). Meanwhile,

scientists working in the Faroe Islands found that children whose prenatal exposures were similar to those observed in the Seychelles population had subtle developmental dose-related deficits that were apparent at 7 years of age. Abnormalities were seen in tests of memory, attention, and language and, to a lesser extent, in neurophysiological end points. Measurements of blood pressure, heart rate, and heart-rate variability were also taken when the children reached 7 years of age. Researchers found that diastolic and systolic blood pressures increased, and hfeartrate variability decreased as cord-blood Hg concentrations rose from 1 to 10 μg/L.

A prospective study carried out in New Zealand (Kjellström et al. 1986, 1989) examined the effects in offspring exposed in utero to MeHg via maternal consumption of fish. Scores on the Denver Developmental Screening Test (DDST), a standardized test for childhood mental and motor development, were compared in groups of children 4 years of age categorized by maternal Hg exposure (as measured in parts per million in maternal hair) (Kjellström et al. 1986). At 6 years of age, a battery of specific cognitive tests was administered (Kjellström et al. 1989). At both ages, the researchers found significant decrements in test performance in the children exposed to moderate-to-high doses of MeHg prenatally (more than 6 ppm).

A correlation was demonstrated between hair Hg concentrations and neurophysiological effects in a study of an adult population in the Amazon, where gold-mining activities have resulted in fish highly contaminated with Hg (Lebel et al. 1996). In that study population, it is likely that the adult population was also exposed to MeHg in utero.

The studies of the Iraqi, Amazon, Seychelles, and Faroe Islands populations were reviewed by an expert panel that met in Raleigh, North Carolina, at the Workshop on the Scientific Issues Relevant to Assessment of Health Effects from Exposure to MeHg. A report of that workshop has been published (NIEHS 1998). In suggesting possible explanations for the discrepant findings of the Seychelles and Faroe studies, the panel pointed to differences in sources of exposures or exposure measures, differences in the neurobehavioral tests used or their administration or interpretation, influences of confounders and covariates, and biostatistical issues involved in the analysis of the data. The differences between those studies are discussed further in Chapter 6.

SUMMARY OF RISK ASSESSMENTS FOR MEHG

State and national governments as well as international organizations have recommended acceptable levels of Hg exposure that are thought to be protective against adverse effects (see Table 1-1). General risk assessment approaches used by the various agencies are described in NRC (1983) and NRC (1984). In this report, information on how EPA derives an RfD can be found in the section on Risk Assessment for Noncancer End Points in Chapter 7. Specific details on the derivation of EPA's MeHg RfD can be found in the section on The Current EPA Reference Dose in Chapter 8. In the United States, responsibility for regulating Hg is shared by two federal agencies: the Food and Drug Administration (FDA) and EPA. FDA is responsible for ensuring that Hg concentrations in commercially sold fish and seafood do not exceed what the agency defines as an action level for this contaminant (FDA 1979). EPA monitors Hg concentrations in the environment and regulates industrial releases to air and surface water. Although not a regulatory agency, the Agency for Toxic Substances and Disease Registry (ATSDR) evaluates the potential for humans to be exposed to MeHg and investigates reported health effects. Currently, each of these agencies uses a different guideline to assess exposure to toxicants.

The differences in guidelines among the agencies are due to the use of different risk-assessment methods, data sets, and uncertainty factors and the different mandates of each agency (EPA 1984, 2000; FDA 1979; ATSDR 2000). For example, EPA used data from the 1971 Iraqi poisoning incident to derive an RfD of 0.1 microgram per kilogram (µg/kg) of body weight per day for MeHg (EPA 1997a). The reference dose was calculated using a benchmark dose of 1.1 µg/kg per day. That benchmark dose was divided by uncertainty factors(UF) to account for the variability in the human population (UF of 3) and for the lack data on reproductive effects, sequelae, and adult paresthesia (UF of 3). Although MeHg is classified by the agency as a possible human carcinogen, no uncertainty factor was used to protect against that effect. The RfD calculated by EPA was in the range of other values obtained by EPA using similar analysis of other data sets.

In 1998, ATSDR used the Seychelles study (Davidson et al. 1998) as the starting point for estimating a minimal risk level for exposure to MeHg (ATSDR 1999). In this study, the investigators examined

TABLE 1-1 Summary of Risk Assessments for Methylmercury

Agency	Key Studies	End Points	Biomarker and Exposure Level	Critical Dose	Uncertainty Factors	Acceptable Level
EPA[a]	Iraqi study (Marsh et al. 1987)	Combined instance of neurological effects following in utero exposure[b]	Maternal hair, 11 ppm; equivalent to intake of 1.1 µg/kg/d	Benchmark dose, 1.1 µg/kg/d[c]	UF, 10[d]	RfD, 0.1 µg/kg/d (based on fetal effects)
ATSDR	Seychelles study (Davidson et al. 1998)	Developmental neurotoxicity measured by neurological evaluation, behavioral, psychological tests	Maternal hair, 15.3 ppm; equivalent to intake of 1.3 µg/kg/d	NOAEL, 1.3 µg/kg/d	UF, 4.5[e]	MRL, 0.3 µg/kg/d
FDA	Japanese data (Friberg et al. 1971)	Overt neurological symptoms in adults	Adult blood, 0.2 ppm; equivalent to intake of 300 µg/d	LOAEL, 4.3 µg/kg/d	SF, 10[f]	Action level in fish, 1 ppm in edible portion[g] (equivalent to 0.5 µg/kg/d)
JECFA[h]	Japanese data (Friberg et al. 1971)	Overt neurological symptoms in adults	Adult blood, 0.2 ppm; equivalent to intake of 300 µg/d	LOAEL, 4.3 µg/kg/d	SF of 10[i]	pTWI, 3.3 µg/kg/wk (equivalent to 0.5 µg/kg/d)
Health Canada	Seychelles study (Davidson et al.1998); Faroe Islands (Grandjean et al. 1997); New Zealand (Kjellstrom 1986, 1989)	Developmental neurotoxicity	Maternal hair, 10 ppm; equivalent to intake of 1 µg/kg/d	Benchmark dose, 1 µg/kg/d[j]	UF, 5[k]	pTDI, 0.2 µg/kg/d (for women of childbearing ages, infants, and young children)[l]

North Carolina	Seychelles study (Davidson et al. 1998)	Developmental neurotoxicity	Maternal hair, 6.8 ppm; equivalent to intake of 0.5 µg/kg/d	Arithmetic mean,[m] 0.5 µg/kg/d	Modifying factor, 3	RfD, 0.2 µg/kg/d (for women of childbearing age and developing fetuses)[n]
Washington State	Faroe Islands (Grandjean et al.1997)	Impaired neurological development and longterm or delayed sequelae in children	Maternal hair, 4.3-10 ppm; equivalent to intake of 0.35-0.8 µg/kg/d	Daily intake range,[0] 0.35-0.8 µg/kg/d	UF, 10[p]	TDI, 0.035-0.08 µg/kg/d

[a]EPA report to Congress states that "a number of additional studies of human populations generally support the dose range of the benchmark dose level for perinatal effects." The agency is awaiting the results of this NRC report before updating its RfD based on more recent data.

[b]The data for delayed onset of walking and talking, neurological scores of less than 3, mental symptoms, and seizures were grouped together for this analysis.

[c]EPA carried out the analysis using the polynomial model and the Weibull model. The results of the two models were within 3% of each other. EPA based its analysis on the Weibull model due to goodness of fit and history of use. The Benchmark dose is an estimate of an experimental dose associated with a specified low incidence of adverse effects.

[d]According to the Integrated Risk Information System (IRIS), the following uncertainty factors were applied: 3 for the variability in human population (variability in the half-life of methylmercury and in hair-to-blood ratio) and 3 for the lack of a two-generation reproductive study and data on the effect of exposure duration on sequelae of the developmental neurotoxicity effects and on adult paresthesia.

[e]The following uncertainty factors were applied: 1.5 for human pharmacokinetic variability, 1.5 for human pharmacodynamic variability and 1.5 to account for domain-specific findings in the Faroe study.

[f]Arbitrary value; the *Federal Register* states that, in cases in which human data are available, the safety factor used is 10.

[g]This conversion was calculated using fish consumption data from the National Marine Fisheries Service.

[h]The Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA) concluded in 1999 that "the information available was insufficient for evaluating the neurodevelopmental effects on offspring of mothers with low intakes of methylmercury."

[i]In the absence of relevant toxicodynamic and toxicokinetic data, the committee uses a safety factor of 10 when the pTWI is based on human data.
[j]An approximate benchmark dose determined by qualitatively looking at the data.
[k]Arbitrary value.
[l]Health Canada also maintains the provisional TDI for adults of 0.47 microgram per kilogram (µg/kg) of body weight per day that was established by JECFA.
[m]Arithmetic mean exposure value for entire Seychelles cohort.
[n]North Carolina also maintains an RfD for nonsensitive populations of 0.5 µg/kg of body weight per day.
[o]Obtained using the algorithm relating Hg levels in blood to a daily intake level as described by ATSDR (1997). The geometric average maternal hair level of 4.3 ppm was used because the regression relationship between MeHg exposure and adverse effects was described from the entire cohort and the average value reflects that cohort (not withstanding that the regression may be driven by values close or below the average value), while 10 ppm represents the cutoff value used in the bivariate categorical analyses which showed a significant difference for MeHg above and below that value.
[p]Accounts for interindividual pharmacokinetic variability associated with determining a tolerable intake level based on hair mercury concentrations, for uncertainty associated with toxicodynamic variations within the populations, and for the lack of ability to address long-term or delayed sequelae.
Abbreviations: EPA, Environmental Protection Agency; ATSDR, Agency for Toxic Substances and Disease Registry; FDA; Food and Drug Administration;NOAEL;no-observed-adverse-effect level;LOAEL, lowest-observed-adverse-effect level; UF, uncertainty factor; SF, safety factor; RfD, reference dose (an amount of a substance that is anticipated to be without adverse health effects in humans, including sensitive populations, when ingested daily over a lifetime; MRL, minimal risk level (an estimate of daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse noncancer health effects over a specified route and duration of exposure); pTDI, provisional tolerable daily intake (maximum daily exposure level to a contaminant; provisional meaning that it is considered temporary until more data are available, especially the completed Seychelles study); JECFA, Joint FAO/WHO Expert Committee on Food Additives; pTWI, provisional tolerable weekly intake.

the correlation between subtle neurological effects and low-dose chronic exposure to MeHg. No correlation between Hg concentrations and neurological effects was seen. ATSDR determined a minimal risk level of 0.3 µg/kg per day, based on a dose of 1.3 µg/kg per day, which reflects the average concentration of the upper quintile of the exposed population but does not necessarily correspond to a no-observed-adverse-effect level (NOAEL). The agency used two uncertainty factors of 1.5 each to account for pharmacokinetic and pharmacodynamic variability within the human population. A modifying factor of 1.5 was applied to account for the possibility that domain-specific tests used in the Faroe Islands study might have allowed detection of subtle neurological effects that were not evaluated in the Seychelles cohort. Although the conventional risk-assessment approach is to multiply uncertainty factors, the agency summed these factors to develop an overall safety factor of 4.5.

According to Tollefson and Cordle (1986), FDA used data from the Minamata Bay poisoning episode to determine the action level of 1 ppm (in the edible portion of fish), which corresponds to a daily intake of 0.5 µg/kg (Friberg et al. 1971). FDA followed the approach taken by the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA), who had determined a provisional tolerable weekly intake (pTWI) of 0.5 µg/kg in adults and stated that the fetus and children might be more sensitive but that the data are insufficient to determine a safe intake in these populations (JECFA 1972). That pTWI was recently confirmed at the JECFA meeting in June 1999 (JECFA 1999). Canadian recommendations are based on the JECFA pTWI in adults; however, Canada also has a provisional tolerable daily intake of 0.2 µg/kg per day for children and women of child-bearing years, an intake based on a qualitative assessment of available data (M.-T. Lo, Food Directorate, Health Canada, personal commun., June 1999). The effect on public health of using one dose rather than another to set acceptable exposure levels might be substantial, leaving open the question of which value best ensures public safety. Differences in acceptable levels can affect many government programs, including state fish advisories, and regulation of such industries as commercial fishing and electric power plants (Renner 1999).

SCIENTIFIC CONTROVERSIES AND SOURCES OF UNCERTAINTY

Many controversies surround the determination of what is an acceptable level of exposure to MeHg. Some of these controversies stem from the science underlying the toxicity data base for MeHg. For example, there is disagreement over which studies and which end points of concern should be used to derive an acceptable level. There is emerging evidence of potential effects on both the immune and cardiovascular systems at low doses. The contradictory findings from the Seychelles and Faroe Islands studies have made it difficult to determine an appropriate point of departure for risk assessment. Scientists also do not agree on whether Hg in hair or blood is the more appropriate biomarker or measurement of exposure. There is debate over the assumptions on the disposition and metabolism of MeHg that are used to extrapolate from a measured biomarker value to a corresponding Hg exposure level. In addition, there is debate over the assumptions on fish intake and the concentration of Hg in the fish that are used to determine a safe amount of fish for consumption. The choice of dose-response model and uncertainty factors, if any, is also controversial.

ORGANIZATION OF THE REPORT

The remainder of this report is organized into six chapters and an appendix. In Chapter 2, information on the chemistry, toxicokinetics, toxicodynamics, and exposure of MeHg is presented. Chapter 3 presents a discussion on toxicokinetic variability and other factors that influence variation in human sensitivity to MeHg. Those factors include age, genetics, and nutrition. In Chapter 4, issues involved in assessing MeHg exposure and dose are presented. The focus is on the selection and interpretation of dose metrics and the implications of the possible dose metrics for dose-response assessment and nutritional assessment. The health effects associated with the ingestion of MeHg are discussed in Chapter 5. Emphasis is placed on the more-recent studies with respect to the choice of end points, possible confounders, and sensitive subpopulations. Evidence from experimental animal studies is also discussed. In Chapter 6, a comparison of studies that are appropriate for risk assessment for MeHg is presented. Chapter 7 provides an evalua

tion of the various data sets and statistical approaches for deriving an acceptable Hg exposure level. Further details of one approach are provided in the appendix. In Chapter 8, the risks from ingestion of MeHg and the sources of uncertainty are characterized and the adequacy of the EPA MeHg RfD for protecting human health is evaluated. The public-health implications of exposure to MeHg, including the implications of choosing one Hg exposure level over another, and how these relate to state and federal concerns, such as fish advisories and consumption, are also addressed.

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2

CHEMISTRY, EXPOSURE, TOXICOKINETICS, AND TOXICODYNAMICS

THIS chapter presents background information that serves as a foundation for understanding the toxicology of MeHg. The chemical, toxicokinetic, and toxicodynamic properties of MeHg are presented. There is extensive literature on MeHg, and this review is not meant to be exhaustive. Although the primary emphasis of this report is on MeHg, this chapter includes discussions of other Hg species to provide a general review of the sources of exposure and toxicological properties of different Hg species. The emphasis is on human Hg data. Animal data are also discussed.

PHYSICAL AND CHEMICAL PROPERTIES

Chemical species of Hg that are of toxicological importance include the inorganic forms, elemental or metallic Hg (Hg^0), mercurous Hg (Hg^{1+}), and mercuric Hg (Hg^{2+}), and the organic forms, MeHg and ethylmercury. Although there are many organic Hg compounds, the emphasis in this chapter is on MeHg. The structure, chemical formula, and physical and chemical properties of some Hg-containing compounds are shown in Table 2-1. A more complete table of physical and chemical properties of some Hg compounds can be found in the Agency of Toxic Substances and Disease Registry (ATSDR) *Toxicological Profile for Mercury (Update)* (ATSDR 1999). Table 2-2 summarizes the informa

tion on some toxicologically relevant Hg compounds discussed later in this chapter.

TABLE 2-1 Physical and Chemical Properties of Some Toxicologically Relevant Mercury Compounds

Chemical Name	Elemental Mercury[a]	Mercuric Chloride	Mercurous Chloride[b]	Methylmercuric Chloride [c]	Dimethylmercury
Molecular formula	Hg^0	$HgCl_2$	Hg_2Cl_2	CH_3HgCl	C_2H_6Hg
Molecular structure		Cl-Hg-Cl	Cl-Hg-Hg-Cl	CH_3-Hg-Cl	CH_3-Hg-CH_3
Molecular weight	200.59	271.52	472.09	251.1	230.66
Solubility	5.6×10^{-5} g/L at 25°C	69 g/L at 20°C	2.0×10^{-3} g/L at 25° C	0.100 g/L at 21°C	1 g/L at 21°C
Density	13.534 g/cm_3 at 25°C	5.4 g/cm_3 at 25°C	7.15 g/cm_3 at 19° C	4.06 g/cm_3 at 20°C	3.1874 g/cm_3 at 20°C
Oxidation state	+1, +2	+2	+1	+2	+2

[a]Also known as metallic mercury.
[b]Also known as calomel.
[c]Methylmercuric chloride is used experimentally to investigate the effects of methylmercury.

At 25° C, elemental Hg has a water solubility of 5.6×10^{-5} g/L. Mercuric chloride is considerably more soluble, having a solubility of 69 g/L at 20° C. In comparison, an organic Hg compound, such as methylmercury chloride, is much less water soluble, having a solubility of 0.100 g/L at 21° C. Dimethylmercury, a very toxic by-product of the chemical synthesis of MeHg (Nierenberg et al. 1998), also has a relatively low water solubility (1.0 g/L at 21° C). Due to its low water solubility, MeHg chloride is considered to be relatively lipid soluble. As discussed later in this chapter, the solubility of the different forms of Hg might play a role in their differential toxicity.

TABLE 2-2 Summary Table Comparing Toxicologically Relevant Mercury Species

Methylmercury (CH_3Hg^+)	Elemental Mercury (Hg^0)	Mercuric Mercury (Hg^{2+})
Sources of Exposure		
Fish, marine mammals, crustaceans, animals and poultry fed fish meal	Dental amalgams, occupational exposure, Caribbean religious ceremonies, fossil fuels, incinerators	Oxidation of elemental mercury or demethylation of MeHg; deliberate or accidental poisoning with $HgCl_2$
Biological Monitoring		
Hair, blood, cord blood	Urine, blood	Urine, blood
Toxicokinetics		
Absorption		
Inhalation: Vapors of MeHg absorbed	Inhalation: Approximately 80% of inhaled dose of Hg^0 readily absorbed	Inhalation: Aerosols of $HgCl_2$ absorbed
Oral: Approximately 95% of MeHg in fish readily absorbed from GI tract	Oral: GI absorption of metallic Hg is poor; any released vapor in GI tract converted to mercuric sulfide and excreted	Oral: 7-15% of ingested dose of $HgCl_2$ absorbed from the GI tract; absorption proportional to water solubility of mercuric salt; uptake by neonates greater than adults
Dermal: In guinea pigs, 3-5% of applied dose absorbed in 5 hr	Dermal: Average rate of absorption of Hg^0 through human skin, 0.024 ng/cm^2 for every 1 mg/m$_3$ in air	Dermal: In guinea pigs, 2-3% of applied dose of $HgCl_2$ absorbed
Distribution		
Distributed throughout body since lipophilic; approximately 1-10% of absorbed oral dose of MeHg distributed to blood; 90% of blood MeHg in RBCs	Rapidly distributed throughout the body since it is lipophilic	Highest accumulation in kidney; fraction of dose retained in kidney dose dependent

MeHg-cysteine complex[a] involved in transport of MeHg into cells		
Half-life in blood, 50 d; 50% of dose found in liver; 10% in head.	Half-life in blood, 45 d (slow phase); half-life appears to increase with increasing dose	Half-life in blood, 19.7-65.6 d; 1st phase, 24 d, 2nd phase, 15-30 d
Readily crosses blood-brain and placental barriers	Readily crosses blood-brain and placental barriers	Does not readily penetrate blood-brain or placental barriers In neonate, mercuric Hg not concentrated in kidneys; therefore, more widely distributed to other tissues In fetus and neonate, blood-brain barrier incompletely formed, so mercuric Hg brain concentrations higher than those in adults
Biotransformation		
MeHg slowly demethylated to mercuric Hg (Hg^{2+})	Hg^0 in tissue and blood oxidized to Hg^{2+} by catalase and hydrogen peroxide (H_2O_2); H_2O_2 production the rate-limiting step	Hg^0 vapor exhaled by rodents following oral administration of mercuric Hg
Tissue macrophages, intestinal flora, and fetal liver are sites of tissue demethylation		Mercuric Hg not methylated in body tissues but GI microorganisms can form MeHg

Mechanisms of demethylation unknown; free radicals demethylate MeHg in vitro; bacterial demethylation enzymes studied extensively, none has been characterized or identified in mammalian cells		
Does not bind or induce metallothionein		Binds and induces metallothionein
Excretion		
Daily excretion, 1% of body burden; major excretory route is bile and feces; 90% excreted in feces as Hg^{2+}; 10% excreted in urine as Hg^{2+}	Excreted as Hg^0 in exhaled air, sweat, and saliva, and as mercuric Hg in feces and urine	Excreted in urine and feces; also excreted in saliva, bile, sweat, exhaled air, and breast milk
Lactation increases clearance from blood; 16% of Hg in breast milk is MeHg		
Half-Life limination		
(Whole body) 70-80 d; dependent on species, dose, sex, and animal strain	58 d	1-2 mo
Toxicodynamics		
Critical target organ		
Brain, adult and fetal	Brain and kidney	Kidney
Causes of Toxicity		
Demethylation of MeHg to Hg^{2+} and the intrinsic toxicity of MeHg	Oxidation of Hg^0 to Hg^{2+}	Hg^{2+} binding to thiols in critical enzyme (e.g., cysteine) and structural proteins

Latency period		
In Iraq, from weeks to month; in Japan, more than a year; differences suggested to be caused by Se in fish; no toxic signs during latency period		
Mobilization		
DMPS, DMSA	After oxidation to Hg^{2+}: DMPS, DMSA	DMPS, DMSA
Possible Antagonists		
Selenium, garlic, zinc		

[a]MeHg-cysteine complex is structurally analogous to methionine.

Abbreviations: $HgCl_2$, mercuric chloride; DMPS, 2,3-dimercapto-1-propane sulfonate; DMSA, meso 2,3-dimercaptosuccinic acid; GI, gastrointestinal tract; RBC red blood cells.

METHODS OF CHEMICAL ANALYSIS

The methods used for analyzing Hg in biological samples include atomic absorption spectrometry (AAS), atomic fluorescence spectrometry (AFS) (Vermeir et al. 1991a, b), X-ray fluorescence (XRF) (Marsh et al. 1987), gas chromatography (GC)-electron capture (Cappon and Smith 1978), and neutron activation analysis (NAA) (Fung et al. 1995). Anodic stripping voltammetry (ASV) has also been used (Liu et al. 1990). Of those procedures, GC-electron capture is able to distinguish MeHg from other species, but only cold vapor (CV)-AAS will detect Hg at parts per billion. CV-AAS, AFS, XRF, and NAA have all been used to analyze Hg content in hair (Zhuang et al. 1989).

To measure total Hg in biological samples, the Hg must first be reduced to the elemental form. CV-AAS is most frequently used to measure Hg in urine (Magos and Cernik 1969) and blood (Magos and Clarkson 1972). For example, CV-AAS, the most commonly used method for analyzing Hg in biological samples, involves reduction of the Hg in the sample with stannous chloride to elemental Hg. To measure inorganic Hg, the analysis is carried out without chemical reduction of the sample. The difference between the total Hg concentration and the inorganic Hg concentration represents the concentration of organic Hg that was present in the sample.

Biological samples containing MeHg can also be analyzed using *Pseudomonas putida* strain FB1. That bacteria converts MeHg to methane gas and elemental Hg (Baldi and Filippelli 1991). This method is one of the most reliable and specific methods for MeHg quantification, because chemical interference is negligible. It can detect 15 ng of MeHg in 1 g of biological tissue with a coefficient of variation of 1.9%.

New methods for analyzing Hg in biological samples have been developed such as inductively coupled plasma-mass spectrometry (ICPMS) (Kalamegham and Ash 1992). Most of the new methods are expensive and beyond the reach of most laboratories. The cost is approximately $150,000-250,000 for the instrument and more than $35,000 a year for gases and maintenance costs.

Regardless of the analytical method used, care must be taken to eliminate or prevent contamination of the sample by Hg during preparation and analysis. All glassware and plasticware used for collection and analysis of the specimen must be acid washed. In addition, care must

be taken to avoid losses due to volatilization of elemental Hg and MeHg, especially when preserving or concentrating the samples.

Many procedures require the digestion of the sample before reduction. When attempting to quantify Hg content, especially in biological samples, data are needed to validate the procedures and their use in a given laboratory. All the methods of analysis are prone to large variations.

Biological monitoring of inorganic Hg, including elemental Hg, requires measurement of Hg concentrations in blood, urine, or both (Clarkson et al. 1988). Biological monitoring for MeHg usually involves measuring Hg content in scalp hair, blood, or both. The MeHg incorporated into hair is stable and can be used for longitudinal timing (historical record) of exposure to MeHg by analyzing segments of hair (Phelps et al. 1980; IPCS 1990; Grandjean et al. 1992; Suzuki et al. 1992). One source of error in hair Hg analysis is the presence of Hg on the hair surface due to external deposition. Adequate washing of the hair sample before analysis minimizes that error (Francis et al. 1982).

An excellent summary of the analytical methods for determining various species of Hg in biological specimens, including blood, urine, hair, breath, and tissues, as well as in environmental samples can be found in Table 6-1 in *Toxicological Profile for Mercury (Update)* (ATSDR 1999) and in the World Health Organization (WHO) report *Methylmercury* (IPCS 1990).

EXPOSURES TO MEHG IN THE U.S. POPULATION

The major source of MeHg exposure in humans is consumption of fish, marine mammals, and crustaceans. Because exposure to MeHg occurs almost entirely through fish consumption and varies according to the types of fish consumed, variations in exposure to MeHg in the U.S. population are based on individual characteristics of fish consumption. Exposure also varies according to the characteristic amounts and types of fish consumed in different regions of the United States. Hg concentrations in commercial fish and seafood in the United States span about two orders of magnitude. For example, herring contains Hg at approximately 0.01 ppm and shark contains Hg at greater than 1 ppm (EPA 1997a). Limited data suggest that coastal regions generally have

higher rates of fish consumption (Rupp et al. 1980). In addition, specific ethnic and cultural subgroups, as well as recreational fishermen, can have increased exposures (EPA 1997a). Population-based estimates of MeHg exposure in the United States have been made on the basis of dietary assessment studies, which provide information on fish consumption by species and by portion size. The combination of intake frequency by species and portion size by species for each individual consumer provides an estimate of the average mass of fish consumed (in grams per day). Summaries of such studies giving national data are provided in EPA's report to Congress (EPA 1997a). Another such dietary assessment study was conducted in New Jersey (Stern et al. 1996). To estimate population-based MeHg exposure from such studies, the gram-per-day amount of each species consumed by each individual is multiplied by the characteristic MeHg concentration of each species (microgram per gram) and then is summed across species to give the average intake of MeHg by each individual (microgram/day). The distribution of individual intakes for the study sample can then provide an estimate of MeHg intake in the underlying population. Uncertainties in such assessments include those in recall and recording of intake frequency and portion size, misidentification of the species consumed, extrapolation of short-term dietary studies to long-term average exposure, and the outdated and incomplete national database on average MeHg concentrations of different fish species. Estimates also typically vary depending on the length of time over which the fish-intake data was obtained (e.g., 1-day recall versus 1-week recall). These uncertainties are discussed by EPA (1997a) and Stern et al. (1996). Table 2-3 presents the EPA (1997c) analysis of MeHg intake for the general population and for the population of women of childbearing age based on fish-consumption data for month-long consumption. Estimates based on intake from such data are generally lower than those based on 1-day dietary data. Table 2-3 also presents data from New Jersey based on a 7-day recall survey. These data, along with the study by Rupp et al. 1980, suggest that the population in that region of the United States has higher intakes than the U.S. population in general. Estimates of population exposure and risk based on the average exposure of the U.S. population might, therefore, underestimate exposure to large subpopulations. Upon completion, data from Continuing Survey of Food Intakes by Individuals (CFSII) and National Health and Nutrition Examination

Survey (NHANES IV) might provide information on regional fish consumption. NHANES IV is also designed to provide information on MeHg exposure in U.S. populations.

TABLE 2-3 Estimated Average MeHg Intake for the U.S. Population and for New Jersey Fish Consumers

Average Daly Intake of MeHg (μg/day)[a]				
Percentiles of the Population	General Population		Women of Childbearing Age	
	U.S.[b,c]	New Jersey[d]	U.S.[b,e]	New Jersey[c,f]
50th	1.4	3.1	0.6	3.2
75th	3.5	5.8	1.8	5.4
90th	9.1	13.1	4.8	10.8
95th	15.6	21.1	7.8	15.7
99th		49.9	22.2	26.5

[a]Assuming body weight of 70 kg for the general population and 60 kg for women of childbearing age.
[b]Data from EPA 1997a.
[c]Unweighted average across ethnic groups.
[d]Data from Stern et al. 1996.
[e]Women 15-45 years old.
[f]Women 18-40 years old.

Consumption of animals or poultry fed fish meal might increase the exposure to MeHg, but data are not available. The use of organic Hg compounds as preservatives in vaccines and medical preparations is also a source of exposure and is of particular importance in young children who might be more sensitive to those mercurials than adults. As many as 219 such products are in use (FDA 1999). Thimerosal (TM) (sodium ethylmercurithiosalicylate) and phenylmercuric acetate (PMA) are the most frequently used compounds, at concentrations of 0.01% and 0.0002%, respectively. The FDA estimates that 75-80 kg of Hg compounds are used annually by the manufacturers of those vaccines and medical preparations. The risks associated with thimerosal use in vaccines have been discussed in an interim report to clinicians (American Academy of Pediatrics 1999).

Small amounts of MeHg can be formed in the gut by intestinal bacte

ria. A.O. Summers (University of Georgia, personal commun., Dec. 1999) estimated that 9 µg of MeHg can be formed per day in the gut of humans. That estimate is based on the bacterial species reported to occur in the human gut and assumes that there are 454 g of feces in the lower bowel of an adult human. However, not all the MeHg that is synthesized would be absorbed. Some of the methylation would occur in the colon, where absorption is less. In addition, intestinal flora can demethylate MeHg to inorganic Hg, which is poorly absorbed by the GI tract (Nakamura et al. 1977; Rowland et al. 1980).

The major source of exposure to elemental Hg in the general U.S. population is due to Hg vapor released from dental amalgams (Goering et al. 1992; Halbach 1994; Lorscheider et al. 1995). Approximately 300 metric tons of Hg are used annually by dentists for amalgams (Arenholt-Bindslev and Larsen 1996). Most amalgams used in the United States contain approximately 50% Hg (IPCS 1991; Aposhian et al. 1992a; Lorscheider et al. 1995). In a study of college students who have dental amalgams, two-thirds of the Hg excreted in the urine appeared to be derived from the Hg vapor released from their amalgams (Aposhian et al. 1992a). Evidence shows that Hg vapor from dental amalgams enters tissues, including the brain, where it is oxidized to inorganic Hg. Pregnant sheep given amalgam fillings labeled with radioactive Hg accumulated radioactivity in maternal and fetal tissues within a few days (Vimy et al. 1990). Significant positive correlations between the number of amalgams in the mouth and the mercury content of human tissues, including the brain, are also seen (Drasch et al. 1994). The mean concentration of total Hg in whole blood (in the absence of consumption of fish with high concentrations of MeHg) is probably of the order of 5-10 µg/L (IPCS 1991; Mahaffey and Mergler 1998). This concentration is most likely due to exposure to Hg vapors from amalgams, because retention of inorganic Hg is very low compared with retention of organic and elemental Hg. Furthermore, exposure to MeHg from non-fish sources is also very low (IPCS 1991).

Occupational exposure to elemental Hg has occurred because of accidents in chloralkali plants (Bluhm et al. 1992). However, there are other potential occupational exposures to elemental Hg. In addition, some Caribbean religions use elemental Hg in religious ceremonies (Wendroff 1995). Children have been known to play with elemental Hg because of its fascinating physical properties (i.e., liquid silver), possibly

severely contaminating living and play areas (ATSDR 1999). In wastewaters, the main sources of elemental Hg are dental offices, hospitals, and laboratories (Arenholt-Bindsley and Larsen 1996). Exposure of humans to mercuric Hg has occurred because of intentional or accidental (e.g., occupational exposures) poisonings with mercuric chloride (Clarkson et al. 1988).

TOXICOKINETICS

Absorption and Distribution

Methylmercury

Most fish contain MeHg. Many freshwater fish in the United States contain more than 2-3 ppm of Hg (Northeast States for Coordination of Air Use Management (NESCAUM 1998). Populations worldwide that eat fish regularly can have concentrations of more than 10 ppm in their hair (Cernichiari et al. 1995). About 95% of the MeHg in fish ingested by humans (Aberg et al. 1969; Miettinen 1973) or about 95% of methylmercuric nitrate given orally to volunteers (Aberg et al. 1969) was found to be absorbed from the gastrointestinal (GI) tract. Although MeHg toxicity following ingestion is the primary focus of this report, it should be noted that MeHg also is readily absorbed through the skin and lungs. The extent of absorption following inhalation exposure is believed to be high.

Once absorbed into the bloodstream, MeHg enters the red blood cells. More than 90% of the MeHg that is found in blood is bound to hemoglobin in red blood cells (Kershaw et al. 1980). Aberg et al. (1969) studied the distribution of Hg compounds in three healthy male volunteers administered [^{203}Hg]-methylmercuric nitrate orally. ^{203}Hg was found in the blood 15 min after administration and peaked within 3-6 hr. The concentration in red blood cells was 10 times greater than that in plasma. MeHg binds to cysteine residue number 104, of the α chain and numbers 93 and 112 of the β chain of hemoglobin. Numbers 104 and 112 are cysteine residues in the contact junction of the hemoglobin molecule. Number 93 is out of the junction and binds to MeHg easily because it is on the external surface of the hemoglobin molecule. The number and

position of the junctional and external cysteine residues on hemoglobin differ in animal species. An extensive table, including the data for the hemoglobin of eight animal species, can be found in Doi (1991). Some MeHg is also bound to plasma proteins. In humans exposed orally to large amounts of MeHg daily, the percentage of the total Hg found as inorganic Hg in whole blood, plasma, breast milk, liver, and urine was 7%, 22%, 39%, 16-40%, and 73% respectively (IPCS 1990). Matsuo et al. (1989) reported autopsy data on Japanese subjects. Kidney and liver contained total Hg concentrations on the order of hundreds of ng/g. Cerebrum, cerebellum, heart, and spleen contained total Hg concentrations on the order of tens of ng/g. Approximately 80% of the Hg in those organs was in the form of MeHg. In the liver, kidney medulla and kidney cortex 33%, 15% and 11% of the mercury was methylmercury, respectively. Consumption of high concentrations of MeHg in fish results in only about 5% inorganic Hg in whole blood and about 20% inorganic Hg in scalp hair (Phelps et al. 1980). It should be emphasized that the exact form(s) in which MeHg exists in the body is still unknown. MeHg ion is hydrated in aqueous solutions. There are pH-dependent reactions giving rise to Hg-substituted oxonium ions (Figure 2-1). Cotton and Wilkinson (1988), state that "the types of complexes formed by the two ions differ markedly; Hg^{2+} compounds of amino acids containing SH groups are polymeric and polar, whereas the CH_3HgR species are nonpolar and monomeric. For example the cysteinate is with a linear C—Hg—S." The chemistry and formation of Hg-substituted oxonium ion complexes may affect MeHg transport, but investigators who study such transport largely ignore them.

About 10% of the body burden of MeHg is found in the brain where it is slowly demethylated to inorganic mercuric Hg (see Figure 2-2). MeHg is also readily transferred to the fetus and the fetal brain. Evidence from rat experiments suggests that MeHg transport across the blood-brain barrier occurs via a MeHg-L-cysteine complex, which is transported by the L-system (leucine preferring) amino acid carrier (Kerper et al. 1992). MeHg-cysteine is released in vitro from a MeHg-glutathione complex by the action of γ-glutamyltransferase and dipeptidases (Naganuma et al. 1988). That action suggests that glutathione might play an indirect role in the transport of MeHg into endothelial cells. The MeHg-cysteine or MeHg-glutathione complex would be expected to be water soluble. That would not support the hypothesis

$$CH_3Hg(OH_2)^+ + OH^- \rightleftharpoons CH_3HgOH + H_2O$$

$$CH_3Hg(OH_2)^+ + CH_3HgOH \rightleftharpoons (CH_3Hg)_2OH^+ + H_2O$$

$$CH_3HgOH + (CH_3Hg)_2OH^+ \rightleftharpoons (CH_3Hg)_3O^+ + H_2O$$

FIGURE 2-1 Hg-substituted oxonium ions formed in aqueous solution. Source: Cotton and Wilkinson 1988.

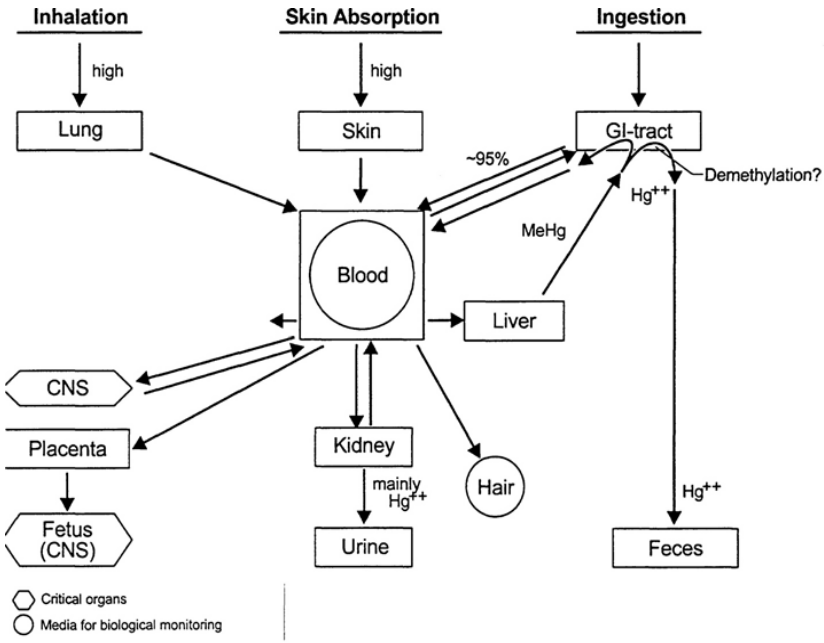

FIGURE 2-2 Methylmercury kinetics. Source: Elinder et al 1988. Reprinted with permission from *Biological Monitoring of Toxic Metals;* copyright 1988, Plenum Publishing Corporation.

that the rapid uptake of MeHg by the brain is due to lipid solubility in body tissues and fluids. Recently, Fujiyama et al. (1994) proposed that the MeHg-glutathione complex is the mechanism by which MeHg can efflux rat astroglia. Aschner et al. (1991), however, proposed that the MeHg-cysteine complex is the mechanism by which MeHg is exported from astroglia.

A case study of family members that developed classic signs of MeHg poisoning due to the consumption of contaminated pork indicates that the cerebrum and the cerebellum are particularly sensitive to MeHg (Davis et al. 1994). Analyses of various regions of the brain of one female member upon autopsy, several years later, revealed that the extent of brain damage correlated with regional-brain Hg concentrations. Inorganic Hg comprised 82-100% of the total Hg, suggesting that most of the MeHg had been converted to inorganic Hg during the period. The highest levels of Hg were found in the cerebrum and cerebellum. Magnetic Resonance Imaging (MRI) studies showed brain damage in the calcarine cortices, parietal cortices, and cerebellum of other family members. The damage in those areas is believed to underlie many of their persistent clinical signs, because those areas of the brain are responsible for coordination, balance, and sensations (see Chapter 5).

Dimethylmercury

Dimethylmercury is a supertoxic form of Hg (Gosselin et al. 1984) that has been fatal after accidental exposure. At Dartmouth College, a chemistry professor died 298 days after several drops of dimethylmercury fell on her latex gloves. The gloves did not appear to act as a barrier, and the compound was rapidly absorbed through her skin. Six to 7 months after her exposure, her blood Hg concentration was 1,000 µg/L (Nierenberg et al. 1998). Typical blood concentrations of Hg are in the range of 1 to 8 µg/L. Mouse studies suggest that the extremely toxic dimethlymercury must be metabolized to MeHg before it can enter the brain (Ostlund 1969).

Elemental Mercury

Absorption of elemental Hg vapor via the lungs is rapid. In humans,

75-85% of an inhaled dose is absorbed (Kudsk 1965; Okawa et al. 1982; Hursh 1985; Hursh et al. 1985). Elemental Hg in liquid or vapor form is not well absorbed from the GI tract (less than 0.01%) (Bornmann et al. 1970). In humans exposed to elemental Hg vapor, 97% of the absorption occurred via the lungs, and less than 3% of the total amount absorbed was via the skin (Hursh et al. 1989).

Because elemental Hg is very lipid soluble, its diffusion across the lungs and dissolution in blood lipids is rapid (Berlin 1986). The fact that it is uncharged with intermediate molecular weight and size might be another reason why it passes readily from air to blood. It is distributed throughout the body, and readily crosses the placenta and the blood-brain barrier (Vimy et al. 1997; Fredricksson et al. 1992, 1996; Drasch et al. 1994) (see Figure 2-3). Elemental Hg is oxidized to mercuric Hg. Eventually, the Hg ratio of red blood cells to plasma is 1:1.

Inorganic Mercury

Approximately 7-15% of an ingested dose of mercuric chloride is absorbed from the GI tract (WHO 1976; Miettinen 1973). Absorption is proportional to the water solubility of the mercuric salt. Mercuric Hg has a high affinity for sulfhydryl groups in the red blood cells and plasma. The half-life in the blood is reported to be 19.7-65.6 days (Hall et al. 1995).

The highest accumulation of mercuric Hg is in the kidneys. The major fraction of inorganic Hg in rat kidney is bound to metallothionein (Jakubowski et al. 1970; Wisniewska et al. 1970; Komsta-Szumska et al. 1976). In contrast MeHg has a low affinity for metallothionein (Chen et al. 1973). Because of its ionic charge, mercuric Hg does not readily penetrate the blood-brain barrier or the placenta.

Biotransformation

MeHg is converted in tissues to mercuric Hg (Magos and Butler 1972; Dunn and Clarkson 1980). The rate of demethylation in rats and most other species is very slow. The mechanisms involved in conversion of MeHg to mercuric Hg are controversial. The enzymes in mammalian

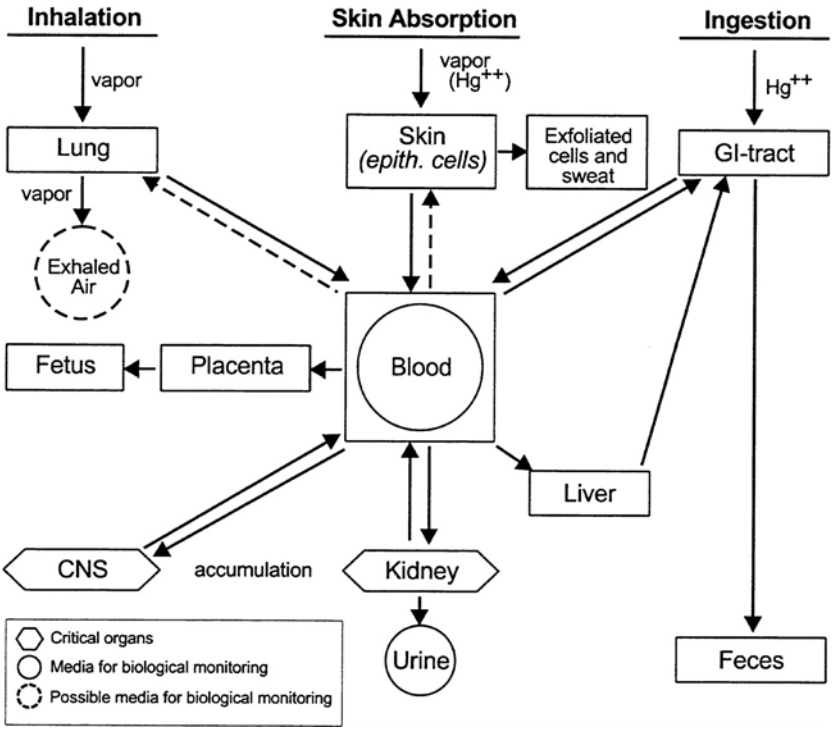

FIGURE 2-3 Inorganic mercury kinetics. This diagram is complicated by the fact that inhaled vapor is oxidized to Hg^{++} so that both species are present. The inhaled vapor is highly mobile, readily crosses cell membranes, the blood-brain barrier, and the placenta. The Hg^{++} species is much less mobile, crossing the blood-brain barrier and placenta much more slowly than dissolved vapor. Source: Elinder et al. 1988. Reprinted with permission from *Biological Monitoring of Toxic Metals;* copyright 1988, Plenum Publishing Corporation.

tissues believed to be responsible for the biotransformation have never been identified. Greater emphasis has been placed on investigating the possible role of a free radical mechanism (Suda and Hirayama 1992). In addition, γ-globulin and serum albumin have been shown to have

similar degradation activity that can be stimulated further by glutathione (Gage 1975). Intestinal flora, tissue macrophages, and fetal liver are all sites of tissue demethylation.

Experiments in bacteria demonstrate many different mechanisms to detoxify heavy metals. For example, some metals are actively transported out of the cell (e.g., arsenite) (Perry and Silver 1982; Mobley and Rosen 1982; Silver and Keach 1982), and other metals are sequestered by protein binding in the cell (Kägi and Nordberg 1979). Organic Hg compounds are detoxified by a microbial organomercurial resistance system (see Figure 2-4). An organomercurial lyase catalyzes the protonolysis of the carbon-Hg bond to give a hydrocarbon and a mercuric ion (Summers 1985; Robinson and Tuovinen 1984; Summers and Silver 1978). Mercuric reductase then catalyzes the reduction of mercuric Hg to elemental Hg. NADPH is the coenzyme in that reaction (Fox and Walsh 1982, 1983; Brown et al. 1983). Because elemental Hg is volatile, it evaporates from the bacterial culture.

GI absorption of MeHg is decreased by intestinal flora that convert MeHg to inorganic Hg (mercuric ion) (Nakamura et al. 1977; Rowland et al. 1980), which is poorly absorbed. Organomercurial lyase has been purified from *Escherichia coli* (Begley et al. 1986). The enzyme is encoded on the plasmid R831. No cofactors are required for enzyme activity, and the enzyme structure does not contain any metals. The enzyme can catalyze protonolysis of the C-Hg bond in primary, secondary, and tertiary alkyl, vinyl, allyl, and aryl organomercurial salts to the hydrocarbon and mercuric ion. A thiol must be present for activity, cysteine being the most active thiol compound, for demethylation of organic mercurials.

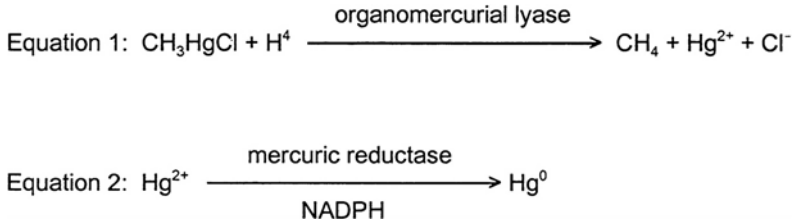

FIGURE 2-4 Organomercurical detoxification pathway in bacteria.

Enzymes similar to those found in bacteria have not been found in mammals. Demethylation of MeHg is thought to occur via a free-radical mechanism in the mammalian brain, possibly eliminating the need for those enzymes. It is also possible that the enzymes have not yet been identified.

Lefevre and Daniel (1973) examined rat, mouse, and guinea-pig liver homogenates for activity that would degrade organic Hg compounds. Although a minimum level of activity was found, phenylmercuric acetate and methoxyethylmercury chloride were degraded, but not MeHg. Fang and Fallin (1974) were able to show cleavage of phenylmercuric acetate (PMA) and ethylmercury chloride in the kidney and liver of rats, but no activity was seen against MeHg.

Elemental Hg vapor is oxidized to mercuric mercury by catalase and hydrogen peroxide (H_2O_2) in blood and tissues (Berlin 1986). H_2O_2 production is the rate-limiting step.

When mercuric Hg is administered orally to rodents, elemental Hg vapor has been detected in the expired air, indicating that some metabolism to elemental Hg must have occurred. Mammals do not methylate mercuric Hg; however, intestinal flora can methylate Hg^{2+} to a small extent (Rowland et al. 1977).

Excretion

Approximately 1% of the human body burden of MeHg is excreted daily (Clarkson et al. 1988). In humans, the major routes of excretion are via the bile and feces. About 90% of a given dose of MeHg is eventually excreted in the feces as mercuric Hg in humans and other species. Approximately 10% is excreted as mercuric Hg via the urine. Much of the biliary MeHg is reabsorbed; MeHg complexed with glutathione is eliminated via the bile.

Following oral administration of [^{203}Hg] methylmercuric nitrate, only about 33% of the administered dose was excreted in 49 days, fecal excretion being the main route of excretion (Miettinen 1973). There was a 0.18% to 0.27% excretion of the dose in the urine in 10 days and 3.3% excretion in 49 days. The extent of urinary excretion continued to increase up to 71 days after ingestion. A maximum of 0.12% of the administered dose of Hg was found per gram of hair. That amount was found 40-50 days after ingestion. Using whole-body measurements, the

half-life of MeHg was 70-74 days. No methylmercuric chloride was found in the sperm, but about 50% of the body content was found in the liver and about 10% was found in the head.

In humans, the whole-body half-life of MeHg was estimated to be 70-80 days (Aberg et al. 1969; Miettinen 1973; Bernard and Purdue 1984; EPA 1997b).

The half-life in blood for MeHg as measured in blood and hair of humans ranged from 48 to 53 days (Miettinen et al. 1971; Kershaw et al. 1980; Sherlock et al. 1984; Cox et al. 1989). Elimination rates for MeHg are dependent upon species, dose, sex, and animal strain (Nielsen 1992).

It is pertinent to note that neonatal rats and monkeys are limited in their ability to excrete MeHg into the bile (Ballatori and Clarkson 1982). Therefore, it takes them longer than mature animals to excrete MeHg (Thomas et al. 1982). In addition, their intestinal flora might also be less able to demethylate MeHg during this suckling period (Rowland et al. 1977; Sundberg et al. 1998; Grandjean et al 1994). If those two phenomena are true for humans, then neonates might be particularly sensitive to exposure to MeHg. GSH may be the major cellular defense against MeHg toxicity. GSH complexation with MeHg is a major mechanism for MeHg excretion from the cell, thus protecting against MeHg toxicity (Kromidas et al. 1990).

MeHg has been measured in the breast milk of rats, humans, and guinea pigs (Sundberg and Oskarsson 1992; Yoshida et al. 1992). Therefore, breast milk is considered a route of excretion, but it is also an important route of exposure to suckling neonates. In human breast milk, 16% of the Hg was found to be MeHg (Skerfving 1988). That percent is much lower than the percent of Hg found as MeHg in whole blood. In animals, the total Hg content of breast milk was found to be proportional to the total Hg content of the plasma (Skerfving 1988; Sundberg and Oskarsson 1992).

A small amount of elemental Hg vapor is excreted unchanged in exhaled air, sweat, saliva, feces, and urine (Cherian et al. 1978). Only small amounts of elemental Hg can be detected in the urine (Stopford et al. 1978) and exhaled air (Hursh et al. 1976). Excretion via sweat and saliva is usually minimal. The hair-life for whole-body Hg excretion was 58 days in humans (Hursh et al. 1976). Elemental Hg is also oxidized in the body to mercuric Hg, which is then excreted in the feces and urine. That is demonstrated by the observation that, after exposure to Hg

vapor, the mercuric Hg content in the feces increases and is four times greater than that in the urine.

Following oral administration of mercuric Hg to humans, about 85% was excreted in the feces within a few days (Miettinen 1973). Fecal excretion of mercuric Hg occurs as the result of secretion through the small intestine epithelium and colon, and bile secretion (Berlin 1986). Mercuric Hg is also excreted in the urine, sweat, lung (Clarkson et al. 1988), and breast milk (Yoshida et al. 1992). Urinary excretion is useful for biological monitoring of inorganic Hg. Absorbed inorganic Hg has been estimated to have a half-life of 40 days (Rahola et al. 1973) or 67 days (Hall et al. 1995). WHO (IPCS 1990) reported a half-life of 35 days. Humans occupationally exposed to inorganic Hg excrete in their urine three forms of this element: a metallic form, a Hg-cysteine complex, and a large unidentified complex (Henderson et al. 1974).

MOBILIZATION OF BODY HG

Synthetic chelating or complexing agents that compete with endogenous ligands for mercuric or organic Hg increase the urinary excretion of inorganic Hg and organic Hg and reduce the body burden (Aposhian 1983; Aposhian and Aposhian 1990). Compounds that have been used therapeutically are 2,3-dimercapto-1-propane sulfonate (DMPS, Dimaval, and Unithiol) and meso 2,3-dimercaptosuccinic acid (DMSA, succimer). DMPS and DMSA are water-soluble, less-toxic chemical analogs of 2,3-dimercapto-1-propanol (British Anti-Lewisite BAL dimercaprol). BAL is lipid soluble and must be given by deep intramuscular injection. DMPS and DMSA can be taken orally. There is an injectable preparation of DMPS. About 55% of patients administered BAL have one or more adverse reactions to it (Klaassen 1996), although most of the reactions are not serious. However, because BAL redistributes Hg, increasing brain Hg concentrations when given to Hg-intoxicated animals, its continued therapeutic use is questionable (Berlin 1986).

DMPS was introduced into the official Soviet drug armamentarium in 1958 (Klimova 1958) and to the western world in 1978. A number of reviews of DMPS and other chelating agents have appeared during the last 18 years (Aposhian 1983; Aposhian et al. 1992b, 1995; Aaseth et al. 1995). It is approved for use by the German and Chinese equivalents of

the U.S. Food and Drug Administration (FDA). Clarkson et al. (1981) used DMPS to treat the MeHg-poisoned humans in Iraq and showed that it is more potent than D-penicillamine *N*-acetyl-DL-penicillamine or a thiolated resin for decreasing inorganic Hg in the blood. Elsewhere, including the United States, DMPS has been used by alternative-medicine physicians concerned with dental amalgam toxicity. It was used recently to increase the urinary excretion of Hg in eight humans exposed to mercurous Hg (Gonzalez-Ramirez et al. 1998). In contrast to BAL, DMPS does not increase brain Hg concentration in rats (Aposhian et al. 1996).

Although it has not been approved for this use, DMSA has been used to treat Hg intoxication (Aposhian 1983; Aposhian and Aposhian 1990). It was approved by the FDA in 1990 for the treatment of children with blood Pb concentrations greater than or equal to 45 μg per deciliter.

CHEMICAL FORMS OF HG IN TOXICITY

There is ample evidence from studies of humans (Takizawa 1979; Matsuo et al. 1987; Takeuchi et al. 1989) and experimental studies using animal models (Vahter et al. 1994) that MeHg is slowly biotransformed to inorganic Hg in the brain. Although the rate of demethylation of MeHg in the brain appears to be dose related, many questions remain concerning the mechanisms by which the brain biotransforms MeHg to inorganic Hg and the slow rate at which it occurs. Davis et al. (1994) reported that a New Mexico patient who died approximately 21 years after eating MeHg-tainted pork had greatly increased total Hg concentrations in various regions of the brain (71 to 300 times greater than controls). A minimum of 82% of the Hg in the patients brain was in the inorganic form. In most regions of her brain, 100% of the Hg was in the inorganic form. Similar results were found in a Minamata patient who died 18 years after the exposure (Takeuchi and Komyo 1977).

Experimental studies have also reported a slow increase in the concentration of inorganic Hg in the brain in a number of species after administering MeHg and analyzing the brain for total and inorganic Hg from days to years after exposure (Friberg and Mottet 1989). When monkeys were exposed daily to high doses of MeHg for long periods of time, there were significant concentrations of inorganic Hg found in the brain (Lind et al. 1988). By 69-166 weeks, 10-33% of the brain Hg was

inorganic. Female monkeys (*Macaca fascicularis*) received daily doses of MeHg for up to 18 months (Vahter et al. 1994, 1995). When the brains were examined for Hg species, inorganic Hg made up about 9% of the total Hg after 6-12 months of exposure and 18% after 18 months of exposure. Six months after a 12-month exposure ended, it was 74%. The authors stated that they believed that inorganic Hg "was formed by demethylation of MeHg in the brain."

The extent to which demethylation of MeHg produces toxicity in the brain is not known. Studies by Norseth and Clarkson (1970) and Syversen (1974) indicated that MeHg itself mediates the toxicity following MeHg exposure. In addition, Magos et al. (1985) provided direct evidence that the extent of brain damage correlates better with the brain concentration of intact organic Hg than inorganic Hg when MeHg or ethyl Hg is administered to rats. A possible hypothesis is that the long half-life of inorganic Hg in the brain once demethylation occurs might be responsible for the latent or long-term MeHg effects that have been reported. No direct evidence to support that hypothesis is available at this time.

In addition to the questions regarding whether inorganic or organic Hg mediates MeHg toxicity at the cellular level, questions have also been raised regarding the species responsible for the Iraqi poisonings. In the Iraqi poisoning episode, some of the grain seeds appeared to contain phenyl Hg instead of MeHg. There is no doubt, however, that gas chromatography identified MeHg in the blood of most of the exposed population, and phenyl Hg would have been quickly converted to inorganic Hg in the blood (T.W. Clarkson, University of Rochester, personal commun., Nov. 1999). In addition, the phenyl Hg was in the barley seeds and no barley seeds were used to make bread (T.W. Clarkson, University of Rochester, personal commun., Nov. 1999).

TOXIC EFFECTS AND TARGET ORGANS

Currently, there is a general consensus that the critical organ for MeHg toxicity is the brain. Both the adult and fetal brains are susceptible to MeHg toxicity (see Figure 2-2), although the developing nervous system appears to be more sensitive. Studies of the Minamata disaster in Japan indicate that prenatal exposure causes damage throughout the fetal brain and, at high doses, results in effects in the offspring that are

largely indistinguishable from cerebral palsy caused by other factors (Harada 1995). Exposure of adults to MeHg resulted in focal lesions (Clarkson 1997). The neurotoxicity of chronic MeHg exposure at lower levels is not immediately evident. A latent period of 1 month or more usually occurs (Bakir et al. 1973; IPCS 1990). Other adverse effects (e.g., cardiovascular and immunological effects) have been reported to occur at MeHg doses lower than those producing adverse effects in the nervous system. Those effects, however, are not as well studied as the neurotoxic effects. The health effects of MeHg are discussed in more detail in Chapter 5.

The target organs of elemental Hg are the brain and kidney. The toxicity of elemental Hg is believed to be due to mercuric Hg. Inhaled elemental Hg vapor readily crosses the blood-brain barrier and is then oxidized to mercuric Hg. The latter becomes firmly bound to macro-molecules in the brain. There does not seem to be any endogenous mechanism for the rapid removal of mercuric Hg from such sites. In humans occupationally exposed to elemental Hg vapor, signs of severe exposure include tremor, psychiatric disturbances, gingivitis, and altered behavior.

The target organ of mercuric Hg toxicity is the kidney due to Hg accumulation there. The earliest signs of renal injury due to Hg compounds are increased urinary excretion of *N*-acetyl-β-glucoseaminidase, β_2-microglobulin and retinol-binding protein. Although the exact mechanism of renal toxicity is not known, it is known that mercuric Hg has a strong affinity for sulfhydryl moieties. The formation constants of Hg sulfhydryl complexes are very high (approximately $K_f = 10^{30}$) (Divine et al. 1999). The formation constant for mercuric Hg and the anionic form of a sulfhydryl group, RS^-, is greater than or equal to 10^{10}-fold higher than that for the carboxyl or amino groups (Ballatori 1991; Divine et al. 1999). Since there is a wide distribution of sulfhydryl groups in the body, especially in proteins, mercuric Hg is believed to cause toxicity by combining with the active centers of critical enzymes and structural proteins.

BIOCHEMICAL MECHANISMS OF TOXICITY

Experimental studies of the possible biochemical mechanisms of MeHg neurotoxicity have been reviewed in detail (Atchison and Hare

1994; Chang and Verity 1995; ATSDR 1999). Mitochondrial changes, induction of lipid peroxidation, microtuble disruption, and disrupted protein synthesis have all been proposed as possible mechanisms. In developmental toxicity, disruption of cell-surface recognition has also been proposed as a possible mechanism (Baron et al. 1998; Dey et al. 1999). To date, no definitive data are available that point to any one mechanism as the proximate cause for the neurotoxic symptoms associated with MeHg exposure in adults.

Exposure of rats to MeHg has long been known to cause biochemical and ultrastructural changes in the mitochondria, but the evidence is not convincing that those changes are the primary mechanism for MeHg toxicity (Denny and Atchison 1994; Yoshino et al. 1966). Sarafian and Verity (1991) showed that MeHg causes membrane peroxidation in nerve cells. Because antioxidants, such as vitamin E and selenium, offer some protection in vivo against MeHg neurotoxicity (Chang et al. 1978; Magos and Webb 1980), free-radical-induced lipid peroxidation might be involved in the cellular damage caused by MeHg. However, lipid peroxidation does not appear to be the critical mechanism that causes cell lethality for many reasons, as summarized by Atchison and Hare (1994).

MeHg disrupts protein synthesis, and disruption has been proposed as the primary mechanism of MeHg neurotoxicity. In the rat, inorganic Hg, however, was 10 times more potent an inhibitor of cell-free protein synthesis than MeHg (Sugano et al. 1975). Stimulation of protein synthesis by MeHg was also reported (Burbaker et al. 1973). Mitotic arrest is one of the most sensitive indicators of MeHg exposure in mice. A single 4-mg/kg dose MeHg on postnatal day 2 resulted in a brain Hg concentration of only 1.8 μg/g of tissue. The ratio of late mitotic figures to total mitotic figures was significantly reduced in the cerebellum of exposed mice, indicating mitotic arrest (Sager et al. 1984).

Oxidative stress might also be involved in MeHg toxicity. Glutathione is the major antioxidant of the cell. After exposure to MeHg, glutathione concentrations decline and then increase. Cells that are made resistant to MeHg toxicity had an increase in the rate of efflux of MeHg and had 4-fold higher glutathione concentrations than normal cells (Miura and Clarkson 1993).

Another proposed mechanism underlying MeHg toxicity is disruption of microtubules in the neuronal cytoskeleton (Miura and Imura 1987). Hg binds to thiols in the tubulin, the protein monomers that form micro

tubules, and blocks the depolymerization and repolymerization of microtubules. Because the breakdown and assembly of microtubules are required for many cell functions, including cell division and migration, disruption of microtubule assembly could disrupt cellular processes. In vitro, MeHg has been shown to disrupt cell-cycle progression in primary rat brain cells (Ponce et al. 1994). The developing nervous system would be particularly sensitive to those effects due to the extensive cell division and migration that occurs during its development.

The ability to exchange between thiols forms the basis of therapeutic techniques following both MeHg exposure and exposure to Hg vapor. The neurotoxic effects of combined exposure to MeHg and Hg vapor have been reported to be similar in nature but more severe than those observed following exposure to each alone (Fredriksson et al 1996). There are many similarities in the biochemistry of the $MeHg^{+}$ and the inorganic Hg cation (Hg^{2+}), which is responsible for the toxicity following Hg vapor exposure (Clarkson 1997). Both cations exhibit a high affinity for SH groups, and association and dissociation reactions are rapid (Carty and Malone 1979). Both are found in tissues bound to large and small molecular-weight thiol-containing molecules (proteins, cysteine, and glutathione). The formation of Hg thiol bonds is believed to underlie the mobility and toxicity of Hg in the body (Clarkson 1997).

Although the exposure patterns and toxicokinetics and toxicodynamics of the different Hg species are usually studied separately, organic Hg and elemental Hg are eventually converted in vivo to inorganic Hg. The estimated average daily intake and retention of various forms of Hg are shown in Table 2-4. Estimates of the retention in the body of Hg from dental amalgams range from 3.1 to 17 µg per day. Estimates of MeHg retention range from 1 to 6 µg per day. The ratio of MeHg to total Hg will be different among those with high fish consumption. The data in Table 2-4 suggest that average exposure to Hg from dental amalgams might be considerably higher than exposure to Hg from MeHg. However, the available data are not adequate to permit a definitive comparison.

MeHg is very slowly but ultimately metabolized in situ in the brain to inorganic Hg. Elemental mercury is also oxidized to inorganic Hg in the brain. It is unclear whether MeHg toxicity at the cellular level is caused by the parent compound itself, due to the inorganic Hg that is its metabolite, or is caused indirectly by the free radicals generated by the

metabolism of MeHg to inorganic Hg. If the ultimate toxic form of MeHg is indeed its inorganic Hg metabolite, that suggests that the dose of inorganic Hg to the brain from elemental Hg exposure (particularly from dental amalgams) and MeHg might be cumulative. That is the case even if oxidation of elemental Hg in the blood before absorption to the brain is considered. Risk-assessment models for MeHg, therefore, should consider additional chronic sources of exposure to Hg such as dental amalgams.

TABLE 2-4 Estimated Daily Intake and Retentiona (micrograms per day) of Total Hg and Hg Compounds in the General Population Not Occupationally Exposed to Hg

Exposure	Elemental Hg Vapor	Inorganic Hg Compounds[b]	MeHg
Air	0.030 (0.024)[b,c]	0.002 (0.001)[b,c]	0.008 (0.0064)[b,c]
Food Sources			
Fish	0[b,c]	0.600 (0.042)[b, c]	1[d, e, f,] 3[e, g, h,] 6[c, g, h]
Non-Fish	0[b, c]	3.6 (0.25)[b, c]	0[b, c]
Drinking water	0[b, c]	0.050 (0.0035)[b, c]	0[b, c]
Dental amalgams	3.8-21 (3-17)[b, c]	0[b, c]	0[b, c]
Total	3.9-21 (3.1-17)	4.3 (0.3)	1-6 (1-6)

[a]Retention is assumed to be 95% of intake for MeHg, 80% for elemental Hg vapor, and 7% for inorganic Hg compounds.
[b]Data from IPCS 1991.
[c]Mean value.
[d]Data are for United States nationwide (per capita), calculated assuming a body weight of 70 kg (EPA 1997).
[e]Median value.
[f]Equivalent data for women of childbearing age: median = 1, assuming a body weight of 60 kg.
[g]Data are for the general population of reproductive age in New Jersey fish consumers, calculated assuming a body weight of 70 kg (Stern et al. 1996).
[h]Equivalent data for women of childbearing age: mean = 5, median = 3, assuming a body weight of 60 kg.
Note: Values given are the estimated average daily intake; the figures in parentheses represent the estimated amount retained in the body of an adult. Values are quoted to two significant figures.

Such considerations are complicated by uncertainty about the mechanisms by which MeHg specifically exerts its neurodevelopmental toxicity. Such mechanisms might not be the same as those responsible for adult neurotoxicity. Nonetheless, the potential implications of additive toxicity from fish consumption and dental amalgams make elucidation of the mechanisms of MeHg toxicity in the brain a critical research priority.

SUMMARY AND CONCLUSIONS

- The major source of MeHg exposure in humans is consumption of fish, marine mammals, and crustaceans.
- The water solubility of mercuric chloride is greater than elemental Hg. That of elemental Hg is greater than MeHg. The solubility of the different forms of Hg might play a role in their differential toxicity.
- Elemental Hg and a portion of MeHg are converted to mercuric Hg in the body. The conversion of MeHg occurs at a very slow rate.
- Analytical methods for analyzing Hg in biological samples include AAS, AFS, NAA, ASV, ICP-MS, and XRF. Care must be taken to prevent contamination by Hg during sample preparation and analysis.
- MeHg is readily absorbed from the GI tract. After ingestion, 90% of the MeHg in blood can be found in red blood cells. It is bound primarily to red-blood-cell hemoglobin, but some is bound to plasma proteins.
- Hg in blood reflects recent exposure to MeHg and inorganic Hg. The half-life in blood for humans averages 50 days but can vary substantially. Because neonates have an immature transport system, they do not excrete MeHg as rapidly as adults.
- Hg in hair is approximately 90% MeHg. Hair measurements have the advantage of providing a historical record of MeHg exposure but do not accurately reflect exposure to inorganic Hg.
- The daily excretion of MeHg is about 1% of the human body burden. It is excreted mainly via the bile and feces as MeHg and mercuric Hg. Complexing with GSH is involved. Urine MeHg concentrations do not accurately reflect MeHg exposure.

- For elemental and inorganic Hg, the half-life in blood is 1-2 months. The whole-body half-life is slightly longer, but that does not take into account Hg in the brain, which is cleared very slowly. Excretion occurs primarily via urine and feces and, to a small extent, saliva, bile, sweat, and lungs.
- DMPS and DMSA can be used to increase Hg excretion. Dimercaprol (BAL), used in the past for chelation, is contraindicated because it redistributes Hg to the brain.
- MeHg readily crosses the blood-brain barrier. The rapid uptake of MeHg in the brain has been proposed to be due to lipid solubility, but evidence in rats suggests that the transport is due to the formation of MeHg-cysteine complexes.
- MeHg accumulates in the brain where it is slowly converted to inorganic Hg. Whether CNS damage is due to MeHg per se, to its biotransformation to inorganic Hg, or to both is still controversial. The mechanisms and cellular site for the biotransformation in humans are not well understood. Both free-radical and enzymatic biotransformation has been proposed.
- The critical organ for MeHg toxicity is the brain. Both adult and fetal brains are vulnerable. For elemental Hg, the critical organs are the brain and kidney. Both MeHg and elemental Hg are converted to mercuric Hg in the brain, where it is trapped. The biological mechanisms for removing mercuric Hg from the brain are limited. The critical organ for mercuric Hg toxicity is the kidney, where it accumulates.
- There is emerging evidence that the cardiovascular and immune systems might be major sites of MeHg toxicity (see Chapter 5).
- The high affinity of MeHg and mercuric Hg for sulfhydryl groups is believed to be a major mechanism that underlies their toxicity. If those sulfhydryl groups are in the active center of critical enzymes, severe inhibition of essential biochemical pathways occurs.
- The toxicology of the three species of Hg — elemental Hg, mercuric Hg and MeHg — are intertwined, because MeHg and elemental Hg are transformed to inorganic Hg in the brain. Risk-assessment models for MeHg in humans are complicated because of inadequate data regarding the cumulative neurotoxic effects of MeHg per se and its biotransformation product mercuric Hg, which has a very long half-live in the brain.

RECOMMENDATIONS

- As data become available, exposure to elemental Hg from dental amalgams should be considered in risk assessment of MeHg. Exposure to other chemical forms of Hg should also be considered.
- Retention of inorganic Hg in the brain for years following early MeHg intake is possibly related to the latent or long-term neurotoxic effects reported. The long half-life of inorganic Hg in the brain following MeHg intake should be considered in risk assessment of MeHg.
- The mechanisms, including any enzymes, involved in the biotransformation of MeHg to mercuric Hg in human tissues need to be investigated, especially at the subcellular level. The effects of Hg on signaling pathways and the conformation of enzymes and structural proteins should be further elucidated, because the development and function of the brain would be particularly sensitive to such effects.
- Exposure assessment of the U.S. population — including those with high fish consumption — is needed to provide a full picture of the distribution of MeHg and total Hg exposure nationally and regionally.

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3

BIOLOGICAL VARIABILITY

INDIVIDUAL responses to MeHg exposure are variable. For example, individuals receiving the same dose of MeHg in the Iraqi accident did not all have the same effects. Even in controlled animal experiments, considerable variability in response is noted (Burbacher et al. 1988; Rice and Gilbert 1990). Differences in susceptibility to MeHg might be due to differences in the uptake, storage, transport, or metabolism of MeHg. Susceptibility to the effects of MeHg can also be predetermined by genetic polymorphisms that affect the delivery of MeHg to the target organs or affect the response of the target organs to MeHg. In addition, other external factors can influence vulnerability to the effects of MeHg. Factors that deserve consideration are age, gender, health status, nutritional status, and the intake of other foods or nutrients that might influence the absorption, uptake, distribution, and metabolism of MeHg. The ability of the individual to compensate for damage caused by MeHg exposure would also affect susceptibility. This chapter discusses those factors that could underlie the variability in response to Hg exposure. The implications of that variability on the study of the toxicokinetics of Hg are discussed.

AGE-RELATED SUSCEPTIBILITY

Exposure to MeHg during the neonatal period, infancy and childhood has different effects due to the different stages of brain development and

organ growth and the ratio of the MeHg concentration to body size. Age also affects the detection of toxic responses to MeHg, because some of the most sensitive end points examined — neurological development and cognitive ability — are dependent upon the age of the subject and the stage of cognitive maturation. There are also natural differences among individuals in performance on tests used. Therefore, the sensitivity of the test or assessment is dependent upon the developmental stage and age of the subject. In addition, many of the tests are carried out during periods of rapid development, which results in greater natural variation between individuals.

Data from Japanese poisoning episodes provide strong evidence that susceptibility to MeHg changes with age. Takeuchi (1968) described three distinct patterns of MeHg neuropathology termed adult, infantile, and fetal Minamata disease. In autopsy cases following fetal exposures, clear evidence of interference with brain development was observed. Disorganized cell layers and misoriented cells were observed, providing evidence of disrupted cell migration. For fetal and infantile exposures, lesions were observed throughout the cortex. A more selective pattern of lesions, localized in the calcarine and precentral cortices, particularly in the depths of the sulci, was observed in adult cases. Lesions in the granular layer of the cerebellum were observed in all cases. Reports of age-related neurological effects due to MeHg exposure in Japan and Iraq have also been described (Bakir et al. 1973; Harada 1968; Marsh et al. 1980). In both cases, mothers with few or no symptoms gave birth to infants severely affected. Studies with animal models also have reported significant age-dependent effects from MeHg exposure. As in human cases, offspring are sometimes severely affected with little or no signs of toxicity in the mother (Spyker et al. 1972; Mottet et al. 1987). Thus, age needs to be considered in the design of studies of MeHg, including in the choice of end points and the determination of how to analyze the results.

GENDER DIFFERENCES

Several reports have described gender differences in the toxicokinetics and the toxicodynamics of MeHg. Evidence of gender-dependent MeHg metabolism has been reported in humans (Miettinen 1973) and

animal models (Thomas et al. 1986; Nielsen and Andersen 1991). However, this gender sensitivity does not apply in the same way for all outcomes. The Iraqi MeHg epidemic appeared to affect three times as many females as males (Magos et al. 1976). Epidemiological studies of human infants and children have reported gender specific effects on development with males exhibiting greater effects than females. (McKeown-Eyssen et al. 1983)

In general, results in animal studies indicate that females exhibit a higher body burden of Hg per given dose than males. That result might be due to higher metabolism and urinary-excretion rates for MeHg in sexually mature male mice compared with female mice (Hirayama and Yasutake 1986). Animal data also indicate gender differences in the sensitivity to MeHg toxicity. Fowler (1972) and Yasutake et al. (1990) found that females are more likely to show renal toxicity following MeHg exposure. Yasutake and Hirayama (1988) found the gender differences to be strain sensitive following oral administration of MeHg chloride at 5 mg/kg per day since male Balb/cA mice died earlier than female Balb/cA mice, but female C57B/6N mice died earlier than male C57B/6N mice. Reports regarding the neurological effects have been mixed; females were found to be more susceptible than males in some studies, and males were observed to be more susceptible than females in others (Magos et al. 1976; Tagashira et al. 1980; McKeown-Eyssen et al. 1983; Vorhees 1985; Tamashiro et al. 1986a).

GENETICS

Aside from gender differences within a population, there is evidence of differences in sensitivity within populations that result in greater damage from a given exposure in one individual than in another. The extent to which that difference is due to familial characteristics compared with nutritional and environmentally mediated susceptibility remains to be determined. Differences in enzymatic expression might result in individual differences in sensitivity to MeHg. Currently, no evidence of polymorphisms affecting the metabolism or detoxification of MeHg exists. The lack of evidence, might be due to the inadequate study of those interactions in human populations and animal models. Therefore, the extent to which interindividual variability in effects at

similar doses is attributable to genetic differences in susceptibility remains unknown (Tamashiro et al. 1986).

MECHANISMS OF NUTRITIONAL INFLUENCE ON MEHG HEALTH EFFECTS

Overall, nutritional status and dietary interactions can affect the outcomes of MeHg studies, either by influencing the toxicity of Hg or by having effects on the end points measured. The main source of exposure to MeHg is through the food chain, largely through consumption of nonherbivorous fish and marine mammals, with smaller amounts contributed by intake of other fish and seafood. The nature of dietary exposures is such that consumption of one food group is generally related to a reduction or avoidance of other food groups. Establishing causality becomes particularly complex under those circumstances. Pathways through which diet and nutrients might affect the results of MeHg toxicity studies include the potential for attenuating a MeHg effect, exacerbating a MeHg effect, or acting as a confounder by causing toxicity due to other common food components or contaminants. Those three pathways are outlined in Figure 3-1.

Potentially harmful effects of MeHg might be attenuated by protective effects of such nutrients as selenium and omega-3 fatty acids. At the other extreme, malnourishment could affect study results either by directly reducing the sensitivity of an end point tested or by exacerbating the effects of MeHg, thereby increasing the sensitivity to MeHg toxicity. Nutritional factors that disrupt neuronal development, such as iron or folate deficiencies, might increase the impact of MeHg on neural development. Conversely, adequate levels of iron and folate in the diet might reduce the impact of MeHg. Such nutrient deficiencies could arise from an inadequate diet or, secondarily, from repeated infection, intestinal parasites, or excessive alcohol consumption.

The available data for the birth weight, gestation, and weight of the children studied in the Faroe Islands, Seychelles, and New Zealand do not suggest that there are energy or macronutrient (protein, carbohydrate, and fat) deficiencies in these populations. However, micronutrient deficiencies, such as iron and zinc, due to low intake of fortified or unrefined grains, fruits, and vegetables are possible. There

is insufficient information on the extent of breast-feeding of the infants to determine whether the use of other sources of milk and milk substitutes affected the outcome because of inadequate levels of iron, vitamins, and other minerals in those sources. The effects of such deficiencies on neurobehavioral end points might be evident long before any clinical signs of deficiency are present, and such deficiencies might not

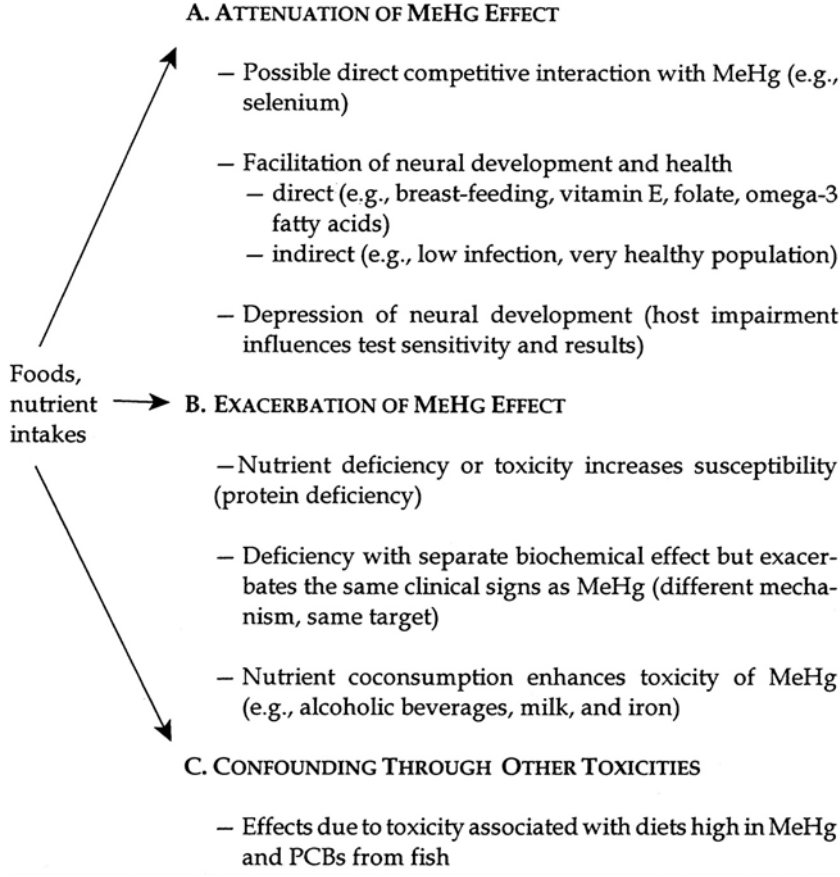

FIGURE 3-1 Hg nutrient interactions. Source: Modified from NIEHS 1998.

have been obvious in the study populations. Although those deficiencies could affect the risk estimate, an artifactual response will be seen only if those deficiencies are disproportionally distributed among the individuals exposed to MeHg at different doses.

Dietary Interactions and Confounding

Dietary factors can also confound studies of the effects of MeHg when consumption of a food contributes to the measured outcome through more than one component in that food. If a factor is associated with both MeHg exposure and outcome measures but is not part of the pathway by which MeHg effects neurological or other responses, it can be considered a confounding factor and must be controlled for in the analyses. Because the primary source of exposure is from fish consumption, it is difficult to determine whether the Hg in that source is the only cause of the fish-related effects. Other contaminants that could be present in fish, such as polychlorinated biphenyls (PCBs) or dichlorodiphenyltrichloroethane (DDT), could confound a study. High fish consumption could also result in the absence of another important food or nutrient from the diet. Conversely, fish consumption might be associated with the intake of protective substances, such as selenium and omega-3 fatty acids. Such an association was seen by Osman et al. (1998), who examined blood MeHg and selenium concentrations in Polish children from Katowice.

The understanding of the causal relationship between MeHg and adverse effects, therefore, would be greatly enhanced by information on the intake of all dietary constituents and adjustment for other toxicants. Availability of quantitative dietary information and incorporation of that information into assessments of MeHg effects could improve the analysis of the studies.

It is important to remember that fish and shellfish are high-quality food sources of protein and nutrients and that they are low in saturated fats. They contain nutrients that are essential for proper central-nervous-system development and function, and they might have potential health benefits in the prevention of cardiovascular disease and cancer. A reduction in the consumption of fish and shellfish might result in dietary patterns that are generally more harmful.

Selenium

Although the effect of selenium on MeHg toxicity has not been well documented in humans, it has been known for over two decades that organic and inorganic selenium can influence the deposition of MeHg in the body and protect against its toxicity in animals (Ganther et al. 1972). In animals, selenium deficiency has been associated with enhanced fetotoxicity following MeHg exposure (Potter and Matrone 1974; Nishikido et al. 1987). At the other extreme, the toxicity of MeHg can be enhanced in the presence of very high selenium supplementation (as in its absence) (Nobunaga et al. 1979). Over 40 studies have examined the interaction of selenium and mercury in various systems. These have recently been reviewed by Chapman and Chan (2000).

Selenium also influences tissue deposition in a form- and dose-dependent manner. Administration of seleno-methionine increased MeHg and total Hg content in the blood of rats exposed to MeHg through fish consumption. Administration of selenium dioxide lowered Hg concentrations by 24-29% in the blood and liver of rats in the same model system. Selenite supplementation in the diet of female rats before mating, during gestation, and during lactation antagonized the central-nervous-system effects following in utero exposure to MeHg (Fredriksson et al. 1993). Selenium injection during gestation has been shown to increase Hg concentrations in the neonatal brain (Satoh and Suzuki 1979), whereas ingestion has been shown to reduce brain levels (Fredriksson et al. 1993).

Therefore, animal experiments show that selenium might be protective in terms of neurodevelopmental responses but this is not clear. The selenium dose, form, and exposure route (injection vs ingestion) might affect the tissue deposition profiles. Although selenium appears to have a protective effect in animals, no association has been confirmed in humans. The mechanism by which selenium influences the deposition of Hg is not established. Proposed mechanisms include the formation of seleno-MeHg complexes, a selenium-induced release of MeHg from sulfhydryl bonds in the blood, and tissue-specific mechanisms that influence intracellular uptake (Glynn and Lind 1995).

Garlic

Garlic might be an important effect modifier in MeHg studies. Many

compounds (or their metabolites) in garlic could act as metal chelating or complexing agents and increase MeHg excretion. Such chemicals can be converted to thiols or include thiols (diallyldisulfide, diallyltrisulfide, propylallyldisulfide, and diallylsulfide), glutathione, vitamin C, and thiol amino acids (see review by Block 1985). Garlic also contains selenium (0.72-1.52 µg of selenium per gram of garlic), which, as previously discussed, might influence Hg toxicokinetics.

Animal studies support a protective role of garlic against Hg toxicity (Cha 1987; Rhee et al. 1985). Male Sprague-Dawley rats were simultaneously administered MeHg (4 ppm), cadmium, and phenylmercury in their drinking water as well as 8% peeled, crushed raw garlic (*Allium satirum*) in the feed (200 ppm allicin) for 12 weeks. Results indicate a statistically significant reduction in Hg tissue concentrations compared with rats that did not receive garlic (Cha 1987). It is not clear from that study whether the garlic removed Hg that had been deposited in the tissues or whether it prevented its accumulation before deposition. Severe pathology was noted in the kidneys of rats receiving the MeHg in the absence of garlic, and only mild or no damage was noted in MeHg-exposed rats receiving 6.7% or 8 % garlic, respectively. Interpretation of that study must be done cautiously, however, because the effects might be due to cadmium and not Hg toxicity. It should also be noted that the protection is against the renal effects of MeHg, not the neurotoxicity.

In an earlier paper, Rhee et al. (1985) exposed rats (40 per group) intraperitoneally to MeHg (5 mg/kg of body weight per day) for 8 days. One group also received garlic. Tissue Hg concentrations were lower in the garlic-exposed animals than in the rats that did not receive garlic.

It should be noted that the doses of garlic used in those studies (6-8% by animal weight) are well above the expected garlic content in the human diet, even in those cultures that use relatively high amounts of garlic in their cooking. More extensive study of the interactions between garlic and MeHg is needed.

Omega-3 Fatty Acids

Polyunsaturated fatty acids are essential for brain development. During perinatal development, docosahexaenoic acid (DHA), an omega-3 fatty acid, accumulates in membrane phospholipids of the nervous

system. Deficiency in DHA impairs learning and memory in rats (Greiner et al. 1999).

The ratio of omega-3 to omega-6 fatty acids might also be important. The largest source of omega-3 fatty acids, in particular eicosapentanoic acid and its metabolite DHA, in the human diet is oily fish, such as salmon, herring, and other cold- water fish. Chalon et al. (1998) demonstrated that fish oil affects monoaminergic neruotransmission and behavior in rats. Omega-3 fatty acids might enhance neurotoxicological function and their deficiency might contribute to lower test results, which would confound MeHg toxicological studies in human populations. Individuals consuming less fish might perform more poorly. Individuals on a diet high in fish might demonstrate the competing effects of enhanced function from these fatty acids and reduced function because of the presence of MeHg in the same food source. A case-control study in Greece concluded that low fish intake is associated with an increased risk of cerebral palsy (Petridou et al. 1998). Populations eating diets rich in fish might have enhanced neural development that could mask adverse effects on development caused by MeHg. Therefore, controlling for intake of essential fatty acids in MeHg studies is important. That can be done by measuring biomarkers of long-term exposure to fatty acids, such as adipose tissue (Kohlmeier and Kohlmeier 1995). However, there is no evidence to date that supplementation of omega-3 fatty acid to the diet of a well-nourished term infant further enhances neurological development or attenuates the toxic effects of Hg.

Protein

The type and amount of protein consumed might affect the uptake and distribution of Hg in the body. Low protein intakes have been associated with increased Hg in the brain of the mouse (Adachi et al. 1994; Adachi et al. 1992). Sulfur amino acid ingestion might also increase blood, renal, and hepatic concentrations of Hg. Cysteine appeared to enhance transport of MeHg to the brains of rodents (Aschner and Clarkson 1987; 1988; Aschner and Aschner 1990; Hirayama 1985) when the amino acid was injected into the animals at the time of oral dosing or injection of MeHg chloride. There is some indication that

leucine might inhibit MeHg uptake (Mokrzan et al. 1995). In contrast, in vitro studies indicate that methionine might stimulate MeHg uptake (Alexander and Aaseth 1982; Wu 1995).

Alcohol

Ethanol has been shown to potentiate MeHg toxicity in mice and rats (Takahashi et al. 1978; Turner et al. 1981). Five studies conducted in rodents examined the potential for alcohol interactions with MeHg. These studies indicate that the coconsumption of alcohol with MeHg can potentiate toxicity, particularly in the kidney (Takahashi et al. 1978 as cited in Chapman and Chan 2000; Rumbeiha et al. 1992; Tamashiro et al. 1986b; Turner et al. 1981; McNeil et al. 1988). Ethanol administered to male rats in conjunction with daily injections of MeHg chloride has resulted in a dose-dependent increase in tissue concentrations of both total Hg and MeHg in the brain and kidneys and in the morbidity and mortality of these animals. The applicability of these findings to human alcohol consumption and MeHg exposure patterns is unknown.

Other Foods That Might Influence Hg Uptake

Two studies indicated that the addition of milk to rodent diets increases the total body burden of Hg as well as Hg concentrations in the brain (Landry et al. 1979; Rowland et al. 1984). Landry et al. (1979) showed a 56% increase in the whole-body retention of Hg in female BALB/c mice fed liquid diets of evaporated whole milk as compared with their standard diet. That increase was attributed to the binding of heavy metals to the milk triglycerides, enhancing gut absorption. Those findings of an increased retention of MeHg with a diet containing evaporated milk were confirmed by Rowland et al. (1984).

There are strong indications that wheat bran, but neither cellulose nor pectin, when consumed concurrently with MeHg administration, might reduce Hg concentrations in the brain. In a study of male BALB/c mice, a dose-response relationship between brain Hg concentrations and the percentage of wheat bran was seen across 0%, 5%, 15%, and 30% wheat bran in the diet. The highest dose of wheat bran decreased the half-time

of Hg elimination by 43%, and decreased the brain Hg concentrations by 24%. Corresponding reductions were seen in the Hg concentrations in the blood of the bran-fed animals. Reductions of that magnitude have been associated with a lower incidence and severity of symptoms of neurotoxicity in rats. The effect has been attributed partially to binding of the Hg to bran, reducing its absorption from the gut and decreasing intestinal transit time. Using evidence of an increase in mercuric Hg in the large intestines of the bran-fed mice, it has also been hypothesized that wheat bran increased the rate of demethylation of organic Hg in the gut (Rowland et al. 1986).

Vitamin E

The protective effect of coconsumption of α-tocopherol supplementation in the diet has been shown to be protective against Hg toxicity in tissue cultures and animals models. For example, in studies of male golden hamsters, the injection of 2 ppm α-tocopherol acetate completely prevented the neurotoxic effects and histological changes associated with injection of 2 ppm MeHg (Chang et al. 1978). The hypothesized mechanism is an antioxidant effect related to lipid peroxidation and to the prevention of neuronal degeneration (Kling and Soares 1982; Kling et al. 1987; Chang et al. 1978; Kasuya 1975; Park et al. 1996; Prasad et al. 1980).

Nutrient Enhancement of Toxicity

In addition to the effects of protein, milk, and alcohol discussed earlier, four other nutrients have been implicated in the enhancement of MeHg toxicity: vitamin A, vitamin C, iron, and β carotene. Welsh (1977) reported in an abstract that vitamin A (10,000 IU/kg) decreased the time of onset of Hg toxicity in Fischer 344 rats given methylmercuric chloride at 10-15 ppm in drinking water. Vitamin C was shown to increase the absorption of Hg from the gastrointestinal tract, shortening the survival time of guinea pigs exposed to methylmercuric iodide at 8 mg/kg per day (Murray and Hughes 1976). The iron chelator, deferoxamine, was shown to inhibit the formation of reactive oxygen species in the cerebel

lum of rats treated with MeHg at 5 mg/kg (LeBel et al. 1992). Finally, Andersen and Andersen (1993) reported that β-carotene at 1,000 to 10,000 IU/kg enhanced Hg-induced lipid peroxidation in the liver, kidney, and brain of CBA mice exposed to methylmercuric chloride. β-carotene did not affect the activity of total glutathione peroxidase or selenium-dependent glutathione peroxidase.

Beneficial Effects of Fish Consumption

The committee is aware of the other nutritional advantages of diets rich in fish, including fish being a rich source of vitamin D, omega-3 fatty acids, protein, and other nutrients that might be marginal in some diets. Cardiovascular disease, osteoporosis, and cancer might be partially prevented by the regular consumption of fish. Those are major chronic diseases that afflict large proportions of the U.S. population. For that reason, the long-term goal needs to be a reduction in the concentrations of MeHg in fish, rather than a replacement of fish in the diet by other foods, such as saturated fat rich sources of protein like red meat.

In the interim, the best methods of maintaining fish consumption and minimizing Hg exposure is the consumption of smaller fish within a species and the selection of species of fish known to have lower MeHg concentrations. Ikarashi et al. (1996) reported that, within a species, the MeHg content of the fish relates to the size of the fish, presumably because larger fish have had a longer life span and more time to accumulate MeHg.

TOXICOKINETIC VARIABILITY

Typically, biomarkers of MeHg exposure (i.e., hair or blood total Hg concentrations) are used as a surrogate for dose in the derivation of a reference dose (RfD) for MeHg. As discussed in Chapter 4, hair Hg is approximately 90% MeHg. Total Hg concentration in blood can reflect exposures to both MeHg and inorganic Hg. One goal of a dose-response assessment is thus to identify a biomarker concentration that is associated with a no-observed-adverse-effect level (NOAEL), low-observed-adverse-effect level (LOAEL), or a benchmark dose. That biomarker

concentration is then translated into an RfD. An RfD is a dose of MeHg that is considered safe to ingest and is expressed in micrograms of MeHg per kilogram of body weight per day. Therefore, to derive the RfD, it is necessary to determine the ingested dose that resulted in the measured Hg concentration in the biomarker. That is referred to as dose reconstruction. That determination requires the back-calculation of dose using a toxicokinetic model. There are several toxicokinetic parameters that determine the tissue (or biomarker) MeHg concentration after ingestion of a given dose of MeHg. Those parameters include the uptake of MeHg from the gastrointestinal tract, the distribution of MeHg to the various body tissues (including the biomarker tissues), and the elimination of MeHg or Hg from those tissues. The uptake, distribution, metabolism, and elimination have been described by a physiologically based pharmacokinetic (PBPK) model (Clewell et al. 1999) and by a one-compartment pharmacokinetic model (IPCS 1990; EPA 1997). Both models require a quantitative description of several physiological and toxicokinetic inputs (e.g., body weight, blood volume, and hair-blood partition coefficients).

The PBPK model of Clewell et al. (1999), illustrated in Figure 3-2, attempts to characterize the distribution and redistribution of MeHg among several body compartments, including maternal hair and fetal cord blood. Although the PBPK model is conceptually more accurate and flexible than the one-compartment model, it is also considerably more complex, and thus, more difficult to evaluate.

In contrast, the one-compartment model, illustrated in Figure 3-3, collapses the maternal-body compartments to a single maternal-blood compartment. The blood concentration of MeHg (and Hg^{2+} resulting from MeHg metabolism) is assumed to be at steady state, and the model permits the estimation of the blood Hg concentration resulting from a given ingested dose. The corresponding hair Hg concentration can then be estimated by using an empirically derived hair-to-blood Hg concentration ratio.

The rate of MeHg entry into the blood, I (micrograms per day), is calculated by

$$I = D \times W \times A \times F, \quad (1)$$

where D is the ingested dose (micrograms per kilogram of body weight per day); W is the body weight (kilograms); A is the fraction of ingested MeHg that is absorbed; and F is the fraction of absorbed MeHg that is distributed to the blood.

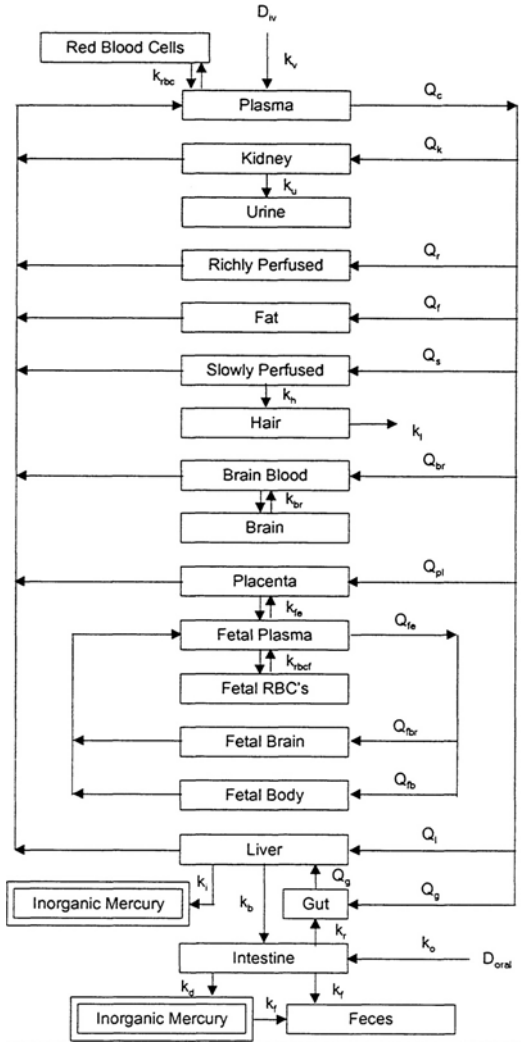

FIGURE 3-2 PBPK model for MeHg. Model parameters denoted by k represent rate constants for MeHg. Model parameters denoted by Q represent plasma flow rates. D represents the dose of MeHg. Source: Clewell et al. 1999. Reprinted with permission from *Risk Analysis*; copyright 1999, Plenum Publishing Corporation.

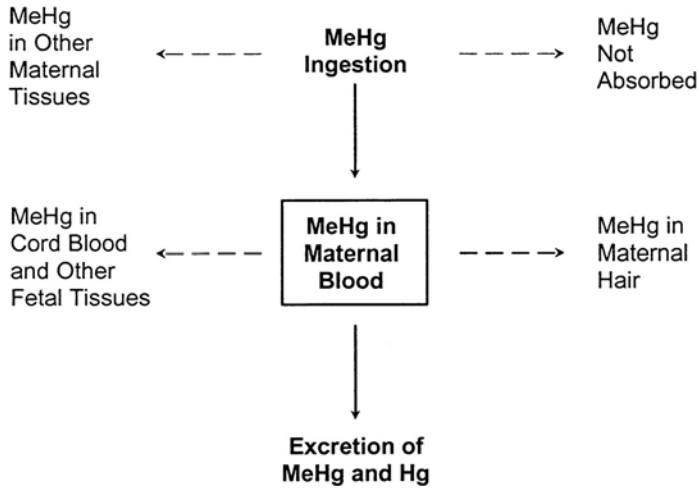

FIGURE 3-3 The one-compartment model relating ingestion of MeHg to MeHg in maternal blood. The one-compartment model predicts the steady-state MeHg concentration in the maternal-blood compartment under the assumption that the daily mass of MeHg entering the compartment from ingestion is equal to the daily mass leaving the compartment by excretion. Dotted lines indicate other toxicokinetic compartments that are not directly considered in the model.

The rate of MeHg elimination from the blood, E (micrograms per day), is calculated by

$$E = C \times b \times V, \quad (2)$$

where C is the concentration of MeHg in the blood (micrograms per liter); b is the elimination-rate constant, expressed as the fraction of the concentration eliminated per day (day^{-1}); and V is the blood volume (liters).

By definition of steady state, the rate of MeHg entry into the blood is

equal to the rate of MeHg elimination from the blood. Therefore, at steady state, $I = E$ and

$$D \times W \times A \times F = C \times b \times V. \quad (3)$$

Equation 3 can be solved for C to calculate the blood MeHg concentration resulting from a given steady-state dose:

$$C = \frac{D \times W \times A \times F}{b \times V}. \quad (4)$$

Equation 3 can also be solved for D to calculate the steady-state dose corresponding to a given blood concentration:

$$D = \frac{C \times b \times V}{W \times A \times F}. \quad (5)$$

The MeHg concentration in hair, H, is related to the concentration in blood, C, through the empirically derived hair-to-blood Hg concentration ratio (μg/g)/(μg/L), R, as follows:

$$C = (1/R) \times H. \quad (6)$$

The inverse form, $(1/R)$, is used to maintain the ratio in the form in which it is traditionally expressed in the scientific literature.

To calculate the ingested dose that gave rise to a measured hair concentration, Equation 6 can be combined with Equation 5 as follows:

$$D = \frac{(1/R)\, H \times b \times V}{W \times A \times F} \quad (7)$$

Equation 5 and 7 can thus be used to estimate the ingested dose of MeHg that gave rise to a maternal-blood and maternal-hair MeHg concentration, respectively, which are associated with a given level of adverse effects.

When fetal-cord-blood MeHg concentration is the biomarker measured, the corresponding maternal-blood concentration can be estimated

using an empirically derived ratio of cord-blood concentration to maternal-blood concentration.

Due to interindividual variability in physiology and kinetics, there is no single correct value that can be assigned to any of the parameters in either toxicokinetic model. Each of the model parameters is a random variable whose possible values in a population can be described by a probability distribution. The ingested dose of MeHg corresponding to a measured biomarker concentration, therefore, is also described by a probability distribution. That distribution is determined by the combination of the distributions of the individual model parameters according to the mathematic form of the model. The central-tendency value of the ingested dose corresponding to a given biomarker concentration could be estimated using the central-tendency value for each parameter of the model. However, no single value, including the central tendency, can capture the range of possible values for a parameter in a heterogenous population. Furthermore, no combination of single-number (point-estimate[1]) parameter values in a model can estimate the range of possible ingested doses. Because the RfD is intended to protect the most sensitive individuals in a population, an estimate based solely on the central tendency of the distribution (without uncertainty adjustment) would not provide a protective RfD. To be protective of the sensitive population, the ingested dose used as the basis for the RfD should be at the lower range of doses that could result in a given MeHg biomarker concentration. Figure 3-4 presents an estimate, using the one-compartment model, of the percentage of women of childbearing age having a hair Hg concentration of 11 ppm with a given MeHg ingested dose. The use of central-tendency values for each of the model parameters would approximate the ingested dose at which 50% of the population would achieve a hair MeHg concentration of 11 ppm. In that example, the dose is approximately 0.4 µg/kg per day. However, 50% of the population is predicted to achieve a hair Hg concentration of a 11 ppm with an ingested dose of MeHg of less than 0.4 µg/kg per day. An RfD based on an ingested dose of 0.4 µg/kg per day without further adjustment would, therefore, be protective of only 50% of the population. In that example, to protect 95% of the population from having a hair Hg

[1]A point estimate is a single value, selected from a distribution of values, that is intended to represent the entire distribution.

concentration above 11 ppm, the ingested dose would be about 0.2 μg/kg per day, or half the dose predicted using central-tendency values for the model parameters.

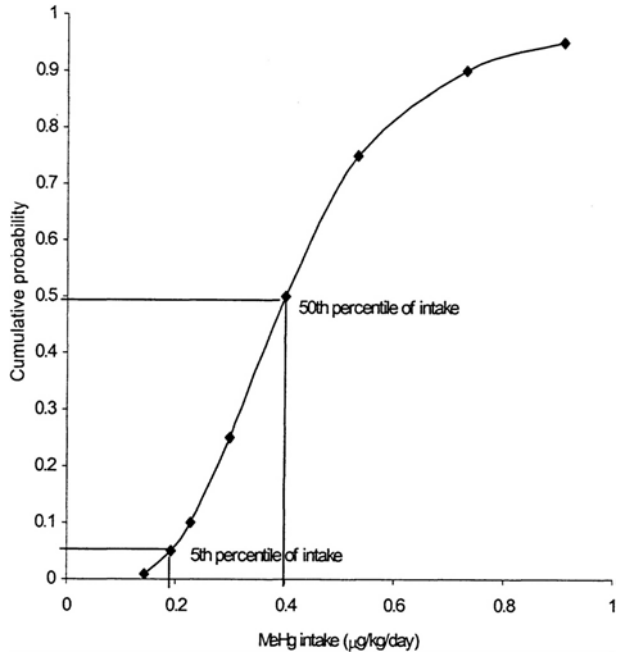

FIGURE 3-4 Predicted mean probability of MeHg intake corresponding to 11 ppm MeHg in hair. Source: Data from Stern 1997.

In estimating the range of ingested doses which could have resulted in a given biomarker concentration, there are three main sources of variability errors in model selection, errors in estimation of model parameters, and true population variability (i.e., heterogeneity). The variability due to the first two sources can be reduced by the collection

of more or better data and through development of more accurate models. However, heterogeneity in toxicokinetics is inherent in human populations, and the variability in estimates due to population variability cannot be decreased.

In its derivation of an RfD for MeHg, the U.S. Environmental Protection Agency (EPA) used point estimates to calculate an ingested dose from its benchmark hair concentration (EPA 1997). EPA did not address the distribution of the model parameters or of the predicted dose, nor did it characterize how inclusive its point estimate of dose was of the range of ingested doses that could have given rise to the benchmark hair concentration. An uncertainty factor of 3, however, was used to account for "variability in the human population, in particular, variation in the biological half-life of MeHg, and the variation that occurs in the hair/blood ratio for Hg." Appendix D of volume 5 of the *EPA Mercury Study Report to Congress* (EPA 1997; see also Swartout and Rice 2000), presents an ad hoc probabilistic assessment of interindividual toxicokinetic variability, using the one-compartment model, in the calculation of the ingested dose. The results of that analysis, however, were not used by EPA in the derivation of its RfD.

In the derivation of an MRL for MeHg, ATSDR (1999) also used point-estimate values in the one-compartment model to calculate the ingested dose without addressing the distribution of the model parameters or of the predicted dose. Parameter estimates in the model were selected to reflect the central tendency of the range of values in the population. Two uncertainty factors of 1.5 each (summed to give an overall uncertainty factor of 3) were applied to the NOAEL to address "variability in hair-to-blood ratios among women and fetuses in the U.S. population, as determined by pharmacokinetic modeling of actual data by Clewell et al. (1998)," and "to address the remainder of any inter-individual variability (i.e., pharmacodynamics) in the U.S. population." The appropriateness of such an overall adjustment that addresses interindividual variability in only one parameter of the toxicokinetic model (i.e., the hair-to-blood ratio) and the poorly characterized adjustment to account for the "remainder" of variability are difficult to assess.

Three analyses have been carried out to characterize the interindividual toxicokinetic variability in the estimates of the MeHg-ingested dose corresponding to a given concentration of Hg in a biomarker (Stern 1997; Swartout and Rice 2000 (see also EPA 1997); Clewell et al. 1999). Each

of those analyses used a Monte Carlo simulation to combine the probability distributions for the individual model parameters to generate a probability distribution of the corresponding ingested dose. That probability distribution estimates the fraction of the maternal population who could achieve a specific hair Hg concentration from a given MeHg ingestion. The analyses by Stern (1997) and Swartout and Rice (2000) are based on the one-compartment model, and that by Clewell et al. (1999) is based on the PBPK model.

Stern (1997) identified data on the distribution of parameters in the one-compartment model from the published literature. Blood volume and body weight were assumed to be correlated. A similar approach was used by Swartout and Rice (2000). In that analysis, however, some of the parameters are described by different distributional shapes or by distributions from different data sources than those used by Stern (1997). Swartout and Rice (2000) assumed correlations between several pairs of parameters: the hair-to-blood ratio and the elimination-rate constant; body weight and blood volume; and the fraction of the absorbed dose in the blood and body weight.

Clewell et al. (1999) likewise identified data on the distribution of parameters from the literature, but because the PBPK model contains many parameters that are not used in the one-compartment model, the distributions used in this analysis are not directly comparable to those used in one-compartment-model analyses. In addition, given the large number of parameters and the inconsistent availability of distributional data for those parameters, Clewell et al. (1999) tended to use default distributions for their model parameters.

The variability in the relationship between the concentration of Hg in maternal hair or cord blood and the ingested dose of MeHg predicted by the three analyses is summarized in Table 3-1. If the ingested dose is calculated from the Hg concentration in hair or blood from the central-tendency estimates of model parameters in either the one-compartment or the PBPK model, then the resulting ingested dose should approximate the 50th percentile of the population distribution. The ratio of the ingested dose corresponding to the 50th percentile of the distribution to the dose at the 5th percentile of the distribution, therefore, is an estimate of the factor by which the central-tendency estimate of the ingested dose should be divided to make the dose estimate inclusive of the variability in 95% of the population. Likewise, the ratio of the ingested dose

corresponding to the 50th percentile of the distribution to the dose at the 1st percentile is an estimate of the factor by which the central tendency estimate should be divided to make the dose estimate inclusive of the variability in 99% of the population. In general, Stern (1997) and Swartout and Rice (2000) predicted similar variability in the relationship between hair Hg concentration and ingested dose, but both predicted a somewhat larger variability than did Clewell et al. (1999). Nonetheless, the three studies differ only by a factor of 1.5 in their predictions of both the 50th:5th and the 50th:1st percentile ratios. Although the three studies predict similar relative variability, examination of the median (i.e., 50th percentile) ingested dose predicted to correspond to 1 ppm Hg in maternal hair (Table 3-1) indicates that the absolute value of the central tendency of the distribution of ingested doses predicted by Stern

TABLE 3-1 Comparison of Results from Three Analyses of the Interindividual Variability in the Ingested Dose of MeHg Corresponding to a Given Maternal-Hair or Blood Hg Concentration

Study	Maternal Medium	50th percentile[a] (μg/kg-d)	50th percentile/5th[b] percentile	50th percentile/1st percentile[c]
Stern (1997)	hair	0.03-0.05[d] (mean = 0.04)	1.8-2.4 (mean = 2.1)	2.3-3.3 (mean = 2.7)
	blood	0.01	1.5-2.2 (mean = 1.8)	1.7-3.0 (mean = 2.4)
Swartout and Rice (2000)	hair	0.08	2.2	Data not reported
	blood[e]	0.02	2.1	2.8
Clewell et al. (1999)	hair	0.08	1.5	1.8
Clewell et al. (1999)	blood[f]	0.07	1.4	1.7

[a]Predicted 50th percentile of the ingested dose of methylmercury that corresponds to 1 ppm Hg in hair or 1 ppb in blood.
[b]Ratio of 50th percentile of ingested dose of methylmercury that corresponds to 1 ppm Hg in hair or 1 ppb in blood to the 5th percentile.
[c]Ratio of 50th percentile of ingested dose of methylmercury that corresponds to 1 ppm Hg in hair or 1 ppb in blood to the 1st percentile.
[d]Range reflects minimum and maximum values among eight alternative analyses.
[e]Data from J. Swartout, U.S. Environmental Protection Agency, personal commun.; June 9, 2000.
[f]Data from H.J. Clewell, ICF Consulting, personal commun.; April 19, 2000.

(1997) is lower than that predicted by the other two studies. In other words, the distribution predicted by Stern appears to be shifted toward lower-ingested dose values compared with the other two analyses. That difference appears to be due to selection of different data sets for several key model parameters. Given the existence of several valid data sets for those parameters, it is not clear which central-tendency estimate is more appropriate.

Each of those analyses (Stern 1997; Swartout and Rice 2000 (see also EPA 1997); Clewell et al. 1999) estimated the ingested dose corresponding to maternal-hair Hg concentration. For studies in which the biomarker measured is the Hg concentration in cord blood (e.g., the Faroe Islands studies), the estimation of the ingested dose would follow the same approach, except that the hair-to-blood ratio would be omitted from the model. The analyses of variability of the ingested dose can be recalculated for the variability of the ingested dose corresponding to a given blood Hg concentration. The results of that calculation for the three analyses are presented in Table 3-1. Comparison of the relative variability in the ingested dose based on the ratio of hair Hg concentration to blood Hg concentration indicates that the variability for maternal-hair Hg concentration is 1.1 to 1.2 times greater than that for the maternal-blood Hg concentration. That result is consistent with the results of sensitivity analyses conducted in each of the three studies, which identified the hair-to-blood ratio as a major contributor to the variability in the predicted ingested dose. Nonetheless, the Table 3-1 data, which are intended to describe the distribution of ingested doses that corresponds to a given cord-blood Hg concentration, actually describe the relationship between the ingested dose and the maternal-blood Hg concentration. The application of estimates based on the ratio of maternal-blood Hg concentration to estimates of cord-blood Hg concentration assumes that those two concentrations are equal. Some observations suggest that Hg concentrations in cord blood are larger than in maternal blood by at least 20-30 % (Dennis and Fehr 1975; Pitkin et al. 1976; Kuhnert et al. 1981), however, such differences are not seen consistently (Fujita and Takabatake 1977;Sikorski et al. 1989). Therefore, the data in Table 3-1 might underestimate the variability in ingested doses calculated from cord-blood Hg concentrations, however, that is not entirely clear.

On the basis of the data in Table 3-1, if an estimate of the ingested

dose from a benchmark hair Hg concentration is generated using point estimates of the central tendency for each model parameter, then dividing this initial estimate by an uncertainty factor of 2 would result in a dose that includes approximately 95% of the interindividual toxicokinetic variability in the population. Dividing the initial estimate by an uncertainty factor of 2-3 would include approximately 99% of the interindividual toxicokinetic variability. Similarly, for estimates of the ingested dose based on a benchmark blood Hg concentration, the data in Table 3-1 indicate that adjustment of a central-tendency estimate of the ingested dose by an uncertainty-factor adjustment of about 2 takes into account 95-99% of the interindividual toxicokinetic variability.

The use of uncertainty factors to adjust a central-tendency estimate of the ingested dose for interindividual variability is an indirect, or "back-end," approach to accounting for such variability in the RfD. A direct, or "front-end," approach would be to select as the starting point for the derivation of the RfD the ingested dose that corresponds to a given (e.g., benchmark) hair or blood Hg concentration for the percentile of the population variability that is to be accounted for. In that case, no uncertainty-factor adjustments would be necessary to account for toxicokinetic variability in the dose conversion. For example, with reference to Figure 3-4, if the benchmark (or NOAEL) hair concentration is 11 ppm and the RfD is intended to include the toxicokinetic variability in 95% of the population, then the corresponding ingested dose would be approximately 0.2 μg/kg per day. The difficulty with using such an approach is that, in the direct approach the estimate of the absolute value of the ingested dose is the critical determination. Whereas in the uncertainty factor approach the estimate of the relative variability in the ingested dose is critical. As discussed previously, for a given hair concentration the absolute value of the ingested dose for any given percentile of the population is not consistent in the analyses of Stern (1997), Swartout and Rice (2000), and Clewell et al. (1999). The analysis of Stern (1997) predicts lower absolute values of the ingested dose for a given percentile of the population than the other two analyses. Therefore, the use of the direct approach requires that a choice be made among the probability distributions predicted by those analyses. The differences in the analyses are due to the use of different data sets for parameter estimates, and there is no clear basis for choosing one data set over another. Even when central-tendency estimates and uncertainty

factors are used, the most appropriate value for each model parameter must be selected. Selection of different values for model parameters could underlie differences in the modeling results. The advantage of the uncertainty-factor approach, however, is that the choice for each model parameter is explicit. That allows for a more reasoned and detailed discussion of those choices. The analyses of Stern (1997), Swartout and Rice (2000), and Clewell et al. (1999) all discuss their choices of parameter estimates. The information presented in those discussions should be considered in the selection of the central-tendency estimates of the individual parameters.

CONCLUSIONS

- Sensitivity to the toxic effects of MeHg is related to the age at which exposure occurs. Because of that, the fetus and young infants exposed during periods of rapid brain development are particularly vulnerable.
- Sex differences appear to affect the metabolism, tissue uptake, excretion and toxicity of Hg.

  — Gender specific effects due to developmental exposure to MeHg typically indicate a greater sensitivity for male offspring.
  — Gender sensitivity in toxicity appears to be dependent on the species used and outcome studied.

- Dietary nutrients and supplements might protect against the toxicity of MeHg. Data regarding the relative presence or absence of such nutrients and supplements either in the populations studied or in the United States are not available. The lack of that information contributes to overall data-base uncertainty, but it does not detract from the suitability of those studies for determining the risk associated with MeHg.
- In addition to the above factors, intraindividual differences are clearly noted in responses to similar exposures. Those are explained, in part, by nutritional factors that might exacerbate or attenuate the effects of Hg toxicity in the host. Currently unknown genetic susceptibilities could be expected to play a role in response variability.
- In any MeHg risk assessment in which the exposure metric is a Hg

biomarker concentration, it is necessary to use a toxicokinetic model to estimate the ingested dose that gave rise to the critical biomarker concentration (e.g., benchmark or NOAEL concentration).

— The simpler and more easily manipulated one-compartment model and the more complex but more realistic PBPK model have been used for that purpose.
— The parameters in those models are variables whose possible values are described by probability distributions reflecting the interindividual variability in the population.
— The ingested doses predicted by the one-compartment and PBPK models, therefore, are also probability distributions that reflect the likelihood that any given ingested dose could give rise to the critical biomarker concentration.

• Failure to consider interindividual toxicokinetic variability can result in an RfD that is not protective of a substantial portion of the population.

— Interindividual toxicokinetic variability can be addressed in the derivation of the RfD by application of an uncertainty factor to a central- tendency estimate of the ingested dose.
— It is uncertain which values are most appropriate for the model parameters used to derive the central-tendency estimates. The basis for each choice should be carefully considered with reference to discussions already presented in the published analyses of toxicokinetic variability.

RECOMMENDATIONS

• Future studies of MeHg exposures in humans should include a thorough assessment of the diet during the periods of vulnerability and exposure. They should involve assessment of the nutritional adequacy of the group, including the assessment of nutritional and environmental factors that might attenuate or exacerbate the effect of MeHg on the health end points measured.

— Dietary assessment should be conducted concurrently with the exposures, because retrospective assessment is influenced by many factors, including memory, changes in eating behavior,

food fortification, and use of prenatal and postnatal vitamin and mineral supplementation. Dietary assessment should be conducted on a person-specific basis, with particular effort to estimate quantitatively individual consumption and consumption patterns of fish and pilot whale.

— For all the studies, the estimates of consumption of fish (and whale meat as appropriate) should be used with information on MeHg concentrations in the food to estimate possible MeHg intake by pregnant women, young children, and adults. Attempts should be made to validate estimates of intake by using experimental data on the relationship between hair Hg concentration and diet intake.

— Future studies should include a standardized measure of the duration of breast-feeding and the quantity of breast milk ingested by infants. The dose of MeHg is dependant on the amount of milk ingested and the MeHg content of the milk. Historical recording of duration of breast-feeding is likely to be biased; therefore, a prospective diary of breast-feeding and weaning should be considered.

• Studies using animal models should examine changes in the dose response characteristics of Hg effects associated with nutritional or genetic factors.

• Any biomarker-based RfD for MeHg should specifically address interindividual toxicokinetic variability in the estimation of dose corresponding to a given biomarker concentration.

— The starting point for addressing interindividual toxicokinetic variability should be a central-tendency estimate of the ingested dose corresponding to a critical biomarker concentration (e.g., a benchmark hair concentration).

— The central-tendency estimate of the ingested dose should be based on careful consideration of the several possible and sometimes contradictory data sets for each parameter. A starting point for such consideration is the discussion of parameter distributions presented in the analyses of Stern (1997), Swartout and Rice (2000), and Clewell et al. (1999).

• An uncertainty-factor adjustment should be applied to any central-tendency estimate of the ingested dose corresponding to the critical biomarker concentration.

- For an RfD based on maternal-hair Hg concentration, an uncertainty-factor adjustment of 2 should be applied to the central-tendency estimate of dose to be inclusive of 95% of the toxicokinetic variability in the population. An uncertainty-factor adjustment of 2-3 should be applied to be inclusive of 99% of the toxicokinetic variability.
- For an RfD based on blood Hg concentration, an uncertainty factor adjustment of about 2 should be applied to the central-tendency estimate of dose to be inclusive of 95-99% of the toxicokinetic variability in the population.
- Because of the recognized nutritional benefits of diets rich in fish, the best method of maintaining fish consumption and minimizing Hg exposure is the consumption of fish known to have lower MeHg concentrations.

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4

DOSE ESTIMATION

In assessing the risks of exposure to MeHg, quantitative exposure assessments are required to derive dose-response relationships from epidemiological data. A quantitative exposure assessment also allows risk assessment of an exposed population by comparing actual exposures to a reference dose (or similar benchmark) derived from critical studies. In contrast to experimental animal studies, in which the dose can be closely controlled, the dose in population-based epidemiological studies is not controlled and is therefore viewed as a random variable distributed across the study population. Three metrics for retrospective dose estimation and reconstruction are available for MeHg: dietary assessment, hair analysis, and blood analysis. Each metric has advantages and disadvantages. Ponce et al. (1998) proposed an approach for examining the relative uncertainties of those metrics.

DIETARY ASSESSMENT

With the exception of intakes through breast milk, which is less well characterized, exposure to MeHg occurs almost entirely from a single dietary category — fish (IPCS 1990, 1991). For that reason, the task of assessing dietary intake or assessing ongoing intake in populations with uncontrolled exposures is relatively straight forward compared to assessment of multiple types of food. There are several basic approaches to the estimation of MeHg exposure from dietary intake: collection of

duplicate portions of foods consumed; food-consumption diaries, in which daily fish intakes are recorded quantitatively; recall methods, such as 24-hr recall of fish consumption; diet histories of usual consumption at various meals; and food-frequency measures of usual frequency of consumption of fish and shellfish. Duplicate-diet collections and food-consumption diaries are prospective approaches, and the others are retrospective approaches.

General considerations for duplicate-diet studies were recently discussed by Berry (1997) and Thomas et al. (1997). In duplicate-diet studies, participants collect an identical portion of the food they consume and provide it to the investigator for laboratory analyses. In theory, duplicate-diet studies have the potential to provide the most accurate information on the ingested dose of MeHg, because the mass of fish and other nutrients and contaminants, in addition to MeHg, can be measured directly. The fact that only the fish portion of any given meal will contain MeHg simplifies the burden of duplicate-diet collection. In practice, however, this approach is limited by the demands it makes on the participants, the difficulty in identifying individuals who are willing to carry out such a study, the influence exerted by investigator observation, and the potential change in diet resulting in response to the burden of food collection. Thomas et al. (1997), working with nine highly motivated households, was able to collect duplicate samples for 97% of meals and 94% of snacks over a 7-day period. The number of uncollected meals, however, tripled after the first 3 days, and participants strongly recommended that future studies be limited to a maximum of 3-4 days. When such studies are confined to fish consumption, 3-4 days of collection might be useful only for populations with very frequent and highly regular patterns of fish consumption. Because of the practical limits on the length of the collection period, the authors recommended that duplicate-diet studies for risk-assessment purposes should be done over multiple intervals of time. Moreover, when the calorie content of collected food was compared with the estimated energy requirements of participants, duplicate portions were found to be underestimated.

Duplicate-diet studies have been specifically applied to the estimation of MeHg exposure by Sherlock et al. (1982) and Haxton et al. (1979). Sherlock et al. (1982) carried out a 1-week duplicate-diet study with 98 participants selected on the basis of frequent fish consumption. In

addition, a 1-month dietary diary was kept by the participants; the last week of the diary corresponded to the duplicate-diet collection. No indication is provided of the completeness of the duplicate-diet collection, but the weight of fish calculated from the diary during the week of duplicate-diet collection corresponded closely to the weight of fish measured from the duplicate samples. The authors noted however, indirect evidence of undercollection of duplicate-diet portions relative to consumed portions. It should also be noted that the preselection of subjects with frequent fish consumption increased the likelihood of collecting a meaningful number of samples over a 1-week period. A similar study with a randomly selected study sample would be less likely to provide adequate representation of infrequent consumers.

Haxton et al. (1979) conducted a 1-week duplicate-diet study with 174 subjects selected from fishermen and their families in coastal communities to obtain a population with high fish-consumption rates. No simultaneous diaries were kept, but the characteristic intake for each individual was identified from pre-collection interviews. No estimate of the completeness of the duplicate-diet collection was provided. However, the authors noted that the measured weight of weekly fish intake from the duplicate-diet samples was lower than that calculated from the interviews, and all measured intakes were below the calculated mean intake. The authors suggested that the discrepancy resulted from misidentification of characteristic intake in the interviews rather than from undercollection of dietary samples. No data are provided to support that assertion. As with the Sherlock et al. (1982) study, the preselection of subjects with frequent fish consumption made the relatively short collection period feasible.

Multiple-day food records (food-consumption diaries) are often used in conjunction with duplicate-diet studies (Sherlock et al. 1982, Thomas et al. 1997). This method, if conducted appropriately, has the advantage of recording information prospectively with little reliance on recall. It also requires less effort from participants than the duplicate-diet approach. However, daily recording of foods eaten at each meal requires a continuous and significant time commitment. Because fish are consumed relatively infrequently, the duration of the recording period might require many weeks to adequately capture infrequent consumers as well as variability in consumption among more frequent consumers. Furthermore, the design must be such that possible seasonal patterns of

consumption are observable. The determination of the mass of food consumed when using food-consumption diaries can be made by weighing samples or by participants' estimating portion size. The former is preferable but more invasive, especially when foods are consumed away from home. Participants' estimation of portion size introduces a degree of measurement error not seen with duplicate-diet methods. Furthermore, if the diary approach is used without duplicate-diet collection, analysis of Hg concentration in each fish meal consumed cannot be made directly but must be based on the characteristic Hg concentration in each reported species. Such studies must, therefore, rely on participants for correct identification of species. Incorrect species identification can lead to errors in estimation of MeHg intake. Consumers, as well as the markets from which they purchase fish, might not know or correctly identify the species that was bought and consumed.

The data from the Continuing Survey of Food Intake by Individuals (CSFII) generated by the U.S. Department of Agriculture from 1989 to 1995 rely on self-administered food consumption diaries for the second and third days of its 3 days of reporting (discussed in EPA 1997). The CSFII data have been used by the U.S. EPA to estimate fish consumption in the U.S. population (Jacobs et al. 1998) and to estimate MeHg intake (EPA 1997). The National Purchase Diary conducted by the Market Research Corporation used dietary diaries over 1-month periods between 1973 and 1974 (discussed in EPA 1997). The fish-consumption portions of these diary data were used to estimate MeHg exposure in the U.S. population (Stern 1993, EPA 1997).

Retrospective dietary-assessment methods are simpler and less expensive than prospective and duplicate-diet methods, and therefore are used more often as the basis of dietary exposure assessments. Food-frequency studies take the form of participants identifying their typical fish consumption (e.g., “How many times per week/month do you usually eat fish A?”). Diet histories involve recollection of specific meals over a specific time (e.g. 24-hr or 1-week periods). In the studies mentioned above, Sherlock et al. (1982) and Haxton et al. (1979) used retrospective assessment of typical consumption to preselect subjects. In a recent study of MeHg exposure among pregnant women in New Jersey (Stern et al. 2000), participants were asked to identify their typical consumption frequency and typical portion size of 17 species of fish and

fish dishes (e.g., fish sticks). MeHg intake was estimated as the product of the characteristic MeHg concentration for each fish species, the self-reported yearly frequency of consumption, and the self-reported average portion size. The yearly MeHg intake estimated in that manner was poorly correlated with the Hg concentration in hair from the same individuals. The authors attributed the discrepancy to the relatively infrequent consumption of fish in general. Therefore, the hair segments might have been too short to provide an adequate sample of the yearly intake. Uncertainty in the reporting of characteristic consumption frequency and portion size was also suspected as a contributing factor to the poor correlation.

The usefulness of studies using dietary recollection over a specific period depends on the participants' ability and willingness to recall information about fish meals over the target period. Recall of fish consumption seems to be much better than recall of other dietary items or of food intake in general. However, short-term recall methods of dietary assessment will tend to underrepresent the consumption characteristics of infrequent consumers (Whipple et al. 1996; Stern et al. 1996). If the species of fish (and thus the characteristic Hg concentration in the fish) consumed by frequent and infrequent consumers differ, or if the average portion size consumed by each group differs, the estimate of MeHg intake in the overall population will not be accurate.

The CSFII data used by EPA to estimate fish consumption (Jacobs et al. 1998) and MeHg exposure (EPA 1997) nationally are, as noted above, based on 1 day of recall and 2 succeeding days of diary entries. The National Health and Nutrition Examination Surveys (NHANES III) dietary data, generated from 1-day recall, were also used by the EPA to generate estimates of MeHg in the U.S. population (EPA 1997). Stern et al. (1996) used data from a fish-consumption-specific telephone survey of New Jersey residents. The survey elicited a 7-day recall. Relatively short-term recall studies can miss long-term patterns of variability in consumption and might not adequately capture consumption patterns of infrequent consumers. To address those issues, information on respondents' usual frequency of fish consumption was also elicited. That information allowed identification of infrequent consumers of fish in the sample. The information was used to investigate reweighting of the data to estimate the distribution of consumption frequency represented

in a hypothetical 1-year recall study. Interestingly, the reweighting of the data using several different approaches resulted in only minor differences in estimates of fish consumption and MeHg exposure.

Retrospective dietary data and diary data on fish consumption have frequently been used to stratify a study population into broad classes of MeHg intake before more quantitative estimation of exposure by measurement of Hg in biomarkers. Such data have also been used to provide a rough validation of biomarker analyses (e.g., Dennis and Fehr 1975; Skerfving 1991; Grandjean et al. 1992; Holsbeek et al. 1996; Vural and Ünlü 1996; Mahaffey and Mergler 1998). Less frequently, retrospective and diary data on fish consumption are used directly in quantitative estimations of MeHg exposure (Buzina et al. 1995; Stern et al. 1996; Chan et al. 1997). Such estimates, however, generally require species-specific Hg concentrations (microgram of Hg per gram of fish), which are combined with the reported consumption frequency (grams of fish per day), to yield an Hg intake rate (micrograms Hg per day). The assignment of species-specific concentration data is a potential source of error in such studies for several reasons. First, the identity of the species on the part of the retailer or the consumer is often ambiguous. Second, Hg concentrations characteristic of a given species in local and regional markets or waters might differ from the characteristic concentrations identified on the basis of nationwide sampling. Finally, characteristic Hg concentrations derived from data that are often decades old might not be valid today.

In the United States, data on Hg concentration in commercial fish are largely available from two sources: (1) the National Marine Fisheries Service (NMFS) study, which sampled fish that were intended for human consumption and which were landed in the United States in the early to mid-1970s (Hall et al. 1978); and (2) the U.S. Food and Drug Administration (FDA) sampling conducted in the early 1990s (FDA 1992). Both data bases represent samples of fish collected from landings and markets in various parts of the United States but do not identify the locations at which samples were obtained or sold. The NMFS data were collected more systematically, represent more species, and generally contain considerably more samples for each species than the FDA data. However, the FDA data are about 20 years more recent than the NMFS data. Analysis of species represented in both data bases by at least three samples (n=15) indicates that, in almost all cases, the Hg concentration

reported by FDA in a particular species is significantly lower than the concentration reported by NMFS. The most likely explanation for the discrepancy is the decreased availability of large fish due to overfishing (Stern et al. 1996). Those data cannot be used, therefore, to reflect potentially important local or regional differences in the characteristic concentrations of Hg by species. Studies addressing smaller populations with fewer varieties of fish (e.g., Buzina et al. 1995) can generate population-specific estimates of Hg concentrations by species. Given the variability in concentration within species, the assignment of a single representative value of Hg concentration is another potential source of error in such studies. The NMFS data base provides no estimate of such variability in U.S. commercial supplies. The FDA data base provides concentration ranges as well as average concentrations by species, but the ability to assess intraspecies variability in Hg concentration is limited by the generally small sample sizes. A study of Hg concentration in canned tuna (Yess 1993) indicates coefficients of variation of 55-120% across the several types of tuna commonly sold in cans. In general, sparse data on fish from commercial sources in the United States (FDA 1992) and data on food fish from noncommercial sources (e.g., Schuhmacher et al. 1994; Castilhos et al. 1998) often show a 2-3-fold difference between the mean and the maximum concentrations of Hg. Interspecies variability can be considerably larger. When data are available on intraspecies variability in MeHg concentrations, the variability can be integrated into estimates of intake through Monte Carlo probabilistic analysis (Chan et al. 1997). Intraspecies variability in Hg concentration might be less of a source of error in studies of frequent consumers of that species. With repeated consumption of a species of fish, total MeHg intake by consumers will approach the average concentration in that species. However, for populations with infrequent or sporadic consumption of a species, the effect of ignoring intraspecies variability in Hg concentrations could be significant.

BIOMARKERS OF EXPOSURE

MeHg lends itself to assessment of exposure through direct measurement in blood and hair. Assessment of Hg exposure through analysis of nail clippings has also been done (Pallotti et al. 1979; MacIntosh et al.

1997), but its correlation with fish consumption has yet to be clearly established. Hg exposure through breast milk has also been investigated (Pitkin et al. 1976; Fujita and Takabatake 1977; Skerfving 1988; Grandjean et al. 1995; Oskarsson et al. 1996). Compared with whole blood, breast milk (which is derived from maternal plasma) contains a much higher proportion of inorganic Hg (Skerfving 1988; Oskarsson et al. 1996). Therefore conclusions regarding the exposure of infants to MeHg from breast milk should use MeHg-specific analysis. Finally, there have been no reports of measurement of Hg in the fetal brain, the ultimate target of MeHg developmental neurotoxicity, although Cernichiari et al. (1995a) reported on a small set of measurements of Hg in infant brain.

The relationship among the several possible indicators of exposure is shown in Figure 4-1. Some of the indicators, such as the biomarkers of hair and blood Hg concentration, are commonly measured directly, whereas others, particularly fetal brain Hg concentration, are assumed to be correlated with the directly measured quantities. For the purposes of risk assessment, biomarker concentrations of MeHg serve two functions. First, a biomarker concentration is used as a surrogate for the unknown biologically relevant dose of MeHg in the developing fetal brain. That permits the development of a "dose"-response relationship in which the dose is represented by the biomarker concentration. Second, once such a dose-response relationship has been established, the biomarker concentration identified as the critical (e.g., benchmark) concentration must be translated into an estimate of the ingested dose. At that point, public-health interventions and regulatory measures can be guided by that estimate. The translation of the biomarker concentration to the ingested dose involves the use of toxicokinetic modeling to recapitulate the steps that precede the measured biomarker compartment in Figure 4-1 (see Chapter 3).

Methylmercury in Blood

The detection limit for total Hg in blood is generally in the range of 0.1 to 0.3 µg/L (ppb) (Grandjean et al. 1992; Girard and Dumont 1995; Oskarsson et al. 1996; Mahaffey and Mergler 1998). The mean concentration reported in U.S. studies in which high-fish-consuming populations were not specifically selected appears to be in the range of 1 to 5

µg/L (Humphrey 1975; Brune et al. 1991; Nixon et al. 1996; EPA 1997; Kingman et al. 1998; Stern et al. 2000). Thus, current methods for blood MeHg determination appear to be adequate for fully characterizing population distributions of MeHg exposure and are, in practice, limited only by the volume of blood that can be obtained. Fish and other seafood, including marine mammals, are the only significant source of MeHg exposure (IPCS 1990). Therefore, the blood Hg concentrations in populations with little or no fish consumption should reflect exposure to inorganic Hg. The mean blood Hg concentration in such populations was reported to be about 2 µg/L (standard deviation (SD) = 1.8 µg/L) (Brune et al. 1991). Blood Hg concentrations in populations with high fish consumption are usually considerably higher than that value. For example, median cord-blood concentration in a cohort with high fish consumption in the Faroe Islands was 24 µg/L (Grandjean et al. 1992). Therefore, the measurement of the concentration of total Hg in blood is generally a good surrogate for the concentration of MeHg in blood in populations with high fish consumption. In populations with relatively low fish consumption, inorganic Hg concentration might constitute a larger fraction of total Hg concentrations. Therefore, for such popula

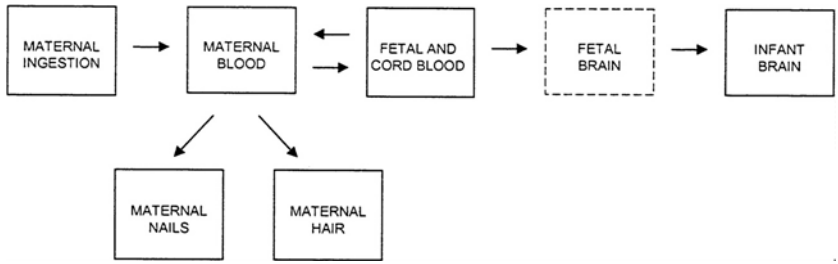

FIGURE 4-1 Relationship among the various indicators of MeHg exposure. Maternal ingestion of MeHg refers to the ingested dose, the magnitude of which depends on the amount of fish consumed and the concentration of MeHg in the fish. The concentration of Hg measured in the maternal blood, fetal blood, cord blood, maternal nails, and maternal hair are all biomarkers of exposure. Concentrations of Hg in the fetal brain, if available, would be considered the effective dose. (Note: The Fetal Brain box is shown with a dotted line because no direct data are available on Hg concentrations in the fetal brain.)

tions, estimates of MeHg exposure from cord blood might be unreliable. Adult blood Hg concentration has frequently been used as a biomarker of adult MeHg exposure, and it has been used to assess dose-response relationships in adult neurotoxicity (e.g., Hecker et al. 1974; Dennis and Fehr 1975; Gowdy et al. 1977; Palotti et al. 1979; Skerfving 1991; Mahaffey and Mergler 1998). Cord-blood or maternal-blood Hg concentrations have also been used with some frequency in assessing exposure to the developing fetus (Dennis and Fehr 1975; Pitkin et al. 1976; Fujita and Takabatake 1977; Kuhnert et al. 1981; Kuntz et al. 1982; Sikorski et al. 1989; Grandjean et al. 1992; Girard and Dumont 1995; Oskarsson et al. 1996).

In assessing the appropriateness of a particular biomarker of exposure, it is important to consider three factors: (1) how well the biomarker of exposure (i.e., the concentration of Hg in hair or blood) correlates with the ingested dose of MeHg; (2) how well the biomarker of exposure correlates with the Hg concentration in the target tissue; and (3) how well the variability over time in the biomarker of exposure correlates with changes in the effective dose at the target tissue over time.

For developmental neurotoxicity, the target organ is the developing fetal brain. The kinetics of MeHg transport among compartments is subject to interindividual variability at each step, and therefore, the more closely a compartment is kinetically related to the target tissue, the more closely the concentration measured in that compartment is likely to correlate with the concentration in the target tissue. As shown in Figure 4-1, the fetal and cord-blood compartment is one compartment removed from the fetal-brain compartment. Thus, the cord-blood Hg concentration might be a reasonable surrogate for the biologically relevant dose to the fetal brain. Having determined a critical concentration of Hg in the blood, it is then necessary to back-calculate the ingested dose (micrograms of Hg per kilogram of body weight per day) corresponding to the critical concentration in blood (Stern 1997). Just as the kinetic proximity of the biomarker compartment to the target tissue increases the correlation between biomarker concentration and dose to the target tissue, the kinetic closeness of the biomarker compartment to the ingested dose will increase the correlation between the critical biomarker concentration and the estimated intake. The cord-blood Hg concentration is more closely linked to the fetal-brain compartment than

to the ingested dose. Maternal-blood Hg concentration is more closely linked to the ingested dose than to the fetal-brain compartment. Thus, with the use of blood as a biomarker of MeHg exposure, there is a trade-off between the precision in the derivation of the dose-response relationship and the precision in the estimate of the corresponding ingested dose.

The mean half-life of total MeHg in blood in humans is about 50 days (Stern 1997; EPA 1997), but much longer half-lives (more than 100 days) are observed. Blood Hg concentration, therefore, reflects relatively short-term exposures relative to the total period of gestation. However, the Hg blood concentration at any given time reflects both the decreasing concentration from earlier exposures and the increase in concentration from recent exposures. Individuals with frequent and regular patterns of fish consumption achieve, or approximate, steady-state blood Hg concentrations (IPCS 1990). At steady state, the daily removal of Hg from the blood equals the daily addition to the blood from intake. Under such conditions, an individual's blood Hg concentration at any given time provides a good approximation of the mean blood Hg concentration over time. For individuals with infrequent or irregular fish consumption, however, recent fish consumption will result in peaks in blood Hg concentration. A single blood sample showing an elevated concentration, without additional exposure information, does not provide a temporal perspective and does not permit differentiation between increasing peak concentrations, decreasing peak concentrations, and steady-state exposure. Conversely, a single blood sample obtained between peak exposures and showing a low blood Hg concentration provides no evidence of peak exposures. That result can introduce error into dose-response and risk assessment in adult populations in whom short-term peak exposures might be relevant to chronic toxicity. The blood Hg concentration can correlate well with the dose presented to the brain at the time of sampling, but such information cannot necessarily be extrapolated to dose at the target tissue at other times. A blood Hg measurement that might be adequate to reflect exposure over time can be determined to some extent by obtaining dietary intake data that corresponds to several half-lives preceding the Hg measurement. In assessing exposure and dose-response relationship in utero, the temporal considerations associated with the use of blood Hg concentration as a biomarker are further complicated by two additional factors: (1) the

fetal brain is developing during much of gestation and might not be equally sensitive to the MeHg during all periods; and (2) the half-life of MeHg in cord blood might not be the same as that in maternal blood.

As summarized by IPCS (1990) and Gilbert and Grant-Webster (1995), there are clear differences between fetal and adult MeHg neurotoxicity. However, few data provide specific information on the differences in sensitivity to MeHg developmental neurotoxicity across the fetal period. The existence of such differences can be inferred, however, from summaries of experimental animal data presented by Gilbert and Grant-Webster (1995) and ATSDR (1999). The timing of maternal dosing in these studies was generally not chosen to relate differences in effect to specific stages of neurological development; therefore, it is difficult to infer specific information about developmental periods of specific sensitivity in the human fetus. It is assumed that there are windows of vulnerability to MeHg during neurological development (Choi 1989), and specific types of developmental effects (e.g., motor and cognitive) might have separate windows of vulnerability. In general, the embryonic period of development (fewer than 4 weeks of gestation), when there is no brain per se, might show little sensitivity to MeHg developmental neurotoxicity. Fetal stages during which the structure of the brain is forming are the periods in which the broad abnormalities in brain architecture, most characteristic of MeHg developmental neurotoxicity, are likely to occur. MeHg exposure during late fetal development, when brain structure is basically established, is likely to produce more function-specific effects on brain architecture. Even within early-to-middle fetal developmental stages, there might be discrete windows of sensitivity. As discussed above, the existence of such windows of sensitivity might have little practical significance if maternal MeHg intake does not vary substantially during pregnancy. However, individuals and populations with irregular patterns of MeHg intake will have peaks of exposure that might or might not occur during a window of vulnerability. If the half-life of MeHg in fetal blood is the same as in maternal blood (~50 days), the cord-blood MeHg concentration would be expected to reflect to some extent fetal exposures over about three half-lives (150 days) prior to delivery. That time (calculating backwards from birth) corresponds approximately to the second half of the second trimester and the third trimester. However, the cord-blood concentration would be most heavily influenced by exposures during

the most recent half-life, which corresponds to the last half of the third trimester. If that period is not critical for MeHg neurological developmental toxicity, dose-response assessments conducted using cord-blood Hg might lead to misclassification of exposure.

Because the fetus (and presumably the infant) has no independent mechanism for excreting or metabolizing MeHg to mercuric mercury (Grandjean and Weihe 1993), any elimination of Hg by the fetus will be by passage across the placenta to the maternal blood. Therefore, if the fetus does not have a specific affinity for MeHg, the half-life of MeHg in the fetal blood will be the same as that in the maternal blood, and the ratio of MeHg in the fetal blood to the maternal blood will be 1.0. However, Dennis and Fehr (1975), Pitkin et al. (1976), and Kuhnert et al. (1981), as well as additional studies cited by the latter two studies, found the concentration of Hg to be about 20-30% higher in cord blood than in maternal blood. On the other hand, Kuntz et al. (1982) and Sikorski et al. (1989) found a ratio close to 1.0. If the Hg concentration in cord blood is 20-30% higher than that in maternal blood (because of a longer half-life in fetal blood), the cord-blood Hg concentration would be more influenced than the maternal-blood concentration by exposures during the latter portion of the second trimester and the first half of the third trimester.

Methylmercury in Hair

In contrast to adult blood sampling, hair sampling is noninvasive and can be done without medical supervision. Although cord-blood collection is also essentially noninvasive, the logistics of its collection can be difficult. Hg concentration in hair is often used to estimate exposure to MeHg. In some studies, hair and blood Hg are measured for comparison. More often, hair is used as the sole biomarker of exposure. Using the standard cold-vapor analytical techniques, the detection limit for total Hg in human hair is generally reported to be in the range of 0.01 to 0.04 μg/g hair (e.g., Airey 1983; Bruhn et al. 1994; Lópes-Artiguez et al. 1994; Holsbeek et al. 1996; Gaggi et a1.1996; Stern et al. 2000). Few studies have reported on hair Hg concentrations in U.S. populations that were not specifically selected for high fish consumption. Among these, the mean hair Hg concentration appears to be in the range of 0.3 to 1.0

μg/g (Smith et al. 1997; EPA 1997; Stern et al. 2000). Thus, the sensitivity of the standard methodology should be adequate to characterize population distributions of MeHg exposure in the United States. Among individuals, whose hair Hg concentrations are presumed to reflect inorganic Hg exposure because of little or no fish consumption, hair Hg concentrations are reported to be in the range of 0.2 to 0.8 μg/g (Pallotti et al. 1979; Grandjean et al. 1992; Oskarsson et al. 1994; Bruhn et al. 1994; Batista et al. 1996; Smith et al. 1997). Populations selected for dose-response analysis on the basis of high fish consumption generally have considerably higher hair Hg concentrations (e.g., the mean maternal-hair Hg concentration in the Seychelles main study cohort was 6.8 μg/g (Cernichiari et al. 1995), and the median maternal-hair Hg concentration in the Faroes cohort was 4.8 μg/g (Grandjean et al. 1992)). Hair Hg concentrations that exceed those attributable to inorganic Hg exposure in fish-consuming populations must arise from MeHg exposure. Thus, the use of total hair Hg concentration in fish-consuming populations as a surrogate for hair MeHg concentration in fish-consuming populations should not lead to significant exposure misclassification.

Blood Hg concentration, unless supplemented by additional temporal exposure data, provides no clear information about the magnitude or timing of the exposures that yield the total Hg concentration observed in a given sample. In contrast, hair Hg concentration as a biomarker of MeHg exposure has the advantages of being able to integrate exposure over a known and limited time and recapitulate the magnitude and the timing of exposure. The ability to obtain such information from hair is predicated on two assumptions: that growing hair shafts incorporate Hg from the circulating blood in proportion to the concentration of Hg in the blood, and that hair shafts grow at a constant rate that does not vary significantly among individuals. The first of these assumptions is necessary to establish a quantitative relationship between hair Hg concentration and MeHg intake, the blood Hg concentration being an intermediate kinetic compartment. The second assumption is necessary to establish a relationship between location along the hair strand and time of exposure.

Although the proximal portion of the growing hair shaft is exposed to circulating blood for several days, that exposure appears to be indirect, as the shaft grows from a group of matrix cells located in the dermis, and these matrix cells are in direct contact with the capillaries

(Hopps 1977). Furthermore, the growing portion of the shaft is also in direct contact with sweat and sebum, both of which can contribute to the incorporation of trace elements into the shaft (Hopps 1977; Katz and Chart 1988). Therefore, measured concentrations of Hg in blood and hair can be separated, at least in part, by one or more kinetic compartments. Interindividual pharmacokinetic variability in these compartmental transfers could explain some of the scatter seen in plots of hair and blood Hg concentrations (e,g., Sherlock et al. 1982; Grandjean et al. 1992).

The growth rate of hair varies both within and among individuals. Among individuals, variations in hair-growth rate occurs because individual hair follicles experience a cycle of growth, transition, and terminal resting (Katz and Chatt 1988). Direct incorporation of trace elements, including MeHg, into the hair occurs only during the growth phase. The growth phase is the longest phase, although for scalp hair (the hair commonly used as an MeHg biomarker), estimates of the proportion of the total cycle during which growth occurs vary from 70% to 90% (Katz and Chatt 1988). In humans, individual hair follicles have independent growth cycles (Hopps 1977), and given the predominance of the growth portion of the follicle's life cycle, a sample of multiple hairs largely reflects hair that was recently incorporating MeHg. However, such a sample potentially has 10% to 30% of its follicles in the terminal resting phase. The Hg concentration in such follicles reflects less-recent exposure than that reflected by follicles in the growth phase. That difference can lead to exposure misclassification for the period of interest. The potential for exposure misclassification due to collection of follicles in the terminal resting phase is a particular concern in single-strand hair analysis for Hg. That analysis implicitly assumes that a point on a hair strand at a given distance from the scalp corresponds to the same point in time on all other strands from that individual.

There appears to be significant interindividual variability in hair-growth rate. An average growth rate of 1.1 centimeters (cm) per month for scalp hair is commonly assumed (Grandjean et al. 1992; Cernichiari et al. 1995; Boischio and Cernichiari 1998). However, Katz and Chatt (1988) characterize hair-growth rates as highly variable and dependent on age, race, gender, and season. They provide a summary of studies of hair-growth rates expressed as ranges. Interstudy values typically range from 0.6 to 1.5 cm per month, but ranges of 2.3 to 3.4 and 3.3 ± 0.6 cm per

month are also reported. Thus, a 9-cm length of maternal hair intended to correspond to approximately 8 months of gestation (assuming a hair-growth rate of 1.1 cm per month) could correspond to a period of 6-15 months (assuming a growth rate of 0.6 to 1.5 cm per month). There is also evidence of intraindividual variability in hair-growth rates (Giovanoli-Jakubczak and Berg 1974). Furthermore, during pregnancy, the rate of hair growth slows slightly (approximately 7% during the second trimester), and the interindividual variability in growth rate appears to increase (Pecoraro et al. 1967), thus adding to the temporal uncertainty inherent in assessing MeHg exposure from hair analysis. In addition, the physical characteristics of the hair alter somewhat, and the percentage of thick hairs increases (Pecoraro et al. 1967). Those physical changes suggest that the uptake and binding of MeHg might be altered. Attempts to identify segments of hair corresponding to all or part of the period of gestation (Grandjean et al. 1992; Cernichiari et al. 1995) by using the average growth rate of 1.1 cm per month might include exposure data from unintended time periods or exclude exposure data from a portion of the intended period. The use of such misidentified segments can result in exposure misclassification in dose-response analysis.

An additional difficulty in identifying the segment of hair corresponding to the entire period of gestation or to any specific period of gestation is the location of the most recently formed portion of the hair shaft, which is below the scalp until pushed out by subsequent growth. To assign an exposure period to a segment of hair, a chronological benchmark on the hair strand is needed to relate measurements of length and time. The proximal end of the shaft, as it emerges from the scalp, is generally taken as such a benchmark, even though the hair is not cut exactly at the scalp level (Hislop et al. 1983). Because the hair below the scalp represents the hair formed at the time of sampling, the proximal end of the cut hair must be assigned a time of formation that accounts for the lag time between formation and sampling (Cernichiari et al. 1995).

Hislop et al. (1983) related the time course of MeHg elimination from blood and hair cut at the scalp with the assumption that the hair Hg concentration is proportional to the blood Hg concentration. The blood was sampled at regular intervals. The hair was sampled once and divided into 8-mm segments. The measurement of the hair-growth rate was 8 mm of growth per 20 days. The presence of a distinct maximal

concentration in the serial blood samples and the segmental hair analysis allowed calculation of the lag between equivalent concentration points in the blood and hair samples. The hair segment with the maximum Hg concentration was found to be offset from the appearance of the maximum concentration in the blood by 20 days. It should be noted that the 20-day estimate is based on a measurement of hair-growth rate specific to this study. Different characteristic hair-growth rates in different populations and variability in the growth rates among individuals in a population would yield different estimates of the time difference in hair and blood measurements. Because the concentration of Hg in the blood represented a precise time point but was compared with the average concentration in the 8-mm segment representing 20 days of exposure, the 20-day estimate is somewhat uncertain.

Cernichiari et al. (1995) attempted to further refine this estimate by assuming that the average concentration in the 8-mm segment is the concentration in the mid-point of the segment and by estimating the time at which that point on the strand appeared just above the scalp. The validity of that assumption is not clear, as there does not appear to be any justification for assuming that the average concentration in a hair segment necessarily represents the concentration at any specific point along that segment. Furthermore, it is not clear that an estimation of the time necessary for a given point along a hair strand to appear just above the scalp is particularly useful unless one is analyzing segments shorter than 8 mm. Grandjean et al. (1998) reported that the appearance of Hg in a hair strand above the scalp is delayed by about 6 weeks. That is more than twice the delay reported by Hislop et al. (1983). However, Grandjean and coworkers provide no specific data to evaluate their assertion.

As discussed for blood Hg analysis, temporal uncertainties might not be critical for individuals with steady-state MeHg concentrations. However, for individuals with variable or peak exposures that might occur at critical periods during development, the uncertainties in assigning a specific time during pregnancy to specific hair segments might result in significant misclassification of exposure.

Despite the potential for temporal misclassification of exposure, the potential for identifying the segment of hair corresponding to a specific period of gestation (and neurological development) has a distinct advantage over cord-blood analysis. However, analysis of Hg concentration

in any given segment of a hair sample will yield only the average exposure over the corresponding time period. Details of exposure within that time period, including peak exposures, will not be elucidated except as they influence the overall average concentration within a segment. As an illustration, consider a 3-cm-long segment of maternal hair (the hair samples analyzed in the Faroe Islands study were generally 3 cm in length (Grandjean et al. 1998) corresponding to approximately 3 months of exposure and intended to correspond to a given trimester of pregnancy. Assume that during that time period, the individual contributing the hair consumed several fish meals high in Hg in close succession and achieved a peak hair concentration that was double the steady-state concentration before consumption of the fish. Assume further, that MeHg is removed from her blood following first-order decay kinetics (IPCS 1990) with a half-life of 50 days (Stern 1997). It can be calculated that (even if blood and hair Hg concentrations are perfectly correlated) the Hg concentration detected in such a hair segment would be only 20% higher than the concentration in the segment before the high-Hg fish consumption. That small observed increase occurs because the rise and return to background of the Hg-concentration peak occurs over a shorter time period than the exposure period represented by the entire 3-cm hair segment. Therefore, the average segment concentration reflects the dilution of the peak concentration by the adjacent stretches of background concentration in the segment. The true peak concentration, representing a doubling in exposure, would likely be identified as a significant increase in exposure if the concentration at that point could be measured, but it is not clear whether the observed 20% increase would be identified as a significant increase in exposure. Such an approach to segmental hair analysis would not give an accurate indication of the magnitude or duration of the peak concentration in the maternal or fetal blood. To some extent, the sensitivity to peak exposures can be increased by analyzing smaller-length segments of hair corresponding to narrower periods of exposure. Following the example above, a 1-cm (approximately 30-day) segment of hair containing the record of a peak doubling of exposure would be seen as an average increase of 50% above the steady-state background concentration. Such an increase is more likely to be recognized as significant but still does not provide a clear indication of the true peak concentration. If peak concentrations of fetal exposure are important to the elucidation of a

dose-response relationship, even the accurate identification and analysis of the segment of hair corresponding to a putative window of developmental sensitivity might result in exposure misclassification. Furthermore, practical considerations might prohibit increasing the number of analyses that would be required for the analysis of shorter hair segments. Despite those limitations, hair samples have the potential to provide temporal information on Hg exposures.

An alternative to segmental hair analysis is continuous single-strand hair analysis using x-ray fluorescence (XRF) (Marsh et al. 1987; Cox et al. 1989). This nondestructive method involves measurement along the length of the strand. It is not truly continuous because determinations are made on consecutive 2-mm segments. Assuming a mean hair-growth rate of approximately 1.1 cm per month, 2 mm corresponds to about 6 days of growth. Assuming first-order decay kinetics, a peak concentration on a single day would decrease by only 8% during this 6-day averaging period. Thus, single-strand analysis will give a much finer picture of exposure peaks than individual segmental hair analysis. In addition, as illustrated in Cox et al. (1989), single-strand analysis avoids errors in the alignment of multiple strands, which will tend to flatten and broaden peaks. Localization of portions of a hair strand corresponding to a given period of gestation, however, is still subject to uncertainty arising from variability in hair-growth rate. In addition, as discussed above, analysis of individual strands in terminal resting phase will give misleading estimates of the exposures corresponding to any time period. For 45 individuals in the Iraqi poisoning, Cox et al. (1989) compared the maximal concentration in two hair strands from the same individual. The overall correlation was good, and the peaks in the Iraqi poisoning episode were distinct and easily identifiable, thus reducing the error in comparing corresponding points in each analysis. Furthermore, it appears that the correlation was based on matching the *value* rather than the *location* of the peak in each strand. Thus, this determination does not necessarily address the errors inherent in the temporal calibration of hair strands or in the selection of hair strands in the terminal resting phase. In the Cox et al. (1989) analysis, a few of the residual errors in the comparison between concentrations on alternate strands appear to be on the order of 25%. Such observations might reflect errors in temporal calibration. Continuous single-strand analysis allows the investigation of multiple plausible dose metrics in dose-response analy

sis. Those metrics include peak concentration in a specific trimester, peak concentration at any time during gestation, average peak concentration, average concentration during a specific trimester, and average concentration during the entire gestation. Overall, single-strand hair analysis by XRF appears to be a powerful tool with the distinct advantage of being able to determine short-term changes in exposure, including peak exposures.

As is the case for blood Hg, the use of maternal hair Hg as a dose metric in the derivation of a reference dose for effects of MeHg on neurological development requires that the hair Hg concentration be used in two separate determinations. The first determination is the derivation of a dose-response relationship between hair Hg concentration and effects. The second determination is the estimation of the MeHg ingested dose that corresponds to the critical Hg concentration in hair identified in the dose-response relationship. In the first determination, the maternal-hair Hg concentration is a surrogate for the unknown dose to the fetal brain. In the second, the critical Hg concentration is used in a pharmacokinetic model to back-calculate the ingested dose.

Comparison of Biomarkers of Exposure

As shown in Figure 4-1, the fetal brain is one kinetic compartment further removed from hair Hg than from cord-blood Hg. Therefore, for the somewhat uncertain period of gestation represented by the cord-blood Hg concentration, the fetal-brain Hg concentration would be expected to correlate more closely with the cord-blood Hg concentration than with the maternal-hair Hg concentration. Cernichiari et al. (1995a), however, presented data comparing the correlations of maternal-hair and infant-brain Hg concentrations, and infant-blood and infant-brain Hg concentrations measured from autopsy samples. The hair samples were collected at delivery, and represent a period of approximately 20 days before delivery. The correlation of maternal-hair and infant-brain Hg concentrations (r = 0.6-0.8, depending on the specific brain region) was generally comparable to the correlation of infant-blood and infant-brain Hg concentrations (0.4-0.8). That finding suggests that, as predictors of Hg concentration in the infant brain, maternal hair and infant blood might have equal validity. However, the error of the regression

slope of infant-brain Hg to maternal-hair Hg is about 3-6 times the error of the slope of infant-brain Hg to infant-blood Hg (although the coefficient of variation for the brain-hair relationship is smaller than that for the brain-blood relationship) (Stern and Gochfeld 1999; Davidson et al. 1999). Perhaps more important in considering the relevance of those comparisons to the choice of dose metric for reference-dose development is the fact that Cernichiari et al. (1995a) examined the correlation between maternal hair and infant brain rather than between maternal hair and fetal brain. Likewise, infant blood rather than cord blood was compared with infant brain. Cernichiari et al. (1995a) do not give the age of the infants in this study, but postnatal infant brain cannot be considered identical to fetal brain, especially since the fetal brain changes substantially during development. Although the vulnerable periods for MeHg effects on neurological development are unknown, they might occur much earlier in gestation than the perinatal period. Furthermore, infant blood is not necessarily comparable to fetal blood due to the ongoing replacement of fetal hemoglobin with adult hemoglobin. At birth, fetal hemoglobin constitutes about 75% of total hemoglobin, but after about 50 days, it constitutes only about 50% of the total (Lubin 1987). Therefore, it is not clear to what extent these observations elucidate the relationship of fetal-brain to either cord-blood, or maternal-hair Hg concentrations.

For the back-calculation of the average ingested dose corresponding to a given biomarker critical concentration, the maternal-hair Hg compartment and the cord-blood Hg compartment are equally distant kinetically from ingestion (see Figure 4-1). The estimation of the ingested dose corresponding to a critical biomarker concentration requires the intermediate estimation of the corresponding maternal-blood Hg concentration. Although no study was found that specifically supplies data on the variance inherent in the ratio of cord-blood to maternal-blood Hg concentrations, the ability of MeHg to pass freely through the placenta (IPCS 1990) suggests that there might be interindividual variability in the extent of transfer of MeHg between the cord-blood and maternal-blood compartments. As discussed above, the mean cord-blood/maternal-blood Hg ratios reported for several populations differed by 20-30% at most. For maternal-hair Hg, the few studies reporting data on the variance in the maternal hair /maternal-blood Hg ratio within a given study population give widely differing coefficients of

variation (Stern 1997). The mean maternal-hair/maternal-blood Hg ratios reported for different population groups can differ at most by a factor of about 2, although nearly all observations fall within approximately 20% of the overall mean of the various observations (Stern 1997; ATSDR 1999). Nonetheless, when the estimation of the ingested dose from a critical concentration in hair is carried out probabilistically and interindividual variability in the various pharmacokinetic inputs is taken into account, sensitivity analysis reveals that the maternal-hair/maternal-blood ratio is one of the key contributors to the variability in the predicated ingested dose (Stern 1997; Clewell et al. 1999).

Overall, in comparing maternal hair and cord blood as possible biomarkers of in utero MeHg exposure, each has significant advantages and disadvantages. At least conceptually, cord blood is kinetically more closely linked to the fetal brain-target and could, therefore, yield a more precise dose-response relationship if the critical period for toxicity coincides with the time period reflected in the cord-blood Hg measurement. However, the cord-blood Hg measurement is not capable of providing information about the specific patterns of exposure during gestation and does not reflect exposure over a clearly delineated period of gestation. In addition, cord blood is not capable of providing information about variability in exposure, even for the time period it most directly reflects. Simple maternal-hair analysis can provide information about average exposure over the entire period of gestation but provides no information about variability in exposure during that period. Identification of the specific portion of a hair strand corresponding to all of gestation is uncertain and is a potential source of exposure misclassification. In addition, maternal-hair Hg concentration is kinetically more distant from the fetal brain than is cord-blood Hg. Segmental hair analysis has the potential to provide information about exposure during specific portions (e.g., trimesters) of gestation, but uncertainties related to hair-growth rate make the identification of segments corresponding to periods as short as a single trimester uncertain. Although segmental hair analysis can provide some information about variability in exposure during different periods of gestation, it is of limited use in identifying either the magnitude or the duration of peak exposures. Continuous single-strand hair analysis, on the other hand, can provide precise information on peak exposures and thus permits the investigation of several different dose metrics in dose-response assessment. This ap

proach is potentially the most powerful for investigation of dose-response relationships. However, single-strand analysis is still hampered by uncertainty in assigning specific periods of gestation to a given section of hair strand. The utility of cord blood and hair as biomarkers of MeHg exposure can be substantially improved by linking them to accurate dietary intake information. Data on frequency, amount, and type of fish consumption in the period during and immediately preceding pregnancy can provide information on the overall variability in exposure as well as on peak exposures. Furthermore, accurate dietary information can provide benchmarks for the temporal calibration of both cord blood and hair Hg data. Recognizing that each of the available metrics provides different and complementary information, the most useful and powerful approach to exposure and dose assessment for MeHg is the collection of comparable dietary, cord-blood and single-strand hair data.

ANALYTICAL ERROR IN BIOMARKER MEASUREMENTS

In comparing the outcomes of the Faroe Islands, Seychelles, and New Zealand studies, it is important to consider the relative analytical errors in the measurement of the biomarker of exposure among those studies. Unfortunately, the reporting of such data in those studies is inconsistent and incomplete. The Seychelles study analyzed only maternal hair. Several analytical methods were used for various purposes in that study, the dose-response analysis used hair Hg concentration determined by cold vapor atomic absorption (CVAA). Although determinations were carried out to compare CVAA results with those from a reference method (counts of exogenously applied ^{203}Hg) (Cernichiari et al. 1995), no summary statistics of the comparison are provided. Results of an interlaboratory comparison of CVAA determinations of hair Hg concentration are reported (Cernichiari et al. 1995), and 100% of all samples analyzed were less than or equal to ± 2 standard deviation (SD) of the target value. The nature of the target value is not, however, discussed. The reporting of analytical quality-control data in the Faroe Islands study is somewhat confusing, because different analytical methods were used at different times for hair and blood, and various analyses were carried out in different laboratories (Grandjean et al. 1992). It appears,

however, that all hair Hg analyses used in the dose-response analyses were carried out in the laboratory of the Seychelles study group (i.e., University of Rochester) using CVAA. Presumably then, the analytical errors in the analyses of hair Hg concentrations in both studies are highly comparable. It appears that all cord-blood Hg analyses used for dose response were carried out in the laboratory of the Faroe Islands group (i.e., Odense University) using ultraviolet (UV) absorption spectrometry. The accuracy of this method was determined relative to four reference samples of trace metals in blood. For the sample with a reference Hg concentration of 9.9 µg/L, the mean reported value was 9.9 µg/L (0% difference). For the three reference samples with much larger Hg concentrations (98, 103, and 103 µg/L), the percent difference between the mean reported values and the reference value was +13.0%, +11.2%, and +10.0%, respectively. The authors report that all the reported values were within the "acceptable range," although this range is not further defined. Analytical imprecision (coefficient of variation for repeated analyses of the same sample) for the first three of those four reference samples ranged from 7.0% to 14.1%, the lowest concentration having the largest imprecision. The New Zealand study generated data only on hair Hg concentration (Kjellstrom et al. 1986, 1989). The reporting of analytical quality control data from the New Zealand study is somewhat complicated because the study was carried out in two stages. During the first stage, no reference samples were available. Reference samples were available for the second stage of the study, and samples from additional mothers were analyzed for that stage. For the most part, however, it appears that samples analyzed during the first stage of the study were not re-analyzed during the second stage. Given the lack of reference samples during the first stage of the study, analytical quality during that stage was based on interlaboratory comparison. Sixteen samples analyzed by CVAA in the laboratory of the New Zealand study group (i.e., University of Auckland) (reporting Hg concentrations of more than 10 ppm) were re-analyzed by CVAA at the University of Rochester. The percent difference (sum of absolute values) for 13 of those samples was 22.8%; 62% of University-of-Auckland values were smaller than the corresponding University-of-Rochester values. The values for the remaining three samples were grossly different. When those three samples were re-analyzed by the University of Auckland, a much closer agreement with the University-of-Rochester values was

achieved. This raises some concern. In the second stage of the New Zealand study, 12 reference samples of hair were analyzed and the results compared with the maximum acceptable deviation (MAD) which was defined as (true $value_{ppm}$ ± (10% of true value ± 1 ppm)). The basis for that metric is not entirely clear. The regression line for the reported values versus the true values was found to lie completely within the MAD lines. Some individual values, however, were marginally outside the MAD lines, and the regression line was biased toward reported values underestimating reference values.

In summary, given the nature of the reporting of the quality-control data in these three studies, it is difficult to assess the analytical error inherent in the biomarker concentrations and ultimately in the dose-response relationships. It is also difficult to quantitatively or qualitatively compare the extent of analytical error in these studies. Some concern, however, is warranted with respect to the analytical error inherent in the New Zealand study. The extent to which that error might affect the interpretation of the dose-response relationship based on the New Zealand study is not clear.

EXPOSURE AND DOSE ASSESSMENT IN THE SEYCHELLES, FAROE ISLANDS, AND NEW ZEALAND STUDIES

Exposure in the Seychelles studies was measured as total Hg in maternal-hair samples. Other biomarkers of exposure were not investigated. Cernichiari et al. (1995) reported that the majority of mothers in the study provided at least two hair samples. The first sample was obtained at delivery, and the second, 6 months after delivery. In the first sample, the hair was cut at the scalp, and the proximal 9 cm was used for Hg analysis. A growth rate of 1.1 cm per month was assumed, and therefore a 9-cm segment of hair corresponded to 8.2 months of gestation. The hair representing the last month of gestation was assumed to lie beneath the scalp at the time of sampling. In the second sample, a segment of hair intended to correspond to the same time period as the first sample of hair was identified by assuming a 1.1 cm per month growth rate. Cernichiari et al. (1995) presented a scatterplot of the correspondence of the mean Hg concentration in those two samples. Regression statistics were not supplied, but the regression slope was

reported to be insignificantly different from unity. There is, however, significant scatter around the regression line, and the data are not symmetrical at the line of equality. The most likely explanation for the scatter and asymmetry appears to be intraindividual variability in hair-growth rates. It is not clear whether the Hg concentration from one of the samples or the average concentration of both samples was used as the actual dose metric in the dose-response assessment. Hair samples from 86% of the main cohort were also divided into segments intended to represent the three trimesters of pregnancy. The average Hg concentration in each of the segments was compared with the average concentration in the complete 9-cm segment. The correlations (r) were all similar and ranged from 0.85 to 0.91. In addition, intercepts were each close to zero. The general comparability of each of the segmental average Hg concentrations to the total average Hg concentration suggests that intake did not vary greatly by approximate trimester for the cohort as a whole. Potential seasonal variations in Hg exposure would not likely be detectable in such an analysis because the cohort was not in synchrony with respect to the onset of gestation. In considering individual variability, the overall strong correlations notwithstanding, a considerable number of outliers can be seen in the scatterplots of these trimester comparisons, particularly in the assumed third-trimester segment. Those outliers suggest that some individuals might have had significant variability in exposure over the course of gestation. As discussed previously however, such analyses are relatively insensitive to short-term peaks in exposure. More specific information about intraindividual exposure variability or peak exposures cannot be deduced from these data. Data from this segmental analysis was not used in dose-response assessment.

Dietary information was obtained from the Seychelles cohort 6 months after delivery (Shamlaye et al. 1995). The extent to which this survey included the entire cohort is not reported. A median fish consumption of 12 meals per week, as well as some additional population percentiles of fish consumption, was reported. Those data, however, reflect self-reported average intake and do not provide information on variability in fish intake during pregnancy. In addition, although data on characteristic Hg concentrations for commonly consumed species of fish were generated (and included some species with relatively high characteristic Hg concentrations) (Davidson et al. 1998), data on con

sumption by species does not appear to have been collected. Thus, dietary data in the Seychelles studies cannot be used to suggest the extent to which individual exposure was variable or peaked during pregnancy.

In the Faroe Islands studies, exposure was measured by the concentration of Hg in maternal hair obtained at delivery and by cord-blood Hg concentration (Grandjean et al. 1992). The collection and analysis of the cord blood appears to be standard. However, the hair samples analyzed were not of uniform length and varied from 3 to 9 cm (Grandjean et al. 1999), thus reflecting exposure over variable times during gestation. As discussed above, cord-blood Hg concentration is influenced by exposure over an indeterminate time period, possibly including the latter part of the second trimester but weighted most heavily toward the latter part of the third trimester. Assuming a delay of about 20 days between incorporation of Hg into a growing hair strand and its appearance above the scalp, a 3-cm hair sample proximal to the scalp would reflect average exposure from the end of the second trimester to the second-third of the third trimester. A 9-cm hair sample would reflect average exposure beginning before conception. If, as asserted by Grandjean et al. (1998), the delay in appearance above the scalp of a section of a hair strand containing a given Hg concentration is 6 weeks rather than 20 days, the 3-cm hair segment would reflect exposure starting before the middle of the second trimester. Taking into account the apparent inconsistency in the length of the hair segments, as well as the inherent variability in hair-growth rates, the extent to which the hair and cord-blood MeHg concentrations reflect common exposures is uncertain. The correlation of hair and blood MeHg concentrations following log transformation ($r = 0.78$) was reasonably strong (Grandjean et al. 1998). However, it is not clear whether that correlation indicates consistency of the hair and blood measurements or it reflects little or no intraindividual variability in exposure during gestation.

Dietary exposure to MeHg in the Faroe population is complicated. The cohort generally consumed fish frequently; 48% ate fish dinners three or more times per week (Grandjean et al. 1992). However, the species of fish generally consumed were coalfish, ling, turbot, and salmon, which characteristically have relatively low concentrations of Hg (Grandjean et al. 1998). On the other hand, pilot whale is a traditional Faroese food that has considerably higher characteristic MeHg

concentrations (less than 1 to more than 3 ppm) (Grandjean et al. 1998). The availability of pilot whale meat is somewhat irregular, as the catch is opportunistic rather than systematic. In the Faroese cohort, 79% of the mothers reported in prenatal interviews that they ate at least one whale dinner per month, but only 27% reported eating three or more whale dinners per month (Grandjean et al. 1992). It should be noted, however, that these data do not provide information on portion size, and refer to dinners only. Grandjean et al. (1998) suggested that whale meat is also eaten at other meals and as snacks (dried). This incomplete dietary intake information makes assessment of variability in exposure difficult. Nonetheless, sporadic consumption of meals high in Hg is expected to result in temporal variability in exposure and possibly in peak exposure. Grandjean et al. (1992) reported on the results of analysis of Hg in multiple segments, each 1.1 cm long, from each of the six women in the Faroese cohort. Coefficients of variation (i.e., comparison among segments from the same individual) ranged from 8.1 to 23.8%. Although that suggests low-to-moderate intraindividual variability in MeHg intake over time, generalization to the entire cohort is not warranted because of the small sample size.

The relative magnitude of potential peak exposures from sporadic consumption of whale meat is possible to estimate. Assume that a pregnant woman consumes whale meals of 113 g each on 3 consecutive days when whale meat is available, and that her maternal-hair Hg concentration is 4.5 ppm (the median maternal-hair concentration in the Faroese cohort (Grandjean et al. 1992). Assume that pilot whale contains Hg at 3.3 ppm (Grandjean and Weihe 1993), and assume that absorption of MeHg from the gastrointestinal tract is 95% complete, that 5% of the ingested dose is distributed to the blood (IPCS 1990), and that the blood volume for a woman of child-bearing age is 3.6 L (Stern 1997). Ginsberg and Toal (2000) have shown that the one-compartment pharmacokinetic model for MeHg provides a reasonable approximation of the accumulation of Hg in hair for single exposures. Using the one-compartment model, therefore, assume that the rate constant for elimination of MeHg from the blood is 0.014 per day (equivalent to a half-life of 50 days) (Stern 1997). Finally, assume that the ratio of maternal-hair Hg concentration to maternal-blood concentration is 0.250 (μg/g)/ (mg/L) (IPCS 1990). Based on those assumptions, the one-compartment model predicts that the hair Hg concentration will increase by about 3.6 ppm to a

total concentration of 8.1 ppm and decrease to the baseline concentration (assuming no additional exposures above background) in about 6 weeks. Thus, this scenario of a fairly large intake over a short time period is predicted to result in a hair concentration that less than doubles the original concentration and returns to the original concentration all within a length of hair slightly greater than 1 cm.

The hair samples analyzed in the Faroe Islands study were generally 3 cm long (Grandjean et al. 1998) and thus represent a longer time period than that incorporating the entire rise and decline of such peaks. As discussed previously, the average Hg concentration in the 3-cm segment is a dilution of the peak value. With the moderate increases that might be represented by such peaks, it is unclear to what extent such peaks would have been discernable when averaged over the length of the longer segment.

In the New Zealand study (Kjellström et al. 1986, 1989), hair Hg concentration was the only biomarker of MeHg exposure used. Cord-blood samples were collected but were analyzed only for lead. Hair samples were obtained from all mothers in the original cohort shortly after delivery. The proximal 9 cm of the sample were analyzed for total Hg to give an average Hg concentration over that entire length. Those 9-cm average values were the dose metric used in the dose-response analyses. As discussed previously, the length of hair approximately corresponding to the last 20 days of gestation remained beneath the scalp, and (assuming a hair-growth rate of approximately 1 cm per month) the distal 1 cm of the 9-cm segment analyzed corresponded to the period preceding conception. In addition to the 9-cm sample of hair, when the mothers provided a sufficient quantity of hair, the sample was split, and another bundle of 9-cm length hair was sectioned into nine 1-cm segments. Analyses of the segments were carried out on samples from 47 of the 237 (19.8%) mothers in the second stage of the study (children at 6 years of age, (Kjellström et al. 1989)). A 1-cm segment of hair represents about 30 days of exposure. As discussed previously, a rapid doubling in Hg exposure during that period, such as that resulting from a few successive high-Hg fish meals, for a 1-cm segment would be reflected as a 50% increase compared with neighboring segments with no such peak exposures. Analysis of these segments would likely detect significant peaks in exposure but would not necessarily provide accurate information on the absolute magnitude of those peaks. Peak concentra

tion was defined as the single largest excursion above the overall 9-cm average concentration. On average, the ratios of individual peak concentrations to the average 9-cm concentrations ranged between 1.4 and 1.6, the highest ratio (1.64) being in the group with hair Hg concentrations in the 6-10-ppm range. The group with the highest average hair concentration (at or above 10 ppm) had a ratio of 1.44. The largest individual ratio of peak-to-average concentration was 3.61, and the next largest value was 1.94. Those data do not permit an assessment of the number of peak exposures during gestation, but the range of average ratios is consistent with actual doublings in exposure at least once during gestation. Generalization to the entire cohort is difficult given the relatively small fraction for which segmental data were obtained. However, those data suggests that MeHg exposure in the New Zealand cohort might have been relatively spiky as opposed to constant and regular. It is interesting that the peak exposures were not regularly distributed across the period of gestation. The largest fraction of peak exposures (30%) occurred in the 9-cm segment most distal to the scalp, and 57% of the peak exposures occurred in the three distal-most segments. Only 19% of peak exposures occurred in the three segments most proximal to the scalp. The reason for the disparity is not clear, but it suggests that, at least for this subsample of the cohort, peak exposures might have been less common during the third trimester.

Information on fish consumption was obtained at about the same time as the hair sample through the administration of a questionnaire. The questionnaire requested information on the overall frequency of consumption of fish and shellfish. In addition, more detailed information on consumption frequency and portion size was obtained for specific fresh fish (lemon fish, snapper, gurnard, and "all other fresh fish"), canned fish (tuna, salmon, smoked, and "all other canned fish"), fish products (fish cakes and fish "fingers"), shellfish (oysters, scallops, mussels, and "all other shellfish"), and fried "takeaway" (i.e., fast food, fish-and-chips) fish. Although consumption of shark was not specifically queried, shark was stated to be a common source of takeaway fish. No data were provided on the characteristic Hg concentration in the species identified by the mothers. That lack precludes quantitative estimates of the contribution of individual species and eating patterns to possible peaks in exposure. In terms of overall fish consumption, 1.5% of mothers claimed daily fish consumption during pregnancy, and

consumption of fish "a few times a week" during pregnancy was identified by 19% of mothers. The most frequently identified fish-consumption category (32% of mothers) was "once a week." Thus, about 53% of the mothers in the original cohort ate fish at least once per week. Therefore, although this population cannot be considered subsistence fish consumers, it is clear that fish constituted a significant fraction of the overall diet. Furthermore, such an overall consumption pattern, in which fish is eaten frequently, but not continuously, is consistent with the possibility of peak or spiky MeHg exposures. Among the possible choices of fish type, consumption of snapper was most closely correlated with hair Hg concentration. Information on the correlation between consumption and hair Hg concentration is not provided for any other species. It appears that additional information on those mothers who were likely to have experienced short-term peak exposures can be recovered from the questionnaire data, particularly from more detailed consideration of the frequency of takeaway fish. Further analysis of these data, therefore, might provide some indication of the influence of peak exposures on MeHg dose-response relationships for neurodevelopmental effects.

The frequency of overall fish consumption was used in the first stage of the study to screen for both the high Hg-dose group (consumption of fish more than three times per week), and the reference group (one or less than one fish meal per week). Ultimately, however, the high Hg-dose group for the first and second stages of the study was selected from among frequent consumers on the basis of hair Hg concentrations of more than 6 ppm. In the second stage of the study, each child in the high Hg-dose group was matched with three control children on the basis of low hair Hg concentration. One of these control children was additionally selected on the basis of frequent (more than three times per week) maternal fish consumption during pregnancy.

Given the differences, uncertainties, and limitations of the exposure-assessment approaches used in the Seychelles, Faroe Islands, and New Zealand studies, none of the approaches can be identified as better or more relevant. It is clear, however, that each of the approaches supplied different, and not necessarily comparable pictures of exposure and dose. Grandjean et al. (1999) noted in the Faroe Islands study that cord-blood MeHg appeared to better predict deficits in cognitive functions (language, attention, and memory), and maternal-hair MeHg appeared to

better predict deficits in fine-motor function. The authors attributed those qualitative differences to the different periods of development reflected by each of the measurements. That conclusion is consistent with the idea that discrete windows of vulnerability in the developmental toxicity of MeHg are differentially represented by hair- and cord-blood Hg measurements. However, the lack of uniformity in the lengths of the hair segments analyzed in the Faroe Islands study (Grandjean et al. 1999) make a clear interpretation of such differences somewhat problematic. Therefore, the uncertainties and limitations in the various biomarkers that are used for MeHg exposure assessment could result in exposure misclassification in the dose-response assessment.

Misclassification of exposure in these studies could take several forms. Those include incorrectly considering exposures that occurred during developmental periods during which there is little or no vulnerability of the observed developmental endpoints to MeHg; failing to identify peak concentrations that might be more toxicologically relevant than the measured average concentrations; and using portions of hair with Hg concentrations that accumulated before or after pregnancy. Generally, exposure misclassification biases to the null — that is, use of an incorrect exposure level in a regression analyses of outcome data leads to decreased power to detect a real effect. Thus, the likely implication of the uncertainties and limitations in the dose metrics used in the Seychelles and the Faroe Islands studies is that the probability of observing true associations of dose and response will be reduced. In addition, the magnitude of those observed associations may be underestimated. Therefore, the existence of uncertainties and limitations notwithstanding, those statistically significant dose-response associations observed with any of the dose metrics are likely to reflect (perhaps indirectly) true associations (if other sources of bias have been adequately addressed). Failure to observe statistically significant dose-response associations could well be due to exposure misclassification resulting from one or more of the uncertainties and limitations discussed above.

SUMMARY AND CONCLUSIONS

- Duplicate diet data can potentially provide accurate data on MeHg intake, although interindividual pharmacokinetic variability creates

uncertainty in the use of such data to estimate the dose to the fetal brain. The collection of duplicate dietary data places demands on study participants. This approach is, therefore, generally limited to short periods of observation that might not capture critical intake variability in populations with high intraindividual variability in intake of fish.

- Retrospective dietary data (diary and recall) are relatively simple to collect, but diary-based data are subject to participant errors in species identification, portion estimation, and assignment of MeHg concentration by species. The number of days of dietary-intake data collected needs to be long enough to characterize adequately the frequent fish consumer and to differentiate the levels of less frequent consumption. Recall-based data are additionally subject to recall errors. Such data might be useful in stratifying exposure and in temporal calibration of hair strands.
- On the other hand, prospective data on all sources of Hg exposure, such as vaccines and dental amalgams and, in particular, dietary intakes of MeHg are essential to understanding the effects of environmental Hg exposures on any outcomes. Quantitative dietary intake data on intakes of all marine food sources can and should be collected in any serious study of this contaminant. Such data are essential for quantifying exposures, separating out the effect modifiers that account for the differences between exposures and target tissue concentrations. Intake data are also essential for identifying possible confounding factors, such as other contaminants or nutrients that are abundant in some of these food sources but not in others.
- Cord-blood Hg concentration is closely linked kinetically to the fetal-brain compartment and should correlate closely with the concentrations at the target organ near the time of delivery. Cord-blood Hg is less closely linked to the ingested dose. That separation can introduce uncertainty into the back-calculation of a reference dose from cord-blood-based dose-response data.
- Cord-blood Hg measurement cannot show temporal variability in exposure. It can provide data on a limited portion of gestation whose duration is somewhat uncertain but which occurs late in gestation. That portion of gestation might not correspond to the periods of greatest fetal sensitivity to MeHg neurotoxicity.

- Maternal-hair Hg concentration is less closely linked kinetically to the fetal-brain compartment than is cord-blood Hg concentration, and the kinetic distance between the maternal-hair and fetal-brain compartments might be a significant source of statistical error in dose-response assessment.
- Hair Hg measurement can potentially provide a range of dose metrics. Analysis of longer strands corresponding to all or part of gestation will provide average exposure data but no information on temporal variability in exposure. Segmental analysis can isolate specific periods of gestation, but peak exposures might be inadequately represented. Continuous single-strand analysis is a powerful technique that can recapitulate MeHg exposure during the entire period of gestation with accurate representation of peak exposures. This approach presents a range of dose metrics that can be investigated in assessing dose response.
- Because of intraindividual and interindividual variability in hair-growth rates, attempts to identify hair Hg concentrations corresponding to specific time periods during gestation might be subject to significant error which can result in exposure misclassification in dose-response assessment. The temporal calibration of Hg measurements along a hair strand can be aided by consideration of corresponding dietary intake data for Hg.
- Each of the dose metrics — dietary records, cord blood, and hair — provides different exposure information. Use of data from two or more of these metrics will increase the likelihood of uncovering a true dose-response relationship.
- In the Seychelles studies, dose was estimated from the average Hg concentration in a length of hair assumed to represent the first 8 months of pregnancy. That approach precluded observing any intraindividual variability in exposure over the course of gestation.
- Fish-consumption data for the Seychelles cohort established the generally high level of fish consumption but could not provide any data on intraindividual variability in exposure.
- In the Faroe Islands studies, dose was estimated from cord-blood and single-sample maternal-hair Hg concentration. The cord-blood Hg data cover exposures over an indeterminate period late in gestation. The hair Hg samples appear not to have been of uniform length and therefore do not necessarily reflect comparable periods

of gestation. Those differences in length are relevant only if there is significant variability in MeHg exposure during gestation. Neither of these metrics has the ability to show intraindividual variability over the course of gestation.

- Fish-consumption data for the Faroe cohort indicated a high rate of consumption of fish with low Hg concentrations, and less frequent consumption of pilot whale containing high concentrations of MeHg. Such a diet suggests a pattern of peaking exposures. Exposure modeling suggests that as reflected by accumulation in hair such peaks might represent a moderate increase above baseline concentrations.
- The uncertainties and limitations in exposure assessment in these studies can result in exposure misclassification, which will lessen the ability to detect significant dose-response associations and might result in inaccuracies in the derivation of dose-response relationships.
- If exposure misclassification occurred in the studies of MeHg, such misclassification would tend to obscure any true effect. Therefore, statistically significant dose-response associations are likely to reflect true dose-response relationships, assuming that other sources of bias are adequately addressed.
- Dose-response assessments using either cord-blood or maternal-hair Hg concentrations are adequate to support the derivation of an RfD.

RECOMMENDATIONS

- Quantitative dietary intake data on patterns of consumption of the primary sources of MeHg including all marine food sources, should be collected in all prospective studies of MeHg exposure. Estimates of exposures will improve dose-response analyses that have implications for regulatory purposes.
- In future studies, data on maternal fish intake by species and by meal should be collected along with Hg biomarker data. Those data should be used to provide estimates of temporal variability in MeHg intake during pregnancy.
- Future studies should collect data on maternal-hair, blood, and

cord-blood Hg concentrations. All three dose metrics should be considered in attempting to identify dose-response relationships.

- Data are needed that reliably measure both Hg intake and biomarkers of Hg exposure to clarify the relationship between the different dose metrics. NHANES IV data should be examined when it becomes available to determine if it satisfies those needs.
- To detect exposure variability, archived hair strands from both the Seychelles and the Faroe Islands studies should be analyzed by continuous single-strand XRF analysis. The possible dose metrics that can be derived from XRF analysis should be examined in the dose-response assessment. Such considerations should also be addressed in future studies.

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5

HEALTH EFFECTS OF METHYLMERCURY

THIS chapter begins with a brief review of the carcinogenicity of MeHg and its immunological, reproductive, renal, cardiovascular and hematopoietic toxicity. Because the central nervous system is widely viewed as the organ system most sensitive to MeHg, the remainder of this chapter focuses on the adverse effects of MeHg on neurological function. Neurological effects in infants, children, and adults are discussed. Studies carried out in populations exposed to high concentrations of MeHg are described, followed by a discussion of epidemiological data on populations exposed chronically to low concentrations of MeHg. Animal data following in utero, early postnatal, and adult exposure are also discussed.

The information available on the human health effects of MeHg are derived from studies of various designs. Each type of design has strengths and weaknesses and might be the most appropriate choice for a given set of circumstances. The methodology, strengths, and weaknesses of environmental epidemiological studies have been discussed in previous NRC reports (NRC 1991, 1997). The data on the Minamata and Iraqi episodes, the collection of which were initiated in response to the occurrence of recognizable illness in the population, are derived from case reports, descriptive studies of convenience samples, and ecological studies of rates. A major advantage of such studies is that the end points assessed are often of clear clinical significance. The inferences permitted from such studies, as described in greater detail in the following sec

tions, can be limited by methodological weaknesses, such as the absence of detailed information on the sampling frame or referral patterns that generated the study sample, the degree to which the study sample is representative of the population from which it was drawn, exposure histories of the subjects, detailed assessments of health status, and the nature of severity of possible confounding biases.

Case-control studies, in which the exposure status (or history) of individuals with a certain health outcome (case) is compared with the exposure status of individuals without the health outcome (controls), can provide a much stronger basis for drawing inferences about exposure-disease associations. Among the challenges of such studies, however, are assembling a representative group of cases and a comparable group of controls, collecting adequate information on critical aspects of exposure history (which, in the case of long-latency diseases, might mean exposures that occurred decades before), and identifying the critical potential confounding biases. A case-control design, however, might be the only efficient way to study rare health outcomes.

Cohort designs (e.g., cross-sectional, retrospective, and prospective) provide a number of advantages. Instead of being selected on the basis of outcome status, as in case-control studies, study subjects are either randomly selected from the target population or selected on the basis of particular exposure characteristics (e.g., over-sampling of extremes of exposure distribution). The former strategy might be used if the goal is to enhance the generalizability of the study inferences to the target population, and the latter might be used if the goal is to estimate, with the greatest precision, the nature of the dose-response relationship within a certain region of the dose distribution. Another advantage of a cohort design is that multiple health outcomes can be measured and related to the index of exposure. A cohort study that incorporates prospective assessments of the study sample generally provides opportunities to assemble more-comprehensive exposure histories of the study subjects and to examine the natural history of a dose-response relationship, including factors that modify risk. As with all epidemiological studies, the methodological challenges of cohort studies include accurate classification of exposure and outcome status and the assessment and control of confounding bias.

CARCINOGENICITY

None of the epidemiological studies found an association between Hg exposure and overall cancer rates; however, two studies found an association between exposure to Hg and acute leukemia. The interpretation of those results is difficult due to the small study populations, the problem of assessing historical exposures to Hg, and the inability of investigators to control for other risk factors. In animals, chronic exposure to MeHg increased the incidence of renal tumors in male mice in some of the studies; however, the increase was observed only at doses that were toxic to the kidneys. Therefore, the tumorigenic effect is thought to be secondary to cell damage and repair. MeHg did not cause tumors in female mice or in rats of either sex. Therefore, in the absence of a tumor initiator, long-term exposure to subtoxic doses of MeHg does not appear to increase tumor formation.

On the basis of the available human and animal data, the International Agency for Research on Cancer (IARC) and the U.S. Environmental Protection Agency (EPA) have classified MeHg as a “possible” human carcinogen.

Human Studies

Four epidemiological studies examined the effect of Hg exposure on cancer incidence or cancer death rate. Those studies are summarized in Table 5-1. Tamashiro et al. (1984) carried out a cohort study that evaluated the causes of death of 334 individuals who had survived Minamata disease (MD) and died between 1970 and 1980. Control cases were selected from deaths that occurred in the same city or town as the MD cases and were matched for sex, age and year of death. No significant difference in cancer death rates was observed between the subjects and the controls, suggesting that the risk of dying from cancer was not correlated with patient history of MeHg poisoning. Specific types of cancer, however, were not evaluated.

Tamashiro et al. (1986) compared the death rates among residents of the Fukuro and Tsukinoura districts with those of age-matched residents of Minamata City. Residents of the two districts were assumed to have a higher intake of local seafood and higher Hg exposure than residents

of Minimata City. No statistically significant increase in the overall cancer mortality was observed. However, an increase in liver- cancer death rates was observed among males who resided in the areas thought to have high Hg exposure (standardized mortality ratio (SMR[1]), 250.5; 95% confidence interval (CI), 133.4-428.4). Males also had significantly higher mortality due to chronic liver disease and cirrhosis in those areas than in Minamata City. The investigators indicated that the increases could not be attributed solely to MeHg, because the alcohol consumption rates and the prevalence of hepatitis B infection were higher in the Fukuro and Tsukinoura districts than in Minamata City. The study is also limited by its failure to fully characterize Hg concentrations in subjects in each cohort.

TABLE 5-1 Summary of Cancer Studies in Humans

Type of Study	Size of Study	Finding	Reference
Retrospective cohort	334 deaths in high-exposure cohort; 668 in low-exposure cohort	No increase in cancer death rate; site-specific rates not analyzed	Tamashiro et al. 1984
Retrospective cohort	416 deaths in high-exposure cohort; 2,325 deaths in low-exposure cohort	Increased liver-cancer death rate among males in high-exposure cohort	Tamashiro et al. 1986
Case-control study of hair Hg concentrations in leukemia patients	47 cases; 79 controls	Increased hair Hg concentrations in acute leukemia patients	Janicki et al. 1987
Retrospective cohort study of Minamata-disease (MD) survivors	1,351 MD survivors; 5,667 referents	Increased leukemia death rate among MD survivors; relative risk, 8.35	Kinjo et al. 1996

In a case-control study in Poland, Janicki et al. (1987) found a statisti

[1]The SMR is the ratio of the number of deaths observed in a study group divided by the number expected (based on age- or sex-specific rates in the general population) and multiplied by 100. An SMR greater than 100 indicates that the death rate was higher than would be expected.

cally significant increase in the Hg content in hair collected from 47 patients with leukemia compared with 52 healthy unrelated subjects (mean 1.24 versus 0.49 ppm). The Hg content in hair from a subgroup of 19 leukemia patients was also significantly greater than that from 52 healthy relatives who had shared the same home for at least 3 years (0.69 versus 0.43 ppm). When those data were analyzed for specific types of leukemia, only patients with acute leukemia had significantly higher hair Hg concentrations. No significant difference was seen in the Hg content in hair collected from nine patients with chronic granulocytic leukemia or from 15 patients with chronic lymphocytic leukemia compared with the healthy unrelated subjects. The study is limited by the small study population, inadequate description of case and control populations, uncertainty about the source of Hg exposure, and lack of adjustment for other leukemia risk factors. In addition, all the hair Hg concentrations were within normal limits.

Kinjo et al. (1996) compared cancer death rates for a cohort (1,351 cases) of MD survivors with those of a referent population (5,667 subjects) who lived in the same region of Japan and consumed fish daily. After adjusting for age, gender, and length of follow-up period, they found no excess relative risk (RR) for overall mortality, all cancer deaths combined, or all noncancer deaths combined. Analysis of site-specific cancers found that Minamata survivors were less likely to die of stomach cancer than the referent population (RR, 0.49; 95% confidence interval (CI), 0.26-0.94). However, on the basis of five observed deaths, survivors were eight times more likely than the referent population to have died from leukemia (RR, 8.35; 95% CI, 1.61-43.3).

Animal Studies

The carcinogenic potential of MeHg was examined in several chronic exposure animal studies. Those studies are summarized in Table 5-2.

Newberne et al. (1972) carried out a 2-year multigeneration study in which Sprague-Dawley rats (30 per sex) were fed diets with MeHg doses of 0 or 0.008 mg/kg per day. Tumor incidence was similar in both groups; however, the maximum tolerated dose (MTD) was not achieved.

A 2-year feeding study conducted by Verschuuren et al. (1976) also failed to provide evidence of carcinogenic effects. Rats (25 per sex per

group) were exposed to MeHg chloride at 0, 0.004, 0.020, or 0.10 mg/kg per day for 2 years. Survival decreased in the mid- and high-dose groups, and kidney weights increased in the high-dose group. However, tumors occurred at similar rates in all the groups.

TABLE 5-2 Summary of Cancer Studies in Animals

Animal	Dose (mg/kg/d)	Tumor response	Study Duration (wk)	Reference
Sprague-Dawley rat	0, 0.008	None	104	Newberne et al. 1972
Rats, unspecified strain	0, 0.004, 0.02, 0.1	None	104	Verschuuren et al. 1976
Sprague-Dawley rats			130	Mitsumori et al. 1983, 1984
Males	0, 0.01, 0.05, 0.28	None		
Females	0, 0.01, 0.06, 0.34	None		
Swiss Albino mice	0, 0.19, 0.95[a]	None	Weaning to death	Schroeder and Mitchener 1975
ICR mice			78	Mitsumori et al. 1981
Males	0, 1.6, 3.1	0/37, 11/16, NA		
Females	0, 1.6, 3.1	0, 0, NA		
Swiss mice	0, 0.03, 0.07, 0.27	Increased tumor response to urethane	15	Blakley 1984
ICR mice			104	Hirano et al. 1986
Male	0, 0.03, 0.15, 0.73	1/32, 0/25,		
Female	0, 0.02, 0.11, 0.60	0/29, 13/26		
		None in any group		
B6C3F$_1$ mice	0, 0.03, 0.14, 0.69	0/60, 0/60,	104	Mitsumori et al. 1990
Male	0, 0.03, 0.13, 0.60	0/60, 13/60		
Female		0/60, 0/60, 0/60, 1/60		

[a]0.95 mg/kg per day for 70 days and then 0.19 mg/kg per day thereafter due to high mortality at 0.95 mg/kg per day.
Abbreviation: NA, not available.

Mitsumori et al. (1983, 1984) also exposed Sprague-Dawley rats to MeHg chloride in feed (males, 0, 0.011, 0.05, or 0.28 mg/kg per day;

females, 0, 0.014, 0.064, or 0.34 mg/kg per day) for up to 130 weeks. Effects were seen in the central nervous system, kidney, arterial wall, and spleen. The MTD was achieved in males in the mid-dose group and exceeded in males and females in the high-dose group. No increase in tumor incidence was observed.

A lifetime study conducted in Swiss albino mice failed to detect a tumorigenic response (Schroeder and Mitchener 1975). Groups of mice (54 per sex per group) were exposed from weaning until death to methylmercuric acetate in drinking water at two doses. The low-dose group received 1 ppm (0.19 mg/kg per day) and the high dose group received 5 ppm (0.95 mg/kg/day) for the first 70 days and then 1 ppm thereafter due to high mortality at the higher dose. Although no increase in tumors was noted, interpretation of the study is limited because of cessation of the high-dose exposure and failure to conduct complete histological examinations.

The incidence of renal tumors was increased in males in a study of ICR mice (60 per sex) fed diets containing MeHg chloride (0, 1.6, or 3.1 mg/kg per day) for 78 weeks (Mitsumori et al. 1981). The majority of mice in the high-dose group died by week 26 of the study. Males in the low-dose group had significantly higher numbers of renal epithelial adenocarcinomas (0 of 37 in control group; 11 of 16 in low-dose group) and renal adenomas (1 of 37 in control group; 5 of 16 in low-dose group) than controls. No renal tumors were observed in females in any group.

Blakley (1984) exposed female Swiss mice to MeHg chloride (approximately 0, 0.03, 0.07, or 0.27 mg/kg per day) in drinking water for 15 weeks. After 3 weeks of exposure, mice were given urethane in a single intraperitonal dose of 1.5 mg/kg. No more than one tumor per mouse was seen in the absence of urethane. With urethane, a statistically significant trend was seen for an increase in the size (0.7, 0.73, 0.76, and 0.76 millimeters (mm) at 0, 0.03, 0.07, and 0.27 mg/kg per day, respectively) and number of tumors per mouse (21.5, 19.4, 19.4, and 33.1 at 0, 0.03, 0.07, and 0.27 mg/kg per day, respectively). These findings suggest that MeHg may act as a tumor promoter.

In a follow-up study to Mitsumori et al. (1981), Hirano et al. (1986) fed MeHg chloride to ICR mice (60 per sex) at lower doses (males, 0, 0.03, 0.15, or 0.73 mg/kg per day; females, 0, 0.02, 0.11, or 0.6 mg/kg per day) for 104 weeks. Kidney and reproductive-system effects indicated that

the MTD was exceeded at the highest dose. An increased incidence of renal epithelial tumors (adenomas and adenocarcinomas) occurred in males. In males in the high-dose group, 10 of the 13 tumors were adenocarcinomas; the incidence of renal epithelial adenomas was not increased. No renal tumors were seen in females.

The incidence of renal tumors was also increased in male $B6C3F_1$ mice following chronic exposure to MeHg chloride. Mitsumori et al. (1990) fed $B6C3F_1$ mice (60 per sex) MeHg chloride (males, 0, 0.03, 0.14, or 0.69 mg/kg per day; females, 0, 0.03, 0.13, or 0.60 mg/kg per day). Following 104 weeks of exposure, adverse effects were seen in the central nervous system, kidney, and testis. The MTD was achieved in males in the mid-dose group and in females in the high-dose group. The MTD was exceeded in males in the high-dose group. The incidence of renal epithelial carcinomas and renal adenomas was significantly increased in males in the high-dose group.

Although chronic exposure to MeHg increased the incidence of renal tumors in male mice in some studies, that effect was observed only at doses that were toxic to the kidneys and is thought to be secondary to cell damage and repair. Exposure to MeHg did not increase tumor rates in female mice or in rats of either sex.

GENOTOXICITY

Human Studies

Evidence that human exposure to Hg causes genetic damage is inconclusive. Several investigators have reported higher rates of chromosomal aberrations among workers who were exposed to elemental or inorganic forms of Hg (Popescu et al. 1979; Verschaeve et al. 1976; Barregard et al. 1991). However, questions have been raised regarding the influence of possible confounders, such as age or simultaneous exposure to other toxicants on these findings. In a recent occupational study, Queiroz et al. (1999) reported a significant increase in the percentage of micronuclei in Hg-exposed workers when compared with unexposed controls.

Skerfving et al. (1970, 1974) reported a positive correlation between blood Hg concentrations and chromosomal aberrations in the lympho

cytes of 23 people who consumed Hg-contaminated fish. However, their findings have been questioned because of experimental problems, such as failure to identify smokers. In addition, significant effects were found only from lymphocyte cultures that were set up several days after collection, and the incidence of aneuploidy in the control and exposed groups was lower than expected. Wulf et al. (1986) reported an increased incidence of sister chromatid exchange in humans who ate Hg-contaminated seal meat. However, information on smoking status and exposure to other heavy metals was not provided for those individuals, making interpretation of the study difficult. More recently, Franchi et al. (1994) reported a correlation between the incidence of micronuclei in peripheral lymphocytes and blood Hg concentrations in a population of fishermen who had eaten Hg-contaminated seafood.

Animal Studies

A single dose of Hg chloride (HgCl) to male Swiss mice (2.2, 4.4, or 8.9 mg/kg) induced a dose-related increase in the frequency of chromosomal aberrations and the percentage of aberrant cells in bone marrow (Ghosh et al. 1991). Chronic exposure of cats to MeHg at doses of 0.0084, 0.02, or 0.046 mg/kg per day for 39 months produced a significant increase in the number of nuclear abnormalities in bone-marrow cells and inhibited DNA repair (Miller et al. 1979). The response, however, was not dose related.

In Vitro Studies

MeHg has been shown to cause DNA damage in cultured *Bacillus subtilis* (Kanematsu et al. 1980); chromosomal aberrations and aneuploidy in human lymphocytes (Betti et al. 1992); and DNA damage in cultured human nerve and lung cells, Chinese hamster V-79 cells, and rat glioblastoma cells (Fiskesjo 1979; Costa et al. 1991). Inorganic Hg concentrations greater than 10 μM have been shown to inhibit mammalian DNA polymerase activity in whole-cell extracts and in purified enzyme preparations (Williams et al. 1987; Robison et al. 1984). Sekow

ski et al. (1997) demonstrated the ability of mercuric ion to impair the fidelity of synthesome-mediated DNA replication at HgCl concentrations as low as 1 μM.

IMMUNOTOXICITY

The immune system appears to be sensitive to Hg. Although there are no data on the effect of MeHg on immune function in humans, occupational studies indicate that Hg compounds can affect the immune system. Animal studies have demonstrated MeHg effects on immune-cell ratios, cellular responses, and the developing immune system. Autoimmune effects have also been associated with exposure to elemental Hg.

Human Studies

The effect of MeHg on the human immune system has not been studied. However, occupational exposure to elemental Hg has been found to alter certain immune parameters. Queiroz and Dantas (1997a, b) evaluated B- and T-lymphocyte populations among 33 workers in a Brazilian Hg production facility. At the time of the study, all the workers had urinary Hg concentrations below 50 μg/g of creatinine. Analysis of T-cell populations found a reverse $CD4^+$-to-$CD8^+$ ratio that was haracterized by a reduction in the number of $CD4^+$ lymphocytes. That alteration was significantly correlated with urinary Hg concentrations. B-lymphocyte counts were also significantly reduced in this cohort; however, that effect was not correlated with urinary Hg concentrations. Analysis of serum antibody levels found increased immunoglobulin E levels but did not detect anti-DNA or anti-nucleolar antibodies. The researchers reported a moderate negative correlation between length of exposure to Hg and IgE levels (Dantas and Queiroz 1997).

Moszczynski et al. (1995) studied lymphocyte subpopulations (T cells, T-helper cells, T-suppressor cells, and natural killer cells) in the peripheral blood of 81 men occupationally exposed to metallic Hg vapors and 36 unexposed men. The average Hg concentration in the workplace air was 0.0028 mg/m^3. Urinary Hg concentrations ranged from 0 to 240

µg/L, and concentrations in the blood varied from 0 to 30 µg/L. Stimulation of T-lymphocytes — manifested by an increased number of T cells, T-helper cells, and T-suppressor cells — was observed.

Animal Studies

Effects on the Adult Immune System

Work in animals has demonstrated that Hg can effect immune function (see Table 5-3). Ilbäck (1991) found that oral exposure to MeHg altered the ratio of lymphocyte subpopulations, enhanced lymphoproliferation in response to B- and T-cell mitogens, and depressed natural-killer-cell activity in mice. Exposure of female Balb/c mice to MeHg (3.9 ppm) in the diet (equivalent to 0.5 mg/kg per day) for 12 weeks significantly decreased thymus weight (22%) and cell number (50%). Lymphoproliferation in response to T- and B-cell mitogens was increased, and natural-killer-cell activity was decreased in exposed mice. Red- blood-cell counts were slightly higher in exposed mice than in unexposed mice, and white-blood-cell counts were unaffected.

Thompson et al. (1998) evaluated the effects of low-dose MeHg exposure in mice. Mice were exposed to MeHg at 0, 3, or 10 ppm in the drinking water for 4 weeks. MeHg altered the proportion of splenocyte and thymocyte subpopulations and caused dose-dependent decreases in splenocyte glutathione concentrations and mitogen-stimulated calcium flux.

Rats were exposed to MeHg (chloride or sulfide; concentrations of 5 or 500 µg/L) in drinking water for 8 or 16 weeks (Ortega et al. 1997). An 8-week exposure to both concentrations of MeHg sulfide enhanced the lymphocyte response to conconavalin A. However, only the 54-µg/L concentration of MeHg chloride had that effect. At 16 weeks, lymphocyte proliferation decreased in the rats exposed to MeHg chloride but increased in those exposed to MeHg sulfide. Those data indicate that the effects of MeHg on T-cell proliferation are dependent upon the dose, duration, and chemical form of the MeHg exposure.

Prolonged exposure to MeHg increased the susceptibility of mice to

viral infections. Koller (1975) fed mice subtoxic doses of MeHg chloride(1 or 10 mg/kg) for 84 days and saw significantly higher mortality after inoculation with encephalomyocarditis virus in exposed mice than in unexposed mice. In the same report, MeHg exposure did not alter the course of neoplasia in mice inoculated with Rauscher leukemia virus. MeHg (3.69 mg/g of diet) also did not alter the lethality of myocarditic coxsackie virus B3 in Balb/c mice but did increase heart tissue damage and viral persistence (Ilbäck et al. 1996).

TABLE 5-3 Summary of Immunological Studies in Animals

Species	NOAEL	LOAEL	Effect	Reference
Rat	None	3.9 ppm in diet of dams	Reduced NK cell activity in pups	Ilbäck et al. 1991
Rat	None	5 ppb in water	Altered mitogen response	Ortega et al. 1997
Rat	None	5 ppb in water of dams	Increased thymic weight in pups	Wild et al. 1997
Mouse	None	1 ppm in diet	Increased mortality when infected with encephalitis virus	Koller 1975
Mouse	None	3.9 ppm in diet (0.5 mg/kg/d)	Reduced NK cell activity; decreased thymus weight.	Ilbäck 1991
Mouse	None	3.69 ppm in diet of dams	Reduced resistance to Coxsackie B3	Ilbäck et al. 1996
Mouse	None	0.5 ppm in diet of dams	Altered immune effects in pups	Thuvander et al. 1996
Mouse	None	3 ppm in water	Altered B-cell and T-cell subtypes; decreased GSH concentrations in splenocytes	Thompson et al. 1998
Mouse	None	0.3 mg/kg/d	Antinucleolar antibody production	Hultman and Hansson-Georgiadis 1999

Abbreviations: NOAEL, no-observed-adverse-effect level; LOAEL, lowest-observed-adverse-effect level; NK, natural killer; GSH, glutathione.

Effects on the Developing Immune System

Prenatal and perinatal exposure to MeHg has long-term effects on the developing immune system. Ilbäck et al. (1991) reported alterations in white-blood-cell counts, natural-killer-cell activity, and the response of thymocytes and splenocytes to T-cell mitogen in Sprague-Dawley rats following prenatal and postnatal exposure of rat pups to MeHg. Wild et al. (1997) exposed rats, in utero and during the nursing period to MeHg (maternal drinking-water concentrations of MeHg chloride at 5 or 500 µg/L, or MeHg sulfide at 5 µg/L). At 6 weeks of age, total body and splenic weights were significantly increased in both MeHg-chloride-exposed groups. Rats exposed to MeHg sulfide had a significant increase in thymic weight at 6 weeks of age. Splenocyte response to pokeweed mitogen was enhanced at 6 and 12 weeks in both MeHg-chloride-exposed groups but was unaffected by MeHg sulfide. Natural-killer-cell activity was not affected in any exposure group at 6 weeks of age but was decreased by 57% in both groups exposed to MeHg chloride at age 12 weeks.

Similar effects have been demonstrated in mice. Female Balb/c mice were fed diets containing MeHg (0, 0.5 or 5 mg/kg) for 10 weeks before mating, throughout gestation, and up to day 15 of lactation (Thuvander et al. 1996). Blood Hg concentrations in the offspring were increased on day 22 (0.5-mg/kg group) and on days 22 and 50 (5-mg/kg group). The number of splenocytes and thymocytes increased, and the antibody response to a viral antigen was stimulated in the offspring of the 0.5-mg/kg group. The response of splenocytes to B-cell mitogen increased in offspring of the 5-mg/kg group. Lymphocyte subpopulations in the thymus were altered at both doses.

In Vitro Studies

The effects of MeHg on lymphocyte function have been studied in cell-culture systems in an attempt to elucidate the mechanisms involved in its ability to modulate immune function. Exposure of cultured lymphocytes to MeHg has been shown to inhibit mitogen-induced DNA synthesis, cell proliferation, and antibody synthesis. Electron micro

scopic analysis of MeHg-exposed lymphocytes revealed nuclear changes characterized by hyperchromaticity and fragmentation. MeHg exposure also induced a rapid and sustained increase in intracellular calcium levels (Nakatsuru et al. 1985; Shenker et al. 1993). Shenker et al. (1999) investigated the mechanism by which MeHg chloride induces human T-cell apoptosis. They reported that the earliest detectable event following MeHg exposure was at the level of the mitochondria. Exposure of T-cells to MeHg chloride caused a decrease in the overall size of mitochondria and changes in the structure of the cristae. Cellular thiol reserves were depleted and mitochondrial cytochrome c was translocated to the cytosol.

Autoimmune Response

Human Studies

There is some evidence that human exposure to metallic Hg can induce an autoimmune response. Renal biopsies of two Hg-exposed workers who had developed proteinuria revealed deposits of IgG and complement C3 in the glomeruli (Tubbs et al. 1982). Examination of 10 patients who complained of illnesses after they received dental amalgams found that 3 of them had antiglomerular basement membrane antibodies, and 2 had elevated antinucleolar antibodies (Anneroth et al. 1992). In addition to those reports, Cardenas et al. (1993) reported high anti-DNA antibody titers in 8 of 44 workers from a chloralkali plant. No studies were located that evaluated autoimmunity in humans following exposure to organic forms of Hg.

Animal Studies

Hg is one of the few chemicals which is able to induce loss of tolerance to self-antigens in animals. This effect is human leukocyte antigen (HLA) dependent and has been demonstrated in genetically susceptible strains of rats and mice. Brown-Norway rats injected with Hg chloride ($HgCl_2$) produce antilaminin antibodies, which attack the kidneys, causing an autoimmune glomerulonephritis (Druet et al. 1994). The

autoimmune response observed following Hg exposure has been linked to a T-cell dependent polyclonal B-cell activation (Hua et al. 1993). Hu et al. (1999) found that Hg exposure induced an autoimmune response in C57BL/6(H-2b) wild-type and interlukin-4 (IL-4)-deficient mice. Antibodies of all classes were induced by Hg treatment, except that in the IL-4-deficient mice, no immunoglobulin E (IgE) and very little IgG1 were produced.

REPRODUCTIVE EFFECTS

Human Studies

In occupational exposure studies, paternal exposure to metallic Hg does not appear to cause infertility or malformations (Alcser et al. 1989; Lauwerys et al. 1985). However, a study of pregnancy outcomes among the wives of 152 Hg-exposed men revealed an increased incidence of spontaneous abortions (Cordier et al. 1991). Preconception paternal urinary Hg concentrations above 50 µg/L were associated with a doubling of the spontaneous abortion risk.

The effect of elemental Hg on fertility and reproductive success has also been examined among occupationally exposed women. The results of various studies are conflicting but are suggestive of an effect on fertility. Elghany et al. (1997) compared the pregnancy outcomes of 46 Hg-exposed workers to those of 19 women who worked in nonproduction areas of the same factory. Among cases and controls during the study period (1948-1977), 104 pregnancies were recorded. Women exposed to inorganic Hg had a higher rate of congenital anomalies. Concentrations were up to 0.6 mg/m^3. No significant differences in stillbirth or miscarriage rates were noted between the two groups of women. Rowland et al. (1994) found that the probability of conception among female dental hygienists who prepared more than 30 amalgams per week and had at least five poor hygiene practices when handling Hg was only 63% of that among unexposed controls. Women with lower exposures, however, were more fertile than unexposed controls. A large study conducted in Norway compared reproductive success rates among 558 female dental surgeons with those of 450 high-school teachers (Dahl et al. 1999). They concluded that exposure to Hg, benzene, and

chloroform was not associated with decreased fertility except for a possible Hg effect on the last pregnancy of multiparous dental surgeons.

No studies were identified that specifically evaluated human reproductive success following exposure to MeHg. However, in a study that described the clinical symptoms and outcomes of more than 6,000 Iraqi citizens who were severely poisoned by bread that had been prepared with MeHg-treated wheat, Bakir et al. (1973) commented on the low number of pregnant women in the cohort. Their report states, in part, that "The admissions frequency of affected pregnant females was remarkably low. One would expect to find approximately 150 pregnant females with diagnosable poisoning in the 6350 cases admitted to hospitals, yet only 31 such females were reported." Although no explanation was offered for the small number of pregnancies among the exposed population, the report provides evidence of a possible effect of MeHg on human fertility.

Animal Studies

The reproductive effects of MeHg exposure in animals are summarized in Table 5-4. Abortion and decreased litter size are the most commonly reported reproductive effects of MeHg in animal studies. Pre- and post-implantation losses have been experimentally induced in rats, mice, guinea pigs, and monkeys exposed to MeHg.

In rats, an oral dose of MeHg at 7.5 mg/kg on gestational days 7-14 resulted in increased fetal deaths and an increased incidence of malformations. A dose of 5 mg/kg was also associated with an increased incidence of malformations as well as reduced fetal weight (Fuyuta et al. 1978).

In Fischer 344 rats, oral doses of MeHg chloride at 10, 20, or 30 mg/kg administered on day 7 of gestation decreased fetal survival by 19.1%, 41.4%, and 91.1%, respectively (Lee and Han 1995). Compared with control animals, implantation sites in the three groups were decreased by 5.9%, 13.7% and 22.5%, respectively. The median lethal dose for fetuses was 16.5 mg/kg.

Oral doses of MeHg hydroxide at 3, 5, or 10 mg/kg on day 8 of gestation in mice caused a significant dose-related decrease in litter size. No effects were seen at 2 mg/kg (Hughes and Annau 1976).

TABLE 5-4 Summary of Reproductive Studies in Animals

Species	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Effect	Reference
Monkey	None	0.05	Abnormal sperm	Mohamed et al. 1987
Monkey	0.05	0.07	Low conception rate	Burbacher et al. 1988
Rat	2.5	5 (males)	Reduced litter size	Khera 1973a
Rat	None	10 on GD 7	Decreased fetal survival	Lee and Han 1995
Mouse	2	3 on GD 8	Decreased fetal survival	Hughes and Annau 1976
Mouse	None	5 on GD 6-13	Fetal malformations	Fuyuta et al. 1978
Mouse	None	10 on GD 10	Embryo resorption	Fuyuta et al. 1979
Mouse	None	0.73	Low sperm counts Tubular atrophy of testes	Hirano et al. 1986 Mitsumori et al. 1990
Guinea pig	None	11.5 on GD 21, 28, 35, or 42	Fetal abortions	Inouye and Kajiwara 1988

Abbreviations: NOAEL, no-observed-adverse-effect level; LOAEL, lowest-observed-adverse-effect level; GD, gestation day.

Fuyuta et al. (1978) reported that an oral dose of MeHg chloride at 7.5 mg/kg on gestational days 6-13 in mice was embryocidal, and doses of 5 or 6 mg/kg reduced fetal weights and increased the incidence of malformations (cleft palate and fused thoracic vertebrae).

Fuyata et al. (1979) also dosed mice with a single oral dose of MeHg at 10,15, 20, or 25 mg/kg on gestational day 10. An increase in resorbed embryos occurred at 25 mg/kg. At the doses of 15, 20, and 25 mg/kg, fetuses weighed less than controls and had an increase in malformations.

A single dose of MeHg chloride at 11.5 mg/kg administered to pregnant guinea pigs on day 21, 28, 35, or 42 of gestation caused half of the litters to be aborted (Inouye and Kajiwara 1988).

Reproductive problems, including decreased conception rates, early abortions, and stillbirths were seen following exposure of female *Macaca fascicularis* monkeys to MeHg hydroxide at 50, 70, or 90 µg/kg per day for 4 months (Burbacher et al. 1988). Although no effects were observed on the menstrual cycle, the number of conceptions decreased with

increasing dose (93% for controls, 81% for group at 50 µg/kg per day, 71% for group at 70 µg/kg per day, and 57% for group at 90 µg/kg per day). A significant reduction in the percentage of viable offspring was observed for the groups at 70 and 90 µg/kg per day (83% for controls, 69% for group at 50 µg/kg per day and 29% for groups at 70 or 90 µg/kg per day). The effects on reproduction were observed at a maternal blood concentration greater than 1.5 ppm. Maternal toxicity was also observed in the doses of 70 and 90 µg/kg per day following prolonged MeHg exposure (½ year to over 1 year), typically at maternal blood concentrations greater than 2 ppm. Maternal toxicity was not seen in monkeys exposed at 50 µg/kg per day.

Effects on reproduction have also been seen following paternal exposure to MeHg. Exposure of male rats to high doses of MeHg chloride (5 to 7 daily doses of 1, 2.5, or 5 mg/kg) before mating with unexposed females produced a dose-related increase in post-implantation losses and reduced litter size (Khera 1973a). Exposure of male mice to those doses had no effect on reproductive success (Khera 1973a). Mohamed et al. (1987) examined the testicular functions of male *Macaca fascicularis* following oral exposure to MeHg hydroxide at 50 or 70 µg/kg per day for 20 weeks. Although there was no significant decrease in sperm counts, MeHg exposure was associated with a decrease in the percentage of motile sperm, a reduction in sperm speed, and an increase in the number of abnormal sperm (primarily bent or kinked tails). No effects were observed on serum testosterone concentrations, and no histological abnormalities were detected in testicular biopsies. Sperm motility returned to normal soon after the cessation of MeHg exposure, and sperm morphology remained abnormal. Chronic exposure to MeHg chloride at 0.73 mg/kg per day decreased spermatogenesis and produced tubular atrophy of the testis in mice (Hirano et al. 1986; Mitsumori et al. 1990). That dose caused renal damage, indicating that it exceeded the MTD.

RENAL TOXICITY

Human Studies

The kidney is sensitive to metallic Hg following inhalation exposure, possibly due to accumulation of Hg. High exposures have resulted in

mild transient proteinuria, gross proteinuria, hematuria, and oliguria. Kidney biopsies from workers with proteinuria revealed proximal tubular and glomerular changes (Kazantzis et al. 1962). Several investigations have found renal changes in workers chronically exposed to Hg vapor (Danziger and Possick 1973; Buchet et al. 1980; Barregard et al. 1988; Cardenas et al. 1993).

However, renal toxicity has rarely been reported following human exposure to organic forms of Hg (see Table 5-5). All cases in which renal damage was confirmed following exposure to organic Hg involved severe poisonings in which neurological symptoms were also present. An autopsy of a man who died following an acute exposure to alkyl Hg vapor revealed necrosis of the tubule epithelium, swollen granular protoplasm, and nonstainable nuclei in the kidneys (Höök et al. 1954). Jalili and Abbasi (1961) described the clinical course of several victims of the Iraqi poisoning incident who displayed symptoms of renal damage, including polyuria, polydypsia, and albuminuria. Similar symptoms were observed in two children who had consumed ethyl-Hg-contaminated pork over a period of several weeks (Cinca et al. 1979). Laboratory analyses conducted shortly after their illnesses began indicated elevated blood urea, urinary protein, and urinary sediment. Both children died of cardiac arrest, and their autopsies revealed severe nephritis and myocarditis.

The only evidence of a renal effect following ingestion of Hg-contaminated fish comes from a death-certificate review conducted by Tamashiro et al. (1986). They evaluated causes of death among residents of a small area of Minamata City that had the highest prevalence of MD using age-specific rates for the entire city as a standard. Between 1970 and 1981, the number of deaths attributed to nephritic diseases was higher than expected among women who resided in that region (SMR, 276.5) but was within the expected range (0.80) among men who resided in this region.

Animal Studies

Although it is well known that the kidney is the target organ for inorganic Hg (Samuels et al. 1982), several reports from animal studies have also described MeHg- induced renal toxicity (see Table 5-6). A

report by Fowler (1972) described the presence of large numbers of spherical masses containing bundles of smooth endoplasmic reticulum in the pars recta of the kidney proximal tubules in rats following a 12-week exposure to MeHg at 2 ppm (0.08 mg/kg per day). Those effects were observed in female rats only. The authors indicated that the sex-specific effects were most likely due to sex differences known to exist in the activity of kidney enzymes associated with MeHg metabolism. In

TABLE 5-5 Summary of Renal Studies in Humans Exposed to Various Organic Mercurials

Exposure source	Effects	Reference
Occupational exposure to alkyl Hg vapors	Necrosis of renal tubules	Höök et al. 1954
Occupational exposure to Hg vapors	Albuminuria, tubular changes	Kazantzis et al. 1962
Occupational exposure to Hg vapors	Proteinuria	Danziger and Possick 1973
Occupational exposure to Hg vapors (urinary > 50 μg/g creatinine)	Albuminuria	Buchet et al. 1980
Occupational exposure to Hg vapors	Increased N-acetyl-B-glucosaminidase	Barregard et al. 1988
Occupational exposure to Hg vapors	Tamm-Horsfall protein, tubular antigen	Cardenas et al. 1993
Ingestion of mercuric chloride (30 mg/kg)	Oliguria, proteinuria	Afonso and deAlvariz 1960
Ingestion of mercuric chloride	Fatal acute renal failure	Murphy et al. 1979
Dermal application of mercuric ammonium chloride	Impaired renal function	Barr et al. 1972
Dermal application of mercuric ammonium chloride	Impaired renal function	Dyall-Smith and Scurry 1990
Ingestion of ethyl-Hg-contaminated pork	Elevated blood urea, urinary protein, urinary sediment	Cinca et al. 1979
Ingestion of MeHg-treated wheat	Polyuria, albuminuria	Jalili and Abbasi 1961
Ingestion of MeHg-contaminated fish	Increase in deaths due to nephritic diseases among women	Tamashiro et al. 1986

a similar study, Magos and Butler (1972) reported fibrosis in the renal cortex of female rats following 12 weeks of MeHg exposure at the lowest dose studied (0.84 mg/kg per day). Increased kidney weight and decreased proximal convoluted tubule enzymes were seen in rats given MeHg chloride in the diet (0.1 mg/kg per day) for 2 years. No histopathological changes were observed (Verschuuren et al. 1976). Subsequent studies of rats and mice reported nephrosis following long-term exposure to MeHg (Mitsumori et al. 1983, 1984, 1990; Solecki et al. 1991). Nephrosis was also observed in rats exposed to phenylmercuric acid in drinking water for 2 years (Solecki et al. 1991).

TABLE 5-6 Summary of Renal Studies in Animals

Species	Duration	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Effect	Reference
Rat	3-12 wk	None	0.84	Fibrosis, inflammation, large foci in renal cortex	Magos and Butler 1972
Rat	12 wk		0.08	Cytoplasmic masses in proximal tubules	Fowler 1972
Rat	2 yr	0.02	0.1	Increased renal weights Decreased renal enzymes	Verschuuren et al. 1976
Rat	0-21 days of age	None	1	Altered renal function and renal hypertrophy	Slotkin et al. 1985
Rat	2 yr		0.4	Nephrosis	Solecki et al. 1991
Mouse	26 wk	0.15	0.6	Degeneration of proximal tubules	Hirano et al. 1986
Mouse		0.03 (males) 0.13 (females)	0.14 (males) 0.6 (females)	Chronic nephropathy, interstitial fibrosis	Mitsumori et al. 1990
Mouse	Once	8 (males) 24 (females)	16 (males) 32 (females)	Decreased phenolsulfonphthalein excretion, increased serum creatinine, swollen tubuler epithelium	Yasutake et at. 1991

Abbreviations: NOAEL, no-observed-adverse-effect level; LOAEL, lowest-observed-adverse-effect level.

Degeneration of the proximal tubules was observed in mice given MeHg chloride in the diet (0.11 mg/kg per day) for 2 years (Hirano et al. 1986). Epithelial degeneration and regeneration of the proximal tubules and interstitial fibrosis were noted in both male and female mice following almost 2 years of exposure to MeHg in the diet (estimated

dose associated with effects was approximately 0.2 mg/kg per day) (Mitsumori et al. 1990). Yasutake et al. (1991) showed in mice that a single oral dose of MeHg (16 mg/kg) impaired renal function, causing increased plasma creatinine concentrations and swelling of tubular epithelium with exfoliation of cells into the tubular lumen. No effects were observed after a single gavage dose of Hg at 8 mg/kg.

A study by Slotkin et al. (1985) examined the renal effects of MeHg exposure during the neonatal period. Rats exposed to daily doses of 1 or 2.5 mg/kg per day from birth to 21 days of age (weaning) exhibited renal hypertrophy and altered renal function (elevated fractional excretions of water, glucose, sodium, chloride, osmotic particles), which peaked at approximately 20 days of age. The authors indicated that the results reflected effects on tubular function and that tests conducted in conjunction with physiological challenge might reveal even greater impairment.

CARDIOVASCULAR EFFECTS

Numerous studies have examined fish consumption and cardiovascular disease risk, and there are strong indications of protective effects of fish. These effects could be due to a number of components in fish, such as omega-3 fatty acids and selenium and might also indicate a different style of eating (diets lower in red meats).

Although inclusion of fish in the diet is generally beneficial, some fish contain agents such as MeHg and PCBs that have been associated with adverse cardiovascular effects. Therefore, future studies should control for co-exposure to these common contaminants in their analyses of the beneficial effects of fish intake.

Hg accumulates in the heart, and exposures to organic and inorganic forms of this metal have been associated with blood-pressure alterations and abnormal cardiac function. Numerous reports of human poisonings have described marked hypertension and abnormal heart rate among victims. Autopsies of two boys who died of cardiac arrest after they were fed ethylmercury-contaminated pork over a period of several weeks revealed myocarditis. Two recent epidemiological studies have found associations between dietary exposure to very low levels of MeHg

and cardiovascular effects. One of those studies found evidence of an effect of prenatal MeHg exposure on heart function at age 7. Additional studies are needed to better characterize the effect of MeHg exposure on blood pressure and cardiovascular function at various stages of life.

Human Studies

The cardiovascular effects of Hg exposure in humans are summarized in Table 5-7. Warkany and Hubbard (1953) reported several cases in which children developed tachycardia and elevated blood pressure after they were treated with mercurous chloride-containing medications for worms or teething discomfort. Increases in blood pressure and heart rate have also been reported following inhalation of high concentrations of metallic Hg (Hallee 1969; Soni et al. 1992; Bluhm et al. 1992). In one of the cases, the increase in heart rate was described as a sinus tachycardia (Soni et al. 1992). Marked hypertension (160/120 mm Hg) and tachycardia (120 beats per minute) were also described in an 11-year old girl who was hospitalized with a diagnosis of acute Hg intoxication (Wössmann et al. 1999). Vroom and Greer (1972) reported a high incidence (five of nine workers) of hypertension among workers in a thermometer plant.

Exposure to organic Hg has also been associated with cardiovascular changes. Three clinical case reports and two epidemiological investigations have reported similar effects. The first evidence of cardiovascular abnormalities following exposure to organic Hg was provided by Jalili and Abbasi's (1961) description of patients who were hospitalized during the Iraqi grain poisoning epidemic. Abnormalities seen in severely poisoned patients included irregular pulse and electrocardiograms showing ventricular ectopic beats, prolongation of the Q-T interval, depression of the S-T segment and T inversion. Electrocardiograms of four family members who consumed ethylmercury-contaminated pork revealed similar findings, including abnormal heart rhythms with S-T segment depression and T-wave inversion (Cinca et al 1979). Deaths of two children in this family were attributed to cardiac arrest, and their autopsies revealed myocarditis. A child who was diagnosed with acrodynia following exposure to vapors from a paint that contained

phenylmercuric acetate exhibited a rapid heart beat and hypertension (Aronow et al. 1990).

Table 5-7 Summary of Cardiovascular Studies in Humans

Exposure source	Effects	Reference
Mercurous Chloride medications	Tachycardia and increased blood pressure in children	Warkany and Hubbard 1953
Occupational exposure to alkyl Hg vapors	Increased blood pressure	Höök et al. 1954
Alkyl Hg-contaminated wheat	Irregular heart rate	Jalili and Abbasi 1961
Ethylmercury-contaminated meat	Irregular heart rate, cardiac arrest, myocarditis	Cinca et al. 1979
Phenylmercuric acetate vapors	Hypertension and rapid heart rate	Aronow et al. 1990
Metallic Hg vapors	Increased blood pressure and heart rate	Hallee 1969, Bluhm et al. 1992, Soni et al. 1992, Vroom and Greer 1972
Dental amalgams	Increased blood pressure	Siblerud 1990
Frequent fish consumption	Higher cardiovascular death rates	Salonen et al. 1995
Hg intoxication (source unspecified)	Marked hypertension in child	Wössmann et al. 1999
Unspecified	High Hg concentrations in myocardium of IDCM patients	Frustaci et al. 1999
Prenatal exposure	Increased blood pressure and decreased heart rate variability at age 7	Sørensen et al. 1999

Two recent epidemiological investigations have found associations between exposure to low levels of MeHg and adverse cardiovascular effects. A recent study by Sørensen et al. (1999) showed an association between prenatal exposure to MeHg and cardiovascular function at age 7. The study of 1,000 children from the Faroe Islands found that diastolic and systolic blood pressures increased by 13.9 and 14.6 mm Hg, respectively, as cord-blood Hg concentrations rose from 1 to 10 μg/L. In boys, heart-rate variability, a marker of cardiac autonomic control,

decreased by 47% as cord-blood Hg concentrations increased from 1 to 10 µg/L.

Salonen et al. (1995) compared dietary intake of fish and Hg, and compared Hg concentrations in hair and urine with the prevalence of acute myocardial infarction (AMI) and death from coronary heart disease or cardiovascular disease in a cohort of 1,833 Finnish men. All study participants were free of clinical heart disease, stroke, claudication, and cancer at the beginning of the study. Daily fish intake ranged from 0 to 619.2 g (mean = 46.5 g per day) and hair Hg concentrations ranged from 0 to 15.67 ppm (mean = 1.92 ppm). Dietary Hg intake ranged from 1.1 to 95.3 µg per day (mean = 7.6 µg per day). Over a 7-year observation period, men in the highest tertile (at or more than 2 ppm) of hair Hg content had a 2.0-fold higher risk of AMI than men in the two lowest tertiles. The relative risk was similar for coronary deaths and cardiovascular deaths, although the difference for coronary deaths did not reach statistical significance due to small numbers. Men who consumed at least 30 g of fish a day had a 2.1-fold higher risk of AMI. For each additional 10 g of fish consumed, there was an increment of 5% in the 5-year risk of AMI.

Trace elements were measured in myocardial and muscle-tissue samples from 13 patients diagnosed with idiopathic dilated cardiomyopathy (IDCM). The subjects had no history of Hg exposure. Findings were compared with Hg concentrations measured in myocardial and muscle biopsies from age-matched patients with valvular (12 patients) or ischemic heart disease (13 patients), papillary and skeletal-muscle biopsies from 10 patients with mitral stenosis, and left-ventricle endomyocardial biopsies from 4 normal subjects. Hg concentrations in myocardial samples collected from patients with IDCM were 22,000 times higher than those in control samples. Antimony, gold, chromium, and cobalt concentrations were also higher in IDCM patients, but the greatest differences were for Hg (178,400 ng/g versus 8 ng/g) and antimony (19,260 ng/g versus 1.5 ng/g). The investigators concluded that the increased concentration of trace elements found in patients with IDCM might adversely affect mitochondrial activity and myocardial metabolism and worsen cellular function (Frustaci et al. 1999). Matsuo et al. (1989) analyzed Hg concentrations in human autopsy tissues collected from 46 cadavers. The subjects (32 males and 14 females aged

4 months to 82 years) were residents of metropolitan Tokyo and had no known exposure to Hg. The average total Hg content in heart tissue was 43 ng/g, with 80% of this being in the form of MeHg.

Animal Studies

Effects of MeHg on the heart and circulatory system have been observed in several animal models (see Table 5-8). A report by Shaw et al. (1979) described cerebrovascular lesions in four nonhuman primates following long-term exposure to near-toxic to toxic doses of MeHg hydroxide (90 to 120 µg/kg per day). Lesions were similar to those observed in humans with hypertension; intimal thickening, smooth-muscle cell proliferation, and adventitial fibrosis were reported.

Mitsumori et al. (1983, 1984) fed Sprague-Dawley rats diets containing MeHg chloride (males, 0, 0.011, 0.05, or 0.28 mg/kg per day; females, 0.014, 0.064, or 0.34 mg/kg per day) for up to 130 weeks. Polyarteritis nodosa and calcification of the arterial wall were seen at the highest

TABLE 5-8 Summary of Cardiovascular Studies in Animals

Species	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Effects	Reference
Monkeys	None	0.09	Cerebrovasular changes, hypertension, intimal thickening	Shaw et al. 1979
Rat	0.05 (males) 0.06 (females)	0.28 (males) 0.34 (females)	Polyarteritis nodosa, calcification of arterial wall	Mitsumori et al. 1983, 1984
Spontaneous hypertensive rat	None	2 (26 d)	Increased blood pressure in females	Tamashiro et al. 1986
Rat	None	0.4	Hypertension	Wakita 1987
Rat	None	12 (2 d)	18% decrease in heart rate	Arito and Takahashi 1991

Abbreviations: NOAEL, no-observed-adverse-effect level; LOAEL, lowest-observed-adverse-effect level.

dose. Histological examination revealed evidence of hemosiderosis and extramedullary hematopoiesis of the spleen.

Tamashiro et al. (1986) reported an increase in blood pressure in spontaneous hypertensive rats (SHR) exposed to MeHg at 2 mg/kg per day for 26 consecutive days. That effect was sex specific, being observed only in females. Considerable variation was observed in blood pressure for both the MeHg-exposed and the control rats. Differences were observed at only two time points, week 3 and week 5 of the study.

In Wistar rats, hypertension was induced after a 30-day exposure to MeHg chloride at 0.4 or 1.2 mg/kg per day (Wakita 1987). The onset of hypertension occurred 42 days after the exposure period ended, and the effect persisted for more than 1 year. In rats, a decrease in heart rate (18%) was observed following 2 daily doses of MeHg at 12 mg/kg per day (Arito and Takahashi 1991).

HEMATOLOGICAL EFFECTS

Hematological changes have not been reported following human exposure to Hg. Studies conducted in animals suggest that Hg exposure might pose a risk of anemia and clotting disorders. Those animal studies are summarized in Table 5-9.

Munro et al. (1980) exposed rats to Hg at 0.25 mg/kg per day for up to 26 months. Exposed males had decreased hematocrit and hemoglobin values, as well as overt signs of neurotoxicity and increased mortality

TABLE 5-9 Summary of Hematological Studies in Animals

Species	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Effect	Reference
Rat	None	0.25 for 26 mon.	Decreased hematocrit and hemoglobin values	Munro et al. 1980
Rat	None	8.0	Decreased clotting time	Kostka et al. 1989
Rat	None	4.2	Decreased hematocrit and hemoglobin values	Solecki et al. 1991

Abbreviations: NOAEL, no-observed-adverse-effect level; LOAEL, lowest-observed-adverse-effect level.

compared with unexposed controls. Hematological changes were not observed in exposed female rats.

Kostka et al. (1989) examined the coagulability of blood in rats exposed to either a single dose of MeHg chloride at 17.9 mg/kg per day or 5 consecutive days of dosing at 8 mg/kg per day. Blood coagulation was measured 1, 3, and 7 days after administration of the single dose or 24 hr after the 5 consecutive days of dosing. A reduction in clotting time and an increase in the fibrinogen concentrations in plasma were observed in both MeHg dose groups. Reduced clotting time was observed in the single-dose group 1 day after exposure.

Decreased hemoglobin, hematocrit, and red-blood-cell counts were seen in rats exposed to phenylmercuric acetate in drinking water (4.2 mg/kg per day) for 2 years (Solecki et al. 1991). The anemia might have been secondary to blood loss associated with ulcerative lesions seen at that dose in the large intestine. Polycythemia developed in rats exposed in utero to a combinations of MeHg chloride, ethylurea, and sodium nitrate. The polycythemia occurred as early as 1 month of age in as many as 24% of the offspring. Many features of this condition were similar to the features of polycythemia vera in man (elevated hematocrit, white- and red-blood-cell counts, splenomegaly, and hyperplasia of bone marrow) (Koller et al. 1977). Because that study involved concurrent exposure to MeHg, ethylurea, and sodium nitrite, the observed effects cannot be attributed to MeHg.

DEVELOPING CENTRAL-NERVOUS-SYSTEM TOXICITY

Human Studies

The central-nervous-system (CNS) effects of MeHg in humans have been extensively studied following accidental poisoning incidents and low-dose exposures. In this section, the Minamata and Iraqi Hg poisoning episodes are reviewed, documenting the severe neurological dysfunctions and developmental abnormalities that occur in children exposed in utero to high doses of MeHg. That review is followed by a review of the effects of low-dose prenatal MeHg exposure on neurological status, age at achievement of developmental milestones, infant and preschool development, childhood development, sensory and neuro

physiological functions, and other end points in children; and neurological, neurophysiological and sensory functions in adults.

High-Dose Poisonings

Poisoning Episode in Japan

The mass poisoning of residents living near Minamata Bay in Japan in the 1950s first raised awareness of the severe neurological sequelae associated with MeHg poisoning, particularly when it occurs prenatally. The primary route of exposure in that episode was the consumption of fish contaminated with MeHg that bioaccumulated as it ascended the aquatic food chain. According to Harada (1995), all children identified as suffering from the most severe form of congenital Minamata disease (CMD) expressed mental retardation, primitive reflexes, cerebellar ataxia, disturbances in physical growth, dysarthria, and limb deformities. Most of the affected children also expressed hyperkinesis (95%), hypersalivation (95%), seizures (82%), strabismus (77%), and pyramidal signs (75%). The incidence of cerebral palsy among children with CMD was also increased (9% of 188 births in three villages versus a national incidence of 0.2% to 2.3%). Some signs and symptoms decreased over time (e.g., paroxysmal events, hypersalivation, primitive reflexes, and ataxia), although others (e.g., reduced intelligence and dysarthria) did not (Harada 1995). Most of the patients with the severe form of CMD were unable to function successfully in society.

It is difficult to reconstruct the MeHg doses in the CMD patients. Measurements of Hg in hair and blood were not made until 1959, several years after the poisoning episode was identified. The Hg concentrations in maternal-hair samples taken 5 to 8 years after giving birth to infants with CMD ranged from 1.8 to 191 ppm (Harada 1995). Analyses of the Hg concentrations in 151 archived umbilical-cord tissue samples dating from 1950 to 1969 confirmed that exposures increased during this period (Harada et al. 1999). Concentrations were highest in patients with CMD, intermediate in patients with acquired MD, and lowest in asymptomatic individuals. On the basis of these data, Akagi et al. (1998) estimated that the mean maternal-hair Hg concentration in CMD patients was approximately 41 ppm (range 3.8 to 133 pm). The uncertainty

associated with that estimate, however, is likely to be substantial. Identification of cases was undoubtedly incomplete, particularly among individuals who suffered milder forms of CMD. For example, even excluding cases of known CMD, the prevalence of mental retardation among children born between 1955 and 1958 in the contaminated area was 29%, far higher than that expected as a background prevalence. That finding suggests that many children with less severe forms of CMD were undiagnosed. Thus, the data cannot provide precise estimates of the minimum dose of MeHg required to produce CMD.

Several observations associated with MD suggest that neurological deficits might emerge decades after exposure to MeHg has ended and that the severity of deficits might increase as a patient ages. It is difficult, however, to definitively rule out continued Hg exposure in adulthood as having a role in progressive neurological disorders. Harada (1995) distinguished three groups of patients with atypical, incomplete, or slight symptoms: (1) gradually progressive type, (2) delayed- onset type, and (3) escalator-progressive type. Evidence consistent with delay in the expressions of MeHg neurotoxicity was reported in a long-term follow-up study of 90% of diagnosed MD patients at least 40 years of age (1,144 patients). Kinjo et al. (1993) found not only that the prevalence of deficits in "activities of daily living" (i.e., eating, bathing, and dressing) was greater among cases than among age- and sex-matched controls but also that the difference between the prevalence rates of the two groups increased significantly with age. Increased deficits with age and delayed effects were also seen in animal studies (Spyker et al. 1972; Rice 1996, 1998; see section on Animal Studies).

Poisoning Episode in Iraq

A second episode of mass MeHg poisoning occurred in Iraq in the early 1970s when seed grain treated with a MeHg-containing fungicide was ground into flour and consumed. Those MeHg exposures were most likely more acute and involved higher exposures than those experienced by the residents of Minamata Bay. Early studies of the most severely affected children exposed to MeHg during fetal development were concordant with the Minamata findings. Those children manifested severe sensory impairments (blindness and deafness), general

paralysis, hyperactive reflexes, cerebral palsy, and impaired mental development (Amin-Zaki et al. 1974). Several follow-up studies of the exposed population were conducted. Marsh et al. (1987) identified 81 children who had been in utero at the time of the episode and collected information from two sources on children's neurodevelopmental outcomes: neurological examination of each child and a maternal interview regarding the age at which the child achieved standard developmental milestones, such as walking and talking. Maximum maternal-hair Hg concentrations during the time when the study child was in utero served as the index of fetal exposure and ranged from 1 to 674 ppm. Developmental retardation was defined as a child's failure to walk a few steps unaided by 18 months of age or to talk (two or three meaningful words) by 24 months of age. A point system was devised for scoring the neurological examination; a score greater than 3 indicated a definite abnormality. There was a dose-response relationship between the prevalence of those indicators of poor outcomes and maternal-hair Hg concentrations. The most frequent neurological findings were increased limb tone and deep tendon reflexes with persisting extensor plantar responses. Ataxia, hypotonia, and athetoid movements were also reported. Boys appeared to be more severely affected than girls. Seven of the 28 children with the highest exposures had seizures (versus none of the 53 children with the lowest exposures). For those seven children, maternal-hair Hg concentrations ranged from 78 to 674 ppm. Many children of mothers with hair concentrations exceeding 100 ppm had normal neurological scores and achieved milestones at the expected times. Moreover, many of the women who had very high hair Hg concentrations and whose infants did poorly experienced only mild and transient signs or symptoms of MeHg toxicity.

Additional analyses of that data set were conducted in an attempt to identify more precisely the shape of the dose-response relationship and, in particular, the threshold for adverse neurodevelopmental effects, if indeed such a threshold exists. Cox et al. (1989) obtained more accurate estimates of peak exposure during pregnancy by applying an X-ray fluorescent method to single strands of maternal hair. Using a variety of statistical models (logit, hockey-stick, and nonparametric kernel-smoothing methods), they estimated a population threshold of approximately 10 ppm for the outcomes investigated (see Figure 5-1, Figure 5-2, and Figure 5-3). However, the uncertainty associated with that estimate is heavily

dependent on the assumed background prevalence of the poor outcomes. (No data were available on the true background prevalence of the poor outcomes among Iraqi children.) For example, for motor retardation, the upper bound of the 95% CI increases from 14 to 190 ppm when the estimate of background prevalence is changed from 0% to 4%. For neurological abnormality, the upper bound of the 95% CI for the threshold estimate is 287 ppm (assuming a 9% background prevalence). In re-analyses of those data, Crump et al. (1995) and Cox et al. (1995) showed that the estimate of population threshold is highly model de

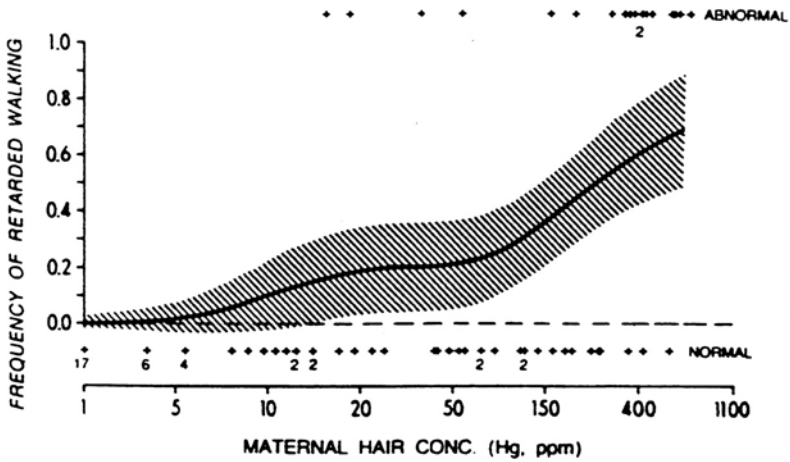

FIGURE 5-1 Nonparametric kernel-smoothing analysis of the relationship between maternal-hair concentration of Hg and retarded walking in the offspring. Maternal-hair concentrations were estimated using XRF single-strand analysis. The exposure value is the maximum level during gestation based on the growth rate of the hair and the birth date of the child. Results from multiple strands were averaged for the final exposure value. The shaded area denotes nonsimultaneous 95% confidence limits for individual points on the smoothed curve (for details, see text). Maternal-hair concentrations for normal and abnormal infants are plotted below and above the graph, respectively. Source: Cox et al. 1989. Reprinted with permission from *Environmental Research*; copyright 1989, Academic Press.

pendent, sensitive to the definition of abnormality, and, in the case of delayed walking, heavily influenced by only four cases of delayed walking among children of women with hair Hg concentrations below 150 ppm. The statistical variability of the threshold estimates appears likely to be considerably greater than that provided by Cox et al. (1989). Crump et al. (1995) concluded that the Iraqi data do not provide convincing evidence of any adverse neurodevelopmental effects of MeHg below maternal-hair concentrations of 80 ppm.

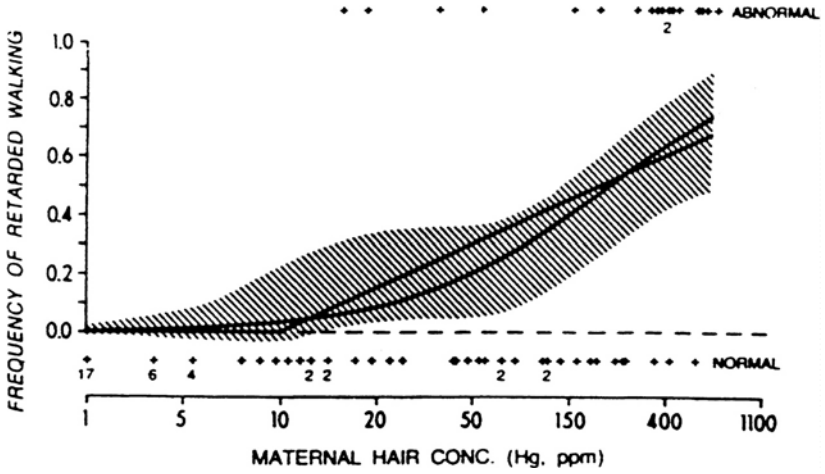

FIGURE 5-2 Plots of the logit and hockey-stick dose-response analysis of the relationship between retarded walking and maternal-hair concentrations during gestation. The two dose-response curves are shown by solid lines. The shaded area represents the 95% confidence limits from kernel smoothing. Source: Cox et al. 1989. Reprinted with permission from *Environmental Research*; copyright 1989, Academic Press.

In evaluating the Iraqi data, it is important to note that the interviews were conducted when the children were a mean age of 30 months. However, some children must have been considerably older, as the ages at which children in the sample were reported to have walked or talked were as high as 72 months. In addition, birth dates are generally not

important among Iraqi nomads. Therefore, maternal recollection of ages at which children achieved milestones had to be referenced to external events, such as the poisoning. The extent of the imprecision in those data is suggested by the strong digit preferences in the mothers responses. For instance, for 70 of the 78 children, the estimated age at walking was an even number of months. Furthermore, 75% of the estimates were multiples of 6 months. For age of talking, 70 of the 73 responses were an even number of months. (It should be noted, however, that the neurological scores were assigned to the children on the basis of a clinical examination and, therefore, were not subject to recall bias.) Finally, the extent of selection bias in this cohort cannot be charac

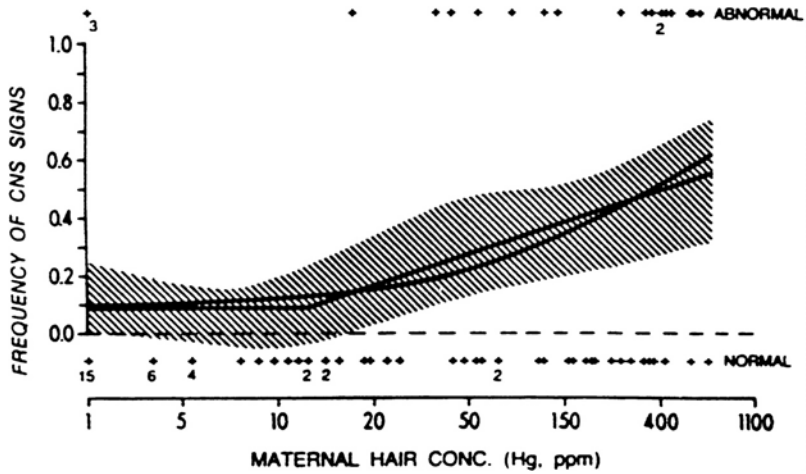

FIGURE 5-3 Plots of the logit and hockey-stick dose-response analysis of the relationship between CNS signs and maternal-hair concentrations during gestation. The two dose-response curves are shown by solid lines. The shaded area represents the 95% confidence limits from kernel smoothing. Source: Cox et al. 1989. Reprinted with permission from *Environmental Research*; copyright 1989, Academic ress.

terized, because the size of the base population from which it was drawn and the referral mechanism that brought mothers and children to medical attention are both unknown. For instance, women who knew that they had consumed large amounts of contaminated grain and had concerns about their children's welfare might have come forward, and women who consumed equally large amounts of contaminated grain but whose children were developing well might not have come forward. That issue is critical, because the calculation of a threshold, a reference dose, or a benchmark dose requires a denominator (i.e., the size of the exposed population) as well as the background prevalence of the adverse outcomes to estimate the added risk associated with the exposure of interest. It appears that the background prevalence of developmental abnormality was extremely high among the Iraqi children who participated in the follow-up studies. The prevalence of delayed walking among children whose mothers had hair Hg concentrations below 10 ppm (and can be viewed essentially as a control group for the purpose of estimating background prevalence) was 36% (11 of 31). In contrast, among the population of U.S. children on whom the Bayley Scales of Infant Development (first edition) were standardized, the prevalence of delayed walking by that criterion was approximately 5%. Similarly, the prevalence of delayed talking (two or three words by 24 months) among the Iraqi children was 22% (6 of 27), and 95% of 24-month-old U.S. children in the standardization sample of the MacArthur Communicative Development Inventory were producing approximately 50 words (Fenson et al. 1993).

Chronic Low-Dose-Exposure Epidemiological Studies

A number of epidemiological studies have been carried out on populations exposed chronically to low doses of MeHg. Table 5-10 summarizes some key methodological aspects of those studies. In this section, those studies are discussed in terms of the end points assessed. End points discussed are status on neurological examination, age at achievement of developmental milestones, infant and preschool development, childhood development, sensory, and neurophysiological functions, and other end points in children.

TABLE 5-10 Summary of Developmental Neurotoxicity Studies in Humans

Study Site	Size of Cohort Identified and Enrolled	Exposure Biomarker	MeHg or Total Hg Concentration	Age at Assessment	Number of Children Assessed	End Points	Reference
Amazon	351	Child hair	Mean, 11.0 ppm; 80% > 10 ppm	7-12 years	354 (Table 1)	Fingertapping, WISC-III: digit span forward, Santa Ana dexterity test, Stanford-inet: copying, bead memory	Grandjean et al.1999
Ecuador	75 (36 children, 39 adults)	Blood	Mean, 17.5 mg/L (3.0 in 34 controls)	Children: 3-15 years Adults: 16-57 years	19-40	Pure tone conduction threshold BAEP	Counter et al. 1998
Faroe Islands	182	Maternal hair	Geometric mean, 4.1 ppm; range, 2.5-7.4 ppm	2 wk, adjusted for gestational age	182	Neurological exam	Steuerwald et al. 2000
		Umbilical cord blood	Geometric mean, 20.4 μg/L; range, 11.8-40.0 μg/L				
		Umbilical cord serum	Geometric mean, 2.5 μg/L; range, 1.7-3.7 μg/L				
	1,023	Maternal hair	Geometric mean, 4.3 ppm; interquartile range, 2.6-7.7 ppm	Maternal interview “during the first year”	583	Developmental milestones	Grandjean et al. 1995

French Guiana	Approx. 400	Maternal hair	Median, 6.6 ppm range, 2.6-17.8 35%>10 ppm	9 month-12 years	248 (neuro exam)	neurological exam fingertapping, Stanford-Binet: block design, copying, bead memory	Cordier and Garel 1999
					206 (psychological exam)	MSCA: numerical memory, leg coordination	
Madeira	149	Maternal hair	Geometric Mean, 9.6 ppm Range, 1.1-54.4 52%> 10ppm	6-7 years	146-149	BAEP, VP NES: fingerlapping, hand eye coordination, continuous performance test WISC-R: digit span, block design Stanford-Binet: bead memory	Murata et al. 1999a
Mancora, Peru	369	Maternal hair	Geometric mean, 7.1 ppm; geometric SD, 2.1; range, 0.9-28.5	?	194 (131 with both exposure and outcome data)	Neurological exam Developmental milestones	Marsh et al. 1995a
Northern Quebec	247	Maternal hair	Mean, 6 ppm; 6%, >20 ppm	12-30 mon	234	Neurological exam	McKeown-Eyssen et al. 1983
New Zealand	10,930 mothers screened, 935 "high" fish consumers identified, 73 "high" Hg mothers identified	Maternal hair	"High" Hg defined 4 yr as >6 ppm; mean, 8.3 ppm in "high" Hg group; range, 6-86 ppm; only 16 values >10 ppm	6 yr	74; 38 "high" Hg, 36 "low" Hg, including 30 matched pairs	DDST, vision, functional neurological exam	Kjellstrom et al. 1986
					237; 57 complete sets of 1 "high" Hg child, 3 matched controls, and 4 incomplete sets	WISC-R, TOLD, MSCA, CDS, BWRT, KMDAT, PPVT, EBRS	Kjellstrom et al. 1989

Seychelles Islands (pilot)	804	Maternal hair	Median, 6.6ppm; range, 0.6-36.4 ppm, interquartile range: 6.1	5-109 wk	789	Neurological exam, DDST-R	Myers et al. 1995a
				66 mon	217	MSCA, PLS, WJTA:LWI, WJTA:AP	Myers et al. 1995c
Seychelles Islands (main)	779	Maternal hair	Median, 5.9ppm; interquartile range, 6.0 ppm; all values, <30 ppm	6.5 mon	712-737	Neurological exam, DDST-R, FTII, visual attention	Myers.et al. 1995b
				19 mon	738	Developmental milestones BSID	Myers et al. 1997; Axtell et al. 1998 Davidson et al. 1995b
				29 mon	736	BSID	Davidson et al.1995b
				66 mon	711	MSCA, PLS, B-G, WJTA:LWI, WJTA:AP, CBCL	Davidson et al.1998

Abbreviations: DDST, Denver Developmental Screening Test (DDST-R is revised version); MSCA, McCarthy Scales of Children's Abilities; PLS, Preschool Language Scale; WJTA, Woodcock Johnson Test of Achievement (AP, applied problems; LWI, letter-word identification); FTII, Fagan Test of Infant Intelligence; BSID, Bayley Scales of Infant Development; B-G, Bender-Gestalt Test; CBCL, Child Behavior Checklist; WISC-R, Wechsler Intelligence Scale for Children-Revised; TOLD, Test of Language Development; CDS, Clay Diagnostic Survey; BWRT, Burt Word Recognition Test; KMDAT, Key Math Diagnostic Arithmetic Test; PPVT, Peabody Picture Vocabulary Test; EBRS, Everts Behaviour Rating Scale; NES, Neurobehavioral Evaluation System; CVLT-C, California Verbal Learning Test-Children; BNT, Boston Naming Test; POMS, Profile of Mood States; VEP, Visual Evoked Potentials; BAEkP, Brainstem Auditory Evoked Responses.

Status on Neurological Examination

McKeown-Eyssen et al. (1983) studied 234 12- to 30-month-old Cree children (95% of eligible children) for whom prenatal MeHg exposure was estimated on the basis of maternal-hair samples. The subjects lived in four communities in northern Quebec. For 28% of the mothers, hair samples were collected during pregnancy; for the balance of the cohort, prenatal exposure was estimated on the basis of hair segments assumed to date from the time the study child was in utero. The measure of exposure used was the maximum concentration of Hg in the segment of hair corresponding most closely to the period from 1 month before conception to 1 month after delivery. The mean maternal-hair Hg concentration was approximately 6 ppm, with 6% of samples exceeding 20 ppm. One of four pediatric neurologists blinded to individual Hg-exposure status, measured height, weight, and head circumference, identified dysmorphologies, and conducted a neurological examination (assessing coordination, cranial nerves, muscle tone, and reflexes). The neurologist made a summary clinical judgment as to the presence of a neurological abnormality. No child was judged to have any abnormal physical findings. Overall, 3.5% (4) of the boys and 4.1% (5) of the girls were considered to have a neurological abnormality. The most frequent abnormality involved tendon reflexes, seen in 11.4% (13) of the boys and 12.2% (14) of the girls. The only neurological findings significantly associated with prenatal MeHg exposure, either before or after adjustment for confounding, were abnormalities of muscle tone or reflexes in boys. Two boys had increased tone in the legs only, five had isolated decreased reflexes, six had generalized decreased reflexes, and two had generalized increased reflexes ($p = 0.05$). The risk of an abnormality of tone or reflexes increased 7 times with each 10-ppm increase in prenatal MeHg exposure (95% CI 1.0-51.0). With log transformation of prenatal MeHg exposure, however, the p value associated with the risk of an abnormality due to MeHg exposure increased to 0.14. When exposure was categorized, the prevalence of tone or reflex abnormality did not increase in a clear dose-response manner across categories (i.e., 15.8%, 5.6%, 26.3%, 0%, 7.1%, and 38.5%). In girls, the only association identified was in the unexpected direction between prenatal MeHg exposure and incoordination (60% decrease in probability of incoordination for each 10-ppm increment; odds ratio (OR), 0.3; 95% CI, 0.1-0.9; $p = 0.02$).

The authors noted five caveats about the one significant adverse association identified: (1) the abnormalities of muscle tone and reflexes in boys were isolated, mild, and of doubtful clinical importance; (2) children exposed to very high MeHg doses manifested as severe generalized neurological disease, including increases in tone and reflexes, rather than the mild, isolated muscle tone and reflex abnormalities (mostly decreased) seen in Cree children; (3) the absence of a coherent dose-response relationship; (4) the absence of consistency across sex; and (5) the possibility that the finding reflects chance, lack of normality in the distribution of the exposure index, or residual confounding.

Infants' status on neurological examination was also evaluated as an end point in a study of 194 children in Mancora, Peru. Although the study was conducted in the early 1980s, it was not published until 1995 (Marsh et al. 1995a). Fish consumption was the primary route of MeHg exposure, and maternal hair was used as the index of exposure (geometric mean, 7.05 ppm; range, 0.9 to 28.5 ppm). Geometric-mean peak hair MeHg concentration was similar (8.34 ppm; range, 1.2 to 30.0 ppm), suggesting that the women were in steady state due to stability in their fish-consumption patterns. Maternal-hair samples and data on child neurological status were available for 131 children. Several elements of the study design are not described, including the size of the eligible population from which the 131 children were sampled, the specific elements of the neurological assessment conducted, and the ages at which the children were examined. However, frequencies are reported for the following end points: tone decreased (two children), tone increased (none), limb weakness (one child), reflexes decreased (one child), reflexes increased (four children), Babinski's sign (an indication of a pyramidal-tract abnormality) (one child), primitive reflexes (none), and ataxia (none). No end point was significantly associated with either mean or peak maternal-hair Hg concentration.

A cross-sectional pilot study was carried out for the Seychelles Child Development Study (SCDS) (Myers et al. 1995a). For 2 years before the start of the study, all women attending an antenatal clinic were asked to provide one or more hair samples during and after pregnancy. A total of 804 infants were subsequently enrolled in the study, and tested during three visits over 2 months in 1987-1988. No data are provided on the size ,of the population from which that sample was drawn. Fifteen infants were excluded due to maternal illnesses during pregnancy (e.g.,

diabetes or eclampsia) or to newborn characteristics thought to place a child at developmental risk (e.g., low birth weight or maternal alcohol ingestion during pregnancy) (Marsh et al. 1995b). A total of 789 infants and children were evaluated between the ages of 5 and 109 weeks by one blinded pediatric neurologist. Mean maternal-hair Hg concentration in the cohort was 6.1 ppm (range, 0.6 to 36.4 ppm). The end points assessed were mental status, attention, social interactions, vocalizations, behavior, coordination, postures and movements, cranial nerves (II-XII), muscle strength and tone, primitive and deep tendon reflexes, plantar responses, and age-appropriate abilities such as rolling, sitting, pulling to stand, walking, and running. The statistical analyses focused on three end points selected due to their apparent sensitivity to prenatal MeHg exposure in the Iraq and Cree studies: overall neurological examination, increased muscle tone, and deep tendon reflexes in the extremities. The overall examination was considered to be abnormal if any findings judged to be pathological were present or if the examiner judged the child's speech or functional abilities to be below age level. Pathological findings included abnormalities of cranial nerves (pupils, extraocular muscles, facial or tongue movement, swallowing, or hearing), alteration in muscle tone or deep tendon reflexes (increase or decrease), incoordination, and involuntary movements. Findings that were not considered to be either normal or pathological were categorized as questionable. Because of the low frequency of abnormal examinations (2.8%), the questionable (11.3%) and abnormal categories were combined. No association was evident between maternal-hair Hg concentration and questionable and abnormal results. The frequency of those results ranged from 16.5% in the group with Hg at 0-3 ppm to 11.7% in the group with Hg at more than 12 ppm. The frequencies of abnormalities of limb tone or deep tendon reflexes were about 8%, and the frequency of both end points did not vary with maternal-hair Hg concentrations in a dose-dependent manner.

The main cohort of the SCDS consisted of 779 mother-infant pairs, representing approximately 50% of all live births during the recruitment period. The final sample size was 740. In addition to 18 infants being excluded for the criteria used in the pilot study, 15 were excluded because of insufficient maternal-hair samples, and 6 were excluded for being a twin. When the infants were 6.5 months old, one blinded pediatric neurologist administered essentially the same neurological exami

nation that had been used in the pilot phase (Myers et al. 1995b). The overall examination was considered abnormal if changes in muscle tone, deep tendon reflexes, or other neurological features were pathological or if functional abilities were not considered appropriate for the age. An examination could also be coded as questionable. A total of 3.4% (25) of the children had overall neurological scores considered abnormal or questionable, a frequency too low to permit statistical analysis of the overall neurological examination. The frequency of abnormalities was 2% for both limb tone and abnormal deep tendon reflexes. Questionable limb tone was identified in approximately 20% of the children, and questionable deep tendon reflexes, in approximately 15%. Although such findings were not considered pathological, they were combined with abnormal findings for statistical analyses. The frequency of abnormal and questionable findings for limb tone or deep tendon reflexes was not significantly associated with maternal-hair Hg concentrations.

Steuerwald et al. (2000) recruited a cohort of 182 singleton, full-term infants born in the Faroe Islands and evaluated the associations between neurological function at 2 weeks of age and various dietary contaminants and nutrients. The cohort represents 64% of all births in the catchment area. The primary outcome variable was the neurological optimality score (NOS), which reflects an infant's functional abilities, reflexes, responsiveness, and stability of state. In addition, two subscores were generated (muscle tone and reflexes). A variety of thyroidfunction indices considered to be outcomes were also assessed. The exposure biomarkers measured were Hg concentration in maternal hair, cord whole blood, and cord serum. Measurements were also taken of 18 pesticides (or metabolites) and 28 polychlorinated biphenyl (PCB) congeners in maternal serum (lipid adjusted) and breast milk, selenium in cord whole blood, and fatty acids (arachidonic, eicosapentanoic, docosahexaenoic, and total omega) in cord serum. There was a significant inverse relationship between NOS scores and cord-whole-blood Hg concentrations. The mean concentration was 20.4 µg/L (range, 1.9-102 µg/L) (see Figure 5-4). Although the unadjusted correlation between cord-whole-blood Hg concentration and NOS score was modest (- 0.16), a 10-fold increase in cord-whole-blood Hg was associated with the equivalent of a 3-week reduction in gestational age based on NOS score. Adjustments for total PCBs and fatty acid concentrations did not appreciably affect the results. Selenium did not appear to function as an effect

modifier. Muscle-tone and reflexes subscores were not significantly associated with any exposure biomarker. Maternal hair-Hg concentrations (mean, 4.08 ppm; range, 0.36-16.3 ppm; 10.4%, more than 10 ppm) were not significantly associated with NOS scores.

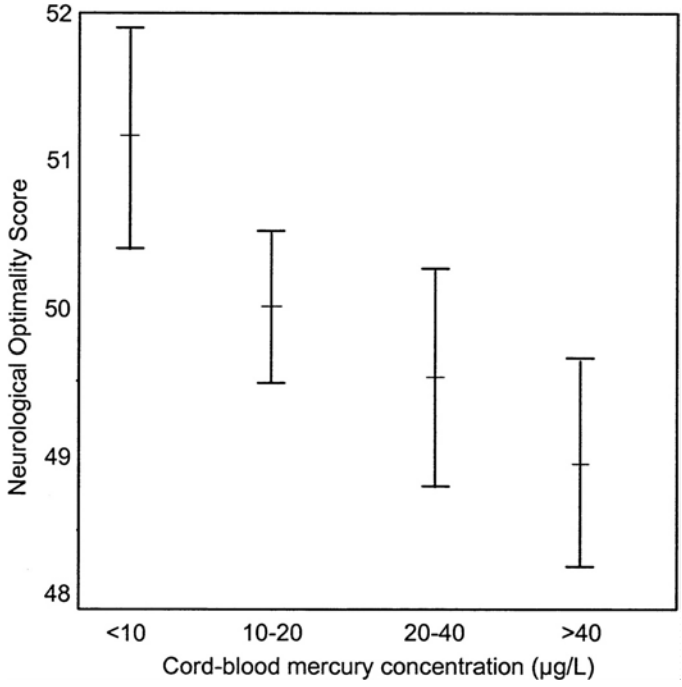

FIGURE 5-4 Neurological optimality score (mean ± standard error of the mean) in relationship to cord-blood Hg concentrations in approximate quartile groups. Source: Stewerwald et al. 2000. Reprinted with permission from the *Journal of Pediatrics*; copyright 2000, Mosby, a Harcourt Health Sciences Company.

A functional neurological examination, as part of a general physical examination, was administered at age 7 years to another cohort of children from the Faroe Islands. The cohort consisted of consecutive deliveries at three hospitals during a 21-month period between 1986 and

1987. Of 1,386 infants born, cord-blood and maternal-hair samples were obtained from 1,022 singleton births (75%) and 917 children were examined (66%) (Grandjean et al. 1992). The mean cord-blood Hg concentration was 22.9 μg/L; the mean maternal-hair Hg concentration was 4.3 ppm. In particular, the examination of the cohort at 7 years of age focused on motor coordination and perceptual-motor performance (Dahl et al. 1996). The coordination tests included diadochokinesia (fast pronation and supination), reciprocal coordination (alternately closing and opening the fists), and finger opposition (the pulpa of the thumb touching the pulpa of the other fingers of the same hand). The perceptual-motor tests included catching a ball with a diameter of 15 cm thrown from a distance of 4 m, finger agnosia, and double finger agnosia. Results were scored as automatic or questionable and poor. Hg concentration was not significantly associated with the number of tests on which a child's performance was considered automatic. On the tests of reciprocal motor coordination, simultaneous finger movement, and finger opposition, fewer than 60% of the children achieved a score of automatic. Finger opposition, however, was the only test in which children with questionable and poor performance (425 children) had a significantly higher mean Hg concentration than children with automatic performance (465 children) (23.9 versus 21.8 μg/L, $p = 0.04$) (Grandjean et al. 1997).

Cordier and Garel (1999) recently reported on the association between MeHg exposure and neurological status in 9-month-old to 6-year-old children living in gold-mining regions of French Guiana. The concentrations of Hg in samples of hair collected from children's mothers at the time of the study were used as a surrogate for exposure during pregnancy. The median concentration was 6.6 ppm (range, 2.6-17.8 ppm; 35%, greater than 10 ppm). Among children 2 years of age and older, the prevalence of increased reflexes was significantly higher with increased Hg concentrations in maternal hair, the association being stronger in boys than in girls. When 10 children who had been found to have increased reflexes were re-examined 9 months later by a different examiner, only three were considered to have increased reflexes. Therefore, the investigators advised caution in interpreting those data.

Overall, the evidence that children's neurological status is associated with low-dose prenatal Hg exposure consists of four findings: (1) an increased prevalence of tone or reflex abnormalities (most often de

creased) in boys with increased maternal-hair Hg concentrations, although that effect is not dose dependent (McKeown-Eyssen et al. 1983); (2) an inverse association between newborns' NOS and umbilical-cord Hg concentration in the Faroe Islands (Steuerwald et al. 2000); (3) a modest but statistically significant increase (2.1 μg/L) in the mean cord-blood Hg samples of 7 year olds who performed suboptimally on a finger opposition test compared with Children whose performance was normal (Grandjean et al. 1997); and (4) an association, especially in boys, between increased reflexes and higher maternal-hair Hg concentrations in a cohort of 9-month-old to 6-year-old children in French Guiana (Cordier and Garel 1999). One limitation in the use of neurological status as an end point is its categorical nature; a child either expresses a particular abnormality or does not. In the SCDS main cohort, the prevalence of abnormal neurological findings was quite low (i.e., 3.4% for abnormal or questionable findings), limiting the statistical power of hypothesis testing. Although the high-dose exposure episodes that occurred in Minamata and Iraq produced classic signs of neurological dysfunction in children exposed in utero, the low doses of MeHg to which the cohorts in the epidemiological studies were exposed prenatally appeared to be associated with subtle neurological effects that are of uncertain clinical significance (e.g., tone or reflex abnormalities). Research on other environmental toxicants such as lead and PCBs has shown, however, that it is important to distinguish individual risk from population risk. A decrement in mean function that is too small to be clinically significant for the individual child might be quite important when it is considered from the standpoint of the impact on the population distribution of the affected function (Weiss 1998).

Age at Achievement of Developmental Milestones

The association between the achievement of developmental milestones and prenatal MeHg exposure was evaluated in the main cohort of the SCDS by Myers et al. (1997) and Axtell et al. (1998). The ages at which a child was able to walk without support and to say words other than “mama” or “dada” were determined by an interview with a child's primary caregiver (person with whom the child spent 5 or more nights per week) conducted at the 19-month evaluation. Those data

were available for 738 of the 779 children enrolled. Prenatal MeHg exposure was estimated as the total Hg in the single longest hair segment dating from the time the study child was in utero (mean, 5.8 ppm; range, 0.5 to 26.7 ppm; 22%, greater than or equal to 10 ppm). Several statistical approaches were carried out, including a standard multiple regression of a log transformation of the age at milestone achievement, hockey-stick models estimating the threshold maternal-hair Hg concentration associated with delay in milestone achievement, and logistic regression analyses of delayed walking, a binary variable in which an abnormal response was defined as greater than 14 months. The mean age at which a child was considered to talk was not significantly associated with maternal-hair Hg in any of the models tested. In regressions stratified by child sex, a positive association was found between age at walking and maternal-hair Hg in boys ($p = 0.043$) but not in girls. A term for the interaction between Hg and sex was not statistically significant in the analyses of the complete cohort, however. The magnitude of the delay in the age at which boys walked was viewed by the authors as clinically insignificant; a 10-ppm increase in maternal-hair Hg was associated with an approximate 2-week delay in walking (see Figure 5-5). The association in boys was not significant when four statistical outliers were excluded from the analysis. Hockey-stick models provided no evidence of a threshold, as the fitted curves were essentially flat. A child's risk of delayed walking was not associated with maternal-hair Hg concentration. Axtell et al. (1998) re-analyzed those milestone data, applying semiparametric generalized additive models, which use smoothing techniques to identify nonlinearities. Those models are less restrictive than the approaches used by Myers et al. (1997), whose approaches make strong assumptions about the true functional form of a relationship.

The major finding of the analyses of Axtell et al. (1998) was that the association between age at walking and maternal-hair Hg in boys was nonlinear, walking appearing at a later age as concentrations increased from 0 to 7 ppm but at a slightly earlier age as Hg concentration increased beyond 7 ppm. The size of the effect associated with the increase from 0 to 7 ppm was very small, corresponding to a delay of less than 1 day in the achievement of walking. Because a coherent dose-response relationship did not hold above 7 ppm, the authors expressed doubt that the association found below 7 ppm reflected a causal effect of Hg exposure on age at walking.

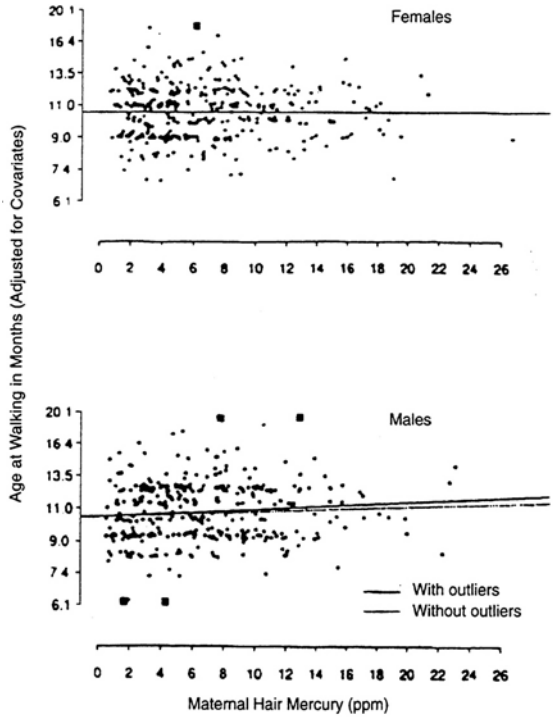

FIGURE 5-5 Plot of partial residuals for log of age at walking versus maternal-hair Hg concentrations for the reduced model with Hg by gender interaction. The partial residual is the natural log of the subject's age at walking adjusted for all variables in the model except Hg. It is computed by adding the Hg effect (estimated coefficient on Hg times the Hg value for that subject) to the raw residual (observed value minus predicted value) obtained from the reduced model. The partial residuals have been rescaled by adding the mean value of log of age at walking to each partial residual. The axis for age at walking (in months) is on a log scale. Outliers are identified on the plot with a different symbol (solid squares). The slope of the solid lines is the regression coefficient for Hg in the originial regression analysis with statistical outliers. The dotted line is the slope with those outliers removed. Source: Myers et al. 1997. Reprinted with permission from *NeuroToxicology*; copyright 1997, Intox Press.

Data on developmental milestones were collected in the Peruvian study conducted by Marsh et al. (1995a). The ages of the children when mothers were queried about the milestones are not stated, although the study was conducted prospectively and data were apparently collected in an ongoing manner over the course of a woman's visits to a postnatal clinic. Regression analyses, including analyses stratified by child sex, did not reveal any significant associations between maternal-hair Hg concentrations and the ages at which children sat, stood, walked, or talked. The geometric mean maternal-hair Hg concentration was 7.05 (S.D. = 2.06). The rates of developmental retardation, especially in speech (13 of 131), were substantial, although the criteria used to define that outcome were not provided. Children's birth weight, height, and head circumference were also unrelated to maternal-hair Hg concentrations.

Ages at milestone achievement of motor development were investigated in a 21-month birth cohort (1022 infants, 1986-1987) of children in the Faroe Islands (Grandjean et al. 1995). Milestone data were obtained from maternal interviews and the observations of district health nurses who visited the homes on several occasions during the children's first year of life. Hg concentrations were determined in maternal-hair samples at delivery, infants' umbilical cord blood, and in children's hair samples obtained at about 12 months of age. Complete data were available for 583 children (57% of the complete cohort). Three motor-development milestones commonly achieved between 5 and 12 months of age were selected for analysis: “sits without support,” “creeps,” and “gets up into standing position with support.” The age at achievement was not significantly associated with either index of prenatal Hg exposure (cord-blood or maternal-hair concentrations) for any of the three milestones. For all three milestones, however, a significant inverse association was found between age at achievement and children's hair Hg concentration at 12 months. Children's hair Hg concentration was interpreted as an index of children's postnatal exposure to MeHg. Nursing was associated with both higher hair Hg concentrations in children at 12 months of age and with more rapid achievement of milestones. Therefore, the authors concluded that the inverse associa

tion reflected residual confounding by duration of breast feeding. That finding suggests that the beneficial effects of nursing on early motor development are sufficient to compensate for any slight adverse impact that low-dose prenatal MeHg exposure might have on the end points.

In conclusion, recent epidemiological studies provide scant evidence that prenatal MeHg exposures, at least those resulting in maternal-hair Hg concentrations below 30 ppm, are associated with the ages at which children achieve developmental milestones. Although the mean age at walking in the SCDS cohort was later among children whose mothers had high hair Hg concentrations, that association was limited to boys, and the risk of late walking did not appear to be dose related. The association was apparent only at concentrations below 7 ppm, and increases in maternal-hair Hg concentrations above 7 ppm were not associated with further delay in walking age of boys. In the Faroe Islands cohort, a negative association was found between children's hair Hg concentration at 12 months and age at achievement of three motor-development milestones. That finding might be due to higher Hg exposure among breast-fed children and might actually reflect beneficial nutritional effects from breast milk. Those recent data are consistent with re-analyses of the Iraqi data (Cox et al. 1995; Crump et al. 1995), suggesting that the population thresholds for delayed achievement of milestones that were originally calculated might be too low. The thresholds appear to be highly dependent on the assumptions made about background prevalence of delay, the definition of late achievement used, and the influence exerted by a small number of data points.

Infant and Preschool Development

In several epidemiological studies, the association between low-dose prenatal MeHg exposure and early child development has been assessed using several widely used standardized tests.

In the Cree study reported by McKeown-Eyssen et al. (1983), the Denver Developmental Screening Test (DDST) was administered to the 12- to 30-month-old children in the cohort. Scores were reported as the percentage of items passed on each subscale (gross-motor, fine-motor, language, and personal and social subscales) and on the entire test.

Although quantitative estimates are not provided for the associations between test scores and maternal-hair Hg concentrations (mean, 6 ppm; 6% greater than 20 ppm), the authors reported that they did not find any significant associations in a direction compatible with an adverse effect of MeHg either before or after adjustment for confounding variables.

Kjellström et al. (1986) studied a cohort of New Zealand children for whom prenatal MeHg exposure was estimated on the basis of maternal-hair samples as well as dietary questionnaires collected during the period when the study child was in utero. Although exposure information was collected on nearly 11,000 women, the authors focused on 935 women who reported eating fish more than three times per week during pregnancy. Seventy-three women had hair Hg concentrations greater than 6 ppm. The 74 children of those women were designated as the "high-Hg group." Efforts were made to match each child in the high-Hg group with a reference child on the basis of maternal ethnicity, hospital of birth, maternal age, and child age. In the follow-up evaluations completed when children were 4 years old, 38 exposed and 36 reference children were tested, including 30 complete matched pairs. On the DDST, the primary outcome used at this age, 52% of the children in the high-Hg group had an abnormal or questionable result compared with 17% of the children in the control group ($p < 0.05$). That result corresponds to an odds ratio of 5.3. Results were similar when pairs that were poorly matched on ethnicity were excluded. It was not possible to identify the specific developmental domains in which performance was most strongly associated with maternal-hair Hg concentrations.

In the SCDS pilot cross-sectional study, a revised version of the DDST (the DDST-R) was administered blindly by one examiner to 789 children between the ages of 1 and 25 months (Myers et al. 1995a). No association was found between maternal-hair Hg concentration during pregnancy (mean 6.6 ppm) and DDST-R results when normal and questionable examinations were combined in the conventional manner, although the prevalence of abnormal findings was so low (three children, less than 1%) that statistical analysis was not meaningful. When abnormal and questionable results were grouped (in 65 children, 8%), as was done in the New Zealand study (Kjellström et al. 1986), however, high maternal-hair Hg concentrations were significantly associated with poor outcomes ($p = 0.04$, one-tailed test). That result was largely attributable

to the higher frequency of abnormal and questionable results (approximately 13%) among children in the highest hair-Hg category (greater than 12 ppm), in contrast to the frequency of approximately 7% among children in each of the other four Hg groups (0-3, 3-6, 6-9, and 9-12 ppm).

In the main SCDS study, the DDST-R was administered by one blinded examiner to a cohort of 740 children at age 6.5 months (mean maternal-hair Hg concentration during pregnancy, 5.9 ppm; interquartile range, 6.0 ppm) (Myers et al. 1995b). The frequencies of examinations considered to be abnormal (three children, 0.4%) or questionable (11 children, 1.5%) were very low, precluding meaningful statistical analysis of the DDST-R data. The Fagan Test of Infant Intelligence (FTII), an assessment of visual-recognition memory or novelty preference, was also administered at 6.5 months to 723 children. The mean percent novelty preference in the entire cohort was 60%, similar to that observed in many other cohorts, and varied by less than 1% across categories of maternal-hair Hg concentration (less than 3 ppm to greater than 12 ppm). Visual attention (the time required to reach visual-fixation criterion on familiarization trials) also was unrelated to maternal-hair Hg concentrations.

The Bayley Scales of Infant Development (BSID) was administered by blinded examiners to children in the SCDS cohort at ages 19 and 29 months (738 at 19 months and 736 at 29 months) (Davidson et al. 1995b). In addition, at 29 months, six items of the Infant Behavior Record (IBR), a rating scale, were completed by the examiner, assessing activity level, attention span, responsiveness to examiner, response to caregiver, cooperation, and general emotional tone. The BSID yield two primary scores: the mental development index (MDI) and psychomotor development index (PDI). At both ages, MDI scores (97.5 and 100.4 at 19 and 29 months, respectively) were similar to the expected mean for U.S. children of 100 ± 16. At both ages, however, the SCDS children performed markedly better on PDI (with scores averaging 126.7 and 121.1 at 19 and 29 months, respectively) than the expected mean for U.S. children. In fact, at 19 months, approximately 200 children in the SCDS cohort achieved the highest possible PDI score of 150 (Davidson et al. 1995a), a finding that most likely reflects the ethnic composition of the cohort. Because of this skew, PDI scores at both ages were expressed as a binary

variable, splitting the distribution at the median score. The MDI scores at 19 or 29 months were not significantly associated with maternal-hair Hg concentration during pregnancy (see Figure 5-6). Similar results were obtained in a secondary analysis that included only children with the lowest (less than or equal to 3 ppm) or highest (greater than 12 ppm) maternal-hair Hg concentrations. Assessments of perceptual skills at 19 months (Kohen-Raz method), dichotomized due to skewing, were not associated with Hg exposure. Scores on that test at 29 months could not be evaluated because of a pronounced ceiling effect. Risk of a PDI score below the median was not significantly associated with maternal-hair Hg concentration in the full logistic regression model but was associated (p = 0.05) with this exposure index in a reduced model in which adjustment was made for a smaller number of covariates selected on an a priori basis. The secondary analysis of the PDI scores of children with the lowest and highest Hg concentrations was not conducted, because the full logistic regression model was not statistically significant.

In the analyses of the six IBR items, maternal-hair Hg concentration was significantly associated only with examiner ratings of activity level during the test session and only in males. The score decreased 1 point (on a 9-point scale) for each 10 ppm. Additional analysis of the data of the main SCDS study cohort failed to identify significant effect modification by factors such as caregiver intelligence, H.O.M.E. score, family income, and gender (Davidson et al. 1999).

Among the four studies that used the DDST (or DDST-R) as a measure of infant development, only in the New Zealand study and the SCDS pilot phase did children's scores appear to be associated with prenatal Hg concentrations, at least when the questionable and abnormal findings were combined. One factor that might partially account for the differences between the findings of those studies is the age at which the examinations were conducted (4 years in the New Zealand study, 1 to 25 months in the SCDS pilot phase and 6.5 months in the SCDS main phase). Another factor is the different rates of abnormal or questionable examinations (50% of the New Zealand group with prenatal maternal-hair concentrations greater than 6 ppm and 17% of controls; 8% of the Seychelles complete cohort in the SCDS pilot phase; and 1.9% of the cohort in the SCDS main phase). That difference is large enough to raise the possibility that the test items were either administered differently in

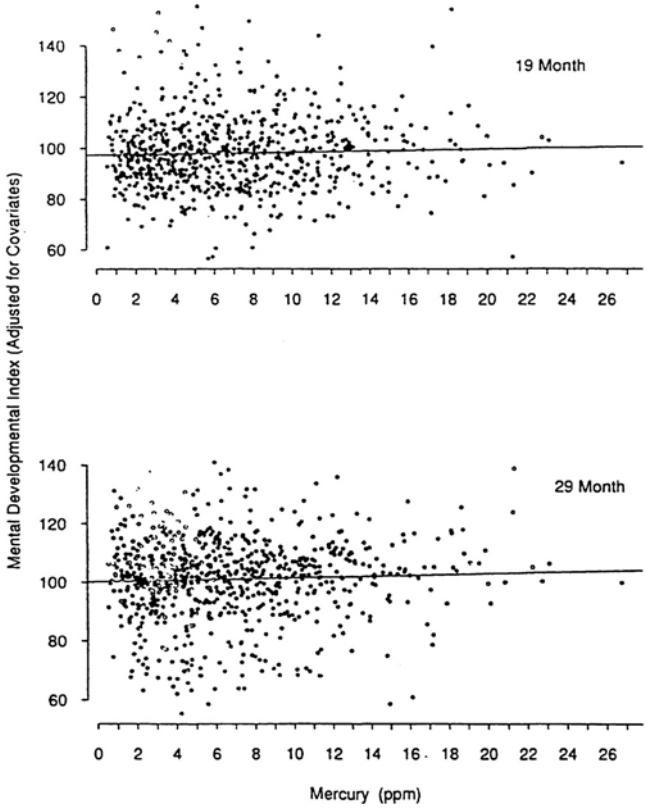

FIGURE 5-6 The 19-month and 29-month mental-developmental-index (MDI) partial residuals from the Bayley Scales of Infant Development. Each data point represents the overall cohort MDI mean plus the partial residual. The partial residual is defined as the subject's MDI score adjusted for all variables in the reduced model except Hg (computed by adding the Hg effect to the residual from the reduced model). The MDI has a U.S. mean of 100 (standard deviation, 16). Scores are plotted as a function of maternal-hair Hg in parts per million. The slope for the 19-month MDI, shown in the upper graph, was 0.125. The slope for the 29-month MDI, shown in the lower graph, was 0.149. Neither effect was significant. Source: Davidson et al. 1995b. Reprinted with permission from *NeuroToxicology*; copyright 1995, Intox Press.

the two studies or that different criteria were used in judging whether an individual passed or failed the tests. Kjellström et al. (1986) reported, however, that among 3- and 4-year-old children in South Auckland routinely assessed with the DDST, the rate of questionable, abnormal, or not testable results was 8-14%, roughly comparable to the rates observed among the low-Hg children in the study sample.

In general, the use of screening tests, such as the DDST, in neurobehavioral toxicology studies is not recommended because of their insensitivity to variations within the range of normal performance (Dietrich and Bellinger 1994). More detailed instruments, such as the BSID, currently considered to be the best in infant assessment, have proved to be sensitive to prenatal exposures to a variety of neurotoxicants, including lead (Bellinger et al. 1987; Dietrich et al. 1987; Wasserman et al. 1992) and PCB's (Rogan and Gladen 1991; Koopman-Esseboom et al. 1996). Among the Hg studies, the BSID was administered only in the SCDS, and no significant associations were found between children's scores and their prenatal exposures. It is notable that the PDI scores were very high in this cohort, requiring that the distribution be split at the median and analyzed as a categorical variable. The median value is not provided by Davidson et al. (1995b), but, based on Figure 3 in Davidson et al. (1995a), appeared to be approximately 130, or 2 standard deviations above the expected population mean.

Childhood Development

Children in the New Zealand cohort were followed up at 6 years of age. In that phase of the study, three controls were matched to each high-Hg child on the basis of ethnic group, sex, maternal age, maternal smoking, area of maternal residence, and the duration of maternal residence in New Zealand. One of the controls for each subject had a hair Hg concentration of 3 to 6 ppm, and the other two controls had hair Hg concentrations of 0 to 3 ppm. For one of the two low-Hg controls, maternal fish consumption was high (more than three times per week), and for the other, it was low. Fifty-seven fully matched groups of four children each and four incomplete sets (resulting in a cohort of 237 children) participated in a follow-up evaluation of neurodevelopmental status at 6 years of age (Kjellström et al. 1989). In the high-Hg group,

the mean maternal-hair Hg concentration was 8.3 ppm (range 6-86 ppm, with all but 16 between 6 and 10 ppm). Extensive information was collected on possible confounding factors, such as social class, medical history, and nutrition. A battery of 26 psychological and scholastic tests was administered, assessing the domains of general intelligence, language development, fine- and gross-motor coordination, academic attainment, and social adjustment. Multiple regression analyses of five primary end points were carried out: the Test of Language Development — spoken language quotient (TOLD_SL), the Wechsler Intelligence Scale for Children-Revised (WISC-R) performance IQ, the WISC-R full-scale IQ, the McCarthy Scales of Children's Abilities perceptual-performance scale (MC_PP), and the McCarthy Scales motor scale. Analyses were adjusted for potential confounders, including maternal ethnic group, maternal age, maternal smoking and alcohol use during pregnancy, length of maternal residence in New Zealand, social class, primary language, siblings, sex, birth weight, fetal maturity, Apgar score, and duration of breast feeding. In addition, robust regression methods were applied, involving the assignment of a weight (0 to 1) to an observation depending on the degree to which it was an outlier. In the robust regressions, maternal-hair Hg concentration was associated with poorer scores (p values ranging from 0.0034 to 0.074) on full-scale IQ, language development (spoken language quotient), visual-spatial skills (perceptual-performance scale) and gross-motor skills (motor scale). The unweighted regression analyses yielded findings that were similar in direction, although generally less statistically significant. The poorer mean scores of the children in the high-Hg group appeared to be largely attributable to the children whose mothers had hair Hg concentrations above 10 ppm (for whom the mean average hair Hg concentration during pregnancy was 13 to 15 ppm and the mean of the peak monthly hair segments was about 25 ppm). Maternal-hair Hg concentrations accounted for relatively small amounts of variance in the outcome measures and generally accounted for less than covariates, such as social class and ethnic group. In additional analyses of that data set, Crump et al. (1998) found that when maternal-hair Hg was expressed as a continuous rather than a binary variable, none of the 5 primary end points studied by Kjellström et al (1989) were associated with Hg at $p < 0.10$. The results were heavily influenced, however, by the data of a child with a maternal-hair Hg concentration of 86 ppm (more than 4

times the next highest concentration), despite the fact that the child's test scores were not outliers by the usual technical criteria. When the data for this child were excluded, scores on the TOLD_SL and MC_PP were inversely associated with maternal-hair Hg concentration at $p < 0.05$. These associations were diminished somewhat in statistical significance, although not in the magnitude of the coefficient, when parental education and child's age at testing were included in the regressions. When these regressions were repeated on all 26 scholastic and psychological tests, 6 were associated with maternal hair-Hg (excluding the child with a level of 86 ppm) at $p < 0.10$: Clay Reading Test — concepts, Clay Reading Test — letter test, McCarthy Scales — general cognitive index, McCarthy Scales — perceptual-performance scale, Test of Language Development — grammar completion, and Test of Language Development — grammar understanding).

Several features of the New Zealand study are noteworthy, including the efforts made to collect data on potential confounding variables and the broad battery of standardized outcome measures administered by trained examiners. In contrast to the acute high-dose exposures experienced by the Iraqi population, the MeHg exposures of the New Zealand cohort were chronic, low dose, and most likely fairly constant over time, reflecting well-established food consumption patterns. In addition, the maternal-hair Hg concentrations were measured prospectively. As part of the SCDS pilot phase, children from the pilot cohort of 789 who turned 66 months old within a 1-year time window underwent developmental assessments (Myers et al. 1995c). Of the 247 eligible children, 217 (87.9%) were administered a test battery consisting of the McCarthy Scales of Children's Abilities, the Preschool Language Scale, and two subtests of the Woodcock-Johnson Tests of Achievement: letter-word identification and applied problems. All 73 children with maternal-hair Hg concentrations greater than or equal to 9 ppm or less than or equal to 4 ppm were assessed. The median maternal-hair Hg concentration in that subsample of the pilot cohort was 7.1 ppm (1.0 to 36.4). The frequency of missing values was substantial for some end points (e.g., 34% for the summary score of the general cognitive index (GCI) yielded by the McCarthy scales). Increased maternal-hair Hg concentrations were associated with significantly lower GCI scores ($p = 0.024$). Scores declined approximately 5 points between the lowest (3 ppm or less) and highest (greater than 12ppm) exposure categories. A similar association

was found on the perceptual-performance scale of the McCarthy scales (p = 0.013). Children's scores on the auditory comprehension scale of the Preschool Language Scale were also inversely associated with maternal-hair Hg concentrations (p = 0.0019). Scores declined approximately 2.5 points across the range of Hg concentrations. Additional analyses identified several outlier or influential data points, whose exclusion from the analyses reduced the estimates of the Hg effect substantially, sometimes to nonsignificance. In the pilot phase of the SCDS, information was not collected on several key variables that frequently confound the association between neurotoxicant exposures and child development. Those variables are socioeconomic status, caregiver intelligence, and quality of the home environment.

In the main SCDS, 711 children (91.2%) from the original cohort of 779 were evaluated at 66 months of age (5.5 years) ± 6 months using a battery of standardized neurodevelopmental tests (Davidson et al. 1998). The major domains assessed (and the tests used) were general cognitive ability (McCarthy Scales of Children's Abilities), expressive and receptive language (Preschool Language Scale), reading achievement (letter-word recognition subtest of the Woodcock-Johnson Tests of Achievement), arithmetic (applied problems subtest of the Woodcock-Johnson Tests of Achievement), visual-spatial ability (Bender Gestalt Test), and social and adaptive behavior (Child Behavior Checklist). Total Hg in a segment of maternal hair taken during pregnancy was the measurement of prenatal MeHg exposure (mean, 6.8 ppm; range, 0.5-26.7 ppm). Total Hg in a 1-cm segment of hair obtained from a child at 66 months served as the measurement of postnatal MeHg exposure (mean, 6.5 ppm; range, 0.9-25.8 ppm). The pattern of scores of the six primary end points did not suggest an adverse effect of either prenatal or postnatal Hg exposure. The associations that were found were consistent with enhanced performance among children with increased exposure to MeHg (see Figure 5-7 and Figure 5-8). For the total score on the Preschool Language Scale, increased prenatal and postnatal Hg concentrations were significantly associated with better scores (both p = 0.02). For the applied problems score, increased postnatal Hg concentrations were associated with better scores (p = 0.05). Among boys, increased postnatal Hg concentrations were associated with fewer errors on the Bender Gestalt Test (p = 0.009) (see Figure 5-8).

The R^2 (square of the multiple correlation coefficient) value (0.10) of

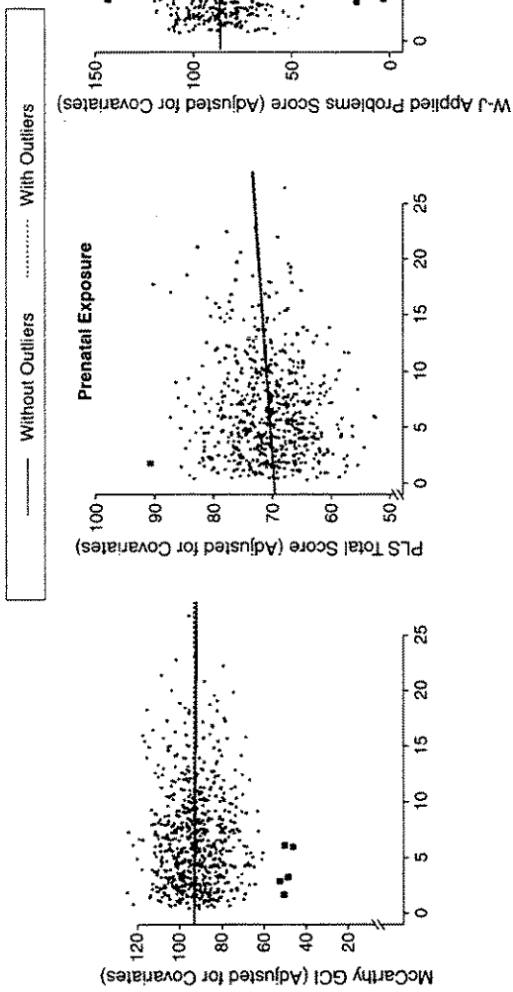

FIGURE 5-7 Partial residuals for prenatal exposure. The measures are the McCarthy Scales of Children's Abilities general cognitive index (GCI), the Preschool Language Scale (PLS)total score, and the Woodcock-Johnson (W-J) applied problems subtest. Each test score was added to the resulting partial residual. The slope of the line in the plot is the regression coefficient for the multiple regression model. Slopes are shown for the model with and without outliers. Black squares indicate outliers. Source: Davidson et al. 1998. Reprinted with permission from the *Journal of the American Medical Association;* copyright 1998, American Medical Association.

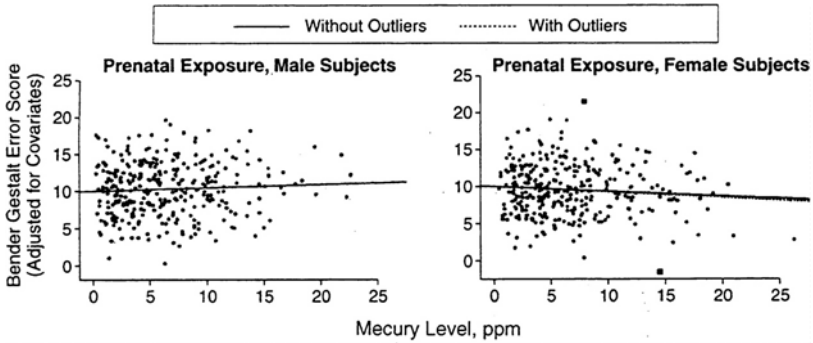

FIGURE 5-8 Partial residuals for prenatal exposure. The measures are Bender Gestalt error scores for male and female subjects. Each test score was adjusted for all reduced model predictors except the exposure value used in the plot. For graphical representations, the overall mean test score was added to the resulting partial residual. The slope of the line in the plot is the regression coefficient for the multiple regression model. Slopes are shown for the model with and without outliers. Black squares indicate outliers. Source: Davidson et al. 1998. Reprinted with permission from the *Journal of the American Medical Association*; copyright 1998, American Medical Association.

the reduced regression model for the GCI score in the main SCDS study was identical to that in the pilot study. That also appeared to be true for scores on the Preschool Language Scale (R^2 of 0.12 for the auditory comprehension scale in the pilot study and 0.14 for total score in the main study). That finding is puzzling because the pilot-study models, as noted previously, did not include several key covariates, including socioeconomic status, caregiver intelligence, and the quality of the home environment, and because the regression coefficients for socioeconomic status and caregiver intelligence were statistically significant for total scores of the GCI and the Preschool Language Scale in the main study cohort. Those differences suggest that maternal-hair Hg concentration is very highly confounded with those key covariates in the Seychelles population, or they suggest that the associations between child neurodevelopment and the covariates differ substantially in the pilot and main study cohorts, or both.

In the Faroe Islands cohort, comprehensive evaluations were con

ducted at approximately 7 years of age on 917 (90.3%) of the surviving members of a 1986-1987 birth cohort of 1,022 singleton births (Grandjean et al. 1997). The neuropsychological battery included three computer-administered tests from the Neurobehavioral Evaluation System (NES) (finger tapping, hand-eye coordination, and continuous performance test), the Tactual Performance Test, three subtests of the WISC-R (digit span, similarities, and block design), the Bender Gestalt Test, the California Verbal Learning Test — Children, the Boston Naming Test, and the Nonverbal Analogue Profile of Mood States. Parents were administered selected items from the Child Behavior Checklist. The primary measure of MeHg exposure was the concentration of Hg in umbilical cord blood (geometric mean, 22.9 μg/L; interquartile range, 13.4-41.3 μg/L; 894 measurements). Measurements were made of the concentration of Hg in maternal hair at parturition (geometric mean, 4.3 ppm; interquartile range, 2.6-7.7 ppm; N = 914), child hair at 12 months of age (geometric mean, 1.1 ppm; interquartile range, 0.7-1.9 ppm, N = 527), and child hair at 7 years (geometric mean, 3.0 ppm; interquartile range, 1.7-6.1 ppm, N = 903).

Not all children were able to complete all tests, and, in some cases, failure was associated with significantly increased Hg concentrations (e.g., finger opposition test and mood test). In multiple regression analyses, increased cord-blood Hg concentration was significantly associated with worse scores on finger tapping (preferred hand, $p = 0.05$), continuous performance test in the first year of data collection (false negatives, $p = 0.02$; mean reaction time, $p = 0.001$), WISC-R digit span ($p = 0.05$), Boston Naming Test (no cues, $p = 0.0003$; with cues, $p = 0.0001$), and the California Verbal Learning Test — Children (short-term reproduction, $p = 0.02$; long-term reproduction, $p = 0.05$). On the basis of the regression coefficients for Hg and age, the investigators estimated that a 10-fold increase in cord Hg concentration was associated with delays of 4 to 7 months in those neuropsychological domains (thus a doubling of Hg with delays of 1.5-2 months).

For two end points (WISC-R block design, Bender Gestalt Test errors), associations indicating adverse Hg effects ($p < 0.05$) were found when an alternative approach to adjustment for confounders (Peters-Belson method) was applied. Results were similar when the 15% of the cohort with maternal-hair Hg concentrations greater than 10 ppm were excluded from the analyses. A term for the interaction between Hg and

sex was not statistically significant, indicating that the Hg effects were similar among boys and girls. In general, children's test scores were more strongly associated with cord-blood Hg concentration than with maternal-hair Hg concentration or with Hg concentrations in samples of children's hair collected at 1 and 7 years of age. Five tests were selected, on the basis of high psychometric validity, to represent key domains of cognitive function: motor, attention, visual-spatial ability, language, and memory. For the tests selected to represent attention, language, and memory, the percentages of children with adjusted scores in the lowest quartile increased significantly as cord-blood Hg concentration increased (see Figure 5-9).

In an additional set of analyses (Grandjean et al. 1998), the investigators compared the neuropsychological scores of two groups of children: a case group of 112 children with maternal-hair concentrations of 10 to 20 ppm (median, 12.5 ppm) at parturition, and a control group of 272 children with maternal-hair Hg concentrations less than 3 ppm (median, 1.8 ppm) matched to cases on age, sex, year of examination, and care-giver intelligence. Median cord-blood Hg concentrations also differed substantially (59.0 µg/L in the case group versus 11.9 µg/L in the control group). On 6 of the 18 end points, the case group scored significantly lower than the control group (one-tailed p value of 0.05). Those end points were finger tapping (both hands), hand-eye coordination (average of all trials), WISC-R block design, Boston Naming Test (no cues, cues), and California Verbal Learning Test — Children (long-term reproduction). The results of those analyses differ in certain respects from those of the main analyses. First, the set of end points on which the cases and controls differed is similar but not identical to the set of end points that were significantly associated with cord Hg concentration found in the main analyses. Moreover, in contrast to the main analyses, a term for the interaction between Hg and sex was statistically significant for several scores, including the Bender Gestalt Test error score, short-term reproduction on the California Verbal Learning Test — Children, all three finger-tapping conditions, continuous-performance-test reaction time, and average hand-eye coordination score. For all scores, adverse Hg effects were noted for boys but not girls.

Grandjean and colleagues assembled an additional study cohort of 351 children 7 to 12 years old from four riverine communities in Amazonian Brazil (Rio Tapajos) with increased exposures to MeHg due to the

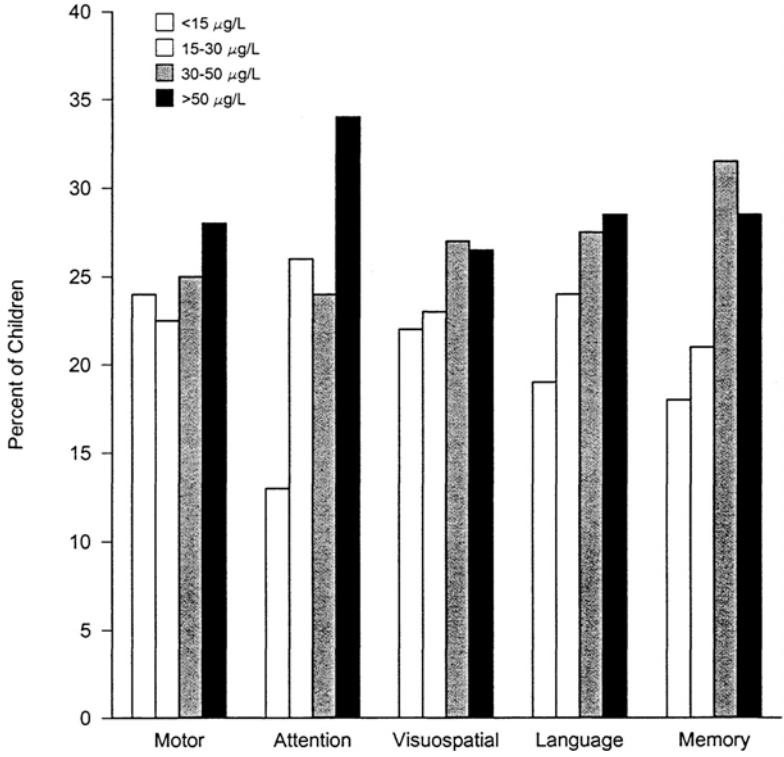

FIGURE 5-9 Prenatal Hg exposure concentrations (in quartile groups) of Faroe Island children with scores in the lowest quartile after adjustment for confounders. For each of five major cognitive functions, one neuropsychological test with a high psychometric validity was selected. Motor: neurobehavioral evaluation system 2 (NES2) finger tapping with preferred hand (p value for trend, 0.23). Attention: Reaction time on the NES2 continued performance test (p = 0.003). Visual-spatial: Bender visual motor gestalt test error score (p = 0.16). Language: Boston Naming Test score after cues (p = 0.02). Memory: California Verbal Learning Test — Children long-delay recall (p = 0.004). Source: Adapted from Grandjean et al. 1997.

consumption of fish contaminated by upstream gold-mining activities (Grandjean et al. 1999). Among children, the mean hair Hg concentration ranged from a geometric mean (range) of 11.9 (35.1) ppm for the lowest exposed of the three communities on the Rio Tapajos to 25.4 (82.9) ppm for the highest; 80% of the children in these villages exceeded 10 ppm. Most of the children reportedly ate fish for two meals per day. In the hair samples available for 63% of the children's mothers, the mean Hg concentration was 11.6 ppm. The battery of neurobehavioral tests administered to the children focused on motor function, attention, visual-spatial function, and short-term memory (finger tapping, Santa Ana dexterity test, WISC-III digit span forward, and Stanford-Binet copying (including recall), and bead memory subtests. In three villages, the tests were administered in Portuguese, although in the fourth (Village D), administration required the services of a Mundurucu interpreter. (The finger tapping, and Santa Ana dexterity tests could not be administered to children in that village.) Combining all four villages, children's hair Hg concentrations were significantly associated with their scores on finger tapping (both preferred and other hand; both $p < 0.001$), Santa Ana dexterity test (preferred hand, $p = 0.005$; other hand, $p = 0.05$), WISC-III digit span ($p = 0.001$), Stanford-Binet copying ($p < 0.001$) and recall ($p < 0.001$), and Stanford-Binet bead memory ($p < 0.001$). Adjustment for community generally reduced the magnitude of the associations, sometimes dramatically (e.g., from $p < 0.001$ to $p = 0.99$ for finger tapping preferred hand). Hair Hg concentrations and village of residence were so highly confounded, however, that adjustment for village might be inappropriate.

In the French Guiana cohort assembled by Cordier and Garel (1999) 206 children 5 to 12 years old were administered a battery of neuropsychological tests that included finger tapping, three subtests from the Stanford-Binet (block designs, copying designs, and bead memory), and two subtests from the McCarthy scales (numerical memory and leg coordination). Median maternal-hair concentration was 6.6 ppm (range, 2.6-17.8 ppm). With adjustment for potential confounders, increased Hg concentrations were associated with copying-design score especially in boys. The findings are complicated, however; when only the children living in the region that has higher exposures were considered and the analyses were stratified by sex, increased Hg concentrations were associated with poorer leg coordination in boys and poorer block-design scores in girls.

Sensory, Neurophysiological, and Other End Points in Children

In the Faroe Islands cohort, the 7-year evaluation included, in addition to the neuropsychological tests, assessments of visual acuity, near contrast sensitivity, otoscopy and tympanometry, and neurophysiological tests (pattern-reversal-visual-evoked potentials at 30' and 15', brainstem auditory-evoked potentials at 20 and 40 clicks per second (Hz), and postural sway) (Grandjean et al. 1997). Visual acuity, contrast sensitivity, auditory thresholds, and visual-evoked potentials were not significantly associated with prenatal MeHg exposures. For brainstem auditory-evoked potential, peaks I, III, and V were slightly delayed at increased cord-blood Hg concentrations at both 20 Hz and 40 Hz (p values, 0.01 to 0.10), although interpeak latencies were not associated with Hg at either frequency. In additional analyses reported separately (Murata et al. 1999b), in which data collected during the second year of this phase of the study were excluded due to concerns about the electromyograph used, higher maternal hair and cord-blood Hg concentrations were associated with lower peak III latencies, as well as with longer peak I-III latencies. Of the four conditions under which postural sway was assessed, only when subjects stood on the platform without foam under it with their eyes closed did the results approach significance ($p = 0.09$). Visual acuity and contrast sensitivity were not related to Hg exposure.

In a cross-sectional study of 149 6- to 7-year-old children living in a fishing village on Madiera, many of the same neurophysiological tests were administered (Murata et al. 1999a). Because patterns of fish consumption were considered to be stable, current maternal-hair Hg concentration was used as a measurement of a child's prenatal Hg exposure (mean, 9.6 ppm; range, 1.1-54.4 ppm). With respect to brainstem auditory evoked potential, maternal-hair Hg was significantly associated with I-III and I-V interpeak latencies at both 20 and 40 Hz, as well as with total latencies for peaks III and V at both frequencies. Those results are similar to the findings in the Faroe Islands cohort, at least among the children who were tested in the first year (see above). With respect to visual-evoked potentials on a pattern-reversal task, maternal-hair Hg concentration was significantly associated with one of the three latencies measured (N145 at 15'), as well as with the N75-N145 and P100-N145 latencies (15' only). As noted above, VEP latencies were unrelated to Hg concentrations in the Faroe Islands cohort.

The relationship between blood Hg concentrations and auditory function in children and adults was investigated by Counter et al. (1998). The study sample consisted of 75 individuals (36 children and 39 adults) from a gold-mining region in Ecuador (study area) and 34 individuals (15 children and 19 adults) from a control area. Blood Hg concentrations were significantly higher in individuals from the gold-mining area than in individuals from the control region (17.5 µg/L versus 3.0 µg/L). Neuro-otological examinations were carried out on all individuals. Audiological evaluations, consisting of determinations of pure tone air-conduction thresholds in each ear at 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz, were carried out on 40 individuals in the study area. Brainstem auditory-evoked-potential studies were carried out on 19 subjects in the study area. The absolute latencies of waves I, II, III, IV, and V and the interpeak latencies of I-III, III-V, and I-V were measured for left and right sides. Blood Hg concentration was significantly associated with hearing threshold at 3 kHz in the right ear only and for children only. A borderline association was found between blood Hg concentration and I-III interpeak transmission time on the left side. The authors concluded that although the end points assessed were generally unaffected at the blood Hg concentrations represented in the cohort of adults and children in the study area, the associations found were consistent with an effect of Hg at the level of the auditory nerve and the cochlear nuclear complex.

Animal Studies

Developmental Effects in Animals

The results of nearly 30 years of experimental studies using various animal models have helped characterize the neurotoxic effects of MeHg following in utero or early postnatal exposures (see Table 5-11). Several excellent reviews on the topic have been published over the years (WHO 1976, Chang 1977, Inskip and Piotrowski 1985, IPCS 1990, Burbacher et al. 1990, Gilbert and Grant-Webster 1995, Clarkson 1997) including a recent “Toxicological Profile for Hg” published by the Agency for Toxic Substances and Disease Registry (ATSDR 1999). In general, experimental studies have reported a continuum of neurodevelopmental effects similar to those reported in studies of humans exposed to MeHg (see

TABLE 5-11 Neurobehavioral Effects of Developmental MeHg Exposure in Animals

Species	Exposure Time	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Effect	Reference
Monkey *(M. fascicularis)*	Birth to 7 yr old	No NOAEL	0.05	Decreased visual-contrast sensitivity (spatial) thresholds at 3-4 yr old	Rice and Gilbert 1982
Monkey *(M. fascicularis)*	In utero	No NOAEL	0.05-0.07	Retarded Object Permanence Development	Burbacher et al. 1986
Monkey *(M. fascicularis)*	In utero	No NOAEL	0.05-0.07	Impaired visual-recognition memory in offspring (abstract)	Gunderson et al. 1986
Monkey *(M. fascicularis)*	In utero	No NOAEL	0.05-0.07	Impaired visual-recognition memory in offspring (social)	Gunderson et al. 1988
Monkey *(M. fascicularis)*	Birth to 7 yr old	No NOAEL	0.05	Increased clumsiness in exercise cage at 13 yr old	Rice 1989
Monkey *(M. fascicularis)*	In utero	No NOAEL	0.05	Reduced social play Increased nonsocial behaviors	Burbacher et al. 1990
Monkey *(M. fascicularis)*	In utero plus 4 yr postnatally	No NOAEL	0.01-0.05	Decreased visual-contrast sensitivity (spatial) thresholds at 5 yr old	Rice and Gilbert 1990
Monkey *(M. fascicularis)*	Birth to 7 yr old	No NOAEL	0.05	Increased pure-tone thresholds at 14 yr old	Rice and Gilbert 1992
Monkey *(Saimiriiureus)*	Gestation wk 11-14.5 to birth (22 wk)	No NOAEL	Not stated (dosed for stable blood concentration)	Retarded schedule-control behavior during transitions	Newland et al. 1994

Monkey *(M. fascicularis)*	Birth to 7 yr old	No NOAEL	0.05	Increased vibration-sensitivity thresholds at 18 yr old	Rice and Gilbert 1995
Monkey *(M. fascicularis)*	In utero plus 4 yr postnatally	No NOAEL	0.01-0.05	Increased pure-tone thresholds at 19 yr old	Rice 1998
Monkey *(M. fascicularis)*	In utero	No NOAEL	0.05-0.09	Decreased visual-contrast sensitivity (spatial)	Burbacher et al. 1999
Rat	Gestation d 1 to postnatal d 42 (68 d)	No NOAEL	0.10	Abnormal swimming; delayed righting reflex; impaired learning in maze	Olson and Bousch 1975
Rat	Gestation d 1 to birth; birth to postnatal d 21; postnatal d 21 to d 30	No NOAEL	2.5	Impaired learning in water T-maze for all 3 groups	Zenick 1974
Rat	Gestation d 10 (in utero only)	6	8	Decreased activity during the postweaning period	Su and Okita 1976
Gestation d 10-12 (in utero only)	No NOAEL	4			
				Decreased activity during the postweaning period	
Rat	Gestation d 1 to birth (in utero plus lactational)	No NOAEL	2.5	Abnormal visual-evoked potentials	Zenick 1976
Rat	Gestation d 7 (in utero plus lactational)	No NOAEL	5	Abnormal visual-evoked potentials	Dyer et al. 1978

Species	Exposure Time	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Effect	Reference
Rat (Wistar)	Gestation d 6-9 (in utero plus lactational)	No NOAEL	0.05	Reduced behavioral performance on DRH operant test	Musch et al. 1978
Rat (Wistar)	Gestation d 6-9 (in utero only)	0.005	0.01	Reduced behavioral performance on DRH operant test	Bornhausen et al. 1980
Rat (Sprague-Dawley)	Gestation d 4 (in utero plus lactational)	No NOAEL	10	Impaired avoidance learning	Schalock et al. 1981
Rat	Gestation d 8 or 15 (in utero plus lactational)	No NOAEL	5	Increased activity during the preweaning period; impaired learning in shuttle box	Eccles and Annau 1982a,b
Rat	Gestation d 6-9 (in utero plus lactational)	No NOAEL	2	Increased auditory startle response; increased activity in figure-8 maze	Buelke-Sam et al. 1985
Rat (Sprague-Dawley)	Gestation d 6-9 (in utero plus lactational)	2	6	Delayed surface righting; delayed swimming ontogeny; decreased postweaning figure-8 activity; increased time and errors in Biel maze	Vorhees 1985
Rat (Sprague-Dawley)	Gestation d 6-9 (in utero only) (cross-fostered)	1.25	2.5	Delayed surface righting; delayed negative geotaxis; delayed swimming ontogeny; decreased activity in open field	Geyer et al. 1985
Rat	2 wk before mating through weaning		0.08	Impaired tactile-kinesthetic function in offspring	Elsner 1991

Rat (Sprague-Dawley)	Gestation d 6-9 (in utero plus lactational)	2 for MeHg No NOAEL (with Hg^0)	2	Potentiated effects of Hg^0: increased activity; increased swimming speed; increased errors in radial maze	Fredriksson et al. 1996
Rat	4 wk before mating through postnatal d 16	6.4	No effects	Normal behavioral performance on DRH operant test	Rasmussen and Newland 1999
Mouse (129/SvS1)	Gestation d 7 or 9 (in utero plus lactational)	No NOAEL	8	Abnormal swimming behavior	Spyker et al. 1972
Mice	Gestation d 8 (in utero only)	No NOAEL	3	Impaired avoidance learning	Hughes and Annau 1976

Abbreviations: NOAEL, no-observed-adverse-effect level; LOAEL, lowest-observed-adverse-effect level; Hg^0, elemental mercury; DRH

Table 5-10). Those effects are largely dependent on the dose, timing, and duration of the MeHg exposure.

Fetal Minamata Disease

Experimental studies using nonhuman primates, cats, and rodent models exposed to high doses of MeHg have reported some or all of the cluster of neuropathological effects consistent with fetal Minimata disease (MD) that were first described from human autopsy cases following the catastrophic exposures in Minamata, Japan, and Iraq (Matsumoto et al 1965; Takeuchi 1968; Choi et al 1978). Those effects include microcephaly, degeneration and atrophy of cortical structures, loss of ceils in the cerebrum and cerebellum, a reduction of myelin, ventricular dilation, gliosis, disorganized cell layers, and ectopic cells. In addition, seizures, spasticity, blindness, and severe learning deficits have been reported. In nonhuman primates, maternal doses above 100 µg/kg per day were associated with MD in offspring autopsied during infancy (Mottet et al. 1987; Burbacher et al. 1990). Similar effects were observed at doses as low as 1 to 1.5 mg/kg per day in mice and rats (Khera and Tabacova 1973; O'Kusky 1983), 2 mg/kg per day in golden hamsters (Reuhl et al. 1981a,b), 12 mg/kg per day in guinea pigs (Inouye and Kajiwara 1988), and 0.25 mg/kg per day in cats (Khera 1973b). Differences in the lowest-observed-adverse-effect levels (LOAELs) for signs consistent with MD do not necessarily represent true species differences in susceptibility to MeHg, because the choices of doses and exposure periods used across the studies are not comparable.

Neurobehavioral Effects

The focus of many of the developmental studies using animal models has been to define the effects of MeHg at exposures that are not associated with gross signs of toxicity. Studies using nonhuman primate and rodent models have reported numerous subclinical effects at doses below those associated with overt maternal or offspring toxicity (see Table 5-11). In a long-term study examining the effects of maternal oral doses of MeHg hydroxide at 50, 70, or 90 µg/kg per day before and

during pregnancy in nonhuman primates (*Macaca fascicularis*), maternal toxicity (blindness and motor incoordination) was observed at the highest dose tested (90 µg/kg per day), and reproductive effects (nonconceptions, abortions, and stillbirths) were observed at 90 and 70 µg/kg per day (Burbacher et al. 1988). The maternal dose of MeHg hydroxide at 50 µg/kg per day was associated with developmental effects in offspring, but not with maternal toxicity or reproductive effects. Impairments in perceptual-cognitive functioning (Fagan Test and Object Permanence Test) and the development of species-specific social behavior were observed in offspring during infancy (Gunderson et al. 1986, 1988; Burbacher et al. 1986, 1990). A significant reduction in the weight gain of exposed males beginning at 2.5 years of age was also observed (Burbacher et al. 1993). That sex-specific effect appeared to be related to the adolescent growth spurt, because adult weight was not affected by MeHg. Studies conducted when the monkeys were adults indicated significant effects due to MeHg exposure on spatial vision (visual contrast-sensitivity functions). Although there were overall group differences in spatial vision, there were large individual differences in the response of the MeHg-exposed monkeys (Burbacher et al. 1999). Tests of adult learning and memory did not indicate significant effects due to MeHg exposure (Gilbert et al. 1993, 1996) and pure-tone auditory thresholds appeared normal when the monkeys were tested at approximately 12 to 15 years of age (Burbacher et al. 1999).

In another series of studies, *Macaca fascicularis* were orally exposed to MeHg at 50 µg/kg per day from birth to 7 years of age (Rice 1989) or at 0, 10, 25, or 50 µg/kg per day in utero plus 4 years postnatally (Rice and Gilbert 1990). No effects of MeHg were observed in the tests on infant or juvenile learning and memory for the in utero plus postnatally exposed animals (Rice 1992). However, impaired spatial vision was observed in monkeys from both dose groups when they were tested on a contrast-sensitivity task between 3 and 5 years of age (Rice and GIlbert 1982; Rice and Gilbert 1990). At 13 years of age, overt toxicity (clumsiness) was observed in some of the monkeys exposed postnatally to MeHg for 7 years (Rice 1989). Tests of those monkeys at 14 years of age indicated impaired high-frequency hearing in four of the five MeHg-exposed monkeys, and tests at age 18 indicated impaired somatosensory function (vibration sensitivity) in the same four monkeys (Rice and Gilbert 1992, 1995). Two of four monkeys exposed to MeHg in utero

plus 4 years postnatally also demonstrated impairments on the vibration-sensitivity test when tested at 15 years of age. Auditory testing of the monkeys exposed to MeHg in utero plus 4 years postnatally at 11 and 19 years of age indicated elevated pure-tone thresholds throughout the full range of frequencies tested (0.125 to 31.5 kHz) at 19 years of age (Rice 1998). Although both controls and MeHg-exposed monkeys showed higher thresholds at 19 years of age compared with 11 years, MeHg-exposed monkeys showed a greater deterioration in auditory function with increasing age. Across studies, MeHg effects were observed in individual monkeys at maternal doses of 10 μg/kg per day to 50 μg/kg per day or a dose of 50 μg/kg per day postnatally. However, the numbers of monkeys in the studies were small (one at 10 μg/kg per day), allowing only individual comparisons.

Newland et al. (1994) examined the effects of in utero exposure to MeHg in squirrel monkeys. Maternal exposure to MeHg varied to provide steady-state blood Hg concentrations between 0.7 and 0.9 ppm. At 5 to 6 years of age, offspring were trained to lever press under concurrent schedules of reinforcement. The results of the study indicated that MeHg-exposed monkeys were not able to change their response rates consistent with changes in reinforcement contingencies. Those effects were most prominent during transitions in reinforcement schedules.

Many of the studies using rodent models have also focused on examining the effects of MeHg exposure on neurobehavioral development. One of the largest studies to examine the effects of developmental exposure to MeHg in rats was the "Collaborative Behavioral Teratology Study" (CBTS), which was performed to compare the results of a standard behavioral test battery across several laboratories (Buelke-Sam et al. 1985). Maternal rats were exposed to MeHg at 0, 2, or 6 mg/kg per day via gavage on gestation days 6-9. Offspring were exposed in utero and during lactation (no cross-fostering). Behavioral assessments of offspring indicated an increase in auditory startle-response habitation, mostly at the high dose. Maze activity increased with increasing MeHg exposure, and performance on a visual discrimination test was affected at the high dose. Two parallel studies, Vorhees (1985) and Geyer et al. (1985), reported similar findings, as well as delayed surface righting and swimming ontogeny. Retarded maze performance at the highest dose tested (Vorhees 1985) and retarded negative geotaxis and pivoting at a

dose of 2.5 mg/kg per day on gestation days 6-15 were also reported (Geyer et al. 1985). The effects observed by Geyer et al. (1985) were related to gestational exposure alone, because the MeHg offspring were cross-fostered to nonexposed dams at birth. Consistent with the results of the nonhuman primate studies, two studies have reported effects of early MeHg exposure on visual functions in rats (Zenick 1976; Dyer et al. 1978). Abnormal visual-evoked potentials were reported following in utero and lactational exposure to MeHg following a single maternal dose of 5 mg/kg per day on gestation day 7 (Dyer et al. 1978) or continuous maternal exposure at 2.5 mg/kg per day (Zenick 1976). Other studies of rats and mice have reported MeHg effects on motor performance and measures of activity and learning. MeHg effects on the swimming behavior of mice was reported following in utero and lactational MeHg exposure (maternal dose of 8 mg/kg on day 7 or 9 of gestation) (Spyker et al. 1972) or following exposure from gestation day 1 to postnatal day 42 (0.1 mg/kg per day) (Olson and Bousch 1975). Reports indicated increased activity in rats during the preweaning period following in utero and lactational MeHg exposure (5 or 8 mg/kg per day on gestation day 8 or 15) (Eccles and Annau 1982a,b), and decreased activity was reported in mice tested postweaning following in utero MeHg exposure alone (8 or 12 mg/kg per day on gestation day 10, or 4 mg/kg per day on gestation days 10-12 with cross-fostering at birth) (Su and Okita 1976). Learning deficits have been reported in both rats and mice following in utero or early postnatal MeHg exposure. Rats exposed prenatally to MeHg displayed impaired learning on a shuttlebox avoidance test (Eccles and Annau 1982a,b), and a single dose of 10 mg/kg per day on gestation day 4 with no cross-fostering of dams (in utero plus lactational exposure) was associated with decreased escape, avoidance, and appetitive learning (Schalock et al. 1981). Olson and Bousch (1975) reported impaired learning in rats on a maze task following exposure to Hg at 0.1 mg/kg per day via a fish diet from gestation day 1 to postnatal day 42. In mice, a maternal dose of 3 mg/kg on gestation day 8 (Hughes and Annau 1976) retarded both active and passive avoidance learning. The results suggested that the effects were due to exposure in utero, because the effects were observed in exposed offspring cross-fostered to control females at birth (no lactational exposure). Zenick (1974) compared the learning performance of rats following prenatal, lactational, or 9 days postweaning exposure to MeHg (2.5

mg/kg per day) in a water T maze. Deficits in learning were observed in the prenatal and postweaning exposure groups but not in the lactational exposure group. Thus far, the Differential Reinforcement of High Rates (DRL) test has proved to be the most sensitive of the behavioral tests used with rodents for detecting effects of in utero MeHg exposure (Müsch et al. 1978; Bornhausen et al. 1980). Rats exposed in utero to maternal doses of MeHg at 0.01 to 0:05 mg/kg per day and cross-fostered at birth displayed abnormal response patterns on the DRL task when tested at 4 months of age. Using a similar DRL paradigm, Rasmussen and Newland (1999), however, were not able to replicate that finding. A procedure designed to measure tactile-kinesthetic function in rodents has also been shown to be sensitive to MeHg exposure. Elsner (1991) reported a decrease with that procedure in the performance of rats following in utero and lactational MeHg exposure at a very low maternal dose (0.08 mg/kg per day, 2 weeks before mating and throughout gestation).

In 1996, Fredricksson et al. reported interactive behavioral effects following exposure of rats to MeHg and metallic Hg vapor. Exposure to Hg vapor at 1.8 mg/m^3 for 1.5 hours per day on gestation days 14-19 was related to hyperactivity and decreased spatial learning. While exposure to MeHg at 2 mg/kg per day on gestation days 6-9 was not related to adverse behavioral effects, co-exposure to MeHg and Hg vapor potentiated the activity and spatial learning effects observed with Hg vapor exposure alone. The reported Hg vapor effects were consistent with previous reports (Danielsson et al. 1993, Fredriksson et al. 1992, 1993). This is the first report, however, of an interactive effect of in utero exposure toHg vapor and MeHg. The results indicate that total exposure to the different forms of Hg during pregnancy is critical in evaluating the effects on the fetus.

Finally, the results of a few of the studies using animal models have provided some preliminary data on the potential effects of early-developmental exposure to MeHg on the functional status of aging animals. An early report by Spyker (1975) summarized the effects of MeHg observed over the lifetime of mice exposed in utero and during lactation. Offspring were normal at birth but exhibited effects of exposure on exploratory activity and swimming ability at 1 month of age and neuromuscular and immune effects after 1 year of age. Those findings

provide the first evidence of delayed neurotoxicity in MeHg-exposed animals. The effects of in utero plus postnatal MeHg exposure described by Rice (1989) also support the notion of delayed neurotoxicity, which might be related to increased functional impairment with aging. Monkeys exposed to MeHg at 50 µg/kg per day from birth to 7 years of age were observed in an exercise cage throughout their life. Obvious motor incoordination was observed only after the monkeys reached 14 years of age (Rice 1989). Subsequent testing of those monkeys indicated higher thresholds for vibration sensitivity, indicating effects on somatosensory functioning (Rice and Gilbert 1995). More recently, monkeys exposed to MeHg at 10-50 µg/kg per day in utero plus 4 years postnatally showed a greater deterioration in auditory function with increasing age when tested at 11 and 19 years of age (Rice 1998). Whether those effects are related to cumulative damage from early MeHg exposure and aging or to a continuous process from long-term retention of inorganic Hg in the brain following MeHg exposure is not known. The results clearly indicate, however, that the health risks associated with early MeHg exposure could last a lifetime (Harada 1995; Kinjo et al 1993).

ADULT CENTRAL-NERVOUS-SYSTEM TOXICITY

Adult Human Neurological, Neurophysiological, and Sensory Function

Several neurological signs and symptoms are among the cardinal features of chronic high-dose exposures to MeHg in adults. As no pathognomonic test is available to confirm the diagnosis of Minamata disease, cases were identified on the basis of a characteristic combination of symptoms (Harada 1997; Uchino et al. 1995; Tsubaki and Takahashi 1986). These included peripheral neuropathy (e.g., sensory impairment of the extremities of the glove-stocking type and perioral dysesthesia), dysarthria, tremor, cerebellar ataxia, gait disturbance, ophthalmological impairment (e.g., visual-field constriction and disturbed ocular movements), audiological impairment (e.g., hearing loss),

disturbance of equilibrium (e.g., vertigo, dizziness and fainting), and subjective symptoms such as headache, muscle and joint pain, forgetfulness, and fatigue. In patients with classic Minamata disease, many of those signs and symptoms were still evident after 20 years. Later studies of patients with Minamata disease reported increased pain thresholds in the body (truncal hypesthesia) and distal extremities (Yoshida et al. 1992).

To evaluate the WHO (IPCS 1990) estimate that 5% of adults with a blood Hg concentration of 200 ppb would manifest paresthesia, Kosatsky and Foran (1996) reviewed 13 studies of neurological status in long-term fish consumers. Although they identified pervasive weaknesses in study design (e.g., crude measures of exposure and outcome, possible selection bias, and absence of blinding), the authors concluded that the studies suggested neurological effects in as few as 11% (95% confidence interval, 4-22) and as many as 31% (95% confidence interval, 19-45) of adults with a blood Hg concentration of 200 ppb or more. Thus, they argued that these data do not support the WHO (IPCS 1990) conclusion that a blood Hg concentration of 200 ppb (corresponding to a hair Hg concentration of 50 ppm) represents a LOAEL for adult paresthesia and identified a need for additional research to define the lower portion of the dose-response curve (20-200 ppb).

Important data on the impact of chronic low-dose MeHg exposures on adult neurological and sensory function are being generated in ongoing studies of fish-eating populations living in the Amazon Basin, where gold is extracted from soil or river sediments and Hg is released. Lebel et al. (1996) studied 29 young adults (ages, 15-35 years; 14 females and 15 males) randomly selected from participants in a previous survey. The geometric-mean hair Hg concentration was 14.0 ppm (range, 5.6 to 38.4 ppm). Subjects underwent a battery of quantitative behavioral, sensory, and motor tests, including tests of visual functions (near and far acuity, chromatic discrimination, near contrast sensitivity, and peripheral visual fields) and motor functions (maximum grip strength and manual dexterity). Individuals with increased hair Hg concentrations had reduced chromatic discrimination. Three individuals with hair Hg concentrations above 24 ppm demonstrated reduced contrast sensitivity, and individuals with concentrations above 20 ppm tended to demonstrate reductions in peripheral visual fields. An increase from 10 to 20 ppm was associated with about a 10 degree difference. Highly exposed

women tended to have lower scores than low-exposed women on both manual dexterity and grip strength. Such a tendency was not seen in men, indicating that association between hair Hg concentration and motor function was sex-specific.

In a subsequent study, Lebel et al. (1998) assembled another sample of 91 individuals (ages 15-81 years), representing approximately 38% of the adult population of the study village. Four measures of exposure were derived based on the Hg concentration in a hair sample (length not specified): mean total hair Hg averaged over all 1-cm segments of the sample (up to 24 segments), total Hg in the first centimeter, maximum total Hg in any segment, and MeHg in the first centimeter. Individuals for whom at least 1 cm of hair contained MeHg at more than 50 ppm were excluded. The mean hair MeHg concentration was approximately 13 ppm. The assessments included the same tests of motor (maximum grip strength and manual dexterity) and visual functions (acuity, chromatic discrimination, and near contrast sensitivity) that were used in the previous study. In addition, a clinical neurological examination was administered to a random sample of the cohort (59 subjects). That examination included the Branches Alternate Movement Task (BAMT), which requires imitation of a prescribed sequence of hand movements. Abnormal performance on the BAMT was significantly associated with all measures of Hg exposure, and abnormal visual fields were associated with mean hair Hg and peak Hg concentrations. Hyper-reflexia (patellar and bicepital) was not associated with any Hg measurement. Increased hair Hg concentrations, most notably peak Hg, were associated with poor scores on the intermediate and higher frequencies of near visual-contrast sensitivity (in the absence of near visual-acuity loss), with poor scores on the manual dexterity test, and with increased muscular fatigue. In women, but not in men, grip strength varied with peak Hg concentration. For many end points, the associations between hair Hg concentration and performance were stronger in younger subjects (less than 35 years) than in older ones. The authors stress that the dose-related decrements in visual and motor functions were associated with hair Hg concentrations below 50 ppm, a range in which clinical signs of Hg intoxication are not apparent. The Hg exposure of the cohort is presumed to have resulted from fish-consumption patterns that are stable and thus relevant to estimating the risk associated with chronic, low-dose MeHg exposure. In fact, the possibility cannot be

excluded that the neurobehavioral deficits of the adult subjects were due to increased prenatal, rather than ongoing, MeHg exposure.

Beuter and Edwards (1998) investigated the prevalence and severity of three types of subtle motor deficits in a cohort of 36 adult Cree (mean age 56 years), comparing them with patients with Parkinson's disease (PD) (21 subjects), cerebellar deficit (6 subjects), essential tremor (3 subjects), or controls (30 subjects). The mean of the annual maximum hair Hg concentration over a period of 25 years varied from 2.2 to 31.1 ppm. Ten of 14 static tremor end points (with visual feedback) and 5 of 8 kinetic tremor end points (during voluntary finger movements) assessed were significantly related to group (i.e. Cree versus PD versus control). Nested analyses were carried out in which the six Cree with the highest hair Hg concentrations (mean of annual maximum hair concentrations greater than 24 ppm; range, 24.34-31.10 ppm) were matched to six Cree with low hair Hg concentrations (mean of annual maximum hair concentrations 6.02-11.89 ppm) and six controls to get a better idea of whether the group differences were likely to be due to Hg or some confounding factor associated with group membership. Despite the reduced number, significant group differences were still found on several end points. Overall, the performance characteristics that best discriminated groups were drift (static tremor), event index (static tremor), mean tracking error (kinetic tremor), and the center of mass harmonicity (static tremor).

The same groups of subjects were administered a test of rapid, precise promixo-distal movements (i.e. eye-hand coordination) (Beuter et al. 1999a). A eurythmkinesiometer recorded subjects' efforts to strike targets with a stylus, yielding measures of precision, imprecision, tremor, Fitts' constant (an index of the trade-off between speed and accuracy), and irregularity. The Cree subjects' performance was more than 1 standard deviation worse than the controls' performance on tremor, Fitts' constant, and irregularity. In the same type of nested analyses carried out in the study of tremor described above, the order of group scores, from best to worst, was control better than low Hg better than high Hg for all three end points, the group differences on Fitts' constant and irregularity being significant.

Rapid alternating movements (diadochokinesia) were assessed in those groups of subjects by asking them to rotate two foam spheres under three conditions: (1) both hands, natural cadence; (2) right and left

hands separately, fast cadence (i.e., as fast as possible); and (3) both hands, fast cadence (Beuter et al. 1999b). Seven dimensions of performance were measured: duration, range, maximum slope, similarity in shape, smoothness, sharpness, and coherence. Significant group difference were found on most end points, and the results of nested analyses provided additional evidence that group differences in Hg concentrations were probably contributory.

Neurotoxic Effects in Adult Animals

Experimental studies of the effects of MeHg exposure on adult animals have reported neurological effects similar to those reported for adult humans. Studies using monkeys, rodents, and cats have reported effects consistent with adult MD (Harada 1995). Some of those studies are summarized in Table 5-12. Neurotoxic signs reported reflect the regional specificity of the neuropathological effects observed in adult subjects. Signs of ataxia, constriction of the visual field, and sensory disturbances are commonly associated with pathological lesions in the calcarine cortices, dorsal root ganglia, and cerebellum (Chang 1980).

A study of macaque and squirrel monkeys has reported ataxia, tremor, and constriction of visual fields in animals with blood Hg concentrations between 1 and 2 ppm (Evans et al. 1977). The latency for the onset of symptoms in that study was 135 to 140 days.

Constriction of the visual field was reported in macaques following variable dosing schedules that produced blood MeHg concentrations from 1.5 to 3 ppm. The onset of visual-field disturbances preceded overt signs of toxicity (Merigan et al. 1983).

Ataxia, tremor, and apparent blindness was reported in adult female macaques exposed orally to doses of MeHg hydroxide at 70 µg/kg per day and above (Burbacher et al. 1988). The durations to onset of symptoms ranged from 177 days to 392 days.

In rodents, several studies have reported severe neurological effects, such as ataxia, paralysis, spasms, and hindlimb crossing in adult rats and mice, from exposure to MeHg (see Table 5-12). In general, the onset of symptoms is dependent on the dose and duration of exposure. In rats, overt signs of neurotoxicity were reported at doses ranging from 0.8 mg/kg per day for 6 weeks (Chang and Hartmann 1972) to 10 mg/kg

TABLE 5-12 Neurological Effects of MeHg Exposure in Adult Animals

Species	Exposure Time	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Effect	Reference
Monkeyss (macaque and squirrel)	135-1,000 d (variable dosing)	NS	NS	Ataxia, tremor, constriction of visual field	Evans et al. 1977
Monkeys (macaque)	20-73 wk (variable dosing)	NS	NS	Tremor, constriction of visual field	Merigan et al. 1983
Monkeys *(Macaca fascicularis)*	177-392 d	0.05	0.09	Ataxia, tremor, blindness	Burbacher et al. 1988
Rat	29 d		2.4	Ataxia, paralysis	Hunter et al. 1940
Rat	1-6 wk		0.8	Ataxia, degeneration of cerebellum and dorsal root ganglia	Chang and Hartmann 1972
Rat	3-12 wk	0.84	1.68	Ataxia, edema and necrosis of cerebellum	Magos and Butler 1972
Rat (Wistar)	2 d		10	Impaired performance in tilting plane test	Fehling et al. 1975
Rat (Wistar)	9, 13, or 21 d	2	4	Hindlimb crossing	Inouye and Murakami 1975
Rat (Wistar)	Gestation d 7-14	4	6	Spasms, gait disturbances	Fuyuta et al. 1978
Rat (Sprague-Dawley)	2 d	1.32	4	Altered sleep cycles	Arito and Takahashi
Rat	15 d (dosed every 3 d)		10	Hindlimb crossing, flailing microgliocytosis and cerebellar degeneration	Leyshon and Morgan 1991

Mouse	24 wk	1.9	Paralysis	MacDonald and Harbison 1977
Mouse (C57B1/6)	17 d 6 d	4 8	Increased auditory brainstem response thresholds	Wassick and Yonovitz 1985
Mouse ($B6C3F_1$) 2 yr	2 yr	0.6	Paralysis, neuropathy	Mitsumori et al. 1990
Rabbit (New Zealand)	7 d	30	Ataxia, decreased muscle tone, reduced splay reflex	Jacobs et al. 1977
Cat		0.05	Ataxia	Khera et al. 1974
Cat	60 wk	0.046	Impaired hopping	Charbonneau et al. 1976

Abbreviations: NOAEL, no-observed-adverse-effect level; LOAEL, lowest-observed-adverse-effect level; NS, not stated.

per day given every 3 days for 15 days (Leyshon and Morgan 1991). Studies in mice reported that doses from 0.6 mg/kg per day for approximately 2 years (Mitsumori et al. 1990) to 1.9 mg/kg per day for 24 weeks (MacDonald and Harbison 1977) caused paralysis. A study by Jacobs et al. (1977) using New Zealand rabbits reported ataxia and decreased muscle tone following a dose of 30 mg/kg per day for 7 days. Two studies using cats reported ataxia and impaired hopping after long-term exposure at approximately 0.05 mg/kg per day (Khera et al. 1974; Charbonneau et al. 1976).

A few studies using rodents have reported less severe symptoms, such as altered sleep cycles, hindlimb weakness, or increased brainstem-auditory-response thresholds following exposure to MeHg. Altered sleep cycles in rats were reported by Arito and Takahashi (1991) following 2 days of exposure at 4 mg/kg per day. Hindlimb weakness in mice was reported by Berthoud et al. (1976) following exposure at 1 mg/kg per day for 60 days. Wassick and Yonovitz (1985) reported increased brainstem-auditory thresholds in mice following 17 days of exposure at 4 mg/kg per day or 6 days of exposure at 8 mg/kg per day.

In summary, reports from animal models of adult MD have provided supportive evidence for the neurological signs reported in humans. These studies have also provided detailed descriptions of the associated neuropathological effects from high-dose MeHg exposures (Chang 1979, 1990). Studies using adult animal models of chronic low-dose MeHg effects have been sparse, most likely because of the focus on neurodevelopmental effects following in utero or early postnatal MeHg exposure.

CONCLUSIONS

- MeHg is highly toxic. The data reviewed in this chapter indicate that the adverse effects of MeHg exposure can be expressed in multiple organ systems throughout the lifespan.
- Studies in humans on the carcinogenic effects of MeHg are inconclusive. Renal tumors have been seen in male mice but only at or above the MTD of MeHg.
- The effect of MeHg on the human immune system is poorly understood. However, studies in vitro and in animals suggest that

exposure to MeHg could increase human susceptibility to infectious diseases and autoimmune disorders by damaging the immune system.

- The reproductive effects of MeHg have not been fully evaluated in humans, but animal studies, including work in nonhuman primates, indicate that MeHg causes functional reproductive effects.
- Damage to the renal tubules and nephron has been observed following human exposure to inorganic and organic forms of Hg. However, symptoms of renal damage have been seen only at Hg exposures that also caused neurological effects. In animals, similar effects have been observed as well as altered renal function and renal hypertrophy have been observed following early postnatal exposure to MeHg.
- Although the data base is not as extensive for cardiovascular effects as it is for other end points (i.e., neurotoxic effects), the cardiovascular system appears to be a target for MeHg toxicity in both humans and animals. Evidence suggests that adverse health effects can occur at very low Hg exposures.

  — Exposure to elemental and organic forms of Hg alters blood-pressure regulation. That effect has been documented in children and adults who were exposed to toxic and subtoxic doses of Hg and have been induced experimentally in rats.
  — Prenatal exposure to MeHg has been shown to alter blood-pressure regulation and heart-rate variability in children. Those effects were observed at cord-blood Hg concentrations that have not been associated with other developmental effects (less than 10 µg/L).
  — Men who consumed at least 30 g of fish per day or had a hair Hg concentration of 2 ppm or more had a higher risk of suffering a fatal or nonfatal acute myocardial infarction. Mercury exposure was also correlated with an increased risk of dying from coronary heart disease or cardiovascular heart disease. A hair Hg concentration of 2 ppm has not been associated with other adverse health effects.

- The human data base on the neurodevelopmental effects of MeHg is extensive, and includes studies of populations following high-dose Hg poisonings and chronic low-dose Hg exposure. Some study results appear to be conflicting. Table 5-10 provides informa

tion about the hair and blood Hg concentrations in the studies on which the following conclusions are based.

— Several studies have detected significant MeHg-associated increases in the frequency of abnormal and questionable findings on standardized neurological examinations, although the functional importance of the apparent effects is uncertain.
— Recent epidemiological studies provide little evidence that the ages at which children achieve major language and motor milestones are affected appreciably by low-dose prenatal MeHg exposure.
— Two out of four studies using the Denver Developmental Screening Test reported an association of low-dose MeHg exposure on early childhood development.
— Of the three major prospective long-term studies, the Faroes study reported associations between low-dose prenatal MeHg exposure and children's performance on standardized neurobehavioral tests, particularly in the domains of attention, fine-motor function, confrontational naming, visual-spatial abilities, and verbal memory, but the Seychelles study did not report such associations. The smaller New Zealand study also observed associations, as did a large pilot study conducted in the Seychelles.

- Recent studies in adults suggest that hair Hg concentrations below 50 ppm are significantly associated with disturbances of the visual system (chromatic discrimination, contrast sensitivity, and peripheral fields) and with neuromotor deficits (tremor, dexterity, grip strength, complex-movement sequences, hand-eye coordination, and rapid alternating movement). Those findings suggest that the current reference dose for adults based on 50 ppm in hair might not be sufficiently protective.
- Neurodevelopmental studies using animal models (nonhuman primates, rodents) exposed in utero and/or early postnatally to MeHg have reported a continuum of effects related to dose. Effects have been reported on sensory, sensorimotor, and cognitive development. Overall, sensory effects seem to be the most long-lasting.
- Experimental studies of adult animal models exposed to MeHg have also reported a continuum of effects associated with dose. The

effects are similar to those observed in cases of human MeHg poisoning.

- Neurodevelopmental effects are the most extensively studied sensitive end point for MeHg toxicity and are appropriate for use in establishing an RfD. New data are emerging, however, indicating that there might be important adverse effects on other end points (e.g., cardiovascular and immune systems) in the same exposure range. Those effects should be considered as the data become available.

RECOMMENDATIONS

- Epidemiological research is needed to evaluate the prevalence of chromosomal aberrations and cancer, especially leukemia and renal tumors, among populations that have chronic exposure to MeHg through ingestion of contaminated fish.
- The ability of MeHg to cause chromosomal damage and promote tumor growth should be considered in the establishment of exposure guidelines.
- Research is needed to determine the effects of MeHg exposure on the immune system, including the effects on the developing immune system, resistance to microbial pathogens, and autoimmunity. Mechanisms by which the immune system is involved in the target-organ toxicity of Hg should also be examined.
- Research is needed to assess the effects of MeHg on reproduction, including the effects on fertility indicators, such as sperm production, conception rates, and pregnancy outcomes.
- Research is needed to evaluate the impact of dietary exposure to MeHg on the prevalence of hypertension and cardiovascular disease in the United States. The risk of fatal and nonfatal heart disease must be considered in the development of a reference dose for this contaminant.
- Research is needed to determine the long-term implications of the neuropsychological and neurophysiological effects of low-level prenatal MeHg exposure detected in children, specifically whether

they are associated with an increased risk for later neurological diseases.

- Research using animal models is needed to better define the immediate and long-term effects of early chronic low-level MeHg exposure. Studies should focus on several important issues:

  — Critical periods for MeHg effects (in utero or postnatal).
  — Low-level dose-response relationships (ppb range).
  — MeHg demethylation in the brain following early MeHg exposure.
  — Synergistic effects of early MeHg and Hg vapor exposure.
  — Neurodegenerative disorders related to early MeHg exposure.

- Animal studies should be conducted to examine the neurodevelopmental effects of continuous versus peak MeHg exposures.

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6

COMPARISON OF STUDIES FOR USE IN RISK ASSESSMENT

UNTIL recently, the data base available for risk assessments of MeHg has been limited to high-dose poisoning episodes in Japan and Iraq. More recently, however, epidemiological studies have been conducted on the health effects of exposure to low doses of MeHg (for details of health effects, see Chapter 5). The low-dose MeHg exposure studies are more relevant to levels of exposures in the United States and, therefore, more appropriate for use in risk assessments. The two largest and most comprehensive studies to address the health effects of MeHg — the Seychelles Child Development Study (SCDS) and the Faroe Islands studies — reached different conclusions. A range of adverse neuropsychological and neurophysiological outcomes were found to be associated with prenatal Hg exposure in the Faroe Islands study, whereas adverse effects were not found in the main Seychelles study. This chapter compares those two studies, as well as data from the pilot phase of the SCDS, and a smaller study carried out on a cohort in New Zealand.

MeHg exposure in the SCDS and Faroe Islands studies were similar; the arithmetic mean maternal hair Hg concentration in the Seychelles cohort (6.8 μg/g) was slightly higher than the geometric mean reported in the Faroe cohort (4.3 μg/g). Several differences in research design and cohort characteristics have been identified that might account for the discrepant findings. Some of those explanations seem less persuasive, however, when the data from the New Zealand study are consid

ered. That study found associations with MeHg exposure in a population whose sources of MeHg exposure were similar to those in the Seychelles and used end points similar to those examined in the Seychelles. Although the New Zealand data have been available for some time, they have not been used extensively for risk assessment, possibly because until recently, they had not been subjected to standard peer-review procedures. A re-analysis of the New Zealand data by Crump et al. (1998), which underwent peer review, reported associations of prenatal MeHg exposure with several end points (when one extreme outlier was excluded), including four that were not found to be related to MeHg in the Seychelles study. The New Zealand study has been criticized for errors in matching exposed children to controls and for testing exposed children and controls at different ages (Myers et al. 1998). Those errors occurred in the 4-year follow-up but were corrected in the 6-year follow-up, which is the data set reviewed in this section. In addition, there is no information that would suggest the presence of differential measurement error across the studies. Any error of that type is likely to be nondifferential (i.e., unbiased), and it would reduce the likelihood of detecting associations between MeHg exposure and neurobehavioral test scores.

Data from the peer-reviewed pilot SCDS of 217 children assessed at 5.5 years (Myers et al. 1995) are also considered in this chapter. (Note that the nonstandard treatment of the data from the Revised Denver Developmental Screening Test (DDST-R) discussed in Chapter 5 was not an issue in the 5.5-year follow-up since the DDST-R was not given at that age.) Two of the four outcomes that were tested in both the pilot and the main Seychelles studies at 5.5 years of age were found to be associated with prenatal Hg exposure in the pilot study. The Seychelles investigators were cautious about drawing inferences from their pilot data, because the effects were substantially weaker when four outliers were excluded from the analyses and because socioenvironmental influences were not adequately assessed and controlled statistically. It is not clear, however, that it is appropriate statistically to exclude influential data points; many statisticians would instead recommend the use of data transformation to reduce their influence. Exclusion is appropriate only where a value appears biologically implausible (see discussion of the New Zealand outlier in the Benchmark Analysis section in Chapter 7). With regard to socioenvironmental influences, T.W. Clarkson

(principal investigator in the SCDS, personal commun., January 20, 2000) indicated to the committee that the most heavily contaminated fish consumed in the Seychelles islands — swordfish, shark, and tuna — tend to be among the most expensive fish, so that, if anything, exposure levels might be higher among mothers with *higher* socioeconomic status. There is, therefore, no reason to expect a confounding of exposure with lower socioeconomic status, and low socioeconomic status is not likely to explain the association of Hg exposure with adverse development outcomes in the Seychelles pilot study.

ASSESSMENT OF PRENATAL HG EXPOSURE: CORD BLOOD VERSUS MATERNAL HAIR AND TIMING OF EXPOSURE

The principal measure of prenatal exposure in the Faroe study was Hg in cord blood; in the Seychelles, it was Hg in maternal hair. The Faroe investigators also analyzed maternal-hair samples, but no cord-blood specimens were obtained in the Seychelles. In a recently published analysis, the Faroe investigators compared the relation of the cord-blood and maternal-hair Hg measures with their 7-year end points (Grandjean et al. 1999). As shown in Table 6-1, cord-blood Hg concentration was significantly associated with a slightly larger number of end points than maternal-hair Hg concentration, and in most cases the associations were slightly stronger. For various pharmacokinetic and neurodevelopmental reasons, cord-blood measurements might be more sensitive indicators of the neurodevelopmental effects of MeHg. However, given that hair Hg concentrations in the Faroe Islands study were only a slightly weaker predictor of Hg effects than cord blood, it would be reasonable to expect that, if children were affected in the main Seychelles study, some indication of an association between child performance and maternal-hair Hg concentration would be apparent in that study. With the possible exception of the Bender Gestalt scores for boys, there is no indication of even a trend in the predicted direction in the data published to date from the main SCDS (e.g., see Figures 5-7 and 5-8).

It should be noted that the maternal-hair samples obtained in the Faroe and Seychelles studies did not necessarily reflect exactly the same period of pregnancy. In part, this is because the Seychelles study obtained

TABLE 6-1 Change in Neuropsychological Test Performance Associated with a Doubling of the Hg Concentration in the Faroese Cohort[a]

	Cord Blood Hg		Maternal Hair Hg	
Test	Change[b]	p[c]	Change[b]	p[c]
NES[d] Finger Tapping				
Preferred hand	−5.37	0.049	−5.99	0.039
Other hand	−1.97	0.460	−4.40	0.120
Both hands	−4.11	0.136	−6.64	0.024
NES Hand-Eye Coordination				
Error score	3.70	0.187	5.40	0.070
NES Continuous Performance Test				
Missed responses	10.08	0.024	5.14	0.241
Reaction Time	15.93	<0.001	8.99	0.035
Wechsler Intelligence Scale for Children-Revised				
Digit Spans	−5.62	0.049	−4.39	0.147
Similarities	−0.37	0.902	−2.07	0.525
Block Designs	−4.36	0.109	−2.86	0.322
Bender Visual Motor Gestalt Test				
Error on copying	3.83	0.154	3.60	0.208
Delayed recall	−4.64	0.104	−1.26	0.679
Boston Naming Test				
No cues	−9.75	<0.001	−6.98	0.016
With cues	−10.47	<0.001	−7.47	0.009
California Verbal Learning Test (Children)				
Learning	−4.33	0.123	−3.96	0.184
Immediate recall	−6.64	0.019	−5.93	0.049
Delayed recall	−5.69	0.047	−5.15	0.092
Recognition	−4.24	0.151	−3.15	0.318

Source: Adapted from Grandjean et al., 1999, Table 2.

[a]All Hg values were log transformed for the analyses presented here.

[b]Expressed as % of standard deviation.

[c]Statistical significance of the effect associated with Hg exposure in a mutiple regression including potential confounders.

[d]Neurobehavioral Evaluation System.

Hg concentrations from a 9-cm length of hair reflecting average MeHg exposure during pregnancy and the Faroe study obtained concentrations from hair samples of variable length, some of 3-cm (reflecting late second and third trimester) and some of 9-cm in length. Additionally, the Faroe maternal-hair samples, which were obtained at delivery, did not include the last 3 weeks of gestation, because it takes approximately 20 days after ingestion for the newly formed portion of the hair strand to emerge above the scalp. If the third trimester is particularly important for the development of the neural substrate for cognitive and neuromotor function, it is perhaps not surprising that the maternal-hair sample obtained in the Faroe Islands might be somewhat less sensitive than the cord-blood sample, which primarily reflects third-trimester exposure (see Chapter 3). A maternal-hair sample that reflected the last 20 days of pregnancy might have been more sensitive. In the SCDS, the maternal-hair samples were obtained at delivery and at 6 months postpartum. The portion of the hair strands corresponding to the pregnancy period was analyzed, assuming 1 cm of hair growth per month. If third-trimester exposure is critical for the neurodevelopmental end points, the SCDS measure of Hg exposure averaged across the entire pregnancy might be less sensitive in detecting them, compared with cord blood, which primarily reflects third-trimester exposure. It might be informative for the SCDS group to re-analyze their data using the concentration of Hg in the portions of hair corresponding only to the third trimester as the exposure measure.

It is also of interest that the neurophysiological end points in the Faroe study (e.g., brain-stem auditory-evoked potentials) were associated only with the maternal-hair Hg measure, not with the cord-blood Hg. Because the hair measure presumably reflects an earlier period of gestation, the data suggest an earlier sensitive or critical period for the neurophysiological effects. In summary, it does not appear that the failure of the SCDS to collect cord-blood Hg samples can account for the discrepancies between their findings and those in the Faroe study because, in the latter study, associations were found between neurobehavioral test scores and both cord-blood Hg and maternal-hair Hg concentrations (Table 6-1). Moreover, the findings reported in New Zealand and the pilot SCDS were based solely on maternal-hair-sample data averaged across the entire pregnancy.

DIFFERENCES IN THE NEUROBEHAVIORAL END POINTS ASSESSED AND THE CHILDREN'S AGES AT ASSESSMENT

The Faroe and Seychelles studies used very different neurobehavioral test batteries. For the most part, the tests selected for the SCDS are considered apical or omnibus tests (e.g., the McCarthy Scales of Children's Abilities), which yield global scores that integrate performance over many separate neuropsychological domains. In contrast, because the Faroe investigators hypothesized multifocal domain-specific neuropsychological effects, their test battery largely consisted of highly focused tests selected from those commonly used in clinical neuropsychology (e.g., California Verbal Learning Test — Children and Boston Naming Test). The Faroe test battery does not include an apical test of global function.

The subscales from the McCarthy test (verbal, perceptual-performance, quantitative, memory, and motor) that assess specific domains of function might be expected to be more directly comparable to the tests administered in the Faroe Islands. For instance, given the finding in the Faroe study that memory, as assessed by the California Verbal Learning Test, was significantly associated with prenatal Hg exposure, it would be expected that children's scores on the McCarthy memory scale in the SCDS would be associated with Hg exposure. However, they were not. In fact, prenatal Hg exposure was not associated with scores on any of the McCarthy subscales. It is important to examine in detail the extent to which the individual McCarthy subscales are comparable to the domain-specific tests selected for the Faroe study. Psychometrically, they are different. The California Verbal Learning Test, for example, involves five learning trials of a 12-word list, with free- and cued-recall trials following short and long delays, and a recognition trial. None of the 18 tests that contribute to scores on the McCarthy scales examine rate of learning, and the memory scale combines scores on four tests that involve recall of differing types of information: pictorial (six common objects arrayed on a page), auditory sequence (xylophone notes), word list (ranging from 3 words in a specified sequence to a 13-word sentence with 9 key words that are scored), connected discourse (recall of individual story elements), and numbers (forward and backward recall of strings of numbers up to seven digits long.) Clearly, a child's score on

the McCarthy memory scale integrates performance on a much wider variety of memory skills than does either the short- or long-delay free-recall trials of the California Verbal Learning Test. Scores on some of the 18 specific subscales of the McCarthy test might offer greater comparability with the key end points of the California Verbal Learning Test assessed in the Faroe study. Each of the 18 subscales is quite brief, however, and thus less psychometrically sound than the richer California Verbal Learning Test, which assesses only one domain of function but does that in considerable depth.

Similarly, although the Boston Naming Test, which was included in the Faroe Islands test battery, and the preschool language scale and the verbal scale of the McCarthy verbal scale which were included in the SCDS 66-month test battery of the SCDS can be considered tests of language skills, the specific skills they assess are quite different. The Boston Naming Test specifically assesses confrontational naming skills, consisting of line drawings of common objects that a child has to name under time pressure (20 seconds). If the child cannot retrieve the correct name spontaneously, semantic and then phonemic cues are provided. In contrast, the total score on the preschool language scale (PLS) integrates a child's performance on the auditory comprehension and expressive communication subscales, both of which assess a broad range of language skills (eg., comprehension and production of vocabulary; concepts of quantity, quality, space, and time; morphology; syntax; and inference drawing). Like the total score on the PLS, the total score on the McCarthy verbal scale integrates a child's performance across many language-relevant domains in the following tests: pictorial memory (same as test described for memory scale), word knowledge (pointing to the picture of an object named by the examiner, providing the name for four pictured objects, and providing word definitions), verbal memory (same as test described for memory scale), verbal fluency (generating words in 20-sec trials to fit specific semantic constraints, such as things to eat or animals), and opposite analogies (providing antonyms). Thus, although the four items of the word-knowledge test that assess naming could be isolated and considered an index of confrontational naming, similar to the Boston Naming Test, the four items are unlikely to possess the same sensitivity insofar as the latter test consists of 60 items.

Thus, although the Faroe Islands and SCDS test batteries include tests of language and memory, it is not appropriate to view the end points

used in the studies to assess each domain to be equivalent either in terms of the specific skills assessed or the test sensitivity.

Although the Bender-Gestalt Test was administered in the Faroe study and SCDS as a measure of visual-spatial abilities, different scoring systems were used (the Gottingen system in the Faroe Islands and the Koppitz system in the Seychelles). The finding of a significant association with Hg in the former but not the latter study is similar to the finding reported by Trillingsgaard et al. (1985) that scores derived using the more-detailed Gottingen system were significantly associated with low-dose lead exposure, and scores on the Koppitz system were not. Thus, the Gottingen system used in the Faroe Islands might be more sensitive. Although the Seychelles data could be rescored using the Gottingen system, the committee was told that the data might still not be comparable, because the more sensitive memory for design conditions was not administered in the Seychelles study.

To help determine the degree to which the discrepant results from the Faroe study and SCDS are attributable to differences in the neurobehavioral tests used, the Seychelles group administered several of the more domain-specific tests from the Faroe battery in their 8-year followup. The results of those assessments, however, are not yet available.

A second important difference in the assessment batteries used in the Faroe study and SCDS relates to the age of assessment — 7 years in the Faroe Islands and 5.5 years of age in the SCDS. The final assessment in the New Zealand cohort was at 6 years of age. Generally speaking, developmental assessments are likely to be less sensitive in detecting subtle neurotoxic effects when they are administered during a period of rapid developmental change. The period covering ages 60-72 months, when the SCDS and New Zealand cohorts were evaluated, is one such period during which marked individual differences in the rate of cognitive maturation are likely to eclipse subtle differences in function attributable to a teratogenic exposure (Jacobson and Jacobson 1991). The assessments performed in the SCDS during infancy, particularly the 19-and 29-month Bayley scales, were also not administered at optimal age points. Studies of prenatal exposure to alcohol and other substances that have administered the Bayley scales at multiple ages have repeatedly failed to detect effects at 18 months, probably because it too is a period of rapid cognitive maturation, involving the emergence of spoken language. Twenty-nine months is likely to be an insensitive testing

point for the Bayley scales because it is at the end of the age range for which the version of this test used in the Seychelles was standardized, leading to a substantial risk of a "ceiling effect" (i.e., too many children receiving the highest possible scores on numerous items). The next round of testing in the Seychelles will be at 8 years of age, a point in development that should be more optimal for detecting neurodevelopmental effects.

Although differences in end points assessed and age of assessment might explain the failure of the SCDS to detect the associations found in the Faroe Islands study, findings from the New Zealand study and the Seychelles pilot study suggest that the discrepancies between the Faroe Islands and the main Seychelles studies are probably not due to differences in the assessments. The New Zealand study found associations between MeHg exposure and scores on the McCarthy Scales of Children's Abilities (the primary outcome measure used in the SCDS) at about the same age of assessment as in the Seychelles study, in a study with full control for potential confounding influences. Associations with prenatal Hg exposure were even seen on the McCarthy scales and the PLS in the 217-member Seychelles pilot study at 5.5 years of age, albeit with only limited control for socioenvironmental influences.

STABLE VERSUS EPISODIC PATTERN OF EXPOSURE

The predominant source of Hg exposure in the Seychelles is daily fish consumption. Maternal fish consumption averages 12 meals per week. Hg exposure in the Faroe Islands, by contrast, is often more episodic. In the Faroe Islands, pilot-whale meals are relatively infrequent (less than once per month on the average), but whale meat has concentrations of MeHg between 10 and 20 times greater than those in many fish consumed in the Faroe Islands (Grandjean et al. 1992); thus, the whale meals might represent toxicologically more significant peak or bolus doses. Laboratory animal experiments on prenatal alcohol exposure have demonstrated that maternal ingestion of a given dose of alcohol over a short time causes greater neuronal (Bonthius and West 1990) and behavioral impairment (Goodlett et al. 1987) than that caused by gradual ingestion of the same total dose over several days. Thus, it is possible that the more episodic exposure pattern in the Faroe Islands, with

heavier doses per occasion, has a more adverse impact on neuronal development than the more gradual exposure in the Seychelles. However, it is difficult to compare the 12 fish meals per week reported in the Seychelles with the three fish "dinners" per week in the Faroe Islands, because the types of fish eaten and their Hg concentrations are different. Moreover, the exposure-associated differences in neurobehavior found in the New Zealand cohort and the Seychelles pilot study where no whale meat was eaten suggest that bolus doses are not necessary to generate cognitive deficits at those levels of exposure.

The importance of high episodic ("spiking") exposures is unclear. However, as discussed in Chapter 4, the degree of spiking in the Faroe study is likely to be in the low-to-moderate range (i.e., less than a doubling in hair Hg concentrations, assuming an individual at the Faroe Islands median exposure level consumes three consecutive 4-ounce whale meals). Spiking might also occur in the Seychelles given the availability of fish species with characteristically moderate-to-high concentrations of Hg (e.g. tuna), although the absence of dietary data does not allow this issue to be examined further.

STUDY DIFFERENCES IN CONTROL FOR CONFOUNDERS

A potential confounder is a variable related to both the exposure of interest (e.g., MeHg) and to the outcome of interest (e.g., neurobehavior). If the relation between exposure and outcome is no longer significant after controlling statistically for a potential confounder, it is inferred that the relation between exposure and outcome is spurious and due to confounding by the control variable being examined. Because random assignment to predetermined exposure levels cannot be used to control for confounding in human exposure studies, it is important to assess whether a broad range of control variables confound any associations observed between exposure and outcome. Table 6-2 lists the control variables examined in the Faroe and Seychelles studies. Both studies evaluated most of the variables that are known to be at least moderately related to childhood cognitive outcome, including maternal cognitive competence (e.g. Ravens test), child age, gender, maternal alcohol consumption and smoking during pregnancy, and parental income. A few variables that are sometimes modestly related to those outcomes

were assessed in one study but not in the other (e.g., maternal age and birth order in the Seychelles study; obstetrical care in the Faroe study). However, the influences of those variables on cognitive outcome are

TABLE 6-2 Control Variables Assessed in the Faroe Islands and the Seychelles Studies

Covariates	Faroe Islands Study	Seychelles Study
Birth weight		X
Maternal cognitive competence (Ravens)	X	X
Child's age	X	--[a]
Child's sex	X	X
Gestational age		X
Smoking during pregnancy	X	X
Alcohol during pregnancy	X	X
Duration breast feeding	X	X
PCBs	X	--[b]
Education (mother and father)	X	
Employment (family income)	X	X
Obstetric care	X	
Daycare	X	X
Computer acquaintance	X	
Examiner	X	
Birth order		X
Maternal age		X
Child's medical history		X
Language at home	N/A	X
Maternal medical history		X
Maternal hair lead	X[c]	X[d]

[a]Test scores adjusted for age, based on U.S. norms.
[b]No PCBs were detected in any of the 49 serum samples obtained at 66 months postpartum. These data support the assumption that there is virtually no PCB exposure in this population.
[c]Whole pregnancy.
[d]At parturition, i.e., pregnancy minus 45 days.
Source: Adapted from NIEHS 1998.

probably too weak to account for any major inconsistencies between the two studies. Parental education was not assessed in the Seychelles study, but it is likely to have added little information over and above family income and maternal cognitive competence.

At a workshop sponsored by the White House Office of Science and Technology Policy in November 1998, the Faroe investigators noted that, apparently due to social-class differences, the maternal Ravens scores and the child verbal-test scores were generally higher among families residing in one of the three Faroe towns than among those living in the countryside. Because more fish and whale meat are consumed by rural residents, the associations of Hg exposure with child verbal-test scores could be spurious, reflecting those social-class differences. (Although the Ravens scores were controlled statistically in the analyses, that single test might not have fully controlled for social-class confounding.) Data presented at the workshop showed, however, that these associations remained significant, even after controlling for a dichotomous town-country control variable (Table 6-3). Although that analysis is reassuring, it would not be appropriate to control for town routinely in all analyses. Because fish and whale consumption constitute a large proportion of the rural diet, the disappearance of associations after controlling for residence could be due to the fact that residing in a rural area leads to increased Hg exposure which, in turn, causes an adverse outcome. It would not necessarily indicate that the lower social class associated with rural residence is the true cause of the Hg-associated deficit. The disappearance of an association between Hg and neurobehavior under those circumstances would be very difficult to interpret, because the interpretation would depend upon what condition is considered the reason for the association between living in a rural area and poor outcome (i.e., lower social class or greater Hg exposure).

Because the rural residents had to travel relatively long distances to the testing site in Torshavn, there has been concern that fatigue and the strangeness of the urban setting might have caused the rural children to perform more poorly. As noted above, however, the data in Table 6-3 make clear that the regression coefficients for prenatal Hg exposure remain significant even after controlling for child's residence.

The neuropsychological test examiner is one potentially important factor that was routinely controlled for in the Faroe Islands study (see NIEHS 1998, section 3.5), but was not controlled for in the SCDS. The omission

TABLE 6-3 Effects of Residence (Town vs. Country) and Prenatal Hg Exposure on Developmental Outcomes in the Faroe Islands Study

	Residence[a]		Hg Without Controlling for Residence[b]		Hg Controlling for Residence[c]	
Test	b[d]	p	b	p	b	p
NES Finger Tapping						
Preferred Hand	0.03	0.95	−1.10	0.05	−1.14	0.04
Other Hand	−0.47	0.26	−0.39	0.46	−0.55	0.31
Both Hands	−1.41	0.11	−1.67	0.14	−2.04	0.07
NES Hand-Eye Coordination						
Error Score	0.001	0.94	0.03	0.19	0.04	0.18
NES Continuous Performance						
Missed Responses	−0.12	0.16	0.27	0.02	0.24	0.04
Reaction Time	−14.55	0.06	40.30	<0.001	35.34	0.002
WISC-R						
Digit Spans	0.06	0.58	−0.27	0.05	−0.26	0.07
Similarities	0.04	0.91	−0.05	0.90	−0.08	0.84
Block Designs	0.19	0.02	−0.17	0.11	−0.12	0.26
Bender Visual Motor Gestalt Test						
Error on Copying	−1.03	0.005	0.67	0.15	0.45	0.35
Delayed Recall	0.35	0.004	−0.25	0.10	−0.17	0.28
Boston Naming Test						
No cues	1.10	0.005	−1.77	<0.001	−1.51	0.003
With cues	1.24	0.001	−1.91	<0.001	−1.60	0.001
CVLT						
Learning	0.89	0.16	−1.25	0.12	−1.10	0.18
Immediate recall	0.37	0.06	−0.57	0.02	−0.49	0.05
Delayed recall	0.02	0.92	−0.55	0.05	−0.56	0.05
Recognition	0.15	0.92	−0.29	0.15	−0.30	0.14

[a]Controlling for all independent variables except Hg; 0 = country, 1 = town.
[b]Controlling for all independent variables except residence.
[C]Controlling for all independent variables.
[d]Raw (unstandardized) regression coefficient.
Abbreviations: NES, Neurobehavioral Evaluation System; CVLT, California Verbal Learning Test.
Source: Adapted from Appendix III-B, Table 3, NIEHS (1998).

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of that control variable might not seem important in light of the lack of observed effects in that study. However, if one examiner who is less adept at eliciting optimal performance from the subjects tested a large proportion of less exposed children, the results could be affected. If those children performed more poorly than they otherwise would have on the test, an association between Hg concentration and test scores might be obscured by failure to control for the examiner. That result could also occur if an adept tester tested a large proportion of the more heavily exposed children, leading them to achieve higher scores than they would have if tested by other examiners.

The SCDS controlled for age by converting the raw test scores to age-corrected standard scores with conversion tables based on U.S. norms (NIEHS 1998). In contrast, the Faroe study analyzed the raw scores by adjusting statistically for the child's age (measured in days since birth). The latter approach is preferable for three reasons. First, the applicability of U.S. norms to these study populations is uncertain. Second, the use of age-corrected standard scores can reduce the sensitivity of the test, because several adjacent raw scores are treated as equivalent in converting to standard scores. Moreover, because age-corrected standard scores use 3-month intervals, for the purposes of conversion of raw to standard scores, a child whose age is 4 years, 3 months, and 31 days is considered to be the same age as a child who is 4 years, 0 months, and 1 day. However, that same child is considered to be different in age from a child who is only 1 day older (i.e., 4 years, 4 months, and 1 day). Finally, the Faroe approach of controlling statistically for age by multiple regression seems appropriate, because the effect of age is likely to be linear across the relatively short age period (3 months in both studies). Although it seems unlikely that the difference in approach to controlling for age could account for the discrepancies in the findings of those two studies, it would be of interest to see a re-analysis of the SCDS data using the approach that was used in the Faroe study.

There appears to have been no need to control for PCB exposure in the Seychelles, because PCB body burdens in that population are exceptionally low. In contrast to North America and Europe, where these contaminants are routinely detected in serum samples, 28 samples obtained from Seychelles study children showed no detectable concentrations of any PCB congeners. In the Faroe study, prenatal PCB exposure was measured in umbilical cord tissue rather than cord blood or maternal blood or milk, as in most previous studies, and specimens were

obtained for only half the newborns. Cord-tissue PCB concentration has never been validated in relation to blood or milk concentration, and because cord tissue is lean, it might provide a less reliable indication of total PCB body burden. Although PCBs are measured most accurately on a lipid-adjusted basis in most tissue, the wet-weight measure used in the Faroes was probably more valid for cord tissues, because the gravimetric approach used to measure fat content is not sufficiently reliable in a lean medium.

With respect to confounding by PCBs, prenatal PCB exposure was associated with four of the eight outcomes whose relation to cord Hg concentration was statistically significant. Those outcomes related primarily to verbal and memory performance, domains found in previous studies to be associated with prenatal PCB exposure (Jacobson and Jacobson 1996; Patandin et al. 1999). When PCBs and Hg were included together in the model, one outcome — continuous performance test (CPT) reaction time — was independently related to Hg exposure (Grandjean et al. 1997, Table 5). For the other three outcomes, however, the associations with both PCB and Hg fell short of conventional levels of statistical significance. One likely explanation is that both of those contaminants adversely affect those outcomes, but their relative contributions cannot be determined given their co-occurrence in the Faroe population (r = 0.41). It is unfortunate that cord specimens were not obtained from a greater proportion of the children.

In a second set of analyses (Budtz-Jørgensen et al. 1999), potential confounding by prenatal PCB exposure was reduced by dividing the sample into tertiles in terms of the infants' cord PCB concentrations. Regressions assessing the associations between Hg exposure and the five principal 7-year outcomes were then run separately for each of the groups. The regression coefficients for Hg in the lowest PCB tertile were no weaker than those among the infants exposed to moderate or heavy PCB doses, lending additional support to the conclusion that the associations between Hg and these outcomes are not attributable to confounding by prenatal PCB exposure.

POPULATION DIFFERENCES IN VULNERABILITY

Vulnerability to prenatal Hg exposure might be enhanced or attenu

ated by differences in genetic susceptibility, diet, or exposure to other contaminants. The SCDS cohort is predominantly African in descent; the Faroe cohort is Caucasian. Moreover, the Faroe population is thought to be descendant from a small number of "founders," which could increase genetic vulnerability to toxic insult. Although racial differences in vulnerability are possible, it should be noted that such differences have not been seen for environmental exposure to lead, which has been studied in racially diverse samples. Moreover, evidence of MeHg neurotoxicity was found in the genetically heterogeneous and racially diverse sample assessed in New Zealand, a sample that was predominantly non-Caucasian.

In principle, poor nutrition might also make a population particularly vulnerable to teratogenic insult. However, the data on birth weight and gestation length in the Faroe and Seychelles studies suggest that energy and macronutrient (protein and carbohydrate) deficiency is unlikely. Nevertheless, micronutrient deficiency in association with low intakes of fortified or unrefined grains or fruits and vegetables is possible. It is also possible that children in one or both samples might have been weaned to breast-milk substitutes or milks of other species that provide inadequate amounts of iron, other minerals, or vitamins. Conversely, certain nutrients found in fish eaten by the Seychelles residents (e.g., omega-3 fatty acids and selenium) could attenuate adverse effects of Hg exposure. The general health status of a population might also enhance or attenuate vulnerability to teratogenic exposure. Because the Faroe and Seychelles populations apparently both receive excellent health care, however, health status seems unlikely to explain the differences in the study findings.

As stated above, one substantial difference between the Faroe and the Seychelles populations relates to their PCB exposure. Whereas PCB concentrations in the Seychelles population are among the lowest observed anywhere in the world, the portion of the Faroe population that eats whale blubber accumulates unusually high PCB body burdens. Although it is conceivable that PCB exposure in the Faroe Islands might enhance fetal vulnerability to Hg, that hypothesis is speculative at present; experimental animal studies would be needed to test its plausibility. The possibility of effect modification by PCB exposure was examined in regression analyses that, in addition to confounders, also included the Hg and PCB exposure variables and their product (Hg ×

PCBs; Budtz-Jørgensen et al. 1999). All five *p*-values for the Hg × PCBs interaction terms exceeded 0.20, suggesting an absence of potentiation of the effects of one of the contaminants by the other. Thus, it seems unlikely that differences in vulnerability due to PCB exposure can explain the differences between the Faroe Islands and the Seychelles findings.

The sample in the main Seychelles study appears to have been developmentally robust. There was an exceptionally low number of abnormal scores on the Denver Developmental Screening Test, an unusually high mean Psychomotor Development Index score, and a very low rate of referral for mental retardation. On the other hand, the means and standard deviations of the cognitive measures administered at later ages were similar to U.S. norms. It is unclear to what extent the developmental robustness of that particular sample might have buffered it from any adverse effects of prenatal Hg exposure.

RANDOM VARIATION IN THE DETECTABILITY OF EFFECTS AT LOW EXPOSURES

The magnitude of the associations found in the MeHg studies resembles that reported with respect to other environmental contaminants, such as low-dose lead and PCBs. When the magnitude of an association is subtle, it is not surprising that it is not detected in every cohort studied. With respect to lead exposure, a strong scientific consensus has developed that blood lead concentrations in excess of 10 µg/dL place a child at increased risk of poor developmental outcomes. However, not all lead studies have found an association, and substantial variability exists in the magnitudes of the reported effects (Bellinger 1995). If two studies from the lead literature were chosen randomly, it is likely that the results of the two would not be entirely concordant. The uncertainties inherent in such studies (e.g., the assessment of exposure histories, the measurement of critical population characteristics, the idiosyncratic pattern of potential confounding factors, and the measurement of neurodevelopmental outcomes) render it likely that evidence of neurotoxicity will not be detected in some of the study cohorts assessed. With respect to the SCDS, the evidence consistent with such effects found in the pilot phase, coupled with the suggestion of unusual devel

opmental robustness in the main study, suggest that the failure to detect apparent adverse effects in the main study could be due to the substantial sample-to-sample variation expected when trying to identify weak associations in an inherently "noisy" system of complex, multi-determined neurobehavioral end points.

Given the large sample size in the main Seychelles cohort, it might seem surprising that that study could lack the power needed to detect an association between increased MeHg exposure and neurobehavioral impairments. However, power analyses that are based on total sample size can be misleading if adverse effects occur primarily among the most heavily exposed children, who typically comprise a very small proportion of the sample. Although the sample size of 700 children in the SCDS would seem to be more than adequate, only about 35 children were exposed at 15 μg/g or higher. Because multiple regression analysis examines associations that are averaged across the entire distribution of exposure, associations that hold only for the most highly exposed children can be difficult to detect. Thus, if adverse effects of prenatal MeHg exposure occur primarily in the upper range, the power to detect them will be limited, and it would not be surprising if associations found in one Seychelles cohort (the pilot study) were not detected in the next cohort (the main study) (see Chapter 7 for further discussion on the issue of statistical power).

CONCLUSIONS

- Three well-designed, prospective, longitudinal studies have examined the relation of prenatal MeHg exposure to neuropsychological function in childhood. MeHg was associated with poorer performance in the Faroe Islands study but not in the SCDS. Little attention has been paid to the New Zealand study because, until recently, it had not been subjected to peer review. Differences in the primary biomarker of Hg exposure (cord blood versus maternal hair), type of neuropsychological tests administered (domain specific versus global), age of testing (7 versus 5.5 years), and sources of exposure (whale meat versus fish) between the Faroe study and the SCDS have been suggested to account for the differences in the findings of the two studies. When the New Zealand

data are considered, however, those differences no longer seem determinative, because the New Zealand study, in which the exposure and research design were very similar to the SCDS, also found associations between higher MeHg levels and worse neurobehavioral test scores, as did the pilot SCDS.

- There is no empirical evidence or hypothesized mechanism to support the suggestion that PCB exposure might enhance vulnerability to MeHg. The lack of any evidence of statistical interaction between Hg and PCB exposure in the Faroes data also makes it unlikely that a difference in PCB exposure can explain the differences between the Faroe Islands and the Seychelles findings.
- The lack of statistical control for examiner in the SCDS, population differences in susceptibility among the study populations, and dietary factors might explain some of the differences among the study findings.
- It is possible that the differences are primarily due to between-sample variability in the expression of neurotoxicity at low doses. Even large sample studies can lack adequate power to detect adverse associations if a relatively small number of children are exposed in the upper ranges of the exposure distributions, where the adverse effects are most likely to be found.
- Although none of the between-study differences noted above appears to be determinative, the combined influence of two or more of these factors is difficult to predict. For example, it is possible that slightly reduced vulnerability in the Seychelles population combined with the use in that study of a biomarker of exposure that averages across pregnancy could make it difficult to detect neurocognitive effects that might be specific to third trimester exposure.
- When the two studies reporting associations between MeHg and neurobehavior are compared, the strengths of the New Zealand study include an ethnically heterogeneous sample and the use of developmental end points with greater predictive validity. The advantages of the Faroe study include a larger sample size, the use of two different biomarkers of exposure, and extensive scrutiny in the epidemiological literature. The Faroe data have also undergone extensive re-analyses in response to questions raised by panelists in the NIEHS (1998) workshop and by this committee in the course of its deliberations.

RECOMMENDATIONS

- It would be helpful to obtain more comprehensive nutritional data from all three populations as well as single-strand hair analyses to address more effectively the issue of spiking or bolus dose. A reanalysis of the 5.5-year SCDS data controlling statistically for examiner might also be useful.
- Most of the MeHg exposure standards currently in effect are based on extrapolations from the Iraqi MeHg poisoning episode, in which exposure was due to the consumption of highly contaminated grain and resulted in body burdens that greatly exceeded those found in the general population of fish consumers. Given the availability of data from three well-designed epidemiological studies in which prenatal MeHg exposures were in the range of general-population exposures, exposure standards should be based on data from these newer studies.

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7

DOSE-RESPONSE ASSESSMENT

THIS chapter focuses on dose-response analysis and its role in choosing a point of departure to be used in the risk assessment for MeHg. The chapter begins with a brief review of risk assessment for noncancer end points. Problems with the traditional approach that is based on no-observed-effect levels (NOAELs) will be discussed, along with advantages of more recent approaches that are based on dose-response modeling and benchmark-dose calculations. The chapter then reviews some of the specific challenges that arise when considering benchmark-dose calculations for MeHg. Foremost among these challenges is the fact that three studies of similar quality yield different results regarding the association between low-level exposures to MeHg and adverse developmental outcomes. After exploring the possibility that differences in power might explain some of this discrepancy, the committee presents and discusses several approaches that could be used to provide a benchmark dose based on data from the three studies. Among the methods considered are traditional approaches based on selecting a single outcome from a single study and an integrative analysis that combines information from different studies and outcomes. Results are found to be sensitive to model choice and recommendations are made for model choice.

RISK ASSESSMENT FOR NONCANCER END POINTS

Quantitative risk assessment for noncancer effects is commonly based

on determination of a NOAEL from a controlled study in animals. In this context, the NOAEL is defined as the highest experimental dose that does not produce a statistically or biologically significant increase in adverse effects over those of controls. An "acceptably safe" daily dose for humans is then derived by dividing the NOAEL by a safety factor, usually 10 to 1,000, to account for sensitive subgroups of the population, data insufficiency, and extrapolation from animals to humans. The U.S. Environmental Protection Agency (EPA) refers to the resulting quantity as the reference dose (RfD), the Food and Drug Administration (FDA) uses the term allowable daily intake (ADI) and the Agency for Toxic Substances and Disease Registry (ATSDR) uses minimum risk level (MRL). The concept is also similar to the upper limits (ULs) recently introduced by the National Academy of Sciences for nutrient recommendations. In the event that the lowest experimental dose shows a significant difference from the control, it is termed a LOAEL (lowest-observed-adverse-effect level), and an extra factor of 10 is used in the determination of the RfD, ADI, or MRL (see, for example, EPA 1998). Various reports have provided RfDs for MeHg that are derived from animal studies (Rice 1992; Gilbert et al. 1993; Zelikoff et al. 1995; Rice 1996). Typically, these calculations have used the results from a series of nonhuman primate studies, which indicate that adverse developmental effects in several outcomes occur at 50 μg/kg per day maternal dose. Uncertainty factors of 10 were used for LOAEL to NOAEL, species differences, and individual variation in response for an RfD of 0.05 μg/kg per day.

In recent years, use of the NOAEL has become controversial among risk assessors and regulators because of several serious statistical drawbacks (Gaylor 1983; Crump 1984; Kimmel and Gaylor 1988; Kimmel 1990; Leisenring and Ryan 1992). For instance, because the NOAEL must, by definition, correspond to one of the experimental doses, it can vary considerably across different experiments, yet this statistical variation is usually ignored when computing RfD values. Furthermore, estimation of the NOAEL is sensitive to sample size: because the NOAEL is based on statistical comparisons between exposed and unexposed dose groups, larger studies have higher power to detect small changes and therefore tend to produce lower NOAELs. In contrast, smaller studies tend to yield higher NOAELs due to their lower power to detect real effects. Because NOAEL calculations are traditionally based on pairwise comparisons of exposed groups and controls, there is

no widely accepted procedure for calculating a NOAEL in settings where exposure is measured on a relatively continuous scale. Indeed, the current definition of NOAEL involves an implicit assumption that the dose levels are grouped in some way. Grouping is common in the context of controlled animal studies, but most epidemiological studies, including the available MeHg studies, measure exposure on a continuous scale.

Problems with the NOAEL and LOAEL approach have led to increasing interest in the development of alternative approaches based on dose-response modeling techniques. The benchmark dose was defined by Crump (1984) as a lower 95% confidence limit on the dose corresponding to a moderate increase (e.g., 1%, 5%, or 10%) over the background rate. Because the benchmark dose generally occurs within the range of experimental data, Crump and others have argued that its estimation is relatively robust to model choice. In an extensive empirical comparison of NOAEL and benchmark-dose calculations, Allen et al. (1994) found that the NOAEL in a typically sized developmental toxicity study was, on average, 6 times larger than the BMDL corresponding to a 5% risk. The NOAEL was higher than even a 10% BMD, on average, by a factor of 3. Leisenring and Ryan (1992) came to somewhat similar conclusions based on analytical considerations. Crump (1984) used the abbreviation BMD to refer to the benchmark dose. Other authors, including Crump (1995), use BMD to denote the estimated dose that corresponds to a specified risk above the background risk and BMDL to denote the corresponding lower limit. This latter notation has become standard usage now and will be used throughout the remainder of this chapter.

BENCHMARK-DOSE CALCULATIONS FOR CONTINUOUS OUTCOMES

Benchmark-dose calculations for quantitative outcomes (e.g., birth weight or IQ) are more complicated than those for quantal responses, such as presence or absence of a defect. Although Crump (1984) discussed how to calculate a BMD for a quantitative outcome, Gaylor and Slikker (1992) were the first to develop the approach in any detail. Their first step is to fit a regression model characterizing the mean of the outcome of interest as a function of dose and assuming that the data are normally distributed. The next step is to specify a cutoff to define values

for which the outcome can be considered abnormal. For example, a weight lower than 0.8 g might be considered abnormal for a teratology study in mice. Using the fitted model, one then calculates the dose-specific probability of falling into the abnormal region. The BMD is estimated as the dose corresponding to a specified increase in that probability, compared with the background probability. The BMDL is the corresponding 95% lower limit on that dose. Figure 7-1 illustrates the ideas behind the approach. The curve in the top panel represents the distribution of IQs in an unexposed population, and the curve in the lower panel has been shifted to the left in response to an exposure. Note that the mean IQ in the unexposed population is 100, and the standard deviation (SD) is 15. The shaded areas in the left tails of each distribution represent the proportion of the exposed and unexposed populations that fall below a specified cutoff point (we will refer to cutoff point as C), designated as the IQ level that indicates an adverse response. In Figure 7-1, we have used a value of C = 75, which represents the lower 5% of the control population. From the figure, it is easy to see that the further left we move the curve corresponding to the exposed group, the higher the percentage of the exposed population that falls below the cutoff point. Gaylor and Slikker's suggestion simply involves finding the exposure level that leads to a specific increase in the proportion of the population falling below the cutoff point. To be more precise, let Y_i represent the outcome for the ith study subject, and suppose that a lowered outcome is considered to be adverse (e.g., as for IQ). Then, let P_0 denote the probability that an unexposed individual falls below the value (C) that defines an adverse effect. The BMD is then defined as the dose, x, such that

$$\Pr(Y < C \mid \text{dose} = x) - P_0 = \text{BMR},$$

where BMR denotes the “benchmark response” and refers to a specific risk increase above background risk. As in the quantal-response setting, BMR values of 0.1, 0.05, or possibly 0.01 are generally chosen. Later in the chapter, the committee focuses mostly on the case where $P_0 = 0.05$ BMR = 10% of the children experiencing an adverse effect. Thus, these choices of P_0 and BMR will result in a BMD that represents a doubling of the proportion of the population that falls into the adverse effect

region. Two broad approaches are available for BMD calculations that are based on continuous outcomes. As described above, one option is to fix P_0 at a specified percentile of performance in the unexposed population (e.g., 0.05 or 0.10). Assuming that the data follow a linear model ($Y_i = a_0 + a_1X_i + \varepsilon_i$, where X_i represents the exposure level for the ith subject, a_0 and a_1 are unknown regression coefficients, and ε_i is random error, assumed to be normally distributed with variance σ_2), specifying a fixed P_0 is equivalent to setting the cutoff value at a specified number of SDs below the mean in the unexposed group:

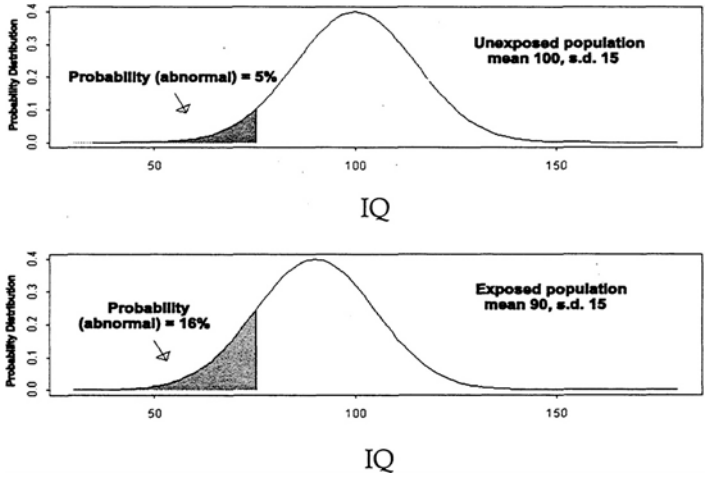

FIGURE 7-1 Hypothetical IQ distribution in an exposed and unexposed population.

$$C = a_0 + \sigma\Phi^{-1}(P_0),$$

where $\Phi(\times)$ represents the normal cumulative distribution function (i.e., the area under a standard normal curve up to and including the value $\times$). When $P_0 = 0.05$, for example, the value of C is $a_0 - 1.645\ \sigma$ (i.e., 1.64 SDs below the control mean). Alternatively, one can choose the cutoff

value directly on the basis of clinical considerations or other information. For example, it might be appropriate to define 2,500 g as the cutoff in an epidemiological study of birth weight. In that case, P_0 can be expressed as a function of C as follows:

$$P_0 = \Phi\left(\frac{C - a_0}{\sigma}\right).$$

As discussed by Crump et al. (1998), there are advantages to using the approach based on specifying a fixed P_0 (i.e., the first option), because the calculations simplify in this setting, particularly in the presence of covariates (see also E. Budtz-Jørgensen, Copenhagen University, N. Keiding, Copenhagen University, and P. Grandjean, University of Southern Denmark, unpublished material, May 5, 2000). Under the assumption that the error terms follow a normal distribution, it follows that the benchmark dose will be the solution, BMD, to

$$\Phi\left(\frac{C - a_0 - a_1 BMD}{\sigma}\right) = BMR + P_0,$$

which is

$$BMD = [\sigma\Phi^{-1}(P_0) - \sigma\Phi^{-1}(BMR + P_0)] / a_1. \qquad (7\text{-}1)$$

Notice that the estimated BMD simply corresponds to a constant divided by the dose-response slope from the regression model. That concept is important, because it provides some theoretical justification for some analyses (presented later) that are based on the inverse of the estimated benchmark doses from several MeHg studies.

Several authors have suggested variations on how to calculate BMDs for continuous outcomes. For example, Kodell and West (1993) and West and Kodell (1993) extended the Gaylor and Slikker approach to allow the model variance to depend on dose level (the calculations above assume a constant σ^2). Crump (1995) developed a more general approach that relaxed the normality assumption required by previous approaches. Bosch et al. (1996) proposed a nonparametric approach that

avoided the need for specifying a distribution altogether. In general, the different approaches are unlikely to yield dramatically different results when the data are approximately normally distributed with constant variance, which is the case in most of the MeHg epidemiological studies.

SOME SPECIFIC CONSIDERATIONS FOR MEHG

Aside from the general issues discussed above, several specific issues further complicate the application of benchmark-dose methods for MeHg. Foremost among these issues is the existence of three studies of comparable quality that lead to seemingly conflicting results in terms of the association between MeHg and adverse developmental or neurological outcomes. Previous chapters have discussed in-depth some of the possible explanations for this conflict (e.g., unmeasured confounders, co-exposures, and variations in population sensitivity). Another possibility is that the differences are due to random chance. Indeed, study results have been presented and summarized largely in terms of *p* values based on statistical tests of the association between exposure and outcome. Only recently have several papers focused on dose-response modeling and benchmark-dose calculations. When the focus is on statistical testing rather than modeling, it is common to encounter apparent contradictions, wherein one study will yield a statistically significant association at $p < 0.05$, and another one does not. To assess study concordance more fully, it is useful to consider the statistical power[1] that each has to detect effects of the magnitude observed.

For simplicity here, suppose that all confounders have already been accounted for, so that we can consider the power that a study will have to detect a true non-zero slope based on a simple linear regression ($Y_i = a_0 + a_1 X_i + \varepsilon_i$, where Y_i, X_i, a_0, a_1, and ε_i are as defined above). It is straightforward to compute the power to detect specific values of the dose-response parameter a_1, but comparing such calculations across studies is complicated, because the computed power depends on the distributions of exposure levels and outcomes within each study (see Zar

[1] Statistical power refers to the probability of correctly rejecting the null hypothesis of no association when, in fact, a true association exists (see Zar 1998).

1998). Cohen (1988, p. 75) argues that standardized regression coefficients provide a useful way to discuss power for the linear regression setting. The standardized regression coefficient corresponds to the raw slope (in our case, a_1) multiplied by the standard deviation of exposure and divided by the standard deviation of the error term. In the simple linear regression setting, the standardized regression coefficient corresponds precisely to the Pearson correlation between X and Y. Because the standardized regression coefficient is a unitless quantity, power calculations are simplified considerably and involve only sample size. According to Table 3.4 of Cohen (1988), the New Zealand study would have had high power (85% or greater) to detect correlations of approximately ± 0.2 or larger, and the Seychelles and the Faroe Islands studies would have had power to detect smaller correlations of approximately ±0.1 or more. Figure 7-2 graphs the power that each study would have had to detect various values of the standardized regression coefficients. The Faroe Islands study, being the largest study, has the highest power, and the New Zealand study has the lowest.

To further aid in interpreting the power calculations summarized in Figure 7-2, we have computed the standardized regression observed in the studies. Table 7-1 shows the standardized regression coefficients for the significant outcomes in the Faroe Islands and New Zealand studies. Five of the eight effects reported in the Faroe Islands study were very small, ranging from −0.05 to 0.08. The power to detect such small effects in the Seychelles study — even with a sample of 700 children — was only about 50% (see Figure 7-2). Thus, some of the inconsistency between the findings of the Faroe Islands and the Seychelles studies could be due to limited power to detect very small effects, even in these very large samples. On the other hand, these analyses cannot explain the failure of the main Seychelles study to detect the neuropsychological effects of the magnitude reported in the New Zealand study, because the Seychelles study should have had adequate power to detect those effects.

There is at least one important caveat to the power considerations discussed above. Standard power calculations for the linear model setting are based on the assumption of a true linear relationship between exposure and outcome. In a real world dose-response setting, such as encountered for MeHg, there is likely to be some nonlinearity. That means that the observed level of statistical significance in a study might depend less on the total sample size than on the spread of the exposure

levels and, in particular, on whether there are sufficient observations at high exposure levels to characterize the true shape of the dose response in that region. In fact, all three studies had fairly skewed exposure distributions, with a large number of subjects clustered at low exposure levels, along with a few subjects exposed at moderate to high levels. Such skewness in the observed exposure levels can be associated with other problems as well. For example, extreme observations have the potential to exert a strong influence on the results in such settings. Indeed, Crump et al. (1998) reported nonsignificant results from a regression analysis on all the children in the New Zealand cohort, but significant results after omission of a single child whose mother's hair Hg concentration was 86 ppm (4 times higher than that of the next highest exposure level in the study). We will see presently that dose-

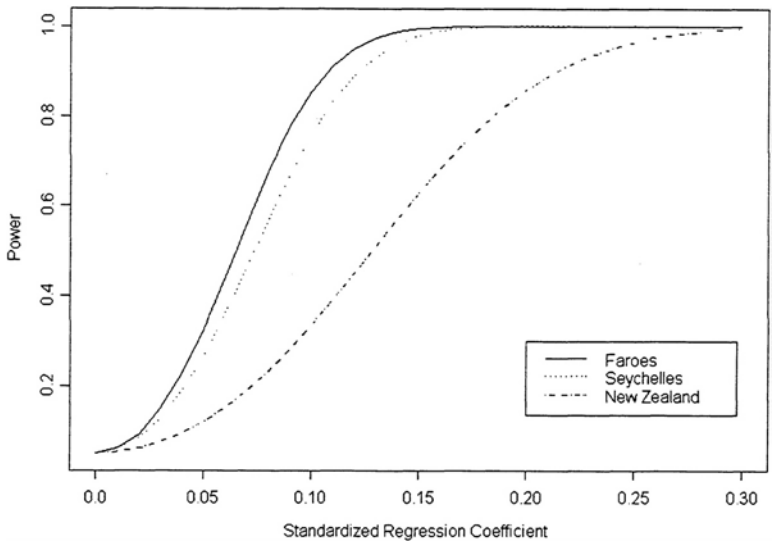

FIGURE 7-2 The power that each study has to detect a given standardized regression coefficient.

response estimates for the Faroe Islands study were also sensitive to omission of some of the observations with very high exposure levels.

TABLE 7-1 Estimates of Standardized Regression Coefficients Based on Reported Study Results

Study	Exposure SD	Outcome	Outcome SD	Raw Regression Coefficient	Standardized Regression Coefficient
Faroe Islands [a]	0.375	Finger Tapping	6.15	−1.1	−0.07
	CPT-Errors [b]	0.54	0.12	0.08	
		CPT-Reaction Time	80	40.3	0.18
		Digit Span	1.5	−.27	−0.06
		Boston Naming Test-no cues	5.3	−1.77	−0.12
		Boston Naming Test-cues	5.3	−1.91	−0.13
		CVLT-Short-term	3.1	−0.57	−0.06
		CVLT-Long-term	3.8	−0.55	−0.05
New Zealand [c]	3.31	TOLD-Language	16	−0.6	−0.12
	Development				
		WISC-R:PIQ	16	−0.54	−0.11
		WISC-R:FSIQ	16	−0.55	−0.11
		McCarthy Perceptual Performance	10	−0.53	−0.17
		McCarthy Motor Test [b]	0.15	−0.007	−0.15

[a]Exposures measured on the log-scale. Exposure SD and regression coefficients provided by study investigators (Grandjean et al. 1997). Outcome SDs estimated by dividing the interquartile range by 1.3.

[b]Log transformed.

[c]Data from Crump et al. 1998.

Abbreviations: CPT, Continuous Performance Test; CVLT, California Verbal Learning Test; TOLD, Test of Language Development; WISC-R:PIQ, Wechsler Intelligence Scale for Children-Revised Performance IQ; WISC-R:FSIQ, Wechsler Intelligence Scale for Children-Revised Full-Scale IQ.

COMPARING BENCHMARK DOSES

From a statistical perspective, reconciling differences among the various studies is more appropriately accomplished by a comparison of dose-response estimates (i.e., regression slopes) rather than *p* values resulting from the application of hypothesis tests. In this section, we present and compare benchmark-dose calculations from the New Zealand, Faroe Islands, and Seychelles studies. These have been reported individually for the New Zealand study by Crump et al. (1998) and also for the Seychelles study (Crump et al. 2000). BMDs for the Faroe Islands study have been calculated in a report prepared for EPA (Budtz-Jørgensen et al. 1999) and in an unpublished technical report (E. Budtz-Jørgensen, Copenhagen University, N. Keiding, Copenhagen University, and P. Grandjean, University of Southern Denmark, unpublished material, May 5, 2000), both of which were made available to the committee. The committee also requested and obtained some additional calculations to be discussed presently.

It might seem counterintuitive to present benchmark-dose calculations for the Seychelles study which did not show statistically significant associations between exposure and outcome. However, the idea makes more sense if we think of a benchmark dose as simply a transformation of the estimated dose response (as we saw in Eq. 7-1). Just as it can make sense to compare slope estimates from several studies, some of which are significantly different from zero and some of which are not, so can it make sense to compare benchmark doses. In the following example, we assume that lower values of the outcomes in question are adverse. Crump et al. (2000) argued that it is possible to calculate a BMDL even for studies where the estimated dose response goes in the ‘wrong' direction. In such settings, the estimated BMD will not even exist. That is, when the estimated regression line suggests a beneficial effect of exposure (as was the case for several outcomes in the Seychelles study), a linear regression model predicts that there will be no exposure level resulting in a 10% adverse response. However, even in such a setting, the BMDL will be finite so long as the estimated regression coefficient is not statistically significantly different from zero, so that its upper or lower confidence limit (depending on whether a larger or smaller response is considered adverse) still goes in the expected direction. Indeed, Crump et al. (2000) presented BMDLs for five outcomes

from the Seychelles study. An important caveat to this discussion is that BMDLs based on negative studies should be interpreted very cautiously. Although such calculations can be useful in a setting like ours where we are interested in comparing results over several MeHg studies, the committee advises that particular care be applied in using this approach in settings involving a single negative study as the basis for a risk assessment. Further research on this topic would be useful.

Crump et al. (1998) calculated BMDs for the New Zealand cohort at age 6, using the K-power model[2] and assuming $P_0 = 0.05$ and BMR = 0.10. Five outcomes were considered: TOLD Language Development, WISC-R Performance IQ, WISC-R Full-Scale IQ, McCarthy Perceptual Performance Scale, and McCarthy Motor Scale. It is important to note again that the results of the analysis reported here are based on omitting the highest exposed individual (86 ppm). A hair Hg concentration of 86 ppm is more than 4 times the next highest hair Hg concentration in the study. If the one-compartment pharmacokinetic model and EPA's standard default input assumption are used, it can be estimated that a 60-kg woman would have to eat an average of 0.5 pounds (227 g) of fish containing 2.2 ppm of Hg to reach a hair Hg concentration of 86 ppm. Consistent exposure at such a dose seems unlikely when the mean Hg concentration in fish from fish-and-chips shops, a principal source of exposure in New Zealand (Kjellström et al. 1986), is 0.72 ppm (Mitchell et al. 1982). On the basis of those considerations, the committee concluded that analyzing the New Zealand data without the data from that individual is appropriate.

Budtz-Jørgensen et al. (1999) presented BMDs and BMDLs for five outcomes measured in the Faroe Islands study: motor speed (finger tapping), attention (CPT reaction time), visuospatial performance (Bender), language (Boston Naming Test), and short-term memory (California Verbal Learning Test). The calculations for each outcome were done using the K-power model, as well as standard linear models applied to the untransformed exposure and square-root and log-transformed exposures. Calculations for the Faroe Islands study were per

[2]The K-power model assumes the following mean: $a_0 + a_1 x^k$, where K is a parameter to be estimated along with a_0 and a_1, thus allowing for a nonlinear dose-response relationship. The estimated value of K is typically constrained to be greater than or equal to 1.

formed for both maternal-hair and cord-blood Hg. Methods similar to those reported by Crump et al. (1998) were used, fixed P_0 values being 0.05 and 0.16 and excess risks (BMRs) being 5% and 10%. For comparability, the committee requested that the Crump analyses on the Seychelles and New Zealand data be expanded to include BMD and BMDL calculations for $P_0 = 0.05$ and 0.16 and for BMR = 0.05 and 0.10. The committee requested these analyses only for the outcomes measured when the children were 5 to 7 years old, because that age period was the only one available from the Faroe Islands study, and data from that age group have better predictive ability than data from earlier ages (E. Budtz-Jørgensen, Copenhagen University, N. Keiding, Copenhagen University, and P. Grandjean, University of Southern Denmark, unpublished material, May 5, 2000). For the Seychelles study, six 66-month end points were considered: Bender Gestalt errors, Child Behavior Checklist-Total, McCarthy-General Cognitive Index, Preschool Language-Total Score, Woodcock-Johnson Applied Problems, and Woodcock-Johnson Letter-Word recognition. For reasons to be discussed in more detail presently, the focus here is on calculations derived from the K-power model applied with $P_0 = 0.05$ and BMD = 0.05. The results of these analyses are summarized in Table 7-2 and graphically represented in Figure 7-3.

Table 7-2 and Figure 7-3 reveal some interesting patterns. First, we see that although study-to-study variability is substantial, within-study consistency (i.e., outcome to outcome) is relatively high. BMDs tended to be lowest for the New Zealand study. BMD and BMDL estimates for the Seychelles study tended to be either nonexistent or quite large (nonexistent values or values greater than 100 are indicated by asterisks in the table). Despite the substantial variability, however, the analyses yield a range of BMD values that are moderately consistent across the three studies. The next section discusses how those data might be used as the basis for a risk assessment.

CHOOSING A CRITICAL DOSE FOR A POINT OF DEPARTURE

An important step in the risk-assessment process is choosing an appropriate dose to be used as the "point of departure" (i.e., choosing the dose to which uncertainty factors will be applied to estimate an

RfD). In a traditional setting, NOAELs are computed for each end point in each study, and the point of departure would most likely be chosen to correspond to the highest observed NOAEL. In the present setting, however, where BMDs and BMDLs are calculated instead of NOAELs, the appropriate choice is not immediately clear. It is not necessarily

TABLE 7-2 Benchmark Dose Calculations (ppm MeHg in maternal hair) from Various Studies and for Various End Points

Study	End Point	BMD[a]	BMDL
Seychelles[b]	Bender Copying Errors	***[e]	25
	Child Behavior Checklist	21	17
	McCarthy General Cognitive	***	23
	Preschool Language Scale	***	23
	WJ Applied Problems	***	22
	WJ Letter/Word Recognition	***	22
Faroe Islands[c]	Finger Tapping	20	12
	CPT Reaction Time	17	10
	Bender Copying Errors	28	15
	Boston Naming Test	15	10
	CVLT: Delayed Recall	27	14
New Zealand[d]	TOLD Language Development	12	6
	WISC-R:PIQ	12	6
	WISC-R:FSIQ	13	6
	McCarthy Perceptual Performance	8	4
	McCarthy Motor Test	13	6

[a]BMDs are calculated from the K-power model under the assumption that 5% of the responses will be abnormal in unexposed subjects ($P_0 = 0.05$), assuming a 5% excess risk (BMR = 0.05).
[b]Data from Crump et al. 1998, 2000. "Extended" covariates.
[c]Data from Budtz-Jørgensen et al. 1999.
[d]Data from Crump et al. 1998, 2000.
[e] *** indicates value exceeds 100.
Abbreviations: WJ, Woodcock-Johnson Tests of Achievement; CPT, Continuous Performance Test; CVLT, California Verbal Learning Test; TOLD, Test of Language Development; WISC-R:PIQ, Wechsler Intelligence Scale for Children-Revised Performance IQ; WISC-R:FSIQ, Wechsler Intelligence Scale for Children-Revised Full-Scale IQ.

appropriate to choose the lowest BMDL as the point of departure because that could easily result in choosing an unreliable end point (i.e., one with great uncertainty). One suitable option might be to choose the BMDL corresponding to the end point with the lowest BMD, selected from among those end points that show a statistically significant effect of exposure. That would lead to choosing the BMD or BMDL based on McCarthy Perceptual Performance from the New Zealand study. The BMD for this end point estimated from the K-power model is 8 ppm; the corresponding BMDL is 4.

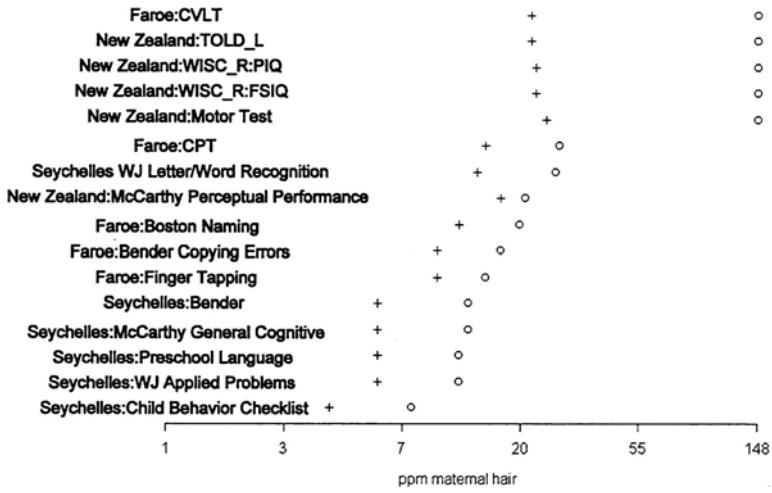

FIGURE 7-3 Benchmark dose (o) and lower 95% confidence limit on the benchmark dose (+): P_0 = BMR = 0.05, K-power model. Abbreviations: WJ, Woodcock-Johnson Tests of Achievement; CPT, Continuous Performance Test; CVLT, California Verbal Learning Test; TOLD, Test of Language Development; WISC-R:PIQ, Wechsler Intelligence Scale for Children-Revised Performance IQ; WISC-R:FSIQ, Wechsler Intelligence Scale for Children-Revised Full-Scale IQ.

The committee had some reservations about choosing the New Zealand study as the basis for risk assessment. First, it is a relatively small study, with only 237 children in contrast to over 700 studied in both the

Seychelles and the Faroe Islands studies. The original study results were not reported in the peer-reviewed literature but in a technical report to the Swedish Government. Although Crump et al. (2000) reported some statistical modeling of the data, the study has not been as comprehensively evaluated nor subject to the same level of scrutiny and re-analysis as the Seychelles and Faroe Islands studies.

The committee concluded that it would be inappropriate to pick the Seychelles study as the basis for risk assessment, given the available evidence for positive effects in the New Zealand and Faroe Islands studies, as well as in the Seychelles own pilot study. The committee felt that a good argument can be made for choosing the Faroe Islands study as the basis for the risk assessment. The Faroe Islands study is large (over 900 children) and measured two biomarkers of exposure. Moreover, it has been extensively analyzed and re-analyzed to explore the extent of confounding and the impact of outliers.

As discussed in Chapter 4, both hair and blood are reliable biomarkers for MeHg exposure. Given the lack of knowledge of differential effects of MeHg at different periods of gestation, there is currently no compelling reason to consider one biomarker of fetal exposure more appropriate than the other. Comparison of the analyses based on hair and cord blood in the Faroe Islands study suggests that the cord-blood measure explains more of the variability in more of the outcomes than hair Hg (see Table 6-1). On that basis, the committee recommends that cord blood be used as the biomaker for a risk assessment of the Faroe Islands data.

Table 7-3 shows the BMDs and BMDLs for the five principal Faroe Islands outcomes based on cord-blood measurements. Normally, the most sensitive adverse end point is selected as the basis for risk assessment. However, in the context of a neuropsychological test battery, the reliability of the individual end points can be highly variable. Therefore, it might not be appropriate in all cases to select the one most sensitive end point as a point of departure for the BMDS. In the Faroe Islands cord-blood analyses, the CPT reaction time measure had the smallest BMD and BMDL. However, because of difficulties in test administration, the data from the second half of the cohort were discarded for the analysis of this end point. Under the circumstances, the committee felt that it would be more appropriate to select the second most sensitive end point, the Boston Naming Test, for which no administration difficulties were encountered. It is noteworthy that the Boston Naming Test

was the most sensitive end point in the analyses based on maternal-hair Hg concentration.

TABLE 7-3 Benchmark Dose Calculations (ppb MeHg in cord blood) from the Faroe Islands Study for Various End Points

End Point	BMD[a]	BMDL
Finger Tapping	140	79
CPT Reaction Time	72	46
Bender Copying Errors	242	104
Boston Naming Test	85	58
CVLT: Delayed Recall	246	103

[a]BMDs are calculated from the K-power model under the assumption that 5% of the responses will be abnormal in unexposed subjects ($P_0 = 0.05$), assuming a 5% excess risk (BMR = 0.05).
Abbreviations: CPT, Continuous Performance Test; CVLT, California Verbal Learning Test.
Source: Budtz-Jørgensen et al. 1999.

The results of the Faroe Islands cord-blood Hg analysis for the Boston Naming Test provide a BMD of 85 ppb and a BMDL of 58 ppb. Corresponding values for hair Hg can be calculated by dividing the cord-blood concentration by a factor of 5 ppb of blood per ppm hair (Grandjean et al. 1992). Such a calculation results in a BMD of 17 ppm and a BMDL of 12 ppm for hair. It is interesting to note that those values are in fact quite close to the BMD and BMDL calculated for the Boston Naming Test based directly on the hair Hg concentration (i.e., BMD, 15 ppm; BMDL, 10 ppm).

Despite several strong arguments in favor of choosing a point of departure based on the Faroe Islands study, there was some concern that the estimated BMDs and corresponding BMDLs could be confounded by PCB exposure, which was not adjusted statistically in the benchmark analysis. To address this question, the committee requested that the Faroe Islands research group provide some additional calculations. Accordingly, Budtz-Jørgensen and colleagues[3] provided estimates of the

[3]E. Budtz-Jørgensen, Copenhagen University, N. Keiding, Copenhagen University, and P. Grandjean, University of Southern Denmark, unpublished material, June 7, 2000.

BMDs and BMDLs for four end points (Finger Tapping, CPT Reaction Time, Boston Naming, and CVLT Delayed Recall) based on (1) models that include log(PCB) as an additional covariate and (2) the subset of subjects in the lowest tertile of PCB exposures. Because PCBs were measured only for children examined in 1993, only about half of the full cohort (approximately 450 children) are used for analysis 1, and only one-sixth (approximately 150 Children) are used for analysis 2. Results were provided for Hg measured in both maternal hair and cord blood (see Table 7-4). The reduced sample sizes in these additional analyses increased the variability among the results. There was no clear pattern with respect to how the PCB-adjusted analyses differed from the original results.

Because of the potential for measurement error to cause additional bias with respect to estimating the Hg effects in the PCB-adjusted models, the committee gave greater weight to interpreting the results of analyses performed in the low PCB subset. Comparing the low PCB subset with the full cohort results, for example, the BMDs for Finger Tapping and CPT Reaction Time were 5-13 ppm lower for maternal hair and 19-99 ppb lower for cord blood, and the BMDs for Boston Naming and Delayed Recall were 5-6 ppm higher for maternal hair and 42-147 ppb higher for cord blood. Thus, the BMDs for the low-PCB-exposed subset for the two end points that were related to PCB exposure — Boston Naming and California Verbal Learning — did not differ from the BMDs for the total sample by any more than the BMDs for the two end points that did not relate to PCB exposure. It should also be noted that the variability seen in Table 7-4 is well within that expected by chance; note that, in all cases, the BMDs and BMDLs for both the PCB-adjusted and the low-PCB subset analyses lie well within the intervals defined by the BMDs and corresponding BMDLs derived for the full cohort. For example, the BMD for the Boston Naming Test based on cord blood in the full cohort (85 ppb) is smaller than the BMD based on the low PCB subset (127 ppb). In fact, the difference between the BMDs based on the full cohort and the low PCB subset is less than one standard error of the BMD based on the low PCB cohort. In weighing all these considerations, the committee concludes that results based on the full cohort provide a reliable basis for establishing a point of departure for a risk assessment for MeHg. Because cord blood explains more of the ob

served variability than Hg in maternal hair, the committee believes that it provides a more suitable biomarker for determining the point of departure.

TABLE 7-4 BMD (BMDL) Estimates from the Faroe Islands Study with and Without Adjustment for PCBs and in the Subset of Low PCB-Exposed Children (Results are reported separately for MeHg measured in hair and cord blood and are calculated using the K-power model.)

		Full Cohort	Adjusted for PCBs	Low PCB subset
Exposure	End Point	BMD (BMDL) [a]	BMD (BMDL)	BMD (BMDL)
Hair	Finger Tapping	20 (12)	17 (9)	7 (4)
	CPT Reaction Time	18 (10)	27 (11)	13 (5)
	Boston Naming Test	15 (10)	24 (10)	21 (6)
	CVLT: Delayed Recall	27 (14)	39 (12)	32 (7)
Cord Blood	Finger Tapping	140 (79)	149 (66)	41 (24)
	CPT Reaction Time	72 (46)	83 (49)	53 (28)
	Boston Naming Test	85 (58)	184 (71)	127 (40)
	CVLT: Delayed Recall	246 (103)	224 (78)	393 (52)

[a]BMDs are calculated under the assumption that 5% of the responses will be abnormal in unexposed subjects ($P_0 = 0.05$), assuming a 5% excess risk (BMR = 0.05).
Abbreviations: CPT, Continuous Performance Test; CVLT, California Verbal Learning Test.
Source: E. Budtz-Jørgensen, Copenhagen University, N. Keiding, Copenhagen University, and P. Grandjean, University of Southern Denmark, unpublished material, April 28, 2000.

AN INTEGRATIVE ANALYSIS

Although the committee felt comfortable with recommending that risk assessment be based on the Boston Naming Test from the Faroe Islands study, it also explored a weight-of-evidence approach based on an integrative analysis that allows a quantitative synthesis of informa

tion available across studies (see Hedges and Olkin 1985 for a more general discussion). Indeed, the recent draft EPA guidelines for carcinogen risk assessment suggest that such approaches can be useful in settings where it is difficult to chose a single study to serve as the basis for a risk assessment (EPA 1999). When well conducted, integrative analysis can provide valuable information to bolster or support a weight-of-evidence argument. Of course, synthesizing data across studies requires a careful statistical analysis that takes proper account of appropriate study-to-study and, in this case, outcome-to-outcome heterogeneity. One approach is to use a hierarchical random effects model. The committee conducted such an analysis using an extension of a method discussed by Dominici et al. (in press). Although the technical details can be complicated, the hierarchical modeling basically serves to smooth away some of the random variation that complicates the interpretation of the data presented in Table 7-2.[4] The approach also provides a way to quantify study-to-study and outcome-to-outcome variability. To motivate the approach, it is useful to consider the graphical presentation of our data in Figure 7-3. The Figure displays estimated BMDs and corresponding BMDLs for the outcomes listed in Table 7-2. Results are presented from the K-power model, the parameters P_0 and BMR both taking the value 0.05. The plot is organized in order of increasing BMD values. The circles indicate BMD and the crosses indicate BMDLs. To allow the eye to distinguish more easily between the values associated with the Faroe Islands and New Zealand studies, the plot is drawn on the log scale. As discussed earlier, several of the BMDs did not exist for the Seychelles study. The committee has arbitrarily assigned those a value of 150 for the purpose of plotting. The figure illustrates the large study-to-study variability relative to the outcome-to-outcome variability. The figure suggests that it might make sense to borrow strength from the different studies and outcomes to gain increased precision. That is what the hierarchical model achieves. The results allow us to do several things. First, we can obtain a revised, smooth estimate of the BMDs in each study. Table 7-5 provides these

[4]To handle nonexistent BMDs, the hierarchical model was applied to the inverse of the BMDs reported in Table 7-2. Nonexistent BMDs were assigned an inverse value of 0. See appendix for more detail.

TABLE 7-5 Results of Applying the Hierarchical Analysis to BMDs (ppm of MeHg in Hair) Calculated Using the K-power Model

		Original	Smoothed
Study	End Point	BMD (BMDL)[a]	BMD (BMDL)
Seychelles[b]	Bender Copying Errors	***[c] (25)	*** (26)
	McCarthy General Cognitive	*** (23)	*** (24)
	WJ Applied Problems	*** (22)	*** (24)
	Child Behavior Checklist	21 (17)	22 (18)
	Preschool Language Scale	*** (23)	*** (25)
	WJ Letter/Word Recognition	*** (22)	*** (24)
Faroe Islands[c]	Finger Tapping	20 (12)	20 (13)
	CPT Reaction Time	18 (10)	19 (12)
	Bender Copying Errors	28 (15)	24 (15)
	Boston Naming Test	15 (10)	17 (12)
	CVLT: Delayed Recall	27 (14)	24 (15)
New Zealand[d]	TOLD Language Development	12 (6)	13 (8)
	WISC-R:PIQ	12 (6)	13 (8)
	WISC-R:FSIQ	13 (6)	13 (8)
	McCarthy Perceived Performance	8 (4)	12 (7)
	McCarthy Motor Test	13 (6)	13 (8)

[a]BMDs are calculated under the assumption that 5% of the responses will be abnormal in unexposed subjects ($P_0 = 0.05$), assuming a 5% excess risk (BMR = 0.05).
[b]Data from Crump et al. (1998) and Crump et al. 2000. "Extended" covariates.
[c]Data from Budtz-Jørgensen et al. 1999.
[d]Data from Crump et al. 1998, 2000.
[e]*** indicates nonexistent values or values greater than 50.
Abbreviations: WJ, Woodcock-Johnson Tests of Achievement; CPT, Continuous Performance Test; CVLT, California Verbal Learning Test; TOLD, Test of Language Development; WISC-R:PIQ, Wechsler Intelligence Scale for Children-Revised Performance IQ; WISC-R:FSIQ, Wechsler Intelligence Scale for Children-Revised Full-Scale IQ.

smoothed BMDs along with corresponding BMDLs. For comparison, the original unsmoothed values are also included. Results are shown for the K-power model with $P_0 = 0.05$ and BMR = 0.05. Note that the effect of the hierarchical modeling is to smooth away much of the random variability observed in the original data. That is especially true of the more extreme values. Estimated BMDs are relatively unchanged for the Faroe Islands study, although even in that study, the outcome-to-outcome variability is reduced. Smoothing increases the BMDs slightly for the New Zealand study. BMDs for the Seychelles study remain high and most are still indicated with asterisks. Another interesting thing to notice from the table is that all the BMDLs tend to move closer to their respective BMDs. That is because the hierarchical model is able to reduce the variability inherent to each individual BMD estimate by drawing strength from the other end points. An important feature of the table is that although much of the outcome-to-outcome variability seems to be smoothed away through the hierarchical modeling, substantial study-to-study variability remains.

Although the hierarchical modeling provides a useful tool for separating random versus systematic variation and provides more stable estimates of study-specific and outcome-specific BMDs, the question remains regarding how the results might be used for risk assessment. There are several possible approaches. One would be to repeat the exercise described in the previous section, basing the risk assessment on either the Faroe Islands or the New Zealand studies but replacing the original BMD and BMDL estimates with the smoothed values from Table 7-5. The argument in favor of this approach is that it will have removed some of the bias associated with selecting an extreme value, and also it will have reduced some of the statistical variability. One could also argue for using the estimate of central tendency derived from the hierarchical modeling approach. The committee's analysis based on the K-power model suggests a mean BMD of 21 ppm, which coincidentally corresponds precisely to the mean of the smoothed BMDs from the Faroe Islands study. (The mean of the unsmoothed BMDs from the Faroe Islands study is 22 ppm). A third approach would be to produce a theoretical estimate of the BMDL on the basis of the lower 5th percentile point from the estimated distribution of BMDs obtained from the hierarchical modeling exercise. Applying this approach to the results for

the K-power model yields an estimate of 7 ppm. The various approaches discussed in this section are summarized in Table 7-6.

MODEL CHOICE ISSUES

As mentioned earlier, the calculations provided by the Faroe Islands research group to the EPA included BMD and BMDL calculations under square-root and log transformations as well as calculations for the K-power model (Budtz-Jørgensen et al. 1999). To enable a full comparison with the results of other studies, the committee requested that the Crump analyses be expanded to include results based on the square-root and log transformations for the New Zealand and Seychelles studies. At first inspection, the results were troubling. Although standard statistical assessments of model adequacy could not distinguish between models based on the K-power model applied to untransformed data, or linear models based on square-root or log dose, the corresponding BMDs and BMDLs differed fairly dramatically. In general, BMDs and BMDLs were lowest for the log model and highest for the linear model. Budtz-Jørgensen and colleagues provided some extended discussion on this issue in the context of the Faroe Islands study (E. Budtz-Jørgensen, Copenhagen University, N. Keiding, Copenhagen University, and P. Grandjean, University of Southern Denmark, unpublished material, May 5, 2000). Because of the profound importance of model choice on estimation of the BMD, the committee requested that the Faroe Islands research group[5] provide some additional calculations to aid the committee's deliberations. The committee wondered, for example, if the influence of a few highly exposed individuals on the estimated dose response might explain the large model-to-model variations. The Faroe Islands study research group conducted sensitivity analyses repeating the regression models after omitting some of the highest observations. The results suggested that the influence of the extreme observations did not explain the model-to-model variability.

[5]E. Budtz-Jørgensen, Copenhagen University, N. Keiding, Copenhagen University, and P. Grandjean, University of Southern Denmark, unpublished material, April 2000.

TABLE 7-6 Approaches to Benchmark Dose Calculation (ppm MeHg in Hair)

Approach	BMD	BMDL
Most sensitive end point from New Zealand	8	4
Median end point from New Zealand	12	6
Most sensitive end point from Faroe Islands study	15	10
Median end point from Faroe Islands study	20	12
Integrative analysis	21[a]	8[b]

[a]Logically equivalent to a BMD.
[b]Logically equivalent to a BMDL. Lower 5th percentile from the estimated distribution of BMDs.

After extensive discussion, the committee concluded that the most reliable and defensible results for the purpose of risk assessment are those based on the K-power model. The argument for this conclusion is as follows. In dose-response settings like those with MeHg, when there are no internal controls (i.e., no unexposed individuals) and where the dose response is relatively flat, the data will often be fit equally well by linear, square-root and log models. The models can yield very different results for BMD calculations, however, because these calculations necessitate extrapolating to estimate the mean response at zero exposure level. Both the square-root and the log models take on a supralinear shape at low doses, that is, they postulate a steeper slope at low doses. Thus, they tend to lead to lower estimates of the BMD than linear or K-power models. From a toxicological perspective, the K-power model has greater biological plausibility, because it allows for the dose response to take on a sublinear form, if appropriate. Sublinear models would be appropriate, for instance, in the presence of a threshold. The K-power model is typically fit under the constraint that $K \geq 1$, so that supralinear models are ruled out. Figure 7-4 contrasts several classes of dose-response models.

The model sensitivity described here might seem in conflict with the concept, put forward by Crump and others, that by estimating risks at moderate levels, such as 5% or 10%, the BMD should be relatively robust to model specification. As discussed by Budtz-Jørgensen and colleagues, key to understanding this apparent contradiction is that the Faroe Islands study does not include any true controls (i.e., subjects with

zero exposure) (E. Budtz-Jørgensen, Copenhagen University, N. Keiding, Copenhagen University, and P. Grandjean, University of Southern Denmark, unpublished material, May 5, 2000). The majority of exposures resulted in hair Hg concentrations that exceeded 5 ppm (24 ppb cord blood). The interquartile range for hair Hg concentration was 3 to 8 ppm (13 to 40 ppb for cord blood) (Grandjean et al. 1992). When models are fitted to the data, they are really capturing the shape of the dose response in this middle range of exposure, as illustrated in Figure 7-5. The figure shows dose-response curves fitted to hair Hg data for the

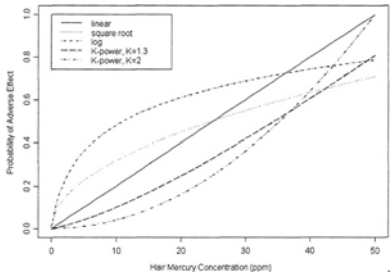

Figure 7-4 The estimated expected excess response due to Hg exposure as a function of the Hg concentration calculated using the linear, square root, and logarithmic (log) model. Source: E. Budtz-Jørgensen, Copenhagen University, N. Keiding, Copenhagen University, and P. Grandjean, University of Southern Denmark, unpublished material, May 5, 2000.

linear, square-root and log transformations. The data and fitted curves are plotted on the log scale, so that the fitted log model appears linear and the linear model shows the highest degree of curvature. What becomes clear from Figure 7-5 is that variations in estimated BMDs are not explained by differences in how well the models fit the bulk of the data but rather what the models predict for the mean response for *unexposed* individuals.

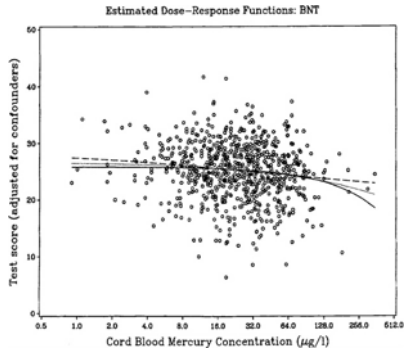

FIGURE 7-5 Dose-response curves fitted to cord-blood Hg data for the linear, square root, and log transformations. Source: E. Budtz-Jørgensen, University of Copenhagen, unpublished material, November 12, 1999.

Because the BMD estimation is based essentially on extrapolation to zero exposure from three models that fit equally well, the committee concludes that the choice regarding which model to use cannot be based on statistical grounds alone. Instead, a more biologically based argument is needed. One useful way to think of differences between the various models is that the linear model implicitly assumes an additive effect of Hg exposure, the log model assumes a multiplicative effect, and the square root lies somewhere in between. All three models fit essentially equally well to data that for the most part correspond to concentrations between 2 and 20 ppm in hair. However, the models differ fairly dramatically with regard to how they extrapolate to values below those levels. The linear model would predict that the change in mean outcome as MeHg concentration goes from 0 to 10 ppm in hair should be the same as the change observed in the mean outcome as concentration increases from 10 to 20 ppm. In contrast, the log-model would predict that the change in mean outcome associated with any doubling of MeHg concentration should be the same as the change observed in the mean outcome as concentration increases from 10 to 20 ppm. Thus, the log model would predict that the same magnitude change in outcome would be expected as the concentration goes from 1 to 2 ppm or from 4 to 8 ppm as that observed for the concentration going from 10 to 20 ppm — that is, the extrapolation down to zero exposure will predict a very steep slope at low doses. Given the relative absence of exposures at very low levels, a decision should be made on biological grounds regarding which model makes the most sense for risk assessment. The committee believes that an additive (linear) or perhaps sublinear model is the most justifiable from a biological perspective, thus ruling out square-root and log-transformed models. For MeHg, the committee believes that a good argument can be made for the use of a K-power model with K constrained to be greater than or equal to 1. That rules out square-root (K = 0.5) and log models (the limiting case as K approaches 0). More generally, the committee concludes that considerable caution should be used in fitting models based on log or square-root transformations of exposure, which might not be appropriate in dose-response settings, such as those for MeHg, where there are no internal controls and where the dose response is relatively flat. In such settings, linear models based on log- or square-root-transformed data are likely to yield

results very similar to those based on untransformed exposures. The supralinear shape of the log and square-root models at low doses will tend to result in smaller BMD estimates than those based on untransformed models.

SUMMARY AND CONCLUSIONS

- Benchmark-dose calculations are available for the Seychelles, New Zealand, and Faroe Islands studies. The calculations reveal fairly high within-study consistency (i.e., outcome to outcome) and high study-to-study variability.
- In general, risk assessments for various toxicants based on animal studies have used a BMR of 0.1, because it usually represents the low range of the observed exposure data. Crump et al. (2000) used a BMR of 0.1 (i.e., 10% of the population is at risk) in their analyses of the New Zealand and Seychelles studies. For the end points studied, the baseline rate in the population is 0.05 (P_0). Selection of a BMR of 0.1, therefore, could result in as much as a tripling of the percentage of the population falling into the abnormal range of neurological performance. The committee, to be more protective of public health, has used a P_0 of 0.05, a BMR of 0.05 (i.e., 5% of the population is at risk). Specification of P_0 in the context of the MeHg studies, however, is somewhat problematic because of the absence of subjects with true zero exposure. The mean response rate at zero is not actually based on observed data but is extrapolated from the fitted model. Because of that, extra caution is needed in choosing a dose-response model as the basis of a risk assessment. Choosing to have P_0 and BMR both equal to 0.05 could lead to a doubling of the proportion of the population falling into the abnormal range. The committee recognizes, however, that the choice of P_0 and the BMR is at the interface of science and policy and should be a science-informed policy judgment. That decision involves choosing a level of risk (i.e., 10%, 5%, or 1%) that is considered to be an "acceptable risk," similar to the choice of an acceptable risk for a carcinogen (i.e., 1×10^{-6} cases). That decision should be guided by the full body of evidence and based on the best available and most relevant data. In choosing the P_0 and the BMR for MeHg, it is

preferable that the range of MeHg concentrations and outcomes observed in the Faroe Islands study be considered.

- Basing the risk assessment on the single most sensitive end point from the most sensitive study would lead to the use of McCarthy Perceptual Performance Scale from the New Zealand study.
- The Faroe Islands study provides the strongest basis for choosing the critical dose for defining a point of departure. This large, high-quality study has been extensively analyzed and re-analyzed to explore the possibility of confounding, outliers, differential sensitivity, and other factors. The Boston Naming Test scores are the most sensitive, reliable end point.
- The potential for confounding by PCB exposure is of some concern for the Faroe Islands study. However, on the basis of a series of sensitivity analyses provided by the Faroe Islands research group, the committee concluded that the PCB exposures were unlikely to be causing serious bias in BMD estimates. Although BMD and BMDL estimates were available in the subset of low PCB exposed subjects, the committee decided to use the estimates based on the full cohort because the considerably larger sample size was felt to result in more reliable estimates.
- It would not be appropriate to base risk-assessment decisions on the Seychelles study because it did not find an association between MeHg and adverse neurodevelopment effects. That finding is not consistent with the weight of evidence demonstrating such an association in the Faroe Islands and New Zealand studies.
- A risk assessment could also be based on an integrative analysis that combines the results of all three studies. One advantage of this approach is that it increases the precision of critical-dose estimates. One could choose either a measure of central tendency (leading to a BMD of 21 ppm in hair) or a lower 5% limit based on the estimated theoretical distribution of benchmark doses (leading to an estimate of 7 ppm in hair). Because the integrative analysis is exploratory, it would be premature to use this approach as the basis for risk assessment for MeHg. However, the approach was useful for facilitating a weight-of-evidence assessment. Furthermore, it is reassuring that the results based on this approach are consistent with those based on the more classic approaches that select a single study.

- Model choice is an important source of uncertainty for the purpose of quantitative risk assessment. Changing the underlying modeling assumptions can have a dramatic effect on the estimated benchmark dose. The committee suggests that the K-power ($K \geq 1$) model results be used.
- Even when such modeling decisions have been made, benchmark-dose calculations require specification of the cutoff point used to define an adverse effect (P_0) and the risk level (BMR) of the benchmark dose. Those are, in part, policy decisions.
- The committee concludes that, given these considerations, the results from the Boston Naming Test in the Faroe Islands study should be used. For that end point, dose-response data based on Hg concentrations in cord blood should be modeled. For that data set, the K-power model ($K \geq 1$) is the model of choice. This analysis estimates a BMD of 85 ppb and a BMDL of 58 ppb. Using a conversion factor of 5 ppb of blood per ppm of hair, that point of departure approximately corresponds to a BMD based on a hair Hg concentration of 17 ppm and a BMDL of 12 ppm. Those values are very close to the values estimated directly from the analysis based on hair Hg concentrations.

RECOMMENDATIONS

- Until better statistical methods become available, risk assessment for MeHg should be based on benchmark dose calculations rather than NOAELs or LOAELs.
- Given the available data, risk assessment should be based on the Boston Naming Test from the Faroe Islands study using MeHg measured in cord blood.
- Despite some potential for PCB exposures to bias BMD estimates based on the Faroe Islands study, the committee recommends using estimates based on the full cohort and not adjusting for PCB exposure, mostly because the larger sample size is believed to result in more reliable estimates.
- Benchmark doses should be based on the K-power model with K constrained to take a value of 1 or greater.
- Because the integrative analysis is exploratory, it would be premature to recommend it for use now. However, the approach should

be considered in context of a weight-of-evidence argument. Further research on the use of integrative models for risk assessment would be useful.

- Further research is generally needed on statistical issues related to risk assessment that is based on epidemiological data. In particular, further research to develop more appropriate methods for handling model uncertainty (e.g., the Bayesian technique of *model averaging* (Carlin and Louis 1998)) would be useful. Further work is also needed to develop risk assessment methods for a setting like MeHg where the study population contains no true controls.

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8

RISK CHARACTERIZATION AND PUBLIC HEALTH IMPLICATIONS

THE purpose of this chapter is to present a summary of the findings of the committee concerning the health effects of methylmercury (MeHg), end points of toxicity, the critical studies, exposure and dose metrics, and sources of uncertainty that should be considered by EPA in deriving the reference dose (RfD). It includes a discussion of the relevant health end points and the scientific basis and public-health rationale for selecting neurotoxicity in children exposed in utero as the critical end point for the EPA RfD.

The committee was directed to investigate the toxicological effects of MeHg and to evaluate research relevant to EPA's MeHg RfD. The activities of the committee included the following:

1. An evaluation of the available human epidemiological and animal toxicity data.
2. An examination of the critical studies, end points of toxicity, and uncertainty factors used in the derivation of the RfD.
3. A review of exposure data from the available epidemiological studies focusing on consumption of MeHg in fish.
4. Consideration of new and emerging health-effects data.
5. Identification of knowledge gaps and recommendations for future research.

The committee evaluated the body of evidence that has provided the

scientific basis for the risk assessments conducted by EPA and other regulatory and health agencies. The committee also reviewed new findings that have emerged since the development of the current RfD and met with the investigators of major ongoing epidemiological studies to examine and compare the methods and results.

Mercury (Hg) is pervasive and persistent in the environment, released from a large variety of natural and anthropogenic sources. The serious health impacts of high-level exposures have long been recognized. Between 1950 and 1975, major poisoning episodes in Japan and Iraq resulted in outbreaks of serious neurotoxic effects, including death, and led to the identification of developmental neurotoxicity as the health effect of greatest concern following high-level episodic exposure. As a result of its well-recognized toxicity, widespread industrial use, and environmental persistence, Hg has been extensively studied. Compared with data bases on many other pollutants, there is a robust data base on Hg, which includes environmental fate and transport; examination of toxicokinetics and toxicodynamics; biological and environmental measures of exposure and dose; and in vitro, animal, and human studies for a broad range of toxicity end points.

Historically, epidemiological investigations have focused on high exposures and related health impacts. More recently, large prospective epidemiological studies have been conducted to examine chronic low-level MeHg exposure. These studies examined the association between subtle end points of neurotoxicity and prenatal exposure measured by maternal markers of prior exposure. These markers are presumed to reflect maternal MeHg exposure from fish consumption. The committee focused on these studies because they provide the most comprehensive evidence of low-dose MeHg toxicity and they examine the exposure pathway most relevant to U.S. population exposures, including the sensitive population of children who were exposed to MeHg in utero.

THE CURRENT EPA REFERENCE DOSE

EPA defines an RfD as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime (EPA 1997a). The

current EPA RfD for MeHg is 0.1 µg/kg-day. The RfD is an important risk-characterization tool that is broadly used as a measure of the "acceptability" of population exposure levels. It is used to guide risk-management decisions and regulatory policies ranging from fish-consumption advisories to air-emission permits. This section provides an overview of the development of the MeHg RfD.

Neurotoxicity in children exposed in utero is the health outcome selected by EPA for the current MeHg RfD. The RfD is based on data from the Iraqi poisoning episode, where the population consumed high levels of MeHg from treated seed grain. The critical study for the RfD conducted by Marsh et al. (1987) identified 81 children who had been in utero during the episode and examined their neurodevelopmental outcomes. Maternal-child pairs were selected from one of five Hg-hair-concentration groups, and the combined incidence of developmental effects (late walking, late talking, mental symptoms, seizures, or increased neurological score) was determined for each group. Exposure levels measured by maternal-hair concentration and combined developmental effects were used to estimate a benchmark dose. The benchmark dose of 11 ppm of Hg in hair was calculated as the 95% lower confidence limit on the maternal-hair concentration corresponding to a 10% extra risk level (Crump et al. 1995). In this report, the lower confidence limit is referred to as the BMDL. The following section describes how EPA derived the current RfD from that value.

A ratio of 250:1 was used to convert hair Hg concentration (mg of Hg/kg of hair) to blood Hg concentration (mg of Hg/L of blood) to derive the RfD critical dose (EPA 1997c):

11 mg/kg of hair would correspond to 11/250 = 44 µg/L of blood.

The following equation was used to obtain a daily dietary intake of MeHg that results in a blood Hg concentration of 44 µg/L:

$$d = \frac{C \times b \times V}{A \times f \times bw},$$

where

d = daily dietary intake (micrograms of MeHg per kilogram of body weight per day),

C = concentration in blood (44 µg/L),

b = elimination constant (0.014 days^{-1}),

V = volume of blood in the body (5 L),
A = absorption factor (expressed as a unitless decimal fraction of 0.95),
f = fraction of daily intake taken up by blood (unitless, 0.05), and
bw = body-weight default value of 60 kg for an adult female.

Using that equation, the total daily quantity of MeHg ingested by a 60-kg female to maintain a blood Hg concentration of 44 µg/L or a hair Hg concentration of 11 ppm would be

$$d = \frac{44\ \mu g/L \times 0.014\ days^{-1} \times 5\ L}{0.95 \times 0.05 \times 60\ kg}$$

$$d = 1.1\ \mu g/kg\text{-}day.$$

A composite uncertainty factor (UF) of 10 was used in the derivation of the RfD to account for human-population variability, lack of a two-generation reproductive study, and lack of data on sequelae resulting from longer durations of exposure (EPA 1997c):

$$RfD = \frac{BMDL}{UF}$$

$$= \frac{1.1\ \mu g/kg\text{-}day}{10}.$$

$$\text{Current RfD} = 0.1\ \mu g/kg\text{-}day.$$

As the calculation shows, the application of UFs has a major influence on the quantification of the final RfD. Although the scientific rationale for the application of these factors is strong, it must be recognized that choosing the ultimate magnitude of the UFs is a policy decision, which is influenced by professional judgment, public-health goals, and the regulatory mandates of EPA.

EVALUATING THE RFD–END POINTS OF MEHG TOXICITY

The committee reviewed human epidemiological results and animal

toxicity data to examine potential human health effects and evaluate the use of neurotoxicity in children exposed in utero as the health end point for the derivation of the RfD. Other end points evaluated are carcinogenicity and immunological, reproductive, renal, and cardiovascular toxicity. Chapter 5 presents an in-depth presentation of the health effects of MeHg. The following is a summary of major findings.

Carcinogenicity

Studies in humans of the carcinogenic effects of MeHg are inconclusive. Although no studies have found an association between MeHg and overall cancer death rates in humans, two studies (Kinjo et al. 1996; Janicki et al. 1987) have found associations between Hg exposure and acute leukemia. Interpretation of these findings is limited because of small study populations and lack of control for other risk factors. Renal tumors have been observed in male mice (Mitsumori et al. 1981; Hirano et al. 1986) but only at or above the maximum tolerated dose. Hg has also been shown to cause chromosomal damage and aneuploidy in a number of in vivo and in vitro systems. On the basis of the available human, animal, and in vitro data, the International Agency for Research on Cancer (IARC) and EPA have classified MeHg as a "possible" (EPA Class C) human carcinogen (EPA 2000).

Immunotoxicity

Occupational studies suggest that Hg exposure can affect the immune system in humans (Dantas and Queiroz 1997; Moszczynski et al. 1999). In vitro and animal studies have shown that Hg can be immunotoxic. They suggest that exposure to MeHg can increase human susceptibility to infectious diseases and autoimmune disorders by damaging the immune system (Ilbäck et at. 1996). Animal studies have also shown that prenatal and perinatal exposure to MeHg produce long-term effects on the developing immune system (Wild et al. 1997). Immunological studies in animals are summarized in Table 5-3.

Reproductive Effects

The reproductive effects of MeHg exposure have not been evaluated in humans. However, an evaluation of the clinical symptoms and outcomes of over 6,000 MeHg-exposed Iraqi citizens found a low rate of pregnancies (79% reduction) among the exposed population (Bakir et al. 1973). That provides suggestive evidence of an effect of MeHg on human fertility. Animal studies, including work in nonhuman primates, have found reproductive problems, including decreased conception rates, early fetal losses, and stillbirths (Burbacher et al. 1988).

Renal Toxicity

The kidney is sensitive to inorganic Hg exposure, and renal damage has been observed following human ingestion of organic forms of Hg. Renal effects from organic Hg exposure have been observed only at exposure levels that also cause neurological effects. Renal damage was observed in the victims of the Iraqi poisoning, and an evaluation of death rates in an area of Minamata City, which had the highest prevalence of Minamata disease, found an increase in deaths from renal disease among women but not men (Tamashiro et al. 1986). Several reports of animal studies have also described MeHg-induced renal toxicity.

Cardiovascular Effects

The cardiovascular system appears to be a target for MeHg toxicity in humans and animals. Blood-pressure elevations have been observed in occupationally exposed men (Höök et al. 1954) and in children treated with mercurous chloride for medical conditions. More recently, there is evidence that suggests effects at low levels of exposure. A recent study of 1,000 children from the Faroe Islands found a positive association between prenatal exposure to MeHg, and blood pressure and heart rate variability at age 7 (Sørensen et al. 1999). A Finnish cohort study of 1,833 men linked dietary intake of fish and Hg concentrations in hair

and urine with increased risk of acute myocardial infarction (AMI) and coronary heart disease and cardiovascular disease (Salonen et al. 1995). Men who consumed at least 30 g of fish a day had a 2.1 higher risk of AMI. Cardiovascular effects have also been observed in several animal models of MeHg toxicity.

Central-Nervous-System Toxicity

The toxic effects of MeHg in the brain have been well documented in human and animal studies. Although both the adult and fetal brains are susceptible, the developing nervous system is more sensitive to the toxic effects of MeHg than is the developed nervous system. It should be pointed out however, that few studies of MeHg effects in adults have investigated the sensitive and subtle types of neurologic endpoints recently examined in children exposed in utero. Studies of Minamata victims indicate that prenatal exposure caused diffuse damage in the brain and adult exposure caused focal lesions. About 10% of the total body burden of MeHg is found in the brain. After ingestion, MeHg accumulates in the brain where it is slowly converted to inorganic Hg. On the basis of available studies, neurodevelopmental effects appear to be a sensitive end point for MeHg toxicity. There is an extensive human data base on neurodevelopmental effects, including studies of populations following high-dose poisonings and chronic low-level Hg exposure. In general, experimental animal studies have reported a continuum of neurodevelopmental effects similar to those reported in studies of humans exposed to MeHg. Of the three major long-term prospective studies, the Faroe Islands study reported an effect of low-level prenatal exposure on children's performance on neurobehavioral tests particularly in the domains of attention, fine-motor function, confrontational naming, visual-spatial abilities, and verbal memory. Similar effects were not found in the main Seychelles study; however, the smaller New Zealand study found effects on standardized tests of cognitive and neuromotor function that were similar to those administered in the main Seychelles study, and there was preliminary evidence of similar effects in the Seychelles pilot study.

SELECTION OF THE END POINT FOR THE RFD

The findings of the committee regarding the end points of MeHg toxicity support the selection of neurotoxicity in children exposed in utero as a suitable end point for the development of the RfD based on the available data. These effects have been well documented in a number of investigations, including prospective epidemiological studies examining low-dose chronic exposure through consumption of contaminated fish and seafood. Evidence from animal studies is consistent with the neurotoxicity findings in humans.

Given the limits of the available data, developmental neurotoxicity is the most sensitive, well-documented health end point. Therefore, its use as the basis for the RfD should be protective for other adverse effects that occur at higher doses of exposure. However, there is emerging evidence of potential effects on both the immune and cardiovascular systems at low doses of exposure. Although these effects are not well understood, emerging data underscore the need for continued research and raise the possibility of adverse effects to other organ systems at or below the current levels of concern for developmental neurotoxicity.

EXAMINATION OF THE CRITICAL STUDIES FOR THE RFD

The traditional approach to development of an RfD and other public-health-based risk guidance numbers is to select a critical study that is well conducted and provides the most sensitive, or lowest, no-observed-adverse-effect level (NOAEL), lowest-observed-adverse-effect level (LOAEL), or a lower 95% confidence limit on the benchmark dose (BMDL). The relevance of the study exposure levels and pathways to the population of concern should also be considered.

The current EPA RfD is based on developmental neurotoxic effects in children exposed in utero to high-level episodic exposure from bread made with grain treated with MeHg as a pesticide (Marsh et al. 1987). Although that study was judged the most appropriate at the time of the development of the current RfD, a number of recognized sources of uncertainty, including possible selection bias in the cohort, cannot be controlled. In addition, the exposure scenario in Iraq is not comparable

to the low-level chronic exposure that the general population of North America might experience through the consumption of fish.

Since the establishment of the current RfD, results from the prospective studies in the Faroe Islands (Grandjean et al. 1997, 1998, 1999a) and the Seychelles (Davidson et al. 1995a,b, 1998), as well as a peer-reviewed re-analysis of the New Zealand study (Crump et al. 1998), have added substantially to the body of knowledge concerning the developmental neurotoxic effects of chronic low-level exposure to MeHg. Each of these studies was well designed and carefully conducted. They examined the relation of prenatal MeHg exposure to neuropsychological function in childhood. MeHg was significantly associated with poorer performance in the Faroe Islands and New Zealand studies, but not in the main Seychelles study.

Much of the debate over the adverse effects of MeHg and the selection of a critical study for the RfD and other guidance has focused on the similarities and differences between the Faroe Islands and the Seychelles studies. The levels of maternal exposure are similar in both studies, but a number of differences in design and cohort characteristics might contribute to the disparate findings. They used different primary biomarkers of Hg exposure (cord blood versus maternal hair), different types of neurological tests (domain specific versus global), and different ages at testing (7 years versus 5.5 years). In addition, the studies had different patterns of exposure (due to whale consumption in the Faroe Islands). When the New Zealand study is considered, those research design differences seem less determinative. In New Zealand, adverse effects were found with exposure measures and a research design similar to the Seychelles study. These studies are contrasted and discussed in detail in Chapter 6.

The Faroe Islands population was also exposed to PCBs. The initial statistical analyses published by the investigators of the Faroe Islands study suggest that the associations of prenatal exposure with language, memory, and verbal-learning deficits might be attributable to prenatal PCB exposure, although the associations with attention and neuromotor-function deficits were not. However, prenatal Hg exposure was associated with deficits in language development in the Seychelles pilot and New Zealand studies, in which there was no evidence of increased PCB exposure. A re-analysis of the Faroe Islands data showed that the association of Hg exposure with language and verbal deficits was as strong among children with low PCB exposure as among those with

high exposure. Furthermore, a series of sensitivity analyses provided by the Faroe Islands research group (E. Budtz-Jørgensen, Copenhagen University, N. Keiding, Copenhagen University, and P. Grandjean, University of Southern Denmark, unpublished material, June 21, 2000) indicated that the PCB exposures were unlikely to be causing serious bias in BMD estimates. On the basis of these considerations, the committee concluded that the neurodevelopmental sequelae found in the Faroe Islands study were not attributable to PCB exposure and that PCB exposure did not invalidate the use of the Faroe Islands study as the basis of risk assessment.

The committee explored the possibility that differences in power might explain the discrepancies in the findings of the major studies. Five of the eight effects observed in the Faroe Islands study were very small. Despite the large sample size of the Seychelles study, its power to detect such small effects was poor. The Seychelles study had adequate power to detect the effects seen in the New Zealand study; therefore, such power considerations cannot fully explain its failure to detect any adverse effects at 5.5 years of age.

Despite their differences, the Faroe Islands, Seychelles, and New Zealand studies represent exposure scenarios that are more consistent than the Iraqi study with the North American experience. However, their conflicting results present a vexing choice for the development of a revised RfD. A conservative approach would be to derive as a point of departure the lowest BMD from the positive end points in the Faroe Islands study or the New Zealand study. It is possible to derive a lower limit approximation of a NOAEL or BMD from the Seychelles results, as was done by the Agency for Toxic Substances and Disease Registry for its minimal risk level (MRL). However, the choice of a negative study to derive guidance numbers when well-designed, plausible positive studies are available is difficult to defend. The committee recommends a more inclusive approach to developing any future RfD or exposure guidance. Given the availability of well-designed epidemiological studies in which prenatal MeHg levels were within the range of general-population exposures, contemporary exposure standards should consider the findings of all three studies — the New Zealand, Faroe Islands, and Seychelles studies.

To synthesize information from the different studies and outcomes, the committee conducted an integrative analysis to derive and compare estimates of BMDLs. This analysis is described in Chapter 7. The

committee debated whether to include the Seychelles study in the BMD evaluation. It concluded that it would be inappropriate to exclude the data from any well-designed study and that the inclusion of the Seychelles study was important to ensure that the analysis would reflect the full range of effects of MeHg exposure.

BMD CONSIDERATIONS: SELECTING A POINT OF DEPARTURE

The current MeHg RfD is based on a BMD estimation. The selection of a particular BMD for the derivation of the RfD represents a critical decision, influenced by both scientific and policy considerations. The BMDL is defined as a lower confidence limit on the dose corresponding to a given increase in response (e.g., 1%, 5%, or 10%) over the background rate (Crump 1984), the benchmark response (BMR). It is intended to be applied as an alternative to the NOAEL to provide a point of departure for low-dose extrapolation. The BMD represents a refinement over the traditional NOAEL or LOAEL, since it is not constrained to be one of the observed or experimental doses, and uses the full-range of dose-response information inherent in the data. Various terms are used for BMD estimates. In this report, the term BMDL denotes the lower confidence limit on the dose corresponding to the BMR of interest, and BMD is used to denote the point estimate of the dose.

The critical studies of MeHg examined a range of neurodevelopmental outcomes. Selection of the most appropriate BMD requires consideration of the biological significance of the effects, including the sensitivity and severity of the outcomes, consideration of the ability to detect both exposure and effects, and selection of an appropriate dose-response model. To examine and compare the results of the critical studies, BMD calculations were conducted and compared for various end points. These results are presented and discussed in detail in Chapter 7.

Various analyses were conducted as part of the committee's consideration of the overall weight of the evidence of developmental neurotoxic effects from low-level MeHg exposure. It is intended as a bounding exercise to evaluate and present the range of effects, BMDs, and BMDLs for each of the major epidemiological studies. The results provide a range of BMDLs, which should be considered in selecting the critical

BMD for development of a revised RfD. The methods considered included (1) approaches based on selecting a single outcome from a single study, and (2) an integrative analysis that synthesizes information over different studies and outcomes. Because the integrative analysis is exploratory, it would be premature to use this approach as the basis for risk assessment for MeHg. However, the approach was useful for facilitating a weight-of-evidence assessment.

The BMDLs derived from the various end points of the critical studies (with a P_0 of 0.05, where P_0 denotes the probability that an unexposed individual falls below the cutoff value that defines an adverse effect, and a BMR of 0.05) range from 4 (New Zealand McCarthy Perceptual Performance Test) to 23 (Seychelles Preschool Language Scale Test) in parts per million (ppm) Hg in maternal hair. It should be noted that the choice of P_0 and the BMR are, in part, policy decisions. The full range of findings is presented in Table 7-2. Table 8-1 lists the BMDLs derived using the K-power model from Table 7-2. The K-power model was suggested because from a toxicological perspective, it has greater biological plausibility, since it allows the dose response to take on a sublinear form, if appropriate. The K-power model is typically fit under the constraint that $K \geq 1$, so that supralinear models are ruled out. As shown in Table 8-1, the data suggest fairly high within-study consistency but high study-to-study variability. However, the ratio between the highest and lowest BMDLs was only 6.

The integrative analysis used a hierarchical model to quantify study-to-study and outcome-to-outcome variability, while smoothing away much of the random variability observed in the original data. Smoothed estimates of the BMDs and BMDL for each study were derived (with a P_0 of 0.05 and a BMR of 0.05), and the distribution was examined. Outcome-to-outcome variability is reduced, but substantial study-to-study variability remains. The smoothed mean of the distribution of the various BMDs is 21 ppm, with a lower 5th percentile of 7 ppm.

The mean of the distribution is in close agreement with the unsmoothed mean of the BMDs from the Faroe Islands study (22 ppm). The integrative analysis does not permit the direct calculation of a BMDL. However, the lower 5th percentile of the theoretical distribution of true BMD values is analogous to a BMDL; that value is 8 ppm.

The examination of the BMDs suggests a number of ways to select a point of departure for the derivation of the RfD. The most sensitive end

point from the most sensitive study is the McCarthy Perceptual Performance from New Zealand (BMD, 8 ppm; BMDL, 4 ppm). The Faroe Islands study represents the central tendency of the three studies, and a central BMD from this study could provide a reasonable point of departure (median BMDL value, 12 ppm). The central tendency of the

TABLE 8-1 BMDLs for Study End Points (ppm Hg in maternal hair, BMR = 0.05)

BMDL (K power)	Study	Age	End Point
Seychelles[a]	66 months	Bender Copying Errors	25
		Child Behavior Checklist	17
		McCarthy General Cognitive	23
		Preschool Language Scale	23
		WJ Applied Problems	22
		WJ letter/word Recognition	22
Faroe Islands[b]	7 years	Finger Tapping	12
		CPT Reaction Time	10
		Bender Copying Errors	15
		Boston Naming Test	10
		CVLT: Delayed Recall	14
New Zealand[c]	6-7 years	TOLD Language Development	6
		WISC-R:PIQ	6
		WISC-R:FSIQ	6
		McCarthy Perceptual Performance	4
		McCarthy Motor Test	6

[a]Data from Crump et al. 1998, 2000.
[b]Data from Budtz-Jorgensen et al. 1999.
[c]Data from Crump et al. 1998, 2000.
Abbreviations: BMDL, lower 95% confidence limit on the benchmark dose; BMR, benchmark response; WJ, Woodcock-Johnson Tests of Achievement; CPT, Continuous Performance Test; CVLT, California Verbal Learning Test; TOLD, Test of Language Development; WISC-R:PIQ, Wechsler Intelligence Scale for Children-Revised performance IQ; WISC-R:FSIQ, Wechsler Intelligence Scale for Children-Revised Full-Scale IQ.

integrative analysis (BMD, 21 ppm) or lower 5% limit (7 ppm) might also be considered. The Seychelles study, because of the lack of positive findings, does not provide an appropriate point of departure for risk assessment. Although the Seychelles study is a well-conducted study, the cohort appeared to be less sensitive than those of the New Zealand and Faroe Islands studies for reasons that are still not understood.

SELECTION OF THE CRITICAL STUDY AND POINT OF DEPARTURE FOR THE REVISED RFD

The committee conducted an in-depth examination of the methods, strengths, uncertainties, and outcomes of each of the major studies. It included an examination of findings and comparison of BMDs and BMDLs. On the basis of its consideration of the body of evidence, the committee concluded that a well-designed study with positive effects provides the most appropriate public-health basis for the RfD. When the two studies with positive effects are compared, the strengths of the New Zealand study include an ethnically heterogeneous sample, in which the observed effects cannot be attributed to the particular vulnerability of a genetically homogenous ethnic group, and the use of developmental end points with greater predictive validity for school performance than that of the discrete neuropsychological tests used in the Faroe Islands study. The advantages of the Faroe Islands study over the New Zealand study include a larger sample size, the use of two biomarkers of exposure, and more extensive scrutiny in the epidemiological literature. In addition, the Faroe Islands data have undergone extensive re-analysis in response to questions raised by panelists at the NIEHS (1998) workshop and by this committee in the course of its deliberations. Therefore, the committee recommends the Faroe Islands study as the critical study for the revision of the RfD. For that study, dose-response data based on Hg concentrations in cord blood should be used to estimate the BMD. Because the data on the most sensitive end point — the Continuous Performance Test — were analyzed for only half the sample, the committee recommends that the BMDL based on the next most sensitive end point — the Boston Naming Test — be considered as a reasonable and representative point of departure for a revised RfD.

SOURCES OF UNCERTAINTY: CONSIDERATION FOR UNCERTAINTY FACTORS

Evaluation of the sources of uncertainty is essential for the development of a RfD. Some uncertainty is inherent in any experimental or epidemiological study. To address these uncertainties in the derivation of the RfD, the NOAEL or BMDL may be divided by one or more uncertainty factors. Uncertainty factors were originally termed safety factors and were used in the derivation of acceptable daily intakes (ADIs) to account for recognized uncertainties by incorporating an additional margin of safety on the NOAEL (NRC 1994). Traditionally, uncertainty factors and modifying factors of 10 or 3 have been applied to address well-recognized issues, which reflect potentials for additional sensitivities or adverse effects not addressed in the dose-response analysis. These issues include variation in sensitivity among humans, animal-to-human extrapolation, extrapolation from subchronic-to-chronic exposure, LOAEL-to-NOAEL extrapolation, and incomplete data to address all possible outcomes. A modifying factor, based on professional judgment, may also be applied to address uncertainties in the data base or critical study (Dourson et al. 1996). Traditional default uncertainty factors of 10 have been acknowledged to be somewhat arbitrary since they were proposed by O.G. Fitzhugh and A. Lehman in the early 1950s (NRC 1994).

At the present time, there is no consistent approach in the application of uncertainty factors across the various regulatory and public-health agencies. The selection and application of uncertainty factors represents a scientific policy judgment that has a major influence on the determination of the RfD or other risk-management guidance numbers. For example, application of large uncertainty factors might overshadow the moderate differences among the various study findings and their NOAELS or BMDs in determining the magnitude of the RfD. That possibility is particularly relevant to the MeHg RfD, because the body of evidence examined by the committee indicates a general convergence of the lower doses associated with neurodevelopmental effects. Given the relatively small differences in BMDLs, a more consistent approach to the application of uncertainty factors could reduce the current inconsistencies between the EPA RfD and other risk guidance numbers.

To identify sources of uncertainty in deriving the current MeHg RfD, EPA conducted an analysis of uncertainties (EPA 1997b, Vol. VI Appen

dix) in relation to the critical study of neurodevelopmental effects from the 1971 Iraqi MeHg poisoning incident (Marsh et al. 1987). Major sources of uncertainty were identified as the variability in susceptibilities within the Iraqi cohort, population variability in the pharmaco-kinetic processes, and response classification error. An additional concern was the applicability of a risk assessment based on a grain-consuming population to the U.S. population for which fish consumption is the primary source of MeHg exposure. A composite uncertainty factor of 10 was applied in the derivation of the RfD to account for several uncertainties, including human-population variability, lack of a two-generation reproductive study, and lack of data on sequelae resulting from longer durations of exposure (EPA 1997c). Although the rationale for the composite uncertainty factor applied in the current RfD is well described, it is not possible to quantitatively validate that it adequately addresses the combined uncertainties in the Iraqi data because some of them have been described only in qualitative terms.

Any refinement of the current RfD will require consideration of sources of uncertainty. The committee has evaluated the body of evidence, focusing on the prospective epidemiological studies of neurotoxicity in children exposed in utero. Refinement of the current RfD based on results from these studies will require both quantitative and qualitative analysis of uncertainties to guide the application of uncertainty factors.

Not all sources of uncertainty require the addition of uncertainty factors in the derivation of the RfD. When the MeHg prospective epidemiological studies provide the basis for the RfD, uncertainty factor adjustments are potentially required only for the following reasons:

- If the uncertainty could result in underestimation of the adverse effects of MeHg exposure on human health.
- If there is reason to suspect that the U.S. population is more sensitive than the study populations to the adverse effects of MeHg.

Although there are multiple sources of uncertainty in the quantitative derivation of the RfD, not all result in an RfD that is insufficiently protective. Table 8-2 lists sources of uncertainty identified by the committee.

Individual responses to MeHg exposure are variable and a key source of uncertainty. Factors that might influence susceptibility include age,

gender, genetics, health status, nutritional influences including dietary interactions, and interindividual toxicokinetic and toxicodynamic variability. For example, data from Iraq indicate that although some individuals were sensitive to low levels of exposure, some members of the cohort were not sensitive to extremely high levels of exposure. That finding suggests a wide interindividual variability in sensitivity. Development of the RfD must consider this individual variation; in particular, any biomarker-based measure should account for the toxicokinetic variability in the population. At present, there is no clear evidence that the U.S. population is more sensitive than any of the key study populations. However, in any given population, there might be sensitive subpopulations whose sensitivity to MeHg is not adequately represented in the dose-response assessment. That possibility could represent an additional source of uncertainty.

TABLE 8-2 Sources of Uncertainty in Key Epidemiological Studies

Susceptible subpopulations

- Interindividual toxicokinetic variability in dose reconstruction
- Toxicodynamic variability
- Nutritional deficits

Measures of exposure

- Lack of dietary-intake data
- Extrapolation from biomarker Hg content to MeHg intake
- Nutritional and dietary confounders and effect modifiers
- Co-exposure to other neurotoxicants (e.g., PCBs)
- Co-exposure to other forms of Hg
- Inability to measure peak exposures
- Temporal matching of exposure to critical periods of susceptibility for the developing fetal brain

Lack of consideration of other key or most-sensitive health end points

- Potential cardiovascular or immune-system effects
- Neurological sequelae (i.e., late emerging effects)

Limitations in the evaluation of exposures also represent a source of uncertainty. Of particular concern is the uncertainty in the linkage between the time and the intensity of exposure to critical periods of

brain development. Each dose metric provides different information about exposure. Dietary-recall data might be useful in stratifying exposure levels, but appropriate dietary data were not collected in the key studies. Measurement of cord blood does not detect temporal variability in exposure and reflects exposure during a period late in gestation. Therefore cord-blood concentrations might not correspond to the periods of greatest fetal sensitivity to Hg neurotoxicity. Similarly, average concentrations of Hg in hair provide no information on peak exposures and, because of variation in length and growth rate, might not reflect comparable periods of gestation.

In any experimental or epidemiological data, there is also some uncertainty on whether the measured effects represent the true most sensitive or critical effects. Neurodevelopmental effects are the most extensively studied sensitive end point for MeHg exposure, but there remains some uncertainty about the possibility of other health effects at low levels of exposure. In particular, there are indications of immune and cardiovascular effects, as well as neurological effects emerging later in life, that have not been adequately studied.

A number of additional sources of uncertainty are not possible to quantify but might contribute to the differences in study findings and BMDLs for the various outcomes. Those might include differences in nutritional and dietary confounders and effect modifiers such as beneficial effects from eating fish. Differences in population susceptibilities and unmeasured coexposure to other pollutants, including other forms of Hg, might introduce uncertainty.

On the basis of an evaluation of the sources of uncertainty in the key epidemiological studies, the committee identified two major categories of uncertainty, which should be considered in the determination of uncertainty factors for the revision of the RfD:

- Interindividual toxicokinetic variability in dose reconstruction (see Chapter 3).
- Data-base insufficiency (i.e., because of consideration of possible low-dose sequelae and latent effects, and immunotoxicity and cardiovascular effects) (see Chapter 5).

On the basis of the analysis presented in Chapter 3, the committee believes that an uncertainty factor of 2-3 for dose reconstruction from

hair Hg concentrations or an uncertainty factor of about 2 for dose reconstruction from blood Hg concentrations is objective and appropriate. Despite ongoing work to provide a data-based and probabilistic basis for uncertainty-factor adjustments in the derivation of the RfD (e.g., Hattis et al. 1999), the choice of values for most categories of uncertainty other than toxicokinetics, and for the aggregate uncertainty-factor adjustment remains, in part, a policy decision. That is particularly the case for the uncertainty factor category of data-base insufficiency. The choice of values for most uncertainty-factor categories (e.g., animal to human) can be related to extant (although limited) analyses of empirical data. In the case of data-base insufficiency, however, the uncertainty-factor value is intended to address the possibility that more accurate or complete information might result in a lower NOAEL or BMD or might result in a more sensitive end point. If data were available to assess such a possibility adequately and quantitatively, such data might well lead to a more appropriate RfD rather than to an uncertainty-factor adjustment. Thus, the selection of an appropriate uncertainty-factor value for data-base insufficiency is inherently uncertain. Nonetheless, the committee believes that there is a reasonable possibility that significant immunotoxicity and cardiovascular effects, as well as neurotoxic sequelae, might occur at exposure levels below the dose corresponding to the neurodevelopmental BMD identified by the committee. Therefore, given the relatively unambiguous starting point for variability in dose reconstruction, the committee believes that an overall uncertainty-factor adjustment of no less than 10 is necessary and appropriate to provide an adequate margin of protection.

IMPLICATIONS FOR PUBLIC HEALTH AND RISK MANAGEMENT

The RfD provides critical guidance for a broad range of public-health and regulatory initiatives aimed at reducing Hg exposures and preventing adverse health impacts. The goal of the RfD is to estimate a level of daily exposure without adverse public health impacts even for sensitive individuals.

EPA has estimated from food consumption surveys that 7% of women

nationwide exceed the RfD. From a food consumption survey in New Jersey it was estimated that 21% of women of childbearing age exceed the current RfD (Stern et al. 1996). EPA has calculated that a hair Hg concentration of 1.0 ppm would approximately result from an intake of MeHg at the current EPA RfD (see calculations in the Current EPA Reference Dose section in this chapter). Although estimates of hair and blood concentrations in the U.S. population are sparse, when that hair Hg concentration (1.0 ppm) is compared with available data, it is again seen that more highly exposed subpopulations frequently exceed the current RfD (EPA 1997c; Stern et al. 2000).

The committee conducted a margin-of-exposure (MOE) analysis to examine the margin of safety between available estimates of population exposure and BMDLs derived from the major epidemiological studies. The MOE approach provides a method of characterizing risks and is being used increasingly to examine potential population risks, particularly for noncancer end points. The MOE approach has been recommended by The Presidential/ Congressional Commission on Risk Assessment and Risk Management (1997) as a common metric to be used by both environmental-protection and public-health agencies for assessing and comparing health risks. The MOE is the ratio of the critical dose (NOAEL or BMDL) to the estimated population exposure level. The smaller the ratio, the greater the cause for concern. Because the BMDLs are not adjusted by uncertainty factors, MOEs less than 10 indicate that population exposures might be approaching levels of public-health concern. Table 8-3 presents the results of the MOE analysis. The analysis compared available estimates of the range of population Hg concentration in hair to BMDLS from the major studies: the cord-blood-derived BMDL for the lowest reliable end point (the Boston Naming Test) from the Faroe Islands study; the 5% lower bound BMD from the committee's integrative analysis; and the Iraq study BMDL, which is the point of departure for the current RfD.

MOEs for the estimates of mean population levels range from 7.5 (New Zealand, most sensitive end point) to 77.3 (Seychelles, median end point). Those results indicate that the risk of adverse health impacts from the current exposure level in the majority of the population is low. However, for those at the high end of the population exposure distribution (95th percentile), the MOEs indicate that the margin of safety for the

TABLE 8-3 Population Margins of Exposure (MOE)[a] for Selected BMDLs and Exposure Estimates (ppm of Hg in Maternal Hair or Estimated Equivalent to Maternal Hair)

		MOE					
		Estimated MeHg Exposure in Selected Populations					
		New Jersey Pregnant Women[b]		EPA Region V Population[c]		U.S. Women of Childbearing Age[d]	
Study	Selected BMDL (value, ppm)	Mean (0.53)	95th Percentile (2.0)	Mean (0.29)	95th Percentile (1)	Mean (0.36)	95th Percentile (2.4)
New Zealand	Most sensitive (4)	7.5	2.0	13.8	4	11.1	1.7
Faroe Islands	Most sensitive (10)	18.9	5.0	34.5	10	27.8	4.2
Faroe Islands	Most-sensitive-reliable, cord-blood derived (12)	22.6	6.0	41.4	12	33.3	5.0
Seychelles	Median (22)	41.5	11	77.3	22	61.1	9.2
New Zealand, Faroe Islands, and Seychelles (integrative analysis)	Lower 5% (7)	13.2	3.5	24.1	7	19.4	2.9
Iraq	(11)[e]	20.8	5.5	37.9	11	30.6	4.6

[a]MOE, BMDL/exposure estimate.
[b]Data from Stern et al. 2000.
[c]Data from Pellizzari et al. 1999.
[d]Data from Smith et al. 1997.
[e]Current RfD basis.
Abbreviations: BMDL, lower 95% confidence limit on the benchmark dose; RfD, reference dose.

most highly exposed is consistently below 10. That indicates that the exposure levels of high-end consumers are close to those at which there are observable adverse neurodevelopmental impacts.

To further characterize the risks of MeHg, the committee developed an estimate of the number of children born annually to women most likely to be highly exposed through high fish consumption (highest 5% estimated to consume 100 g per day). Available consumption data and current population and fertility rates indicate that over 60,000 newborns annually might be at risk for adverse neurodevelopmental effects from in utero exposure to MeHg.

The MeHg-associated performance decrements on the neuropsychological tests administered in the Faroe Islands and New Zealand studies suggest that prenatal MeHg exposure is likely to be associated with poorer school performance. In the Faroe Islands sample, MeHg-related deficits were seen across a broad range of specific domains, including vocabulary, verbal learning, visuospacial attention, and neuromotor function. Deficits of the magnitude reported in these studies are likely to be associated with increases in the number of children who have to struggle to keep up in a normal classroom or who might require remedial classes or special education.

Revision of the RfD for MeHg can have far-reaching implications for public health and environmental protection. Currently, 40 states have issued advisories concerning consumption of certain freshwater fish. Any revision of the RfD will have implications for the market for fish and seafood and the dietary choices of Americans. Regulatory impacts might also be substantial, because federal and state agencies use the RfD to develop water-quality criteria and set limits on Hg releases in air and water. Additionally, there are implications for industrial use of Hg and Hg-containing materials, as well as decisions about disposal methods and recycling options.

Ideally, the application of the RfD in risk management should provide a margin of safety for all of the population. The application of the RfD to guide regulatory and risk-management policies must also consider risk tradeoffs, economic and technological limitations, as well as cultural and political influences. It must be recognized that the refinement of the RfD might not eliminate agency differences in risk management. However, improving the scientific basis for decision-making represents an important step forward in developing a cohesive strategy to prevent adverse effects from MeHg.

COMMITTEE FINDINGS AND RECOMMENDATIONS

- Hg is pervasive and persistent in the environment. Its use in products and emission from industrial processes and combustion have resulted in global circulation and atmospheric deposition. There have been well-documented instances of population poisonings, highly exposed occupational groups, and worldwide chronic low-level environmental exposures. The bioaccumulation of MeHg can lead to high concentrations in many species of fish and result in unacceptable levels of exposure and risk to highly exposed or susceptible subpopulations.
- The weight of the evidence of developmental neurotoxic effects from exposure to MeHg is strong. There is a strong data base, which includes multiple human studies and experimental evidence in animals and in vitro tests. Human studies include both high-exposure scenarios and evaluations of effects of chronic low-level exposure. The epidemiological studies also include well-established biomarkers to evaluate exposure levels in study populations.
- The weight of evidence from multiple epidemiological studies supports the selection of neurotoxicity in children exposed in utero as the most sensitive well-documented effect and a suitable end point for the derivation of the BMD. However, emerging evidence of other potential effects should also be considered in the calculation and the implementation of the EPA RfD.
- Given the availability of results from large prospective epidemiological studies, the Iraq study results should no longer be considered the critical study for the EPA RfD. The exposure scenarios in Iraq are not comparable to the low-level chronic exposures in North America. In addition, there are well-recognized uncertainties concerning exposure and response classification in the Iraq study.
- The New Zealand, Faroe Islands, and Seychelles studies are well-designed epidemiological investigations in which prenatal MeHg exposures were within the range of at least some U.S. population exposures. Any revision of the RfD or other exposure standards should consider the findings of these studies.
- After considering the weight of evidence and range of results from the three major epidemiological studies, the committee concludes

that a positive study will provide the strongest public-health basis for the RfD and recommends the Faroe Islands study as the critical study. Within that study, the lowest BMD for a neurobehavioral end point considered to be sufficiently reliable is the Boston Naming Test. The BMDL estimated from that test is 58 ppb Hg in cord blood (approximately corresponding to 12 ppm Hg in hair). That value should be considered a reasonable point of departure for the development of the revised RfD.

- An MOE analysis using available estimates of population exposure levels indicates that average U.S. population risks from MeHg exposure are low. However, those with high exposures from frequent fish consumption might have little or no margin of safety.
- The population at highest risk is the offspring of women of child-bearing age who consume large amounts of fish and seafood. The committee estimates that over 60,000 children are born each year at risk for adverse neurodevelopmental effects due to in utero exposure to MeHg.
- There is a critical need for improved characterization of population exposure levels to improve estimates of current exposure, track trends, and identify high-risk subpopulations. Characterization should include improved nutritional and dietary exposure assessment and improved biomonitoring for all population groups. Exposure to other chemical forms of Hg, including exposure to elemental Hg from dental amalgams, should also be investigated.
- The application of uncertainty factors in the revision of the RfD should be based on a thorough quantitative and qualitative evaluation of the full range of uncertainties and limitations of the critical studies. Uncertainty factors applied in the development of a revised RfD should include data-base insufficiency and interindividual toxicokinetic variability in dose reconstruction. As a starting point, an uncertainty factor of 2-3 should be applied to a central tendency estimate of dose derived from maternal hair, or a factor of about 2 should be applied to a central tendency estimate of dose derived from cord blood to account for interindividual pharmacokinetic variability in dose reconstruction. The choice of an uncertainty factor for data-base insufficiency is, in part, a policy decision; however, given the data indicating possible low-dose sequelae and latent effects and immunotoxicity and cardiovascular effects, the

committee concludes that an overall composite uncertainty factor of no less than 10 is needed.

- Concurrent with the revision of the RfD, harmonization efforts should be undertaken to establish a common scientific basis for the establishment of exposure guidance and reduce current differences among agencies. Harmonization efforts should address the risk-assessment process and recognize that risk-management efforts reflect the differing mandates and responsibilities of these agencies.
- Recent studies have found associations between exposure to MeHg and impairments of the immune, reproductive, and cardiovascular systems. Immune and cardiovascular effects have been observed following both prenatal and adult exposures. MeHg exposure levels associated with those effects are comparable to and in some cases lower than those known to cause neurodevelopmental problems. Additional research should be done using animal models and human populations that have chronic, low-dose exposure to MeHg. Effects of exposure during fetal development through the entire life span is needed. Further research is also needed to evaluate MeHg-induced chromosomal aberrations and cancer.
- The committee recommends that results from the Boston Naming Test in the Faroe Islands study be used in the calculation of the RfD. For that study, dose- response data based on Hg concentrations in cord blood should be modeled using the K-power model ($K \geq 1$). On the basis of that study, that test, and that model, the committee's preferred estimate of the BMDL is 58 parts per billion (ppb)[1] of Hg in cord blood (approximately corresponding to 12 ppm Hg in hair). To estimate this BMDL, the committee's calculations involved a series of steps, each involving one or more assumptions and related uncertainties. Alternative assumptions could have an impact on the estimated BMDL value. In selecting a single point of departure, the committee followed established public-health practice of using the lowest value for the most sensitive, relevant end point.

[1]The BMDL of 58 ppb is calculated statistically and represents the lower 95% confidence limit on the dose (or biomarker concentration) that is estimated to result in an increased probability that 5% of the population will have an abnormal score on the Boston Naming Test.

- The BMDL of 12 ppm is nearly identical to the BMDL currently used by EPA (11 ppm). Given the toxicokinetic variability and uncertainties in the data, an uncertainty factor of at least 10 is supported by the committee. Therefore, on the basis of its analysis of the available data, the committee finds that the value of EPA's current RfD for MeHg (0.1 µg/kg per day) is scientifically justifiable for the protection of public health.

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APPENDIX TO CHAPTER 7

DOMINICI et al. (2000) used a two-stage Bayesian model to pool dose-response information across a relatively large number of studies. The first stage of their analysis estimated dose-response slopes from each study, adjusting for various confounding factors measured for each study. The second stage involved fitting a hierarchical Bayesian model to the estimates obtained at the first stage. The approach is heuristically appealing and is in fact similar to the ad-hoc two-stage algorithm that was often used to fit linear growth curve models before the advent of programs such as SAS PROC MIXED (see, for example, Laird 1990). As noted by Dominici et al., the approach approximates a fully Bayesian analysis on the original data. The authors justified this approximation by (1) empirically checking this approximation for their particular application and (2) pointing to theoretical justification for the approximation given by Daniels and Dass (1998). A two-stage analysis along the same lines is attractive in the context of MeHg for several reasons. First, the approach is natural in settings in which the original study-specific data are unavailable. That is, one can simply fit the second stage of the model to published summary measures (i.e., dose-response slopes and corresponding standard errors) from each study. Second, the approach easily extends to the case of multiple outcomes, because outcome within a study simply represents an additional level in the hierarchical model. As discussed in the chapter, data available to the committee included estimated BMDs and BMDLs computed for each of the individual outcomes assessed for the Faroe Islands, Seychelles, and

New Zealand studies (see Table 7-3). One approach might be to apply the hierarchical analysis directly to the estimated BMDs, although the committee felt it appropriate to apply the analysis to the inverse BMDs instead. One advantage of working with the inverse BMDs is that very large and undefined values are transformed to zero. Working with the inverse BMDs also has some theoretical justification, because in the context of a linear model, the estimated BMD is simply a constant divided by the estimated dose-response slope (see Equation 7-1).

To describe the committee's approach in more detail, it is useful to define some notation. Let $\hat{\beta}_{ij}$ be the inverse of the BMD estimated for the jth outcome, $j = 1, \ldots Ji,$ within study, $i = 1, \ldots I$. The corresponding standard errors, $\hat{\sigma}_{ij}$, can be estimated by subtracting $\hat{\beta}_{ij}$ from the inverse of the BMDL and then dividing by 1.64. The hierarchical model can be expressed as

$$\hat{\beta}_{ij} \Big| \beta_{ij} \approx N(\beta_{ij}, \hat{\sigma}_{ij}^2)$$

$$\beta_{ij} \Big| \beta_i \approx N(\beta_i, \gamma^2)$$

$$\beta_i \Big| \beta \approx N(\beta, \tau^2)$$

$$\beta \approx N(m,n),\ \gamma^2 \approx \text{InvGamma}(a,b),\ \tau^2 \approx \text{InvGamma}(c,d),$$

where *a, b, c, d, m,* and *n* are chosen so that the priors are all relatively noninformative. In other words, we assume that the true inverse BMDs for each outcome are normally distributed around a study-specific mean value and that these study-specific values are in turn normally distributed around an overall mean. We fit the hierarchical model using the BUGS (Bayesian inference Using Gibbs Sampling) software package (Spiegelhalter et al. 1996). The product of the analysis is a series of simulated distributions of the various random variables defined in the model. Applying an inverse transformation again converts those results to yield estimates of the distribution of the quantities of interest, namely, BMDs. In addition to providing an estimate of distribution of true BMDs corresponding to different outcomes from different studies, the output from the program allows computation of so-called posterior estimates of the true BMDs, given the observed values. The advantage

of working with the posterior estimates instead of the original values is that they have removed some of the random variation inherent in the observed estimates. The "smoothed BMDs" referred to in Chapter 7 and also in Figure 7-3 are posterior estimates.

Because the method proposed here is new and exploratory in nature, the committee does not recommend it as the primary approach to the MeHg risk assessment at the present time. Indeed, there are a number of questions associated with the approach that would require further exploration before it could be used as the basis of a definitive analysis. For example, one concern is the relatively small number of studies (three) available for the MeHg study. The Dominici et al (2000) analysis involved a relatively large number of studies, and therefore, does not have the same concern.

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GLOSSARY

Absorbed dose – The amount of a substance that penetrates an exposed organism's absorption barriers (e.g., skin, lung tissue, gastrointestinal tract) through physical or biological processes. The term is synonymous with internal dose.

Administered dose – The amount of a substance given to a test subject (human or animal) in determining dose-response relationships, especially through ingestion or inhalation. In exposure assessment, since exposure to chemicals is usually inadvertent, this quantity is called potential dose.

Adverse effect – Any effect that produces functional impairment and/or a pathological lesion that may affect the performance of the whole organism, or that reduces an organisms ability to respond to an additional challenge (Stara et al. 1985)

Anthropogenic – Of human origin.

Applied dose – The amount of a substance in contact with the primary absorption boundaries of an organism (e.g, skin, lung, gastrointestinal tract) and available for absorption.

Autoimmunity – A condition resulting from the production of autoantibodies, characterized by cell-mediated or humoral immunological responses to antigens of one's own body, sometimes with damage to normal components of the body.

Benchmark dose analysis – A technique for quantitative assessment of noncancer health effects.

Benchmark dose – An exposure level that corresponds to a statistical lower bound on a standard probability of an effect, such as 10% of people affected.

Bioaccumulation – An increase in concentration in living organisms as they take in contaminated air, water, or food because the substances are very slowly metabolized or excreted.

Bias – Any effect tending to produce results that depart systematically from the true values. Two principle forms of bias in human epidemiological studies are misclassification, when there are misassignments in exposure or adverse outcome, and selection, in which subjects selected for study differ systematically from those not selected.

Bioactivation – A metabolic process wherein an inactive chemical is converted to an active one in the body.

Bioavailability – The state of being capable of being absorbed and available to interact with the metabolic processes of an organism. Bioavailability is typically a function of chemical properties, physical state of the material to which an organism is exposed, and the ability of the individual organism to physiologically take up the chemical.

Biomarker of Effect – A measurable biochemical, physiological, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease.

Biomarker of Exposure – An exogenous substance, the metabolite(s) or the product of interactions between a xenobiotic agent and some target molecule or cell that is measured in a compartment within an organism.

Biologically effective dose – The amount of the deposited or absorbed contaminant that reaches the cells or target site where an adverse effect occurs or where an interaction of that contaminant with a membrane surface occurs.

Biotransformation A series of chemical alterations within the body whereby a foreign substance is transformed to a more or less toxic substance.

Case-control study – An epidemiological study in which persons are selected because they have a specific disease or other outcome (cases) and are compared to a control (referent comparison) group without the disease to evaluate whether there is a difference in their reported frequency of exposure to possible disease risk factors. Also termed a retrospective study or case referent study.

Chronic exposure – Multiple exposures occurring over an extended period of time or over a significant fraction of an animal's or human's lifetime (Usually seven years to a lifetime.)

Chronic toxicity – The capacity of a substance to cause long-term poisonous health effects in humans, animals, fish, and other organisms.

Cohort study – An epidemiological study in which a defined group of persons known to be exposed to a potential disease risk factor is followed over time and compared to a group of persons who were not known to be exposed to the potential risk factor to evaluate the differences in rates of the outcome. Also termed a prospective study, followup study, incidence study, retrospective cohort, or historical cohort study.

Concentration (C) – The total quantity of substance present in a given unit volume (of gas or liquid). It may be expressed in any unit or mass per unit of volume such as milligrams per cubic meter (mg/m_3), or as volume per volume such as parts per million (ppm).

Confidence interval (95%) – A range of values for the effect estimate within which the true value is though to lie with a 95% level of confidence.

Confounder (confounding factor) – A factor that is associated with both the exposure and outcome of interest and can distort the apparent magnitude of the effect of the study factor.

Developmental toxicity – The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse development effects may be detected at any point in the life span of the organism.

Dose – The amount of a risk agent that enters or interacts with organisms. An administered dose is the amount of substance administered to an animal or human, usually measured in milligrams per kilogram of body weight; milligrams per square meter of body surface area; or parts per million of the diet, drinking water, or ambient air. An effective dose is the amount of the substance reaching the target organ.

Dose estimation – The process by which a delivered dose is estimated from an exposure dose or from a biomarker of exposures.

Dose-response assessment – The determination of the relationship between the magnitude of administered, applied, or internal dose and specific biological response. Response can be expresses as measured or observed incidence, percent response in groups of subjects (or populations), or the probability of occurrence of a response in a population.

Dose-response curve – A graphical representation of the quantitative relationship between administered, applied, or internal dose of a chemical or agent, and a specific biological response to that chemical or agent.

Dose-response model – A mathematical description of the relationship between exposure levels and the incidence rates of an effect.

Dose-response relationship – A relationship between the amount of an agent (either administered, absorbed, or believed to be effective) and changes in certain aspects of the biological system (usually toxic effects), apparently in response to the agent.

End points of toxicity – Adverse effects elicited as a result of exposure to a substance.

Epidemiology – The core public health science, investigating the causes and risk factors of disease and injury in populations and the potential to reduce such disease burdens.

Exposure – An event that occurs when there is contact at a boundary between a human and the environment with a contaminant of a specific concentration for an interval of time; the units of exposure are concentration multiplied by time.

Exposure assessment – The determination or estimation (qualitative or quantitative) of the magnitude, frequency, duration, and route of exposure.

Exposure dose – The level of contaminant in the air, water, or soil to which people are actually exposed.

Genotoxic – Capable of altering the structure of DNA and causing mutations.

Half-Life – The time required for the elimination of half a total dose from the body.

Human health risk assessment – A process used to estimate the likelihood of adverse health outcomes of environmental exposures to chemicals.

Immediate versus Delayed Toxicity – The immediate effects that occur or develop rapidly after a single administration or exposure of substances; delayed effects are those that occur after a lapse of some time. These effects have also been referred to as acute and chronic, respectively.

Immunological toxicity – The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

Ingested dose – The amount of a substance consumed by an individual, usually expressed as amount per kilogram body weight over a given time period.

Intake – The amount of material inhaled, absorbed through skin, or ingested during a specified period of time.

Internal dose – In exposure assessment, the amount of a substance penetrating the absorption barriers (e.g., skin, lung tissue, gastrointestinal tract) of an organism through either physical or biological processes.

Latency – Time from the first exposure of a chemical until the appearance of a toxic effect.

Lifetime exposure – Total amount of exposure to a substance that a human would receive in a lifetime (usually assumed to be 75 years).

Lipid solubility – The maximum concentration of a chemical that will dissolve in fatty substances. Lipid soluble substances are insoluble in water. They will very selectively disperse through the environment via intake in living tissue.

Lowest-observed-adverse-effect level (LOAEL) – The lowest exposure level at which there are statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group.

Margin of exposure – A ratio defined by EPA as a dose derived from a tumor bioassay, epidemiological study, or biological marker study, such as the dose associated with a 10% response rate divided by an actual or projected human exposure.

Mechanism of action – The way in which a substance (e.g., a chemical) exerts its toxic effect(s).

Metabolism – All the biological reactions that take in a cell or an organism.

Neurotoxicity – The occurrence of adverse effects on the nervous system following exposure to chemical.

No-observed-adverse-effect level (NOAEL) – An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered as adverse, nor precursors to adverse effects. In an experiment with several NOAELs, the regulatory focus is primarily on the highest one, leading to the common usage of the term NOAEL as the highest exposure without adverse effect.

Point of departure – An estimate or observed level of exposure or dose which is associated with an increase in adverse effect(s) in the study population. Examples of points of departure include NOAELs, LOAELs, BMDs, and BMDLs.

Population at risk – a population subgroup that is more likely to be exposed to a chemical, or is more sensitive to the chemical, than is the general population.

Power – The probability of detecting a specified difference in effect between experimental and control groups.

Probability – A numerical value between 0 and 1 that represents the likelihood of something.

Reference Dose (RfD) – an estimate (with uncertainty spanning perhaps an order of magnitude) of daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

Reproductive toxicity – The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcome, or modifications in other functions that are dependent on the integrity of this system.

Risk – A measure of the probability that damage to life, health, property, and/or the environment will occur as a result of a given hazard.

Risk assessment – An organized process used to describe and estimate the likelihood of adverse health outcomes from environmental exposures to chemicals. The four steps are hazard identification, dose-response assessment, exposure assessment, and risk characterization.

Risk characterization – The last phase process of the risk assessment process that estimates the potential for adverse health or ecological effects to occur from exposure to a stressor and evaluates the uncertainty involved.

Risk management – The process of evaluating and selecting alterative regulatory and non-regulatory responses to risk. The selection process necessarily requires the consideration of legal, economic, and behavioral factors.

Solubility – The amount of mass of a compound that will dissolve in a unit volume of solution. Aqueous Solubility is the maximum concentration of a chemical that will dissolve in pure water at a reference temperature.

Standardized mortality ratio (SMR) – The ratio of observed deaths to expected deaths.

Statistical control – The process by which that variability of measurements or of data outputs of a system is controlled to the extent necessary to produce stable and reproducible results. To say that measurements are under statistical control means that there is statistical evidence that the critical variables in the measurement process are being controlled to such an extent that the system yields data that are reproducible within well-defined limits.

Susceptibility – The extent to which an individual is liable to infection or the effects of substances, such as toxicants, allergens, or other influences. The antithesis of resistance.

Toxicant – A harmful substance or agent that may injury an exposed organism.

Toxicity – A degree to which a substance or mixture of substances can harm humans or animals. Acute toxicity involves harmful effects in a organism through a single or short-term exposure. Chronic toxicity is the ability of a substance or mixture of substances to cause harmful effects over an extended period, usually upon repeated or continuous exposure sometimes lasting for the entire life of that exposed organism. Subchronic toxicity is the ability of the substance to cause effects for more than one year but less than the lifetime of the exposed organism.

Toxicokinetics – The processes of absorption, distribution, metabolism, and excretion that occur between the time a toxic chemical enters the body and when it leaves.

Uncertainty An estimate of the extent to which a risk estimate reflects reality.
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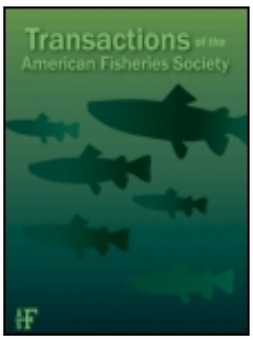
Uncertainty factor – One several, generally 10-fold factors, used in operationally deriving the Reference Dose (RfD) from experimental data. UF's are intended to account for (1) the variation in sensitivity among the members of the human population; (2) the uncertainty in extrapolating animal data to the case of humans; (3) the uncertainty in extrapolating from data obtained in a study that is of less-than-lifetime exposure; and (4) the uncertainty in using LOAEL date rather than NOAEL data.

Weight of the scientific evidence – Considerations involved in assessing the interpretation of published scientific information — quality of methods, ability of a study to detect adverse effects, consistency of results across studies, and biological plausibility of cause-and-effect relationships.



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Spatial Heterogeneity of Mercury Bioaccumulation by Walleye in Franklin D. Roosevelt Lake and the Upper Columbia River, Washington

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Spatial Heterogeneity of Mercury Bioaccumulation by Walleye in Franklin D. Roosevelt Lake and the Upper Columbia River, Washington

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Abstract.—We examined mercury concentration in muscle of walleye *Stizostedion vitreum* from three reaches in Franklin D. Roosevelt Lake, a reservoir on the Columbia River, and from the upper Columbia River, an area contaminated by wastes from metal mining and associated processing activities. Our objectives were to describe the relation between size and age of walleyes and tissue concentrations of mercury and to compare mercury concentrations within a single reservoir system among spatially segregated cohorts. Overall, mercury concentrations in walleye muscle ranged from 0.11 to 0.44 mg/kg (wet weight) and were positively correlated with age, weight, and length of the fish. Mercury concentrations in walleyes varied spatially within the system; the highest concentrations were in fish from the lower and middle reaches of the reservoir. Condition factor of age-2+ fish was inversely related to tissue concentration of mercury and was lower in fish from the lower and middle reaches than in fish from the upper reach. Spatial patterns in condition factor and mercury in walleyes were unrelated to concentrations of total mercury in surficial bed sediments, which ranged from less than 0.05 to 2.8 mg/kg (dry weight). We suggest that the observed spatial differences in the concentrations of mercury in walleyes may be attributed to the fish preferring to spawn and forage in specific areas where the bioavailability of mercury varies due to local differences in the physical and chemical environment.

Mercury is a pollutant of concern throughout the United States; detections in fish occur in approximately 92% of areas sampled (EPA 1992). Areas of concern include those where mercury has historically been released into waters containing sportfish. Franklin D. Roosevelt Lake (hereafter Lake Roosevelt) is a reservoir formed on the Columbia River by Grand Coulee Dam, which was constructed in the late 1930s and early 1940s to supply irrigation water, to control flooding, and to produce hydroelectric power. The upper Columbia River and Lake Roosevelt are major recreational and economic resources due largely to the sport fishery. The principal sportfish species in Lake Roosevelt include walleye *Stizostedion vitreum*, rainbow trout *Oncorhynchus mykiss*, kokanee *Oncorhynchus nerka* (lacustrine sockeye salmon), yellow perch *Perca flavescens*, and smallmouth bass *Micropterus dolomieu* (McDowell and Griffith 1993). Contamination of fish from Lake Roosevelt was discovered in the early 1980s, when elevated concentrations of trace elements were found in fish collected near Grand Coulee Dam (Lowe et al. 1985). In a recent review, Serdar (1993) reported that several studies have since confirmed elevated concentrations of certain trace elements, including mercury, in fish from Lake Roosevelt.

The trace elements in Lake Roosevelt have been attributed to the transport of metallurgical waste and slag from a lead–zinc smelter in Canada (Smith 1987). Since 1900 the smelter has discharged slag into the Columbia River—approximately 360 metric tons per day in recent years (Cominco Metals 1991); the smelter has also discharged metals via its wastewater system. Other sources of trace elements in Lake Roosevelt include the Spokane River, which transports metals from mining areas around the Coeur d'Alene drainage (Yake 1979), and additional historical mining activities in the region. The high loading of trace elements prompted studies to assess the occurrence and distribution of trace elements in bed sediments (Johnson et al. 1990; Bortleson et al. 1994). In 1992, Bortleson et al. (1994) reported that the bed sediments of Lake Roosevelt contained elevated concentrations of arsenic, cadmium, copper, lead, zinc, and mercury relative to metal concentrations at reference sites. While all these trace elements are of environmental concern, Munn et al. (1995) reported that only mercury was

elevated in fillets of walleye, smallmouth bass, and rainbow trout.

Mercury, a potentially toxic nonessential metal, enters aquatic systems mostly in inorganic forms but can be methylated by bacteria to form the more toxic methylmercury, which then biomagnifies in the food chain (Eisler 1987). To reduce health risks of methylmercury, regulating agencies in 47 states have issued consumption advisories for mercury-contaminated fish (EPA 1996). Of the sportfish in Lake Roosevelt and the upper Columbia River, walleyes had the highest concentrations of mercury (Serdar et al. 1993).

Many field studies of mercury in fish have compared tissue concentrations among spatially isolated populations and have attributed differences in concentration levels, in part, to differences in physical and chemical characteristics among water bodies and the effects of these properties on bioavailability and uptake of mercury (Lathrop et al. 1989; McMurtry et al. 1989; Jackson 1991). We described the relation between size and age of walleyes and associated tissue concentrations of mercury and also compared mercury concentrations among spatially segregated cohorts within a single reservoir system. We then compared spatial patterns of mercury in sediment and fish tissue.

Study Area

Lake Roosevelt, a reservoir on the Columbia River formed by Grand Coulee Dam, is the largest reservoir by volume in Washington and one of the largest in the United States in total storage (Figure 1). Located in north-central Washington, Lake Roosevelt extends 217 km upstream from the dam to within 24 km of Canada. The surface area of the lake is 32,400 ha, and the full-pool elevation is 393 m. The stage level of the lake varies due to operation of Grand Coulee Dam by as much as 15 m, and the mean annual water retention time is about 40 d. The average depth is 36 m and maximum depth is 114 m. Major tributaries include Colville River, Kettle River, Spokane River, and Sanpoil River. Additional physical data describing Lake Roosevelt and the upper reach of the Columbia River in the United States are provided by Bortleson et al. (1994).

Three reaches were sampled: (1) The Kettle Falls reach was defined as the Columbia River from near Northport, Washington, to Lake Roosevelt where Sherman Creek enters the reservoir just downstream of Kettle Falls, Washington. In this reach the Columbia River is swift-flowing with riffles, runs, and pools. The river–reservoir transition zone in this reach depends on the flow to and surface elevation of the reservoir. (2) The Spokane reach was defined as a small part of Lake Roosevelt and the lower Spokane River. The Spokane River is the second largest contributor in discharge to the reservoir. The lower Spokane River is a low-gradient system dominated by fine sediment and numerous backwater habitats for fish. (3) The Sanpoil reach was defined as a small part of Lake Roosevelt in the vicinity of the Sanpoil River and the lower part of the Sanpoil River that included a small, lakelike embayment. These three reaches were selected because (1) they are preferred spawning areas and contain a larger percentage than other areas of the older age-class walleyes; (2) they are popular sportfishing areas and the fish caught are for human consumption; and (3) they provided sufficient spatial coverage to allow us to investigate regional differences in mercury concentrations in walleyes.

Methods

Field collection.—Walleyes collected for analyses of mercury content were categorized based on total length (TL) into four groups (25–33 cm, >33–41 cm, >41–48 cm, and >48–56 cm). The minimum and maximum size limits for each group and the overall range of sizes were selected in order to obtain a more or less equal representation of walleye age-classes in the reservoir and were based in large part on angling survey records. Each of 34 walleye composite samples analyzed contained eight individual fillets from fish of the same size-class. Average differences in mercury concentrations between left-side fillet composite samples and right-side individual samples (mean values) for walleyes (>33–41 cm, TL) were less than 10% (Munn et al. 1995).

Fish were sampled during May 16–21 and June 17–19, 1994, by angling and by boat electrofishing. Morphometric measures and tissue samples were taken within 24 h of collection. Measurements included total length (mm) and wet weight (g). Sex was determined once fillets were removed; however, reliable sex determinations could not be made on approximately 38% of collected walleyes, the majority of which consisted of reproductively immature individuals. Accordingly, fish of similar length were composited for mercury analysis regardless of gender. Fish scales were collected for age determination, which was done by the Washington State Department of Fish and Wildlife. Similarly sized fillet samples, including the belly flap, were removed for each composite in accordance

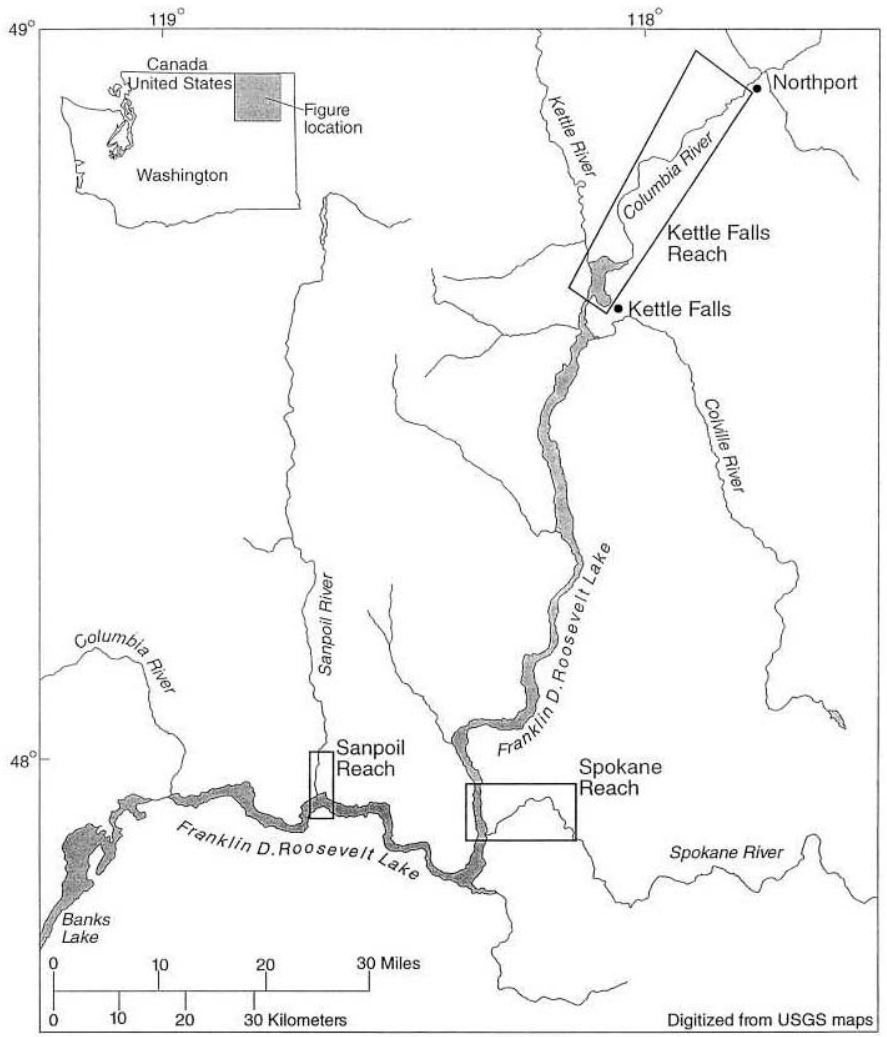

FIGURE 1.—Map showing the location of the three sampling reaches on the Columbia River and Franklin D. Roosevelt Lake.

with procedures described in EPA (1993). Filleting was done on glass cutting boards with stainless steel dissecting equipment. Once the fillet was obtained and the skin was removed, the fillet was weighed, sealed in a plastic bag, and shipped on dry ice to the U.S. Geological Survey (USGS) National Water Quality Laboratory in Arvada, Colorado.

Laboratory analysis and quality control.—Entire composite samples were homogenized at the Arvada laboratory in stainless steel blenders, then were placed in precleaned jars, labeled, and shipped frozen (with dry ice) to the U.S. Environmental Protection Agency (EPA) laboratory in Manchester, Washington, for analysis. Samples were prepared for laboratory analysis by using the hot water bath permanganate digestion method, yielding a 0.2-g final sample for the analysis. Total mercury in tissue was determined with cold vapor atomic absorption spectrophotometry (EPA 1991). The detection limit for this procedure is 0.05 parts per million (ppm, wet weight).

Quality control measures used to assess data quality included field and laboratory blanks to assess potential contamination, laboratory matrix spike samples to assess analytical procedures, and analysis of duplicate sample material to assess analytical accuracy and data precision. Results from

the field and laboratory blanks indicated no contamination from either field or laboratory activities. Data accuracy was assessed through interlaboratory comparison of duplicate samples and the analysis of standard reference material (DORM-2). The relative percent difference in the reported concentration of mercury from duplicate samples to multiple laboratories was within the 20% acceptance range. All laboratories reported the concentration of mercury in the DORM-2 standard reference material within the acceptance range (80–120%); two of the laboratories reported concentrations within the certified range, which is the 95% tolerance limit cited by the supplier. Blind samples were sent to the EPA laboratory to assess analytical precision. The relative percent differences of replicate analyses were within the quality assurance criteria of 20%, indicating acceptable laboratory analytical precision (Munn et al. 1995), and ranged from 0.5% to 11.4% for the six blind samples and 1.3–12.5% for the six duplicate laboratory-generated sample pairs.

Data analysis.—We compared the concentrations of mercury in walleyes among the three reaches with data adjusted for differences in mean total length of walleyes within a composite sample by one-factor analysis of covariance (ANCOVA). The *F*-test examined differences between regression coefficients and determined homogeneity of slopes. The GT2 method tested for differences among adjusted means (Sokal and Rohlf 1981). The relation of the total mercury concentration in walleyes with total length, weight of whole fish, and age was determined with Pearson's correlation coefficients with $\log_{10}$-transformed length and weight data. Regression was used to develop a predictive model of the relationship between the mercury in tissue to the mean total length ($\log_{10}$-normalized) and mean age of walleyes in each composite sample.

Condition factor (K) for walleyes was calculated as $K = 10^3 \times (\text{wet weight, g})/(\text{TL, cm})^3$ (Anderson and Gutreuter 1983). Owing to the comparatively few numbers of individuals in the shortest (25–33 cm) and longest (>48–56 cm) size categories at some of the sampling locations, comparisons of condition factor for walleyes among reaches were limited to individuals representing the two most abundant size categories (>33–41 and >41–48 cm). Assumptions of normality and homogeneity of slopes were valid for these data, and comparisons of condition factor among reaches were performed with single-factor analysis of variance (ANOVA). Pairwise comparisons among means were done with the GT2 method.

Results

Thirty-four composite walleye samples were collected from the three reaches. Individual walleyes ranged in total length from 28 to 54 cm and from 1 to 8 years in age. Eighty-six percent of the walleyes were from 1 to 4 years old with age-2 fish making up 43% of the total. The most abundant size category (>33–41 cm) consisted of individuals with a mean age of 2.4 years. Fish in the second most abundant group (>41–48 cm, 26%) had a mean age of 4.1 years. Fish in the 25–33-cm group (21%) had a mean age of 1.6 years, and the least abundant group (>48–56 cm, 9%) had a mean age of 4.6 years.

Concentrations of mercury in fillet tissue of composite walleye samples ranged from 0.11 to 0.44 mg/kg (wet weight) with an average of 0.34 mg/kg (SD = 0.07; Table 1). Mercury concentrations in composite walleye samples were significantly correlated ($P < 0.01$) with mean total length ($R = 0.57$), mean weight ($R = 0.56$), and mean age ($R = 0.54$).

The regression model that best described the relation between average walleye age and mercury concentration was a curvilinear regression ($R = 0.57$, $P = 0.004$; Figure 2). The concentration of mercury in walleyes increased between ages 1 and 2 and leveled off in fish older than 3 years. The relation between fish length and concentration of mercury in tissue was best described by linear regression (Figure 3). To assess differences among the three reaches, length-standardized mercury concentrations were analyzed for all walleye samples by using ANCOVA. Concentrations of mercury were lower ($P < 0.01$) in walleyes from the Kettle Falls reach than in fish from the Spokane and Sanpoil reaches; and mercury concentrations in walleyes from the Spokane and Sanpoil reaches were not significantly different from each other.

Condition factors of walleyes from the most abundantly collected size-class (>33–41 cm) were significantly different among reaches ($P < 0.002$). Condition factor was significantly lower in walleyes from the Sanpoil ($P < 0.01$) and Spokane ($P < 0.005$) reaches than in those from the Kettle Falls reach. Moreover, condition factor was inversely related to tissue mercury concentrations ($R = -0.59$; $P = 0.02$; Figure 4). Condition factors in the next largest size-group (>41–48 cm) were also significantly lower in the Sanpoil and Spokane reaches when compared with walleyes from the

TABLE 1.—Physical characteristics and age of walleyes in composite samples and results of laboratory tissue analysis for total mercury by sampling location and total length group. A composite sample consisted of eight fillets with skin removed. Ranges for multiple replicates are in parentheses.

Length group (cm)	Number of composite replicates	Mean length (cm)	Mean weight (g)	Mean age (years)	Laboratory analysis	
					Moisture (%)	Mercury (mg/kg wet weight)
Kettle Falls Reach						
25.4–33.0	1	31.8	261	2	80	0.21
>33.0–40.6	6	37.4	426	3	79	0.26
		(36.5–38.9)	(386–491)	(2–4)	(78–81)	(0.21–0.29)
>40.6–48.3	4	43.3	636	4	80	0.31
		(42.9–43.8)	(610–650)	(4–5)	(80)[a]	(0.25–0.36)
>48.3–55.9	1	50.3	1,047	5	79	0.32
Spokane Reach						
25.4–33.0	5	31.1	229	2	77	0.27
		(30.3–32.0)	(206–251)	(1–2)	(68–80)	(0.20–0.37)
>33.0–40.6	7	35.5	344	2	79	0.31
		(34.6–36.0)	(330–367)	(2)[a]	(79–80)	(0.23–0.36)
>40.6–48.3	3	43.7	647	5	80	0.37
		(43.4–44.1)	(632–666)	(4–5)	(80)[a]	(0.35–0.40)
>48.3–55.9	2	50.9	1,028	5	78	0.38
		(50.5–51.2)	(1,021–1,034)	(4–5)	(77–78)	(0.33–0.44)
Sanpoil Reach						
25.4–33.0	1	30.4	205	1	79	0.11
>33.0–40.6	2	36.7	377	2	79	0.36
		(35.3–38.0)	(344–409)	(2–3)	(78–80)	(0.36–0.37)
>40.6–48.3	2	43.1	672	3	78	0.39
		(42.7–43.4)	(617–726)	(3)[a]	(78–79)	(0.36–0.42)

[a] All replicate values were identical.

Kettle Falls reach; however, there was an insufficient number of composite samples for comparing tissue mercury and condition factor for this group.

Mercury concentrations in walleyes did not vary among sampling reaches in accordance with spatial differences in total mercury in surficial bed sediments reported by Bortleson et al. (1994) (Figure 5).

Discussion

Mercury is found in fish from a large number of lakes and rivers throughout the United States and Canada. In a review of whole fish and fillet

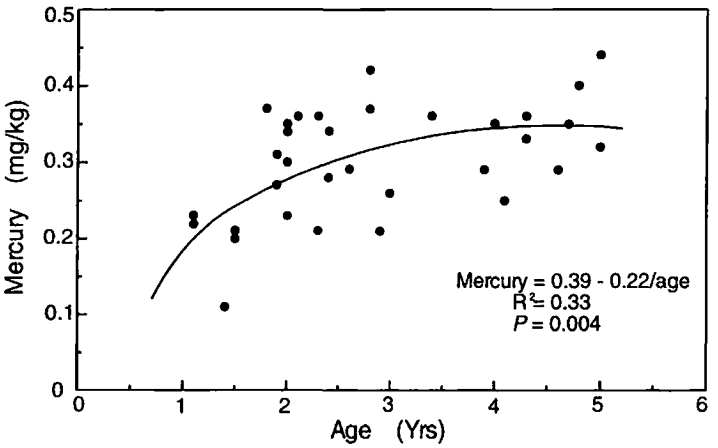

FIGURE 2.—Relation between the concentration of mercury (mg/kg wet weight) in walleye tissue and average walleye age (years).

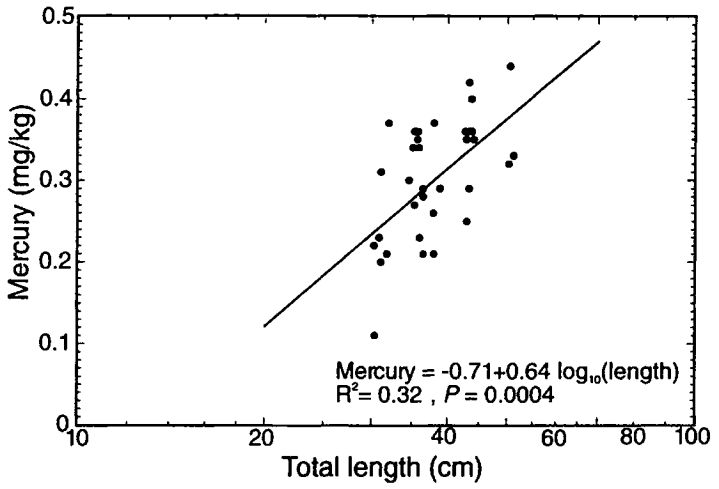

FIGURE 3.—Relation between the concentration of mercury (mg/kg wet weight) in walleye tissue and log-transformed average total length.

data from around the United States, mercury was detected in samples from 92% of the 374 sites studied (EPA 1992). Tissue concentrations of mercury at these sites ranged from less than the detection limit to 1.8 mg/kg (wet weight). In the present study, 50% of the walleye samples collected had concentrations of mercury that exceeded the national median value of 0.17 mg/kg, but none exceeded the U.S. Food and Drug Administration action level of 1.0 mg/kg or the Canadian guideline of 0.5 mg/kg (Norecol 1989). Concentrations of mercury in walleyes collected from Lake Roosevelt in our study were similar to concentrations in walleyes reported from Canadian studies conducted in 1986 and 1987 (Norecol 1989) and were somewhat higher than Serdar et al. (1993) found in walleyes in Lake Roosevelt and the Columbia River above the confluence with the Spokane River (0.17–0.22 mg/kg).

In a survey of mercury in sportfish in Lake Roosevelt, Munn et al. (1995) reported that mercury was detected in all samples of smallmouth bass (0.16–0.62 mg/kg), native rainbow trout (0.16–0.24 mg/kg), and net-pen rainbow trout (0.11–0.16 mg/kg). The median concentration of mercury in age-2 smallmouth bass was lower (0.19 mg/kg) than the median concentration in age-2 walleyes (0.31 mg/kg). Similarly, the median mercury concentration in age-4 to age-5 native rainbow trout was lower than in age-4 to age-5 walleyes (0.20

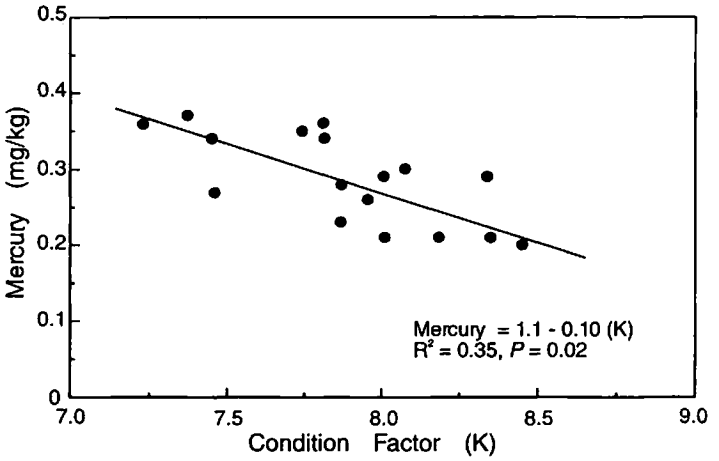

FIGURE 4.—Relation between the concentration of mercury in edible walleye tissue and condition factor of age-2+ fish (mean total length = 36.4 ± 1.2 cm).

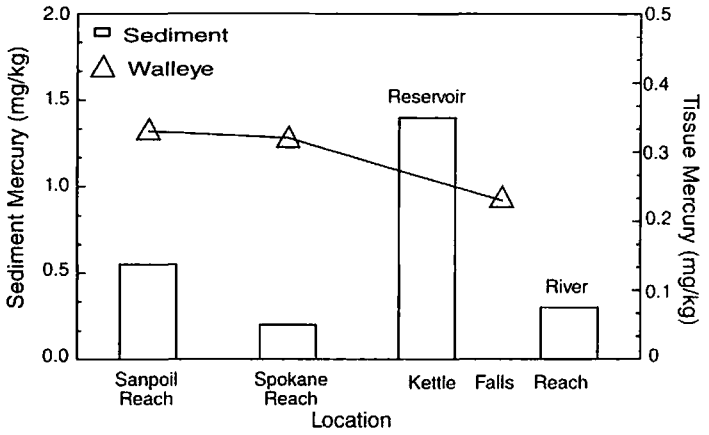

FIGURE 5.—Concentrations of mercury in surficial bed sediments of the upper Columbia River and Lake Roosevelt (from Bortleson et al. 1994) compared with the length-standardized mercury concentrations in walleye tissue.

mg/kg and 0.35 mg/kg, respectively). The median mercury concentration was 0.13 mg/kg in age-3 net-pen rainbow trout and 0.32 mg/kg in age-3 walleyes.

Mercury concentration in fish is age-related and, hence, size-related (Johnels et al. 1967; Huckabee et al. 1979; Windom and Kendall 1979). Whereas our study demonstrated that both age and length of walleyes can be used to predict the concentration of mercury in tissue, the two regression models provided slightly different interpretations of the concentration of mercury in relation to age or length. The curvilinear model used to establish the relation between walleye age and mercury concentration reflects the differential rate of mercury uptake during development. Rate of mercury bioaccumulaton appears to decrease in fish age 3 and older, and this age generally coincides with the onset of reproductive maturity for walleyes in this system (Wydoski and Whitney 1979). The rapid growth rate of juvenile (age-0+ to age-2+) walleyes, coupled with ontogenetic shifts in prey selectivity may account for age-related differences in mercury uptake in walleyes. For example, Griffith and Scholz (1990) reported that fish made up 75–97% of the diet of juvenile walleyes in Lake Roosevelt, and the remainder of the diet consisted of zooplankton and benthic invertebrates. Moreover, preferred prey species shifted from cottids for juvenile walleyes to percids (primarily yellow perch) for adult walleyes. Although not investigated as part of this study, differences in mercury concentrations between prey species may account, in part, for observed age-related differences in mercury uptake in walleyes.

In their study of mercury uptake in yellow perch, Driscoll et al. (1994) found that the relative rate of weight-specific bioaccumulation of mercury decreased with older fish. Typically, older fish put a greater amount of energy into reproduction than into growth and development and, thus, dietary uptake of mercury-contaminated food may decline with age. Accordingly, in the present study, ontogenetic shifts in the extent of dietary assimilation may account, in part, for the lower rate of uptake by older fish. In addition, the more extensive home range of older fish may further limit chronic exposure to local areas where environmental mercury may be elevated.

Our findings with respect to length-related uptake of mercury ($R^2 = 0.32$) were consistent with findings reported by Lathrop et al. (1989) in their study of mercury levels in walleyes ($R^2 = 0.37$) from Wisconsin lakes. Moreover, Jackson (1991) suggested that length is the best predictor of mercury uptake by walleyes because this measure is less prone to short-term variations due to feeding. The strong relationship between mercury uptake and length of walleyes in the present study occurred apparently because walleyes were composited for contaminant analysis based on total length.

Walleyes of >33–48 cm in total length comprised 70% of the fish collected for tissue analysis, and those collected in the Kettle Falls reach were found to have significantly lower ($P < 0.05$) concentrations of mercury than cohorts collected in the Spokane and Sanpoil reaches. This variation of tissue mercury concentration among reaches may be explained by the way mercury enters and moves through the system and by the effects of these transport characteristics on spatial differences in mercury occurrence and bioavailablilty.

Bortleson et al. (1994) reported that most of the mercury that enters the Columbia River is associated with fine-grained sediment (mainly silt), and that in the free-flowing riverine part of the upper Columbia River, the concentration of mercury in suspended sediment is approximately six times greater than that found in coarse, sand-sized bed sediment. On the basis of this finding, a high percentage of mercury in the river appears to originate either from wastewater effluent from a lead–zinc smelter in Canada or from other sources, and that little mercury originates from the sand-sized waste slag that is the source of other metals. The relatively higher sediment concentrations of mercury in the upper reaches of the reservoir suggest that most of the transported mercury is deposited in this area. In general, patterns of mercury distribution in surficial sediments in Lake Roosevelt are not well defined, and characterization of mercury distribution in sediment is confounded by fluctuations in water levels during withdrawal and storage that alter sedimentation patterns through redistribution, resuspension, and erosion of deposited sediments. Much of the bed sediment found in the middle and lower reaches of the reservoir is probably derived from erosion and slumping of bank deposits along the shoreline of the reservoir (Jones et al. 1961) caused by variations in reservoir levels in response to dam operations.

Elevated mercury concentrations in fish have been associated with a variety of physical and chemical water quality characteristics including decreased pH (Wiener et al. 1990; Haines et al. 1992; Lange et al. 1993), elevated water temperature (Bodaly et al. 1993), and decreased specific conductance and hardness (Allard and Stokes 1989; McMurtry et al. 1989; Cope et al. 1990; Lange et al. 1993). Although detailed assessments of both reservoir and tributary water chemistry were not conducted as part of this study, results from previous studies suggest that water chemistry and physical conditions vary little within the main body of the reservoir (Stober et al. 1981; Stober and Nakatani 1992). The system achieves only partial stratification during the summer months and, owing to an average water retention period of only 40 d, the reservoir's deep water remains fairly well mixed throughout most of the year. For example, Stober et al. (1981), in their 1980 limnological study of Lake Roosevelt, found that temperature and pH varied little with depth, based on measurements taken at eight locations along the longitudinal axis of the reservoir. This lack of a strong spatial difference among limnological measurements was recently confirmed by G. Wilson (Washington State University, personal communication, 1996).

Although reservoir-wide physical and chemical conditions were not expected to be markedly different, site-specific factors associated with varying lake morphometry, such as differences in water temperature, could possibly alter local conditions and, hence, bioavailability, particularly in the shallow littoral regions that are the preferred foraging locations for walleyes. Bodaly et al. (1993), for instance, found that mercury concentrations were greater in muscle tissues of walleyes and northern pike *Esox lucius* from small, relatively shallow lakes than in fish from larger and colder, deep lakes. Specific rates of mercury methylation in the lakes were positively correlated with water temperature, whereas specific rates of methylmercury demethylation were negatively correlated with temperature. Furthermore, from whole-lake experiments, Harrison et al. (1990) indicated that mercury enters food chains more rapidly in small, shallow lakes with high littoral-area : pelagic-area ratios than in large, deep lakes. Similarly, Ramlal et al. (1993) found that mercury methylating activity was 20–40 times greater in epilimnetic than hypolimnetic sediments, presumably owing to higher epilimnetic water temperatures. A detailed sediment–water interface study is needed in shallow foraging areas in Lake Roosevelt in order to understand mercury cycling in the system.

Walleyes collected in this study may represent fairly localized assemblages of the overall population that are segregated spatially in accordance with the location of the major tributaries. Griffith and Scholz (1990) reported that although many walleyes migrate throughout the reservoir to and from spawning areas, approximately 50% are recovered in the vicinity of the release site. Furthermore, Griffith and Scholz (1990) found that walleyes collected in the lower reservoir use the area as both a home range and spawning grounds, thus supporting our conclusion of some spatial separation of walleyes within the reservoir. In general, walleyes in oligotrophic lakes tend to occupy the more eutrophic littoral zones where prey are likely to occur (Ryder and Kerr 1978; Schupp 1978) and may limit their activities to a relatively small home range (Ney 1978). Adult walleyes have been observed to limit migrations between home spawning and home foraging areas (Olson et al. 1978) and to not stray to other spawning areas. Moreover, movement during postspawning migrations does not appear to be extensive, and some

walleyes select the same general locations for feeding in successive years. In addition to the mainstem Columbia River flowing into the upper reach, the three major tributaries emptying into Lake Roosevelt represent walleye spawning areas and spatially define the three sampling reaches.

The trophic structure of a water body can influence mercury concentrations in fish, particularly in species that are predominantly piscivorous, such as walleyes. In addition, differences in foraging activities among the walleye assemblages, particularly site-specific differences in mercury content of prey species, might have contributed to variation in mercury concentrations in walleyes among reaches. Dietary uptake is the primary source of tissue methylmercury in fish predators (Dallinger and Kautzky 1985; Wren and MacCrimmon 1986; Miller et al. 1993). Cope et al. (1990) suggest that mercury levels in yellow perch are indicative of levels in walleyes, their main predator. Akielaszek and Haines (1981) found that lake trout *Salvelinus namaycush* have higher mercury concentrations when rainbow smelt *Osmerus mordax*, the principal forage fish, are present. Similarly, mercury concentrations in northern pike in a Finnish lake lacking forage fish were about one-fourth those in northern pike in nearby, similar lakes with forage fish (Rask and Metsälä 1991).

Although the concentrations of mercury in walleye muscle tissue differed among reaches within the reservoir, no consistent relationship was found between the concentrations of mercury in tissue and the concentrations in bed sediment. The significant correlations between condition factor and mercury concentrations in tissue reported here may reflect the fact that elevated environmental concentrations of trace elements can reduce both the quality and quantity of food resources (Miller et al. 1992). For instance, Munkittrick and Dixon (1988) suggested that observed reductions in growth of female white suckers *Catostomus commersoni* and corresponding decreases in fecundity probably resulted from a decrease in available food rather than a direct effect of metal accumulation. Although the detrimental effects of mercury on growth and development cannot be ruled out as factors affecting fish condition in the present study, given that mercury levels in walleyes and bed sediment were not markedly elevated or highly correlated, differences among reaches in condition factor of walleyes were probably responses to site-specific factors affecting growth and development, such as reservoir morphometry and associated effects on temperature, productivity, and prey availability (Parsons 1971; Schupp 1978).

Most studies dealing with the bioaccumulation of mercury in fish inhabiting lakes and reservoirs have either examined differences among co-occurring species or compared mercury concentrations for a single species among different systems. In contrast, we observed a differential bioaccumulation of mercury in walleyes within a single system. Our study indicates that for walleyes, concentrations of mercury among localized aggregrations of individuals can vary significantly and that assessment of potential mercury contamination based on concentration levels in fish tissue requires a spatially comprehensive sampling approach. Furthermore, spatial patterns corresponding to differences in tissue concentrations of mercury cannot be predicted from spatial differences in concentrations of mercury in surficial sediments.

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New Insights into Traditional Health Risk Assessments of Mercury Exposure: Implications of Selenium

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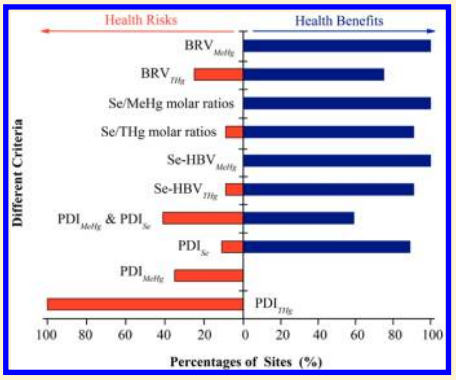
ABSTRACT: There is increasing evidence that selenium (Se) has a significant effect on mercury (Hg) toxicology; however, Hg exposure risk assessments usually consider only the amount of Hg present in the environment or in food. On the basis of the present understanding of mechanisms of interaction between Se and Hg, the physiology/toxicology of Se, and the toxicology of Hg, we propose a new criterion for Se/Hg exposure assessment. This criterion, which is based on Se−Hg interactions, considers not only the toxicological consequences of Hg exposure but also the benefits and/or adverse effects of Se intake, especially the adverse effects related to a Se deficiency/excess. According to an illustrative assessment based on the new criterion and nine existing criteria, large knowledge gaps in the traditional assessments of exposure to Hg and/or Se were found, including those that assessed the interactions between Hg and Se. These results suggest that future assessments of Hg exposure (or Se intake) should include both Se and Hg.



INTRODUCTION

Mercury (Hg) is an exogenous, toxic, and ubiquitous trace element that is nonessential to humans and animals. Methyl-Hg (MeHg), one of its most toxic organic forms, can easily cross the blood-brain and placental barriers; high exposure may cause severe and irreversible damage, particularly to the fetal central nervous system.[1] The MeHg concentrations in water, soil, and sediments are usually negligible when compared to its less toxic inorganic form;[2,3] however, MeHg can bioaccumulate and be biomagnified in aquatic food webs and even some terrestrial plants (e.g., rice[3]), eventually posing a serious threat to humans through the consumption of fish and/or rice.[2] At present, the consequences of long-term, chronic exposure to MeHg remain poorly understood; however, recent epidemiological studies have shown a dose−response relationship at much lower levels of MeHg exposure than those previously recognized as hazardous.[4]

Selenium (Se) is an essential trace element and nutrient that is of vital importance to human health.[5,6] Se exists in human and animal selenoproteins as selenocysteine (Sec) and selenomethionine (SeMet) and is incorporated into the active sites of antioxidant selenoenzymes (glutathione peroxidase and thioredoxin reductase).[7,8] The human selenoproteome includes 25 genetically encoded selenoproteins (including multiple forms of glutathione peroxidases and thioredoxin reductases).[5] Through its incorporation into selenoenzymes (primarily via Sec in mammals), Se exerts important biological functions that affect processes such as free radical metabolism, immune function, reproductive function, and apoptosis.[8,9] Se is particularly fundamental for the redox-mediated prevention and repair of oxidative damage in the brain and neuroendocrine tissues.[10] Epidemiological studies indicate that Se deficiency is necessary for the occurrence of a well-known cardiomyopathy endemic to China (Keshan disease), which is associated with >90% mortality and affects many young children in areas of China where the Se intake is lower than 10 μg/day.[11] Other effects of Se deficiency include muscular dystrophy, reproductive disorders, dental caries, necrosis of the liver/kidney/heart, and cancer.[7,8] Therefore, an adequate intake of Se is important for maintaining the normal physiological synthesis and activity of essential selenoproteins.

The recommended dietary allowance (RDA) of Se for adults in the US is 55 μg/day (the same as that set by the World Health Organization (WHO), equivalent to 0.79 μg/kg body weight [bw]/day, assuming a 70-kg bw for US residents.[12,13] In general, humans obtain Se through dietary intake alone, and many common foods such as fish meals, seafood, seaweeds, meat, cereals, and eggs are important sources of Se.[14,15] However, Se can also be harmful to humans and animals at high exposures due to the narrow margins between the amount that is essential and the levels associated with deficiency or toxicity.[8] Long-term exposure to high levels of Se in food and water may result in health problems, including loss of nails and hair, tooth decay and discoloration, skin lesions, nervous system disorders,

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paralysis, and death.[8] The tolerable upper limit (UL) of Se intake for an adult set by the U.S. Food and Drug Administration (US FDA) and the WHO is 400 μg/day (equivalent to 5.71 μg/kg bw/day, assuming a 70-kg bw for US residents.[12,13] However, the UL of 400 μg/day has been considered to be too conservative considering it was derived arbitrarily by defining one-half the estimate made by Yang et al.[16] Using the same study conducted in Enshi China by Yang et al.[16] as the reference case, Poirier[17] pointed out that no adverse effects were observed with the Se intake for an adult as great as 853 μg/day.

The coexistence of Se and Hg in animal tissues and protective effect of Se against inorganic Hg toxicity has been recognized for nearly half a century, since 1967.[18−24] For a number of years, the protective roles of Se against MeHg have inconsistent.[6] Only recently, the protective effects of organic Se against MeHg toxicity in fetal brain and development have been confirmed by a series of animal studies.[25,26]

MeHg can pass the blood brain barrier and placenta to exert toxic effects on the central nervous system of adults and fetuses.[1] MeHg can exert its neurotoxicity by altering the activity of Na^+/K^+-ATPase, disrupting intracellular calcium homeostasis, and causing oxidative stress, and disrupting neurotransmission.[27] Besides, MeHg toxicity has been considered to be linked to its reactivity to the thiol ligands (-SH) of the proteins in the organisms.[28] Previous study revealed that the biologically active MeHg may predominantly bind to cysteine thiols as MeHg−cysteines complex (MeHg−Cys).[29] The MeHg−Cys complex is molecularly similar with SeMet, which thus can readily cross the placental and the blood-brain barrier.[30] When MeHg−Cys reaches at the active sites of selenoenzyme, the S atom of MeHg−Cys can be directly replaced by the ionized Se of Sec and form the unavailable MeHg−Sec complex owing to the extremely high binding affinity between Se and Hg than that between S and Hg.[31] The formation of the unavailable MeHg−Sec complex thereby inhibits the bioavailability of MeHg yet simultaneously results in efficient sequestration of the biologically required Se in intracellular cycles of Sec synthesis that maintain normal selenoenzyme metabolism in these otherwise protected tissues. Therefore, MeHg has been considered to be a highly specific, irreversible selenoenzyme inhibitor,[32] which implies that impairing selenoenzyme activity and synthesis is one of the possible mechanism of MeHg toxicity especially when the organism is in a Se-deficient state.

Although several physiologic/biochemical mechanisms have been proposed to explain the antagonism between Hg and Se (well summarized by e.g., Yang, et al.[23] and Khan and Wang[24]), the molecular mechanism likely involves the formation of insoluble, equimolar, and biologically unavailable mercury selenide (HgSe) precipitates. Approximately 1:1 molar ratios of Se/Hg have been commonly observed in various species, for example, marine mammals (plasma, erythrocyte, liver) and sea birds and in human (Hg miners, brain, kidney, liver, muscle tissue and urine; and residents, urine) of Hg-mining areas.[24,33,34] The binding affinity between Hg and Se is exceptionally high (with a constant of 10^{45}); in particular, it is one-million-fold higher than the binding affinity (10^{39}) between Hg and sulfur in the production of mercury sulfide (HgS). Thus, an interaction between Se and Hg should readily result in the formation of metabolically inert HgSe precipitates, which have an extremely low solubility (10^{-58} to 10^{-65}) compared to that of HgS precipitates (10^{-52}).[35] It has been proposed that the Hg and Se bind to plasma protein to form high molecular weight complexes, which was described as $(Hg−Se)_n$-selenoprotein P (or (Hg−Se)*n*-SelP).[23,24] The (Hg−Se)*n*-SelP was considered to be the precursor of the HgSe(s).[24] Recently, the existence of inert HgSe(s) granules *in vivo* was unambiguously confirmed using X-ray absorption near edge structure (XANES).[24]

As mentioned earlier, the extensive formation of inert Hg−Se would consequently compromise the biological availability of both Hg and Se, which is consistent with the results of numerous studies reporting alleviation of acute toxicity after simultaneous exposure to Hg and Se in doses higher than their threshold limit values.[20,23,24] Another possible mechanism of the Se protective effect is antioxidation. MeHg disrupts the glutathione (GSH) system maturation resulting in a decrease of GSH-Px in the developing brain, but this toxic effect can be protected by Se as Se can decrease the overall oxidative stress induced by MeHg.[26]

Because Se plays important physiological and biochemical roles in humans and animals, the formation of HgSe precipitates may result in Se deficiency and a corresponding impairment of selenoenzyme activity and synthesis,[7,8] with consequent adverse effects. However, the observed toxicity may be affected by both MeHg toxicity and Se deficiency, especially when there is a greater exposure to MeHg than to Se. After reviewing a large number of studies on this subject, Khan and Wang [24] proposed that Hg toxicity is caused, at least in part, by Hg-induced Se deficiency. In other words, the antidotal effect of Se for counteracting Hg occurs by ensuring that normal selenoenzyme activity and synthesis is maintained. Hence, some of the adverse effects of Hg exposure may be prevented by consuming sufficient Se to result in a greater than 1:1 molar ratio of Se/Hg,[36] while attempting to maintain the Se intake in the physiologically appropriate range. One good example is the study recently conducted in Wanshan Hg mining area in China by Li et al.[34] In their study, supplementation of organic selenium significantly increases Hg excretion and protects against the oxidative damage of long-term Hg exposed local residents.

Despite the decades-long establishment of protection against Hg toxicity by Se in general [18] and by an Se/Hg molar ratio of >1:1 in particular,[36] the current criteria for safe levels of Hg exposure do not consider Se, primarily because the exact Se/Hg ratio that confers protection is unclear. Nonetheless, Se/Hg molar ratios have been commonly used in research and/or assessments of Hg exposure to simplify assessments of the nutritional benefits of Se intake and the risks of MeHg exposure from the consumption of fish and ocean-sourced foods. For instance, a recent animal study indicated that MeHg toxicity could not be explained by MeHg alone but could be explained by considering Hg and Se together (based on Se/Hg molar ratios).[37]

Recently, Kaneko and Ralston [38] proposed a new safety criterion for Hg exposure assessment, the Se-Health Benefit Value (Se-HBV), which is calculated as Se-HBV = Se × (Se/Hg) − Hg × (Hg/Se). This equation includes both the absolute molar concentrations and the relative molar ratios of Se and Hg. The Se-HBV indicates the health benefits (if positive) or health risks (if negative) of Se in terms of Hg exposure. At first glance, the Se-HBV appears more elegant than the molar ratio alone, and it has also been commonly cited in many studies to assess Hg exposure from seafood. Unfortunately, however, the Se-HBV and the traditional Se/

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Table 1. Probable Daily Intake of Se versus Hg by Adults (60 kg bw) for Rice-Based Rural Population Living around the Wanshan Hg Mined Area, Including Values Assessed Using Different Criteria and the Corresponding Percentages of Sites with Health Risks and Benefits[a]

No.		mean ± SD	range	percentage of sites with risks	percentage of sites with benefits	assessment criteria
based on μg/kg/day						
(1)	PDI_{THg}	1.9 ± 1.5	1.2−6.1	100%	0%	[$PTWI_{THg}$ (<0.57 μg/kg bw/day)][b]
(2)	PDI_{MeHg}	0.096 ± 0.17	0.015−0.46	34%	0%	[RfD_{MeHg}(<0.10 μg/kg bw/day)][c]
(3)	PDI_{Se}	2.1 ± 1.5	1.4−8.0	12%	88%	[SIR_{Se}(0.83−3.33 μg/kg bw/day)][d]
(4)	PDI_{MeHg} and PDI_{Se}			41%	59%	[RfD_{MeHg} and SIR_{Se}][e]
based on nmol/kg/day						
(5)	Se−HBV_{THg}	150 ± 260	−55−1700	9%	91%	[Se(Se/THg) − THg(THg/Se) > 0][f]
(6)	Se−HBV_{MeHg}	2200 ± 12400	140−88000	0%	100%	[Se(Se/MeHg) − MeHg(MeHg/Se) > 0][f]
based on nmol/kg/day						
(7)	Se/THg	3.0 ± 2.6	0.58−16	9%	91%	[Se/THg >1][g]
(8)	Se/MeHg	80 ± 150	6.1−860	0%	100%	[Se/MeHg >1][g]
based on nmol/kg/day						
(9)	BRV_{THg}	9.1 ± 21	−28−84	25%	75%	[$0 < PDI_{Se} - \nabla_{Se} - PDI_{THg} < \nabla_{Se}'$][h]
(10)	BRV_{MeHg}	45 ± 120	3.2−770	0%	100%	[$0 < PDI_{Se} - \nabla_{Se} - PDI_{MeHg} < \nabla_{Se}'$][h]

[a]Abbreviations: BRV, benefit-risk value; PDI, probably daily intake; PTWI, provisional tolerable weekly intake; RfD, reference dose; Se-HBV, Se-Health Benefit Value; SIR, safe intake range. [b]Equivalent to 4 μg/kg bw/week.[40] [c]Equivalent to 0.7 μg/kg bw/week.[41] [d]Equivalent to 50−200 μg/kg bw/week.[14,15] [e]Concurrently meet criterion (2) and (3), i.e., $PDI_{MeHg} < RfD_{MeHg}$ (0.10 μg/kg bw/day) and PDI_{Se} within the SIR_{Se} (0.83−3.33 μg/kg bw/day). [f]Kaneko and Ralston.[38] [g]Ganther et al.[36] [h]Present study.

Hg molar ratio both have a serious limitation: in certain extreme cases, although the safety requirement (Se/Hg molar ratio > 1 or Se-HBV > 0) is met, the Se intake may be either below the level required for normal selenoenzyme activity and synthesis (deficiency) or above the safe range (poisoning). Although the Se-HBV and Se/Hg molar ratio may both appear ideal, these are associated with hidden risks. Therefore, an assessment based on either criterion may be misleading. Besides, we noticed that the criterion of Se-HBV= Se(Se/Hg) − Hg(Hg/Se) was recently "updated" as HBV_{Se} = (Se − Hg)/Se*(Se + Hg) by Ralston and Raymond.[39] Unfortunately, it still has a similar limitation: for example, when we assume Hg exposure is zero and Se intake is 10^5 nmol/kg/day (far greater than 170 nmol/kg/day, the threshold value for Se poisoning[14,15]), then the calculated HBV_{Se} should be 10^5 (indicates "great health benefit"). However, this value is actually associated with hidden risks of Se poisoning and thus misleading.

Our main objectives of this study were (1) to develop a new criterion for Se/Hg exposure assessment, which is based on Se−Hg interactions and considers not only the toxicological consequences of Hg exposure but also the benefits and/or adverse effects of Se intake, especially the adverse effects related to a Se deficiency/excess, as mentioned above; (2) to examine the knowledge gaps in previous studies that considered Hg or Se alone versus those that considered Se−Hg interactions (using the new criterion and other existing criteria).

MATERIALS AND METHODS

Proposal for a New Criterion. On the basis of our present understanding of Se−Hg interactions, the physiology/toxicology of Se, and the toxicology of Hg, we propose a new criterion for assessing Hg exposure and Se intake, as shown below:

$$BRV = PDI_{Se} - \Delta_{Se} - PDI_{Hg} \quad (1)$$

$$PDI = \Sigma(C^i \times IR^i)/bw \quad (2)$$

where BRV represents the benefit-risk value, which indicates either health benefits (if $0 < BRV < \nabla_{Se}$) or health risks (if $BRV < 0$ or $BRV > \nabla_{Se}$); Δ_{Se} represents the minimal Se amount required for normal biological function when Hg exposure is zero; ∇_{Se} represents a threshold value for Se poisoning which considered the protective effects from Hg exposure; PDI represents the probable daily intake of Se (PDI_{Se}), Hg (PDI_{Hg}), or MeHg (PDI_{MeHg}); C is the concentration of the exposed medium; IR is the intake rate (the rate of ingestion or inhalation); and i is the intake of a potentially Hg-contaminated substance such as water, rice, fish, vegetable, corn, meat, or poultry. All of the above calculations are based on units of molar concentrations; for example, PDI is measured in nmol/kg bw/day.

Some researchers may prefer a format that directly reflects the molar ratio of Se/Hg. The BRV mentioned above can also be expressed as a molar ratio, that is, a benefit-risk ratio (BRR), as shown below:

$$BRR = (PDI_{Se} - \Delta_{Se})/PDI_{Hg} \quad (3)$$

Similarly, the BRR indicates health benefits if $1 < BRR < 1 + \nabla_{Se}/PDI_{Hg}$ (equivalent to $0 < BRV < \nabla_{Se}$), or it indicates health risks if $BRR < 1$ or $BRR > 1 + \nabla_{Se}/PDI_{Hg}$ (equivalent to $BRV < 0$ or $BRV > \nabla_{Se}$).

The value of Δ_{Se} temporarily represents the lowest safe intake of Se for a human, which is 11 nmol/kg/day (equivalent to 50 μg/day recommended by the Chinese Nutrient Society (CNS)[14,15] or 0.83 μg/kg bw/day if bw is assumed to be 60 kg for Chinese residents; or equivalent to 55 μg/day recommended by the US FDA and the WHO or 0.79 μg/kg bw/day if bw is assumed to be 70 kg for US residents). Similarly, the value of ∇_{Se} temporarily represents the threshold value for Se poisoning set by the CNS,[14,15] which is 170 nmol/kg/day (equivalent to 800 μg/day, or 13.3 and 11.4 μg/kg bw/day, respectively, for Chinese residents and US residents). The dietary Se intake in most populations is far below this threshold value,[15] but it should still be assessed. The intention of the proposed criterion is to examine the use of alternate indices

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that may more accurately reflect health risks and benefits for use in future studies.

Comparison of Different Criteria. We used the new criterion (BRV) proposed above together with existing criteria (PDI, Se-HBV, and Se/Hg molar ratio; Table 1) to assess the health benefits and/or risks of combined Hg and Se exposure through dietary sources (e.g., rice, fish, meat, poultry, vegetable, and drinking water) for residents of 59 locations around a heavily Hg-contaminated area of China covering over 700 km^2 (Wanshan, the largest Hg mining region in Asia). Detailed information about the local settings were provided in our recently published articles.[2,3,35]

The design of this illustrative assessment included four different scenarios: (I) considering only Hg levels using the criteria established by the US Environmental Protection Agency (USEPA) and the Joint Food and Agriculture Organization (FAO)/WHO Expert Committee on Food Additives (JECFA); (II) considering only Se levels using the criteria established by the CNS; (III) considering both Se and Hg independently using the criteria established by the USEPA, JECFA, and CNS; and (IV) considering Se−Hg interactions based on their molar concentrations.

The assessments for the four different scenarios were based on each of the 10 criteria (i.e., PDI_{THg}, PDI_{MeHg}, PDI_{Se}, PDI_{Se} and PDI_{MeHg}, Se-HBV_{THg}, Se-HBV_{MeHg}, molar ratio of Se/THg, molar ratio of Se/MeHg, BRV_{THg}, and BRV_{MeHg}), as shown in Table 1 and Figure 1. It should be mentioned here that all of

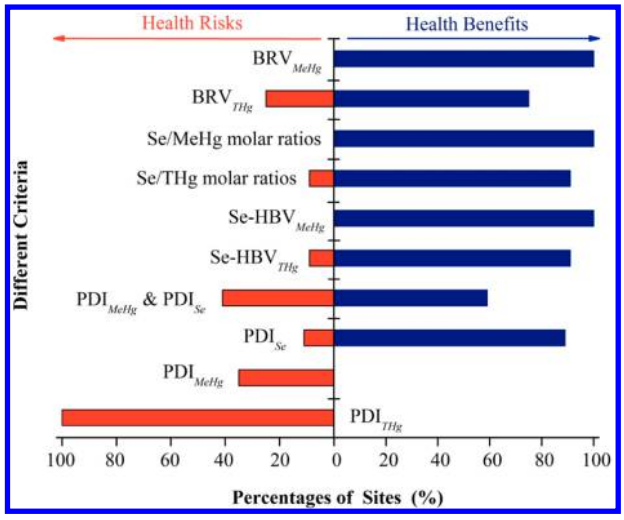

Figure 1. Percentages of sites with health benefits or risks using different criteria.

the calculations in the present illustrative assessment for the Wanshan adult residents were based on 60 kg bw rather than the 70 kg that is commonly used for similar assessment for US residents.

The main purpose of this illustrative study was to examine the knowledge gap between our previous study[4] assessing Hg alone and the present study, which concurrently assessed both Hg and Se individually and the interaction between them. This assessment was primarily based on data from our recently published studies, which are summarized in Table 2.

RESULTS AND DISCUSSION

Differences observed among the results of the assessments using each of the 10 criteria mentioned above were shown in Figure 1 and Table 1.

Scenario I. *Criteria Considering only Hg.* As reported in our previous study,[2] all the sites in Wanshan exhibited levels of Hg exposure associated with health risks if they were assessed using the PDI_{THg} criterion alone based on the provisional tolerable weekly intake (PTWI) of 4 μg/kg bw/week (equivalent to 0.57 μg/kg bw/day).[40] In that study, however, we concluded that PDI_{THg} should not be used to evaluate Hg exposure in the Wanshan area because 95% of the Hg to which the local residents were exposed was inorganic Hg (Table 2), which is much less toxic than MeHg and has a low (only 7%) absorption rate compared to that of MeHg (95%). Alternatively, if assessed using the reference dose (RfD) of 0.1 μg/kg bw/day recommended by the USEPA,[41] the proportion of Wanshan sites with risky levels of Hg exposure was greatly reduced (to 34%). The main reason for this large difference is that rice consumption accounts for ∼95% of the total MeHg exposure among the local residents, whereas fish accounts for only 1% (the local residents rarely eat fish).[2]

The development of the $PTWI_{THg}$ by the JECFA was based on a fish-eating population (derived from toxicity data from poisoning incidents at Minamata and Niigata in Japan) that was primarily exposed to MeHg. The $PTWI_{THg}$ was originally set at 5 μg/kg bw/week (equivalent to 0.7 μg/kg bw/day).[42] More recently, this value was adjusted to the present level of 4 μg/kg bw/week (equivalent to 0.57 μg/kg bw/day).[40] The $PTWI_{THg}$ of 0.57 μg/kg bw/day may be acceptable for fish-eating populations in regions where MeHg is the primary Hg species (i.e., at least more than 40% of THg, see Results and Discussion in what follows) and where MeHg data are unavailable, because inorganic Hg is much less toxic than MeHg and its absorption rate by human body through dietary intake has been estimated to be only 7% while the absorption rate for MeHg is about 95%.[2] As there are great variations in the MeHg/THg ratios among fish species or geographic regions,[43] MeHg concentrations should be measured based on the $PTWI_{MeHg}$ or the RfD_{MeHg} to better provide health guidelines for fish-eating populations.

Similar with $PTWI_{THg}$, the $PTWI_{MeHg}$ has also been adjusted, from 3.3 μg/kg bw/week (equivalent to 0.47 μg/kg bw/day)[42] to the present level of 1.6 μg/kg bw/week (equivalent to 0.23 μg/kg bw/day).[2] This adjustment reduced the ratio of MeHg/THg from 66% to approximately 40%. USEPA recommended a more conservative RfD (MeHg) of 0.1 μg/kg bw/day (equivalent to 0.7 μg/kg bw/week),[41] compared to the $PTWI_{MeHg}$ (1.6 μg/kg bw/week).

However, for rice-eating populations in inland China (e.g., Wanshan in the present study) or other regions where Hg exposure is dominated by inorganic Hg (exceeding 90% of THg[2]), the JECFA PTWI (THg and MeHg) and the USEPA RfD (MeHg) may both inadequately reflect the level of health risk because rice does not contain several important neurologic development-enhancing micronutrients found in fish, such as docosahexaenoic acid (DHA, an omega-3 long-chain polyunsaturated fatty acid), arachidonic acid (an omega-6 fatty acid), and iodine.[43]

Fortunately, Se, another important micronutrient for human health and a well-known efficient antidote to Hg exposure as mentioned earlier, can be absorbed and significantly bio-

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Table 2. Average Concentrations of Hg versus Se and the Average Estimated Daily Intake of Se versus Hg by Adults (60 kg bw) with Percent Contributions (Values in Parentheses) from Different Sources for Rice-Based Rural Population Living around the Wanshan Hg Mined Area[a]

						Hg intake	Se intake	MeHg intake
source	unit	Hg	Se	MeHg	intake rate[c]	μg/day	μg/day	μg/day
rice	(μg/kg, DW)	78[b]	98[b]	9.3[b]	600 g/day, DW	49 (43%)	59 (43%)	5.6 (96%)
vegetables	(μg/kg, WW)	130[c]	29[d]	0.097[c]	370 g/day, WW	47 (41%)	11 (8.0%)	0.036 (1.0%)
meat	(μg/kg, WW)	220[c]	690[e,f]	0.85[c]	79 g/da,y WW	17 (15%)	55 (40%)	0.067 (1.0%)
poultry	(μg/kg, WW)	160[c]	1500[g]	2.4[c]	4.9 g/day, WW	0.77 (0.60%)	7.5 (5.0%)	0.073 (1.0%)
fish	(μg/kg, WW)	290[c]	3000[g]	60[c]	1.2 g/day, WW	0.35 (0.30%)	3.6 (3.0%)	0.011 (0.20)
water	(ng/L)	50[c]	1010[h]	0.064[c]	2.0 L/day	0.10 (0.10%)	2.0 (1.0%)	0.0010 (0.020)
total					μg/day	110	140	5.8
					μg/kg/day	1.9	2.1	0.096

[a]Abbreviations: DW, dry weight; PDI, probably daily intake; WW, wet weight. [b]Zhang et al.[35] [c]Zhang et al.[2] [d]Li et al.[34] [e]Gou et al.[49] [f]Estimated based on 65% water content. [g]Ji et al.[50] [h]Zhang et al.[44]

accumulated in many foods, including rice.[35] Rice is a staple food in most of Asian countries. Indeed, rice consumption has been observed to be the primary route (70%) of Se intake among rice-based rural populations in inland China.[14,15] Because they rarely eat fish and ocean-sourced foods, the general populations of rice-based areas of inland China, except heavily Hg-contaminated areas (e.g., Wanshan), have Hg exposure levels well below the MeHg RfD of 0.1 μg/kg bw/day.[2] In such populations, it may be more beneficial to assess the local residents' Se intake status than their Hg exposure because either excessive or inadequate Se intake is associated with serious health risks.

Scenario II. *Criteria Considering only Se.* According to our estimates from the present illustrative assessment, most (88%) of the sites in the Wanshan area exhibited PDI_{Se} values well within the safe intake range of Se (SIR_{Se}) of 50−200 μg/kg (equivalent to 0.83−3.33 μg/kg bw/day for a bw of 60 kg) established by the CNS.[14,15] Approximately 12% of the Wanshan sites had PDI_{Se} values higher than the UL of the SIR_{Se} (3.33 μg/kg bw/day). However, the highest PDI_{Se} in Wanshan, 8 μg/kg bw/day, was still below the threshold value for Se poisoning (13.33 μg/kg bw/day; equivalent to 800 μg/kg; Table 1). No sites had PDI_{Se} values below the lowest limit of the SIR_{Se}.

The PDI_{Se} range in Wanshan (85−478 μg/day) was comparable to that in countries with adequate Se intake levels (e.g., the US range of 71−152 μg/kg[12,13]); however, the average PDI_{Se} in Wanshan (128 μg/day) was 6−18 times greater than that in regions with high rates of Se deficiency (e.g., 7 μg/day in an endemic Keshan disease area of China and 17 μg/day in Burundi) and 3−4 times greater than in regions with moderate rates of Se deficiency (e.g., 34 μg/day in the UK, 39 μg/day in Greece, and 44 μg/day in Suzhou, China[45]).

The Se levels in food are mainly determined by the Se levels in the soils where the plants are grown. In our recent study, the average soil Se levels in Wanshan (2.1 mg/kg) were elevated compared to the background concentrations in Guizhou (0.38 mg/kg) and China as a whole (0.24 mg/kg), reaching levels comparable to those in the Enshi seleniferous region (4.1 mg/kg).[35] Therefore, the high Se levels in the local soils produced high Se levels in foods such as rice, vegetables, meat, fish, and poultry (Table 2). For instance, the total Se levels in the local rice averaged 98 μg/kg, which was 3−4 times greater than in China as a whole (32 μg/kg) and similar to the average Se levels in rice (81 μg/kg) from the Se-rich Kaiyang region in Guizhou Province.[35] According to the results, rice (43%), meat (40%), and vegetables (8%) were the main routes of Se intake for residents in Wanshan, whereas a combination of fish, poultry, and other foods accounted for only 9% of the total PDI_{Se} (Table 2).

Scenario III. *Criteria Considering Hg and Se Independently.* When Hg and Se were considered independently, few sites (approximately 5%) showed an additive risk. Approximately 36% of the sites showed a single type of risk, e.g., 29% of the sites had an PDI_{MeHg} higher than 0.1 μg/kg bw/day but an Se intake in the safe range, and 7% of the sites had an PDI_{Se} exceeding the safe range but an MeHg intake below the RfD_{MeHg}. Approximately 59% of the sites showed a complete absence of risk; that is, neither MeHg nor Se was in excess of the acceptable limits (Table 1). Overall, approximately 41% of the sites had some health risk (either a single risk or double risks) when Hg and Se were considered independently. This number was higher than those found when MeHg (34%) or Se (12%) was assessed alone.

Compared to Hg exposure, the health problems associated with the incorrect intake of Se are seriously overlooked by the general population. Most people are familiar with the health risks of MeHg toxicity, but few are aware of the physiological importance of Se. Similarly, researchers often consider the ability of Se to inhibit the toxicity of Hg, but we rarely consider that Hg can also inhibit the toxicity of Se. Therefore, a criterion that considers Se−Hg interactions is fundamental to the appropriate evaluation of risk from exposure to both Hg and Se.

Scenario IV. *Criteria Considering Se−Hg Interactions.* We found that all the sites showed health benefits rather than health risks when assessed using criteria that considered the protective interactions between Se−MeHg based on their molar concentrations. All of the three methods, that is, Se/Hg molar ratios,[36] Se-HBV,[38] and BRV (the present study) (Table 1) indicated that the health risks of MeHg exposure were offset by Se intake. The reverse was also true: the health risks of excessive Se intake were neutralized by moderate MeHg exposure. Hence, the 41% of sites with health risk of Se and MeHg exposure under scenario III above exhibited little or no health risk. These results indicate that our previous study[2] considering only the Hg in the environment and foods in this area may have overestimated the level of risk for the local residents. This may be ubiquitous for the previous Hg exposure assessment for fish-eating population as molar ratios of Se/Hg > 1:1 are commonly observed in most marine fish, similar with that in rice, except for pilot whale which contains much more Hg than Se.[35,37]

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Although THg was not used in this assessment, the results based on Se and THg using the three corresponding criteria (Table 1) are shown to elucidate the differences among the three criteria based on the aforementioned molar concentrations above. The results revealed that there was no difference between the results using the Se/Hg molar ratios criterion and the Se-HBV criterion, both of which indicated that 9% of the sites may be associated with health risks. This observation is not surprising because there is no difference in the underlying mechanisms. However, the use of the BRV criterion proposed in the present study increased the proportion of sites with health risks from 9% to 25%, likely because the BRV criterion considers both the health risks of Se excess/deficiency and the Se amount (∇_{Se}) required for normal biological function.

IMPLICATIONS

On the basis of the present study, the traditional method of assessing the health risks of Hg exposure clearly does not fully reveal the actual health risk because this method neglects the contribution of Se. Dietary Se intake may have an important impact on the toxicological consequences of Hg exposure; similarly, assessments of Se intake alone may inadequately reflect the health risk/benefit of Se if its interactions with Hg are not considered. Recently, Laird et al.[46] emphasized the importance of including the benefits of nutrients when issuing dietary advice on Inuit traditional food in Canada. The proposed assessment criteria can potentially be applied as the sources of Se and Hg were reported coming from the same food items.

The most noteworthy finding of the present study is that assessment criteria that consider Se−Hg interactions should also take into account the Se amount (Δ_{Se}) required for normal selenoenzyme synthesis and activities that is critical for human health (e.g., peroxide detoxification) as well as the threshold value (∇_{Se}) for Se poisoning, considered the modulation effects from Hg exposure, although the specific values may require further validation. These factors, which have commonly been omitted by previous studies, may be critical for understanding the "paradox" in previous epidemiological studies, that is, higher exposures to MeHg producing lower toxicological consequence (e.g., studies conducted in the Seychelles and the Faroe Islands and other regions[24,47,48]).

The BRV criterion proposed in the present study is concise and intuitive, and its use can help deepen our understanding of previous assessments. More importantly, this criterion has potential for broad applications in future research. Although the illustrative evaluation in the present study was conducted for the rice-based population, it is also appropriate in application for the fish-eating population. As all calculations in the BRV criterion are based on molar concentrations, Hg and Se can be viewed as a molar relationship: the number of Se atoms versus Hg atoms present or consumed. Thus, essentially, there is no real distinction of applications of this criterion between the two populations regarding the interactions between the two elements. Furthermore, this criterion may be sufficient to protect the fish-eating population against the toxicity of Hg exposure, or at least its evaluated result may be "safer" than that of rice-based populations (given their Hg and Se exposure status are equal) considering fish contains other important nutrients (e.g., *n*-3 polyunsaturated fatty acids) while rice does not.[2,6,43] Despite this, it should be noted here that, until substantial epidemiological evidence is collected, the application of such novel criteria should be limited to scientific inquiry and research rather than prematurely replacing the traditional means of assessing risks/benefits in actual populations.

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Notes

The authors declare no competing financial interest.

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Dietary selenium's protective effects against methylmercury toxicity

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ABSTRACT

Dietary selenium (Se) status is inversely related to vulnerability to methylmercury (MeHg) toxicity. Mercury exposures that are uniformly neurotoxic and lethal among animals fed low dietary Se are far less serious among those with normal Se intakes and are without observable consequences in those fed Se-enriched diets. Although these effects have been known since 1967, they have only lately become well understood. Recent studies have shown that Se-enriched diets not only prevent MeHg toxicity, but can also rapidly reverse some of its most severe symptoms. It is now understood that MeHg is a highly specific, irreversible inhibitor of Se-dependent enzymes (selenoenzymes). Selenoenzymes are required to prevent and reverse oxidative damage throughout the body, particularly in the brain and neuroendocrine tissues. Inhibition of selenoenzyme activities in these vulnerable tissues appears to be the proximal cause of the pathological effects known to accompany MeHg toxicity. Because Hg's binding affinities for Se are up to a million times higher than for sulfur, its second-best binding partner, MeHg inexorably sequesters Se, directly impairing selenoenzyme activities and their synthesis. This may explain why studies of maternal populations exposed to foods that contain Hg in molar excess of Se, such as shark or pilot whale meats, have found adverse child outcomes, but studies of populations exposed to MeHg by eating Se-rich ocean fish observe improved child IQs instead of harm. However, since the Se contents of freshwater fish are dependent on local soil Se status, fish with high MeHg from regions with poor Se availability may be cause for concern. Further studies of these relationships are needed to assist regulatory agencies in protecting and improving child health.

1. Introduction

A nutraceutical is a food known to have a medical or health benefit, including the prevention and treatment of disease. Selenium (Se), an essential trace element for humans and animals, is increasingly recognized for its biological importance and is increasingly considered a nutraceutical component. As reviewed by Rayman (2000), many metabolic processes and, hence, many diseases and clinical conditions directly or indirectly involve disruptions of Se physiology. Selenium can act as a growth factor (Ramauge et al., 1996), has powerful antioxidant (Behne et al., 2000) and anticancer (Combs and Lu, 2001) properties, and is essential for normal thyroid hormone homeostasis (Ramauge et al., 1996) and immunity (Roy et al., 1995). Studies indicate Se has important roles in development, reproduction, cardiovascular disease, and mood disorders (see Rayman, 2000; Taylor et al., 2009, for reviews).

The role of defects of Se physiology in the etiologies of certain diseases is also becoming apparent. Links have been found between compromised Se-dependent metabolic processes and congenital muscular dystrophy, autism, Alzheimer's and Down syndromes, brain tumors, diabetes, liver diseases, and conditions associated with increased oxidative stress or inflammation, such as rheumatoid arthritis, pancreatitis, asthma, and obesity (Whanger, 2001; Rayman, 2000; Köhrle et al., 2000).

Less known, but equally important, is the fact that Se is a natural methylmercury (MeHg) and inorganic Hg antagonist that potently counteracts or eliminates symptoms of toxicity that would otherwise accompany high MeHg/Hg exposures. Because Hg's binding affinities for Se (10^{45}) are up to a million times higher than its affinity for sulfur (10^{39}) in analogous forms (Dyrssen and Wedborg, 1991), Se's "protective effect" was initially presumed to involve Se sequestration of Hg, thereby preventing its harmful effects. However, as more has become understood about Se physiology, the mechanism of MeHg/Hg toxicity and the mechanism of Se's protective effect have also become clear. The high affinity between Hg and Se results in Hg binding to Se, thus compromising Se's biological functions and availability. By biochemical definition, MeHg is a highly specific irreversible inhibitor of selenoenzymes. Since MeHg has the ability to cross the placental and blood–brain barriers, its high affinity for Se enables it to specifically sequester Se at the active sites of essential Se-dependent enzymes (selenoenzymes) in fetal neuroendocrine tissues that lack adequate reserves of Se because of their rapid growth. As intracellular concentrations of MeHg approach, and especially as they exceed 1:1

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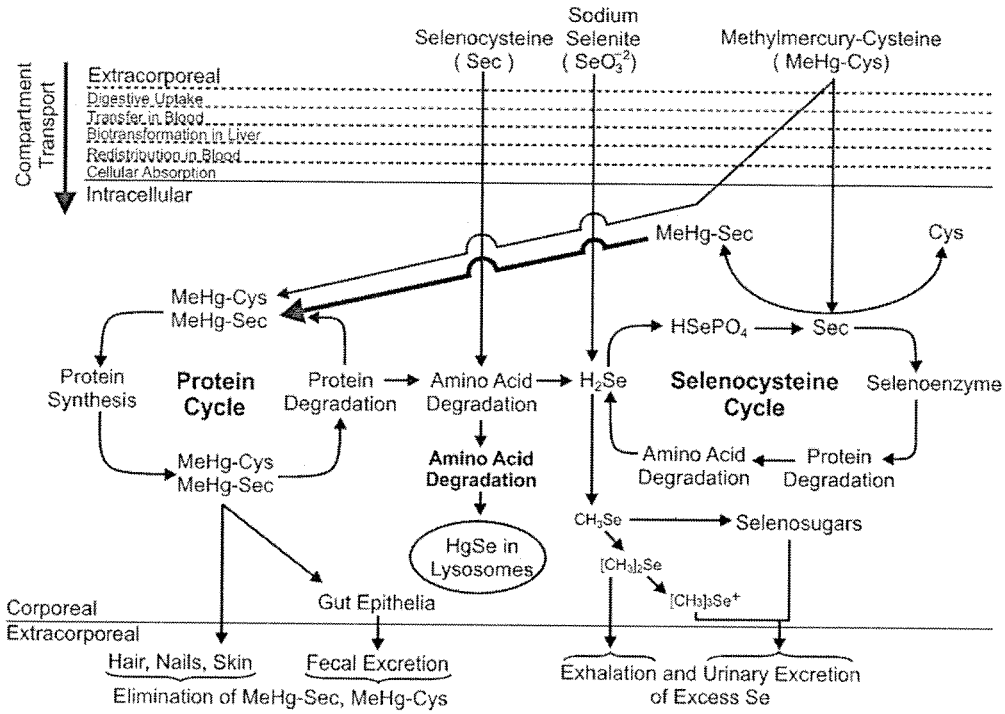

Fig. 2. General scheme of vertebrate Se metabolism and the interactive influences of MeHg.

three-dimensional enzyme active site structure that performs the enzymes' principal functions (Table 2).

The SECIS binding proteins responding to the UGA Sec insertion codon initiate de novo Sec synthesis by catalyzing a selenophosphate reaction with serine to form Sec (Fig. 2), which is inserted at the carboxy terminus of the protein primary structure. In mRNA of many selenoproteins, the UGA of the Sec insertion codon is followed by a second UGA, which is read as the stop codon, and the protein is terminated and released.

In addition to its unique synthetic pathway, Sec is unusual and distinct from other amino acids in several other respects. At physiological pH, the sulfur of Cys is predominantly protonated, but the Se of Sec is predominantly ionized (as shown in Fig. 1). Being the strongest intracellular nucleophile naturally makes it a target for binding by the electrophilic Hg of MeHg, and its proximity to the adjacent nucleophilic α-carboxyl group may further potentiate Hg binding.

In contrast to other amino acids, Sec is not recycled for reincorporation into new proteins but is, instead, degraded to release inorganic Se (Fig. 2). As indicated, all Se sources in the diet or present in endogenous intracellular molecules must first be degraded into inorganic forms before their Se content can be used for de novo synthesis of Sec. Therefore, organic forms of Se are slower than selenite to form selenide. Inorganic selenite, as well as Sec or SeMet from proteins, must first be absorbed from the diet and progress through various compartments before finally arriving in cells such as brain or neuroendocrine tissues. But regardless of their chemical forms, all must be degraded and reduced to selenide prior to incorporation in newly formed Sec. Metabolically, the only difference between inorganic Se and organic Se in the Sec or SeMet forms that occur in

Table 1
Selenoprotein/selenoenzyme functions[a].

GPx1	Detoxifies peroxides in aqueous compartment of cytosol
GPx2	Selectively expressed in cytosol of liver and tissues of the digestive system
GPx3	Primarily synthesized in kidney; active in plasma Se transport to other tissues
GPx4	Prevents and reverses oxidative damage to lipids in brain and other tissues
TrxR1	Interacts with and/or recycles most other redox regulating metabolic pathways
TrxR2	Located in mitochondria, controls and regulates redox state
TGR	Reduces glutathione disulfide, specific physiological functions undefined
MsrB1	Repairs oxidatively damaged methionine (R-sulfoxides)
DIO1	Activates thyroid hormone, converts T4 into T3 (thyroxine)
DIO2	Regulates thyroid hormone status, activates or inactivates T3
DIO3	Activates thyroid hormone, in brain, placenta, and pregnant uterus, important in fetus
SPS2	Catalyzes formation of Se-phosphates required for synthesis of all other selenoproteins
SelM	Expressed in a variety of tissues, with increased levels in the brain
SelN	Mutational defects associated with congenital muscular dystrophy and other disorders
SelP	Primary Se transporter in plasma (10 Sec/molecule)
SelW	Expressed in a variety of tissues, may regulate redox state of 14-3-3 proteins
Sel15	An oxidoreductase that may assist in disulfide formation and protein folding

[a] Information presented in this table was compiled from: Dikiy et al. (2007), Aachmann et al. (2007), Linster and Van Schaftingen (2007), Moghadaszadeh and Beggs (2006), Gladyshev et al. (2004) and Gromer et al. (2005).

GPx1-GPx2 double knockout mice are prone to inflammatory bowel disease and bacteria-induced tumors.

Glutathione peroxidase 3 (GPx3; SwissProt p22352, gene loci 5q23.1) occurs extracellularly in the plasma (and thus, is often called pGPx) and in the intestine. GPx3 is the second most abundant selenoprotein in the plasma after selenoprotein P. It is a homotetrameric (23 kDa/monomer) enzyme, but its physiological functions are not well characterized. It may be primarily involved in transport of Se from the digestive tract to the rest of the body and appears to be involved in homeostatic redistribution from the body to neuroendocrine tissues during times of inadequate dietary Se intake.

Glutathione peroxidase 4 (GPx4: SwissProt p36969, gene loci 19p13.3, EC 1.11.1.12) is an unusual and important monomeric 23 kDa enzyme that exhibits broad substrate specificity and can reduce phospholipid hydroperoxides (for this reason, it is often referred to as ph-GPx) and may act as a universal antioxidant in the protection of biomembranes. It is also involved in redox signaling and regulatory processes including inhibiting lipoxygenases and apoptosis. As a secondary function, it helps prevent oxidation of low-density lipoproteins (LDL). GPx4 accounts for the bulk of Se present in the testes and is abundantly incorporated in the midpiece of sperm. GPx4 knockouts are lethal at an early embryonic age, apparently because of disrupted structural compartmentalization. Loss of this enzyme's essential functions as a result of MeHg inhibition and Se sequestration would be expected to accentuate oxidative damage to lipid membranes of the brain and other neuroendocrine tissues.

Thioredoxin reductase 1 (TRxR1: Swissprot: q16881, gene loci 12q23-q24.1, EC 1.8.1.9) is a ubiquitous cytosolic homodimeric oxidoreductase containing 1 Sec and 1 FAD per 55 kDa subunit, with Sec as the penultimate amino acid (Gladyshev et al., 2004). TrxR1 is a cytosolic housekeeping enzyme with pivotal involvment in redox regulation (Söderberg et al., 2000) and DNA synthesis (Spyrou and Holmgren, 1996). Deletion of this gene is embryonically lethal, indicating the essentiality of its enzyme functions (Bondareva et al., 2007). TrxR1 reduces a broad variety of oxidized substrates; thioredoxin (Trx) dehydroascorbate, lipoic acid/lipoamide, H_2O_2, lipid hydroperoxides, vitamin K, ubiquinone, S-nitrosoglutathione, selenodiglutathione, selenite, methylseleninate, and Sec (Fig. 3). It also reduces oxidized proteins including protein disulfide isomerase, glutaredoxin, glutathione peroxidase, NK-lysin/granulysin, and various oxidized molecular species of exogenous origin; e.g., HIV Tat protein, ninhydrin, juglone, alloxan, and DTNB. If synthesized without Sec at its terminus, thus losing its enzyme activity, the disabled protein is a potent apoptosis-initiator known as GRIM-12 (Anestal and Arner, 2003). Therefore, MeHg-dependent loss of the Se necessary for synthesis of the Sec required to complete formation of this enzyme would not only result in the loss of its vital functions, but would also initiate apoptosis of the Se-deprived cells.

Thioredoxin reductase 2 (TRxR2: formerly known as TR3, Swissprot: q9nnw7, gene loci 22q11.21, EC 1.8.1.9), located in mitochondria, is a ubiquitous homodimeric pyridine nucleotide-disulfide oxidoreductase (Fig. 2), with Sec as terminal amino acid. Highest levels are observed in prostate, testes, liver, uterus, and small intestine, with intermediate levels in brain, skeletal muscle, heart, and spleen.

Thioredoxin glutathione reductase (TGR, formerly known as TR2 or TrxR3, GENE name: TXNRD3; Accession no: XP 051264.6, gene loci 3p13-q13.33) can reduce glutathione disulfide since it contains an N-terminal 1-Cys glutaredoxin-like domain, differentiating it from TrxR1 and TrxR2 (Fig. 3), but its specific physiological functions remain unknown at present. It is testes-specific, where it is localized in the ER.

Iodothyronine Deiodinase 1 (DIO1: Swissprot p49895, gene loci 1p32-p33, EC 1.97.1.10) is a homodimeric plasma membrane protein that cleaves the iodine-carbon bond of T_4 (thyroxine) to form T_3, thus activating thyroid hormone. Its activity is high in the liver, kidney, and pituitary gland, even though it occurs in only trace quantities in most tissues other than brain, where its concentrations are even lower.

Iodothyronine Deiodinase 2 (DIO2: Swissprot q92813, gene loci 4q24.2-q24.3, also EC 1.97.1.10) is a homodimeric plasma membrane protein that cleaves the iodine-carbon bond of T_4 (thyroxine) with a preference for T_4 over rT_3. DIO2 is present in the central nervous system, pituitary and thyroid glands, skeletal and heart muscle, and placental and brown adipose tissue. Only low levels are detectable in kidney and pancreas. Since there is minimal absorption of bloodstream T_3 across the blood–brain barrier, DIO2 is responsible for more than 75% of the T_3 production in the brain.

Iodothyronine Deiodinase 3 (DIO3: Swissprot p55073, gene loci 14q3, EC 1.97.1.11), unlike DIO2, deiodinates the 5-position of the tyrosyl ring. The brain, placenta, and pregnant uterus express higher amounts of DIO3. High DIO3 and low levels of T_3 may have deleterious effects upon central nervous system development and brain function. Therefore, high DIO3 expression may protect the

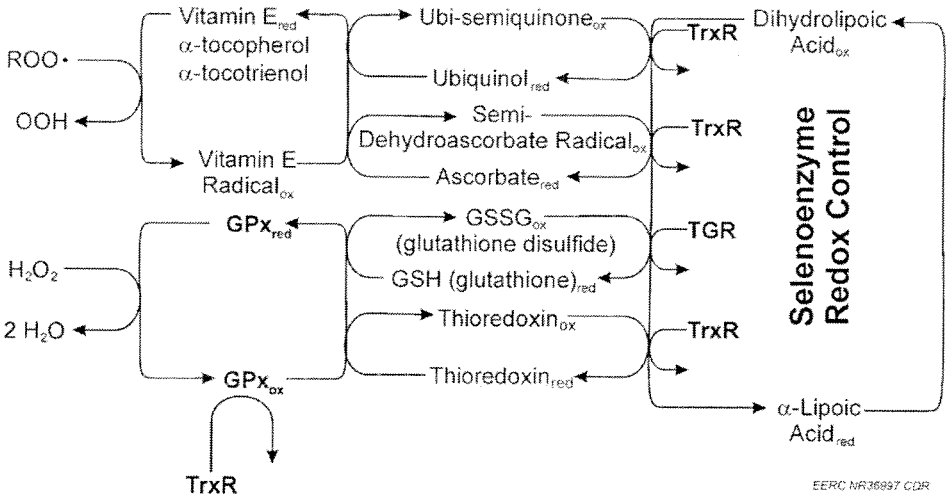

Fig. 3. Roles of selenoenzymes in intracellular control of redox state. Thioredoxin reductase 1 and 2 (TrxR) glutathione peroxidase 1, 2 and 4 (GPx), and thioredoxin glutathione reductase (TGR) are pivotally involved in maintaining intracellular redox tone.

2.4.2. Thioredoxin reductases

The thioredoxin reductases (TrxR) and their substrate thioredoxin (Trx) regulate a range of cellular systems. Thioredoxins (Trx) are 12-kD proteins with dithiol/disulfide active sites that are ubiquitous in organisms from bacteria to humans and are essential for sustaining life in mammals (Nordberg and Arneĭr, 2001). Thioredoxin is a central regulator of the cellular redox status. It is required for the redox-regulated function of transcription factors and hormonally regulated nuclear receptors. It is critical in DNA production, gene expression, cell survival, and embryogenesis. Thus, TrxR enables basic processes and regulates multiple metabolic events. Their antioxidant functions occur because they directly facilitate reduction of oxidized proteins through cysteine-thiol-disulfide exchange. TrxR contributes to more than simply maintaining intracellular redox homeostasis; it is also directly involved in prevention and repair of damage caused by H_2O_2-based oxidative stress. Since it contains Sec in its primary sequence and contributes to intracellular reduction of the selenite that is the required precursor for de novo synthesis of all selenoproteins, TrxR clearly has a central role in Se physiology. It is assumed that Se's pivotal role in TrxR explains why targeted disruption of the thioredoxin gene is lethal (Matsui et al., 1996; Jakupoglu et al., 2005).

Since TrxR is essential for cell survival, it is an important target of many pharmaceutical drugs, such as anticancer and antirheumatic agents. Recent investigations have shown that a truncated form of TrxR1 (GRIM-12) functions as an apoptosis-initiator. Remarkably, the only difference between the truncated and full-length protein is the presence of the two final sec amino acids. When the terminal Sec is compromised in TrxR1, either through Se-deficiency resulting in impaired Sec synthesis or when its Sec is selectively derivatized, the Sec-deficient TrxR1 ceases to have its normal function and, instead, becomes an apoptosis-initiator that rapidly induces cell death. The researchers suggest this enzyme may be important for the pathophysiology of Se deficiency as well as for the efficacy of antiproiferative drugs targeting TrxR (Anestal and Arner, 2003). Therefore, GRIM-12 may also have a contributing role in various consequences of Sedepletion that occur secondary to MeHg toxicity.

2.4.3. Glutathione peroxidases

The glutathione peroxidases (GPx) are Se-dependent enzymes involved in antioxidant defense and redox regulation and modulation. GPx provide protection against oxidative damage and aid in the maintenance of membrane integrity by catalyzing the reduction of hydrogen peroxide. Thyroid hormone synthesis requires a continuous production of high concentrations of H_2O_2 which appears to be its rate-limiting step (Corvilain et al., 1991, 1994; Bjorkman and Ekholm, 1984). Therefore, since the thyrocyte is continually exposed to potentially toxic concentrations of H_2O_2 and lipid hydroperoxides, appropriate antioxidant defense systems are essential to resist this oxidative stress. Any impairment of thyroidal peroxide- metabolizing systems by Se deficiency will allow damage to occur in the thyrocyte. Three of the five GPx are expressed in thyrocytes and thyroid tissue (Villette et al., 1998; Zagrodzki et al., 1998). The thyrocyte synthesizes and secretes GPx in a controlled manner, presumably to provide an additional mechanism for controlling thyroid hormone synthesis through regulating the concentration of H_2O_2. Additionally, studies indicate a distinct regulation of expression, secretion, and function of these selenoproteins for controlling thyrocyte growth, differentiation, and function (Howie et al., 1995, 1998; Zagrodzki et al., 1998; Oertel et al., 1991; Schreck et al., 1994; Beech et al., 1993, 1995; Bermano et al., 1995). When Se intake is adequate, the intracellular GPx and TR systems protect the thyrocyte from peroxides; however, in Se deficiency the thyrocyte's apoptotic response to H_2O_2 is increased (Demelash et al., 2004). Furthermore, in iodine deficiency where hyperstimulation of the thyroid-stimulating hormone (TSH) receptor signals increased H_2O_2 production, GPx production is also stimulated, thus up-regulating, antioxidant protection. During MeHg induced Se sequestration, GPx would be expected to diminish in most body compartments, but could be preferentially retained in the neuroendocrine tissues until Se availability was compromised beyond the capacities of homeostatic response.

2.4.4. Other roles of selenoproteins

In addition to DIO, TrxR, and GPx, further selenoproteins have recently been implicated in processes known to be involved in neurodegenerative diseases, including protein folding, degradation of misfolded membrane proteins, and control of cellular calcium homoeostasis. Likewise, selenoprotein expression is required for interneuron development, and cerebral Se deficiency is associated with neurological disorders such as seizures and ataxia.

The importance of Se in the endocrine system is further emphasized by the fact that mechanisms have evolved to maintain normal concentrations of Se in these tissues even when there is severe dietary Se deficiency. Se deficiency occurs in experimental animals continuously fed diets that contain negligible amounts of Se. After a period of months, the Se concentrations in peripheral tissues such as liver, skeletal muscle, and blood of these animals will become drastically reduced to levels below 1% of normal. However, their brain tissues retain 60% of the Se concentration found in control animal brains (Behne et al., 2000; Ralston et al., 2006; Ralston, 2008a). Behne et al. reports that offspring will maintain ~60% of normal Se contents in their brains through six generations of continuous feeding of Se-deficient diets.

Although brain Se concentrations in Se-deficient animals have not been reduced to less than 60% of normal, Hill showed that feeding diets containing less than 0.1 ppm Se to SelP knockout mice reduced their brain Se concentrations to 43% of normal, the lowest brain Se concentration achieved in any experimental animal model (Hill et al., 2003). While rats with brain Se at 60% of normal appear asymptomatic, the knockout mice demonstrated pronounced loss of motor coordination. However, the motor coordination could be restored and brain Se replenished by feeding them a 2-mg Se/kg diet. When the Se-null mice were fed a Se-deficient diet, neurological dysfunction and death resulted within several weeks (Hill et al., 2003, 2004), however feeding them a high-Se diet prevented all but minor neurological deficits. As further evidence demonstrating the importance of Se-dependent physiology, the total disruption of selenoprotein synthesis in mice, achieved by knocking out the Sec-tRNA gene, resulted in early embryonal lethality (Bosl et al., 1997).

Consequently, any substance that can enter the brain and disrupt selenoprotein synthesis will accomplish what multigenerational Se deficiency cannot. Hg not only has the ability to cross the placental and blood–brain barrier, but its high Se affinity enables it to specifically sequester the brain's Se by forming insoluble HgSe, thereby diminishing selenoprotein synthesis in these otherwise protected tissues.

3. Selenium's relationship to mercury toxicity; "molecular tonic" or "molecular target"?

The ability of Se compounds to decrease the toxicity of Hg has been established in all investigated species of mammals, birds, and fish (Suzuki, 1997; Whanger, 1992; Beijer and Jernelov, 1978; Culvin-Aralar and Furness, 1991; Freidman et al., 1978; Ohi et al., 1980; Ralston et al., 2006, 2007). This phenomenon had previously been speculated to be the result of supplemental dietary Se binding to Hg, thereby preventing Hg from exerting its toxic effects (Suzuki, 1997; Whanger, 1992). However, when considering the importance

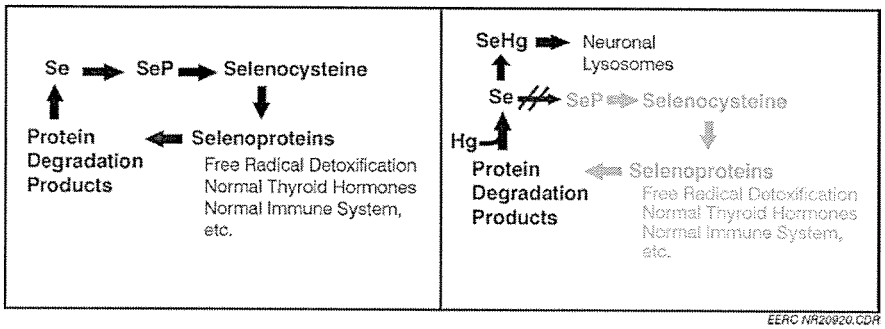

Fig. 4. Schematic of Se sequestration mechanism of Hg toxicity. A simplified portrayal of the normal cycle of selenoprotein synthesis is depicted on the left. Disruption of this cycle by exposure to toxic quantities of Hg (MeHg) is depicted on the right. Selenide freed during selenoprotein breakdown becomes bound to Hg, forming HgSe that accumulates in cellular lysosomes. If Hg is present in stoichiometric excess, formation of insoluble Hg selenides abolishes the bioavailability of Se for protein synthesis (indicated by gray text) and results in loss of normal physiological functions that require selenoenzyme activities.

icity, but fish Se prevented it. Therefore, the organic forms of Se present in ocean fish are bioavailable and effective in counteracting MeHg toxicity. This may explain why studies that examined effects of maternal exposure to MeHg from typical varieties of ocean fish (Davidson et al., 1998; Myers and Davidson, 1998; Hibbeln et al., 2007; Oken et al., 2008; Lederman et al., 2008) have not found the adverse effects that had been expected, but have, instead, found substantial beneficial effects accompany increasing seafood consumption (Hibbeln et al., 2007; Oken et al., 2008) including increases of up to 10 IQ points (Lederman et al., 2008).

In contrast, the studies that have found increasing MeHg exposure from seafood consumption were associated with neurodevelopmental impairments (Crump et al., 1998; Grandjean et al., 1992, 1997, 1998) uniformly involved consumption of foods that contained Hg in molar excess of Se such as pilot whale (5:1 reported by Julshamn et al., 1987) or varieties of shark (>2:1, reported by Kaneko and Ralston, 2007). The New Zealand population had extremely poor dietary Se status at the time of this study (Robinson, 1988). This would have accentuated their vulnerability to MeHg exposure (Ralston, 2008a,b). Since the Se present in fish protects against the concurrent Hg exposures, risks of MeHg exposure from fish consumption need to assess both elements. Furthermore, variation between individuals in their intakes and status of Se and Hg is highly sensitive to differences in amounts and types of fish consumed. For example, red cell Se, plasma Se, and blood Hg is strongly correlated with oily fish, but not significantly correlated with the intake of white fish (Bates et al., 2007).

The Selenium-Health Benefit Values (Se-HBV) of seafoods reflect not only the Hg that is present, but also the Se content of the seafoods. This approach incorporates the molar ratios and absolute amounts of Hg and Se present to calculate an index that has proven to be more reliable for predicting risks associated with MeHg exposure (Ralston et al., 2008; Ralston, 2008a,b). The pilot whales and shark meats whose consumption has been associated with causing harm to children have negative (Se-HBVs) of −80 and −11, respectively (Kaneko and Ralston, 2007). In contrast, the ocean fish that have been associated with beneficial effects on child IQ have Se-HBVs that range between 40 and 250.

Ocean fish tend to be generally rich in Se relative to Hg. However, in freshwater fish, the health risks of MeHg exposure may vary in response to individual and regional differences in Se intake. Environmental availability of Se is highly variable, abundant in soils of one area, and dangerously low in regions only miles away. Although the overall Se status in the United States is good, certain populations of the world are severely Se-compromised. Variations in geologic distributions of Se in soils influence the amounts present in foods, potentially predisposing for or protecting against potential risks of Hg exposure.

Understanding Se's bioavailability and the factors that influence its metabolism are especially important in Se-deficient regions. Although typical varieties of ocean fish are Se-rich, the Se status of freshwater fish is more variable and can be low in certain regions. Methylmercury accumulates at higher levels and at accelerated rates in fish growing in lakes where Se availability is limited, and Se supplementation to normal levels has resulted in MeHg levels in fish diminishing by more than 75% after 3 years (Paulsson and Lindbergh, 1989). Therefore, fish from low-Se lakes would not only have low-Se contents, they would also tend to have higher MeHg contents, a dangerous combination for consumption by pregnant mothers and other vulnerable subpopulations.

Research indicates that Se is also involved in decreasing Hg accumulation in lake fish. Selenium bioavailability in Hg-contaminated lakes is inversely related to bioaccumulation of MeHg in fish (Paulsson and Lindbergh, 1989; Southworth et al., 1994, 2000; Turner and Rudd, 1983). These environmental and physiological processes are likely related and due to the high binding affinity between these two elements, the mechanisms involved in this bioaccumulation pathway remain poorly understood. The HgSe complexes that form when Hg and Se bind together have extremely low solubility, thus HgSe present in tissues of prey species consumed is unavailable for dietary absorption and likely to be retired to the sediments (Fig. 5). Sequestration by Se and formation of HgSe would diminish MeHg absorption and accumulation by predators at each level of the aquatic food chain. Evidence for this effect has been reported from both intervention studies (Paulsson and Lindbergh, 1989) and natural experiments (Peterson et al., 2009; Belzile et al., 2004, 2009) This process continually retires Hg from participation in the biogeochemical cycle and may be responsible for lower Hg levels in fish from certain regions with abundant Se availability, while absence of biologically available Se may be responsible for certain Hg "hot spots." Knowing the concentrations of Se in soils is not sufficient information to assess its environmental availability. A variety of additional factors such as soil or water pH conditions strongly influence availability of Se and its ability to accomplish Hg retirement as HgSe.

5. Discussion

5.1. Need for examination of Hg:Se ratios in freshwater fish

Examinations of risks associated with consumption of foods with high Hg contents have resulted in regulatory advisories designed to minimize maternal MeHg exposures. However, the distinctions between exposure to pilot whale meats with high Hg:Se molar ratios and consumption of ocean fish with low Hg:Se ratios has diminished the practical utility of the advisories. The

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DEPARTMENT OF
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State of Washington

Washington State Water Quality Standards: Human health criteria and implementation tools

Overview of key decisions in rule amendment

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Water Quality Program
Washington State Department of Ecology
Olympia, Washington

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Glossary and List of Acronyms

303(d)	Ecology's list of impaired waters that violate the Water Quality Standards.
BCF	Bioconcentration Factor
BMP	Best Management Practices
BSAF	Biota Sediment Accumulation Factor
BW	Body Weight
CFR	Code of Federal Regulations
CSF	Cancer Slope Factor
CSO	Combined Sewer Overflow
DI	Drinking water Index
DOC	Dissolved Organic Carbon
Ecology	Washington State Department of Ecology
EIM	Environmental Information Management system
EPA	United States Environmental Protection Agency
ESA	Endangered Species Act (US Federal)
FCR	Fish Consumption Rate
HHC	Human Health Criteria
HQ	Hazard Quotient
IRIS	Integrated Risk Information System
Kg	Kilograms
K_{ow}	chemical specific octanol-water partition coefficient
mg/l	Milligrams Per Liter
NOAA	National Oceanic and Atmospheric Administration
NPDES	National Pollutant Discharge Elimination System Permitting Program

NRWQS	National Recommended Water Quality Criteria
NTR	National Toxics Rule
PBDEs	Polychlorinated Biphenyls
PCBs	Polychlorinated Biphenyls; manufactured chemicals which persist and accumulate in food chains
POC	Particulate Organic Carbon
RAGS	Risk Assessment Guidance for Superfund
RCW	Revised Code of Washington
RfD	Reference Dose
RL	Risk Level
RSC	Relative Source Contribution
SDWA	Safe Drinking Water Act
TMDL	Total Maximum Daily Load, or Water Clean-Up Plan
µg/L	Micrograms per liter
USFWS	United States Fish and Wildlife Service
WAC	Washington Administrative Code (The Water Quality Standards for Surface Waters of the State of Washington are in WAC 173-201A)

Overview

What is this rulemaking about and is it required of the state?
This state rulemaking is a revision to the Water Quality Standards for Surface Waters of the State of Washington (Chapter 173-201A WAC). This rulemaking addresses two specific areas of the water quality standards:

1. Development and adoption of new human health criteria (light grey highlighted area in Figure 1); and
2. Revision, expansion, and clarification of some of the tools in the standards that help in criteria implementation (darker grey highlighted area in Figure 1).

This document explains the changes and the rationale supporting the changes, including specific risk management input to Ecology by Governor Inslee. The rule language can be seen at Ecology's Water Quality Standards website: www.ecy.wa.gov/programs/wq/ruledev/wac173201A/1203ov.html.

All states are required to adopt surface water quality standards by a federal law titled the Federal Water Pollution Control Act (hereinafter called the Clean Water Act). Surface waters include streams, lakes, river, bays, and marine waters. States adopt water quality standards to:

- Protect public health or welfare.
- Enhance the quality of water.
- Serve the purposes of the Clean Water Act.

Section 303(c) of the Clean Water Act provides the federal legal basis for the water quality standards program. Section 303(c)(2)(b) specifically requires states to adopt criteria for toxic priority pollutants. The federal regulatory requirements governing the water quality standards program, the Water Quality Standards Regulation, are published by the federal government in the *Code of Federal Regulations* (CFR) at 40 CFR 131.

Washington State law gives Ecology authority and responsibility to protect the quality of Washington waters and implement federal Clean Water Act programs. The authority and responsibility regarding water quality standards can be found in the Revised Code of Washington (RCW): RCW 90.48.030, RCW 90.48.035, and RCW 90.48.260(1).

What is in Washington's surface water quality standards?
The surface water quality standards regulation (WAC 173-201A) defines the water quality goals of the surface waters in Washington. As required by federal regulation, the water quality standards include:

- Designated uses (also called beneficial uses) for all surface waters, such as aquatic life habitat, recreational uses, harvest, public and industrial water supply, and others.
- Water quality concentrations or levels (called criteria) necessary to protect the uses. These criteria can be numeric (such as concentrations of chemicals or maximum

temperatures) or narrative (descriptions such as "…must not … offend the senses of sight, smell, touch, or taste…").

- Antidegradation provisions that prevent degradation of the water quality.

Washington's water quality standards also contain other provisions that aid in and direct the implementation and future changes to the standards.

The designated uses, criteria, antidegradation provisions, and other provisions are illustrated in Figure 1.

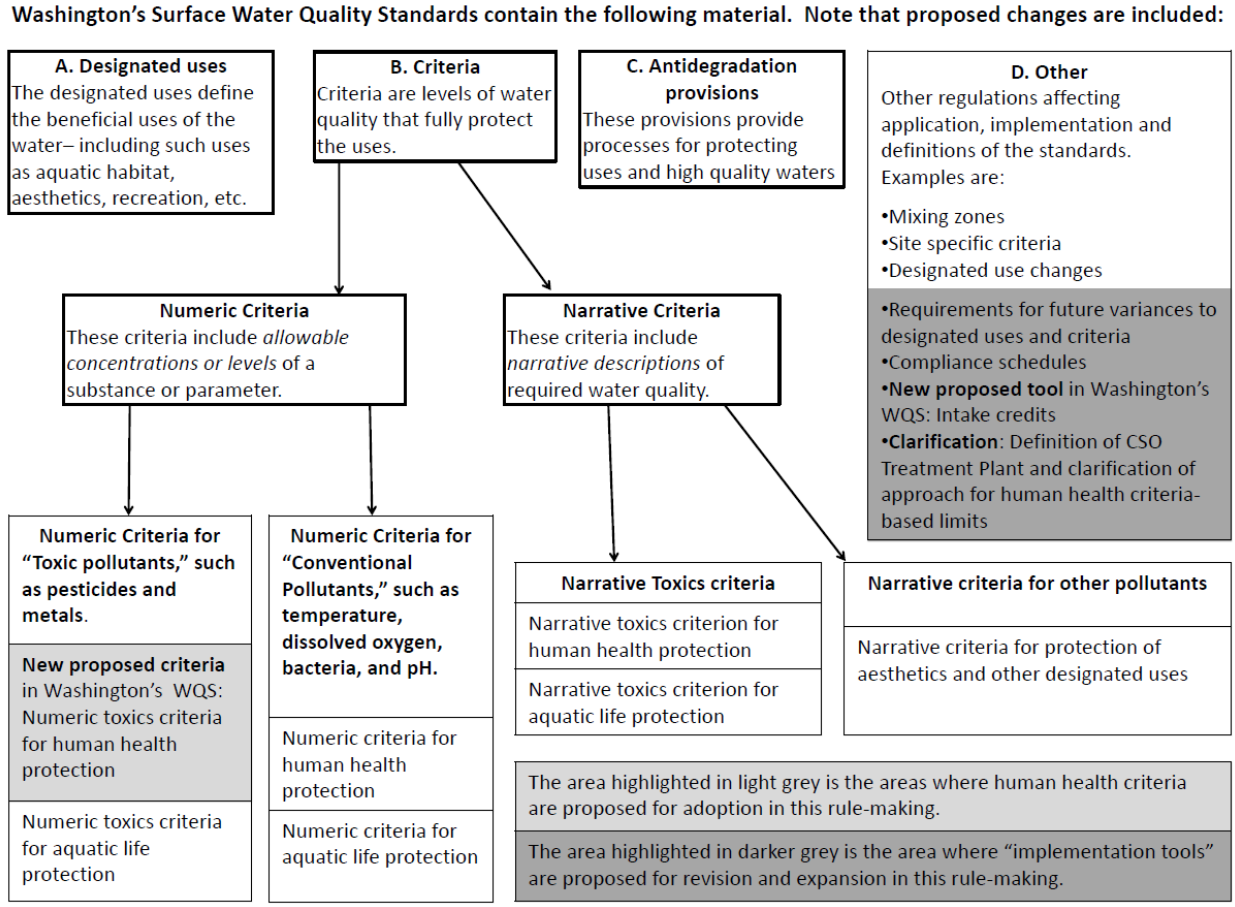


Figure 1: Description of Washington water quality standards with changes highlighted

How are water quality standards revised?

Washington's water quality standards are revised periodically through a formal public rulemaking process. Revisions are made to incorporate new science, to meet new federal or state requirements, to provide additional clarity, and for many other reasons. All water quality standards revisions are submitted to the United States Environmental Protection Agency (EPA) for Clean Water Act approval prior to use. If Endangered Species Act (ESA)-listed species are affected by new water quality standards, then EPA is required to consult with the National Oceanic and Atmospheric Administration (NOAA) and United States Fish and Wildlife Service

(USFWS) regarding effects of the new water quality standards on the ESA-listed species prior to federal approval.

An important part of the state's rule revision process, and in determining which revisions are most important to make, is public review and discussion about the water quality standards. Federal regulations require that states hold public hearings at least once every three years to review applicable surface water quality standards and, as appropriate, adopt new or modified standards. This process is called a *triennial review*.

The triennial review provides an opportunity to discuss the priorities and commitments that Ecology makes with EPA and others regarding the surface water quality standards. Ecology then places activities (guidance development, research needs, or rulemaking) on schedules that match their complexity and importance, rather than trying to force them into a three-year cycle. The latest (2010) triennial review and the Water Quality Program's five-year plan for water quality standards can be seen at http://www.ecy.wa.gov/programs/wq/swqs/triennial_review.html.

Because the triennial review and subsequent rulemaking processes are an ongoing set of actions, this approach results over time in a balanced ongoing update to the water quality standards, with higher priority items taking precedence in rulemaking efforts:

Selection of rulemaking topics

- Topics are selected based on the goal of getting the greatest environmental and/or administrative benefit.
- Topics are prioritized based on the expected environmental benefits, technical complexity, available staff resources, federal mandates, and need for change in the water quality standards guidance, rule, or process.
- A long-term list of prioritized topics is maintained, with commitments to implementing changes (rulemaking or otherwise). Those short-term (<1-5 years) priorities are built into the Ecology and EPA Performance Partnership Agreement (Ecology commitments to EPA), based on Ecology's ability to anticipate and commit staff resources.
- The long-term list of topics is reviewed, and modified where appropriate, during each Triennial Review.

What are the specific areas of the rule that were modified?

This rulemaking modified two specific areas of the water quality standards: (1) adoption of new human health criteria: and, (2) revision and expansion of some of the tools in the standards that help in implementation. These are discussed separately below.

New human health criteria

Numeric criteria: The human health criteria (HHC) are water concentrations for toxic substances that protect people who consume fish and shellfish from local waters and who drink untreated water from local surface waters. HHC for Washington waters are also under the federally promulgated National Toxics Rule (NTR). The NTR criteria are applicable to Washington until EPA approves the state's new HHC.

HHC are calculated from a variety of different factors, including chemical-specific toxicity to humans, how chemicals move from water into fish and shellfish and then into humans, as well as other factors. The criteria calculation and these factors are discussed at more length in the section on HHC Variables. Specific information on arsenic is found in the section on Challenging Chemicals: Arsenic. The development and adoption of new HHC includes consideration of new science on toxicity factors and new information on body weight and Washington-specific fish consumption. The factors that are included in the criteria calculations are a mix of average and higher percentile values, and in general are consistent with EPA guidance and practice. This approach results in high levels of consumer protection from pollutants that could be found in untreated surface water, fish, and shellfish from Washington. These factors were applied to 94 of 97 different chemicals in this rule (see section on Criteria Chemicals). The criteria for arsenic, copper, and asbestos are not calculated values. Instead, they are based on the regulatory level used in the Safe Drinking Water Act (SDWA; 42 U.S.C. § 300f and as amended).

As well as incorporation of new science, this rulemaking also included several risk management decisions that affected the final criteria values. Governor Inslee announced a proposal for the new criteria on October 8, 2015 (http://www.governor.wa.gov/news-media/inslee-announces-new-path-water-quality-rule-continues-work-broader-toxics-reduction). This included direction to use an updated fish consumption rate in the criteria calculations for carcinogens and non-carcinogens (an average fish consumption rate of 175 g/day) and to continue use of the existing risk level in the water quality standards: one-in-one-million (10^{-6}). Criteria for arsenic, copper, and asbestos are values based on the Safe Drinking Water Act, and a chemical-specific approach is used for PCBs.

Narrative criteria: The water quality standards include narrative provisions that address chemicals that are not included in the list of 97 chemicals for which Ecology is developing criteria.

Revised and expanded implementation tools.
The water quality standards contain a number of tools that relate directly to how the criteria are met. These tools are implemented both in permits and in orders, and specify how the current designated uses and criteria can be changed if certain factors can be demonstrated. Ecology revised two of the tools (compliance schedules and variance requirements) that were already in the water quality standards, and added a new tool (intake credits). These three tools and the rule changes associated with them are fully discussed in this document under implementation tools. Ecology also added implementation clarification language for Combined Sewer Overflows (CSOs). Here is a brief summary of the three tools and CSO language changes:

Compliance schedules: Compliance schedules are tools used in Ecology discharge permits, orders, or other directives that allow time for dischargers to make needed modifications to treatment processes in order to meet permit limits or requirements. They are commonly used for construction and treatment plant upgrades, and cannot be used for new or expanding discharges. Compliance schedules are used when there is an expectation that the discharge will meet permit limits at the end of the schedule. The prior water quality standards contained a maximum time

limit of ten years for compliance schedules. In 2009, the Washington legislature passed a law requiring Ecology to develop longer compliance schedules for certain types of discharges.

Variances: A variance is a time-limited designated use and criterion as defined in 40 CFR 131.3, and must be adopted by EPA. A variance temporarily waives water quality standards for a specific chemical criterion and designated use for either a single discharge or for multiple discharges, or, for specified stretches of surface waters (e.g., for a specific tributary, a lake, a watershed). Variances are used in situations where it can be demonstrated that: (1) a discharge can eventually meet the permit limit or a water body can eventually meet the criteria and designated use, but a longer time frame is needed than allowed in a compliance schedule, or, (2) it is not known whether the discharge will ever be able to meet the permit limit or whether a waterbody will meet a criterion and/or designated use. Because a variance is a temporary change to a criteria and use, variances are considered changes to the water quality standards and must go through a rulemaking and subsequent EPA Clean Water Act approval to be effective. The prior water quality standards gave a brief list of the requirements for granting variances and set a maximum five-year period. The federal water quality standards regulations were recently revised and now include substantial requirements for granting variances (40 CFR 131.14; http://www2.epa.gov/wqs-tech/final-rulemaking-update-national-water-quality-standards-regulation). The new state rule language on variances expands on the prior rule language and is consistent with the new EPA regulations. Demonstrating the need for a variance could be very labor intensive, depending on the specific situation. More detailed specifications in the water quality standards will help set clearer expectations for both dischargers and the state, and will result in more predictable outcomes for dischargers.

This rule change does not grant any specific variances to water quality standards. Instead, this rule change gives more details on the information requirements for granting variances, and on the types of actions that would be required of dischargers during variance periods. This includes extending the duration of variances beyond five years if necessary.

Intake credits: Intake credits are a permitting tool that allows a discharge limit to be calculated in a way that does not require the discharger to "clean-up" pollutants in the discharge that are in the intake water, when the intake water and receiving water for the discharge are the same water body. This tool is also used to calculate technology-based limits. This tool is used to calculate water quality-based limits in several other states, including Oregon and the Great Lakes states.

This new rule contains language describing how and when intake credits could be used.

Implementation Clarification for Combined Sewer Overflows Treatment Plants (CSOs): Ecology adopted new language to be explicit about how the permitting process of combined sewer overflow treatment facilities occurs. A new definition has been added to define a Combined Sewer Overflow (CSO) Treatment Plant as "a facility that provides At-Site treatment as provided for in chapter 173-245 WAC. A CSO treatment plant is a specific facility identified in a department-approved CSO Reduction Plan (Long-term Control Plan) that is designed,

operated, and controlled by a municipal utility to capture and treat excess combined sanitary sewage and stormwater from a combined sewer system."

Ecology also added new language at 173-201A-510 WAC to describe implementation of these facilities: "The influent to these facilities is highly variable in frequency, volume, duration, and pollutant concentration. The primary means to be used for requiring compliance with the HHC shall be through the application of narrative limitations, which includes but is not limited to, best management practices required in waste discharge permits, rules, orders and directives issued by the department."

CSOs are driven by influxes of stormwater into combined sanitary and stormwater collection systems. Because of the episodic and short-term nature of CSO discharges, it is infeasible to calculate effluent limits that are based on criteria with durations of exposure up to 70 years. The federal regulations (40CFR122.44(k)) allow use of best management practices (BMP)-based limits in NPDES permits if it is infeasible to calculate numeric limits.

Public Discussion

In December 2011, Ecology started public discussions around implementation tools, and in October 2012, started public discussions around state adoption of HHC. The agency has held many public meetings in a variety of formats to encourage participation. These meetings, and the materials used for the meetings, are at Ecology's Water Quality Standards rule website www.ecy.wa.gov/programs/wq/ruledev/wac173201A/1203ov.html. Ecology has also met many times with various interested groups, including business, municipalities, environmental groups, counties, the US EPA, and Tribes. Ecology received comment from the public and has provided a Response to Comments in its Concise Explanatory Statement.

First Proposed Rule and Supporting Risk Management Decisions

The first proposed rule for HHC and implementation tools was released in January 2015, but was not finalized. The first proposed rule was coupled with an innovative and comprehensive approach to toxics reduction. On July 9, 2014, Governor Inslee released an integrated strategy to reduce pollutants that end up in fish and water. This strategy was based on two joined parts: (1) adoption of HHC and revised and new implementation tools into the state's water quality standards, and, (2) passage of a toxics reduction bill as part of the state's water quality standards rule submittal to the U.S. Environmental Protection Agency.

This strategy included two risk management decisions in the proposed rule: (1) an increase in the risk level from one-in-one-million ($10^{-6)}$ to one-in-one-hundred thousand (10^{-5}); and (2) a risk overlay that dictated that no criterion, except arsenic, would be a higher concentration than the NTR criterion. Adoption of HHC using these risk management decisions, coupled with the draft legislative bill, would have resulted in reductions to a broad suite of toxics at their sources.

July 9, 2014 http://www.governor.wa.gov/news-media/inslee-takes-new-approach-create-meaningful-effective-state-clean-water-standards?id=293

Excerpts from Governor Inslee's 2014 announcement on the first proposed rule

"Gov. Jay Inslee today announced his proposed update to the state's water quality standards, saying he worked until he found a solution that advanced the values of human, environmental and economic health."

"Washingtonians' actual risk to cancer and other harmful effects will be reduced by this proposal," Inslee said. "We are making our waters cleaner and safer."

"But Inslee said the state must also act on the many toxic chemicals from other unregulated sources that the Clean Water Act doesn't address. Inslee said ***he is calling on the Legislature next year to pass a toxics reduction bill as part of the state's submittal to the U.S. Environmental Protection Agency."***

"We could set standards at a thousand grams per day with a cancer risk rate of 10^{-20}, but it still wouldn't do anything to protect our children from exposure to too many toxics that cause neurological and reproductive damage," Inslee said. "This toxics reduction bill gives us the tools to tackle pollutants at their source and make meaningful improvements in the health of our water, our fish and our children."

"Inslee is directing the Department of Ecology to issue a preliminary draft rule no later than Sept. 30 (2014). ***He will submit legislation to the Legislature in 2015 and will make a decision on whether to adopt the final rule only after seeing the outcome of the session. He will ask the EPA to consider the benefits of the full package in determining federal approval of Washington's clean water standards."***

"I believe this approach honors our commitment to keep our children healthy and protect those who regularly eat fish, and doesn't create ineffective and undue requirements on a small number of businesses and governments," Inslee said. "I look forward to working with legislators, businesses, tribes, health care professionals and others to ensure we do the right thing for Washington state and work together for successful implementation of this integrated plan."

Figure 2: Excerpt from Governor Inslee's July 9, 2014 Announcement

In December 2014, Governor Jay Inslee reiterated his comprehensive plan combining the proposed water quality standards with proposed legislation and funding to provide stronger and broader controls on toxic threats in our environment (see the Governor's Policy Brief at: http://www.ecy.wa.gov/water/standards/Gov-Dec2014-ReducingToxicPollution.pdf). In January 2015, Ecology issued a proposed rule establishing new HHC to protect designated uses and provide predictable regulatory implementation tools to help dischargers comply with existing and new source control requirements or discharge limits. The Governor's proposed toxics

reduction bill passed the House during the regular legislative session, but the Senate failed to act on it before the legislative session concluded.

Based on the Governor's decision to hold up adoption, Ecology did not adopt the initial proposed rule. Instead, Ecology proposed a new water quality standards rule.

The Second Proposed Rule
Governor Inslee announced a new direction on the second proposed rule on October 8, 2015. That direction included proposing a fish consumption rate of 175 grams per day, staying with the state's currently adopted risk rate of one-in-one-million (10^{-6}), continuing forward with implementation tools, and chemical-specific approaches to arsenic and PCBs. The second proposed rule incorporated the risk management directions given by Governor Inslee. However, the second proposed rule was not linked with any proposed legislation to reduce toxics.

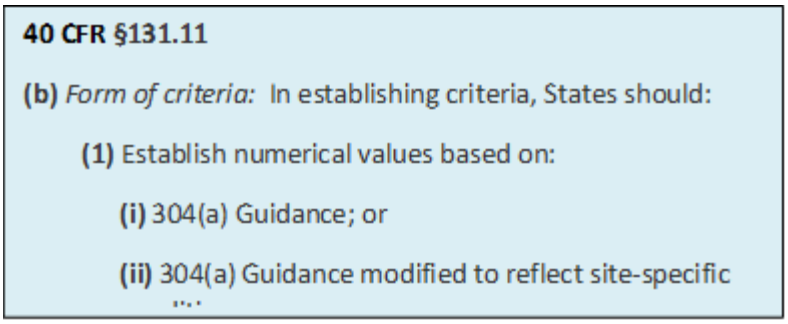
The Final Rule
The final rule was adopted on August 1, 2016. After adoption, Ecology will submit the rule to the EPA for Clean Water Act approval. The new water quality standards do not become effective for Clean Water Act purposes until approved by the EPA.

The new toxics table gives a different look to the water quality standards
The new HHC adds several additional pages of information to the standards. In the new rule, the aquatic life and human health criteria for toxics are combined into one large table.

The aquatic life criteria for toxics, and the accompanying footnotes (WAC 173-201A-240(3), Table 240(3)) are in this section and table. These changes have not modified the aquatic life toxics criteria or their application in any way – this is simply a formatting change. This is considered a non-substantive change. Any references to the aquatic life toxics table in the water quality standards have been updated to reference the new section.

Other changes since the first proposed rule
Subsequent to the publication of the first proposed rule, three federal regulatory actions were taken that affected HHC development in Washington:

1. ***June 2015***. EPA finalized new Clean Water Act 304(a) National Recommended Water Quality Criteria (NRWQC) for human health (80FR No.124, Monday, June 29, 2015, pages 36986-36989: See: (http://water.epa.gov/scitech/swguidance/standards/criteria/current/hhfinal.cfm). Several of the inputs to the new 304(a) guidance values were changed from earlier versions. Because the federal regulations recommend that states consider EPA's 304(a) Guidance when adopting criteria (40 CFR §131.11 (b); see the following text box), this Decision Document for the second rulemaking includes discussion of EPA's most recent NRWQC.



2. ***August 21, 2015***. EPA published a final rule updating six key areas of the federal water quality standards regulation that helps implement the Clean Water Act. The final rule was published in the Federal Register on August 21, 2015 (80 FR 51019) and is in 40 CFR 131. Several different program areas are addressed in the final rule, including water quality standards variances. The new language on variances in this revised rule is aligned with the new EPA regulation on variances.
3. ***September 2015***. EPA proposed a new regulation (80 FR No. 177, Monday, September 14, 2015. Pages 55063 – 55077) that would promulgate new federal HHC applicable to Washington's waters. In 1992 and 1999, EPA finalized HHC for Washington State in the NTR, and this federal regulation contains HHC currently applied to Washington waters. The newest EPA proposal (September 2015) contains updates for 99 priority pollutants. If Ecology submits the final HHC criteria to EPA for Clean Water Act review and approval before EPA finalizes the new federal regulation containing human health water quality criteria for Washington, EPA will review and act upon the state's submission prior to any final action on the federal criteria. If EPA approves criteria submitted by the state, the corresponding federal criteria will not be finalized. See: (http://www.epa.gov/sites/production/files/2015-09/documents/washington-rule-factsheet-2015.pdf).

Specific decisions used to develop the new criteria and implementation tools

The following sections in this document explain the rationale for the substantive portions of this rule revision.

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What Chemicals and Criteria Are Included

Decision

Ecology adopted HHC for all Clean Water Act 307(a) priority toxic pollutants (except for mercury/methylmercury) for which EPA has developed a national recommended numeric HHC. The existing rule language includes a narrative statement for protection from priority pollutants that do not have numeric criteria and from non-priority toxic pollutants.

The state's prior HHC are found in the federal NTR. The NTR contains calculated HHC for 85 priority pollutants, which includes 84 pollutants with calculated criteria values and one pollutant (asbestos) with a Safe Drinking Water Act-based human health criterion. Ecology's revised rule contains calculated and Safe Drinking Water Act-based HHC for 97 priority pollutants. The increased number of chemicals (from 85 to 97) is based on EPA's development of new criteria since the NTR was first issued and last revised.

Background

NTR HHC chemicals: HHC that apply to Washington's waters are found in the federal NTR (EPA, 1999). The NTR contains the complete listing of all 126 of the Clean Water Act 307(a) priority toxic pollutants (priority pollutants), and calculated HHC concentrations for 85 of the priority pollutants (some of the priority pollutants names are *not* accompanied by HHC concentrations). Of the 126 priority pollutants, 85 have numeric criteria for fresh water (exposure routes of drinking untreated surface waters and ingestion of fish and shellfish), and 84 have criteria for marine water (ingestion of fish and shellfish only). The NTR HHC apply to Washington's waters until EPA approves the newly adopted HHC.

EPA's recommended national criteria for chemicals: Since the 1992 NTR was published (and subsequently updated in 1999), EPA developed and published several additional Clean Water Act 304(a) recommended national HHC values for both priority pollutants and for non-priority pollutants. EPA's current recommended national criteria table (EPA, 2015) indicates that EPA has developed national recommended HHC for 99 of the priority pollutants and approximately 18 non-priority pollutants. Washington adopted new criteria for 97 of the chemicals that EPA has indicated are priority pollutants. This lower number of proposed chemicals (97) is because Washington is deferring adoption of new criteria for methylmercury, and will stay under the NTR criteria for mercury. Another chemical that Ecology is not adopting criteria for is bis(2-chloroisopropyl) ether, because it was determined that it does not have a 304(a) national recommended criteria associated with it (see further explanation later in this section).

EPA's recommendations to states on selecting chemicals for criteria adoption: EPA's *Water Quality Standards Handbook: Second Edition* (EPA, 2012) provides guidance to states that are choosing chemical criteria. These include recommendations for priority pollutants and

nonpriority pollutants, as description follows. An explanation of an exception to adopting the chemical bis(2-chloroisopropyl ether is also included.

Priority pollutants (Clean Water Act 303(c)(2)(B) requirements): the following are excerpts of guidance from EPA's *Water Quality Standards Handbook: Second Edition* (EPA, 2012, Chapter 3.4.1):

Excerpt 1

"Section 303(c)(2)(B) addresses only pollutants listed as "toxic" pursuant to section 307(a) of the Act, which are codified at 40 CFR 131.36(b). The section 307(a) list contains 65 compounds and families of compounds, which potentially include thousands of specific compounds. The Agency has interpreted that list to include 126 "priority" toxic pollutants for regulatory purposes. Reference in this guidance to toxic pollutants or section 307(a) toxic pollutants refers to the 126 priority toxic pollutants unless otherwise noted."

Excerpt 2

"States may meet the requirements of Clean Water Act section 303(c)(2)(B) by choosing one of three scientifically and technically sound options (or some combination thereof):

1. *Adopt statewide numeric criteria in state water quality standards for all section 307(a) toxic pollutants for which EPA has developed criteria guidance, regardless of whether the pollutants are known to be present;*
2. *Adopt specific numeric criteria in state water quality standards for section 307(a) toxic pollutants as necessary to support designated uses where such pollutants are discharged or are present in the affected waters and could reasonably be expected to interfere with designated uses;*
3. *Adopt a "translator procedure" to be applied to a narrative water quality standard provision that prohibits toxicity in receiving waters. Such a procedure is to be used by the state in calculating derived numeric criteria, which shall be used for all purposes under section 303(c) of the Clean Water Act. At a minimum, such criteria need to be developed for section 307(a) toxic pollutants, as necessary to support designated uses, where these pollutants are discharged or present in the affected waters and could reasonably be expected to interfere with designated uses,*

Option 1 is consistent with state authority to establish water quality standards and meets the requirements of the Clean Water Act. Option 2 most directly reflects the Clean Water Act requirements and is the option recommended by EPA, but is relatively more labor intensive to implement than Option 1. Option 3, while meeting the requirements of the Clean Water Act, is best suited to supplement numeric criteria from Option 1 or 2…"

Non-priority pollutants (see 40 CFR 131.11). Under these requirements, states must adopt criteria based on sound scientific rationale that cover sufficient parameters to protect

designated uses. Both numeric and narrative criteria may be applied to meet these requirements.

Exception for Bis(2-chloroisopropyl) ether*:* Ecology has determined that bis(2-chloroisopropyl) ether does not have a 304(a) national recommended criteria associated with it, thus the proposed criteria for this chemical were deleted from the final rule. Ecology has determined that the older NTR criteria for bis(2-chloroisopropyl) ether were incorrect, and were not developed for that particular priority pollutant. Ecology is adopting criteria only for the priority pollutants for which EPA has published 304(a) criteria documents. Further rationale for this decision:

Background information on bis(2-chloroisopropyl) ether: Appendix A to 40 CFR Part 423 lists the 126 Priority Pollutants (PP) published by EPA. Bis(2-chloroisopropyl) ether is priority pollutant number 42 on that list. The priority pollutant list does not specify Chemical Abstract Service numbers (CAS #'s); only names are specified. In EPA's most recent revisions to the 304(a) national recommended criteria for human health, EPA did not publish new criteria for this chemical, and further examination of the history of the criteria for this chemical indicates that the criteria in the NTR for Bis(2-chloroisopropyl) ether were in fact calculated for a different chemical. Bis(2-chloroisipropyl) ether was paired with the CAS # 108-60-1 in the 1992 NTR. This CAS number is incorrect. The CAS # for bis(2-chloroisipropyl) ether is CAS # 39638-32-9.

HHC were promulgated in the NTR for the chemical with CAS # 108-60-1, which is the unique identifier for bis(2-chloro-1-methylethyl)ether. This chemical has a different chemical structure than bis(2-chloroisipropyl)ether, and is an isomer. Bis(2-chloro-1-methylethyl) ether is not on the EPA's Priority Pollutant list at 40 CFR Part 423.

In its most recent (2015) revisions to the 304(a) national recommended criteria for human health EPA published new criteria for bis(2-chloro-1-methylethyl) ether (CAS # 108-60-1). EPA did not publish criteria for the priority pollutant bis(2-chloroisipropyl) ether (CAS # 39638-32-9). It appears that over the years EPA synonymized the two different chemicals during development of criteria, but instead of focusing on the actual pollutant priority name in 40 CFR Part 423, it chose to focus on the CAS # that was paired with the priority pollutant name in the NTR, and developed criteria for the non-priority pollutant. Subsequent information from EPA confirms that EPA drafted the criteria to apply to the non-priority pollutant bis(2-chloro-1-methylethyl) ether (CAS # 108-60-1).

Decision on bis(2-chloroisipropyl) ether for this Rulemaking: In the proposed rule Ecology included criteria for bis(2-chloroisipropyl) ether (CAS no. 108-60-1), based on EPA's NTR chemical list and CAS #s and the matching CAS # for EPA's new criteria for bis(2-chloro-1-methylethyl)ether. Subsequent examination (described previously) brought to light the differences in CAS #'s and chemical names for these two

compounds, and the lack of criteria values for the priority pollutant bis(2-chloroisipropyl) ether (CAS # 39638-32-9).

Because the chemical bis(2-chloro-1-methylethyl) ether (CAS no. 108-60-1) is not on EPA's priority pollutant list at Appendix A to 40 CFR Part 423, and because Ecology has made the decision to adopt HHC for priority pollutants only, Ecology is not adopting HHC for this chemical. Because the older criteria for bis(2-chloroisipropyl) ether in the NTR was developed for the non-priority pollutant bis(2-chloro-1-methylethyl) ether (CAS no. 108-60-1) Ecology is not adopting the NTR criteria for this chemical. When Ecology submits final adopted water quality standards to EPA for approval, it will include a recommendation that EPA revise the priority pollutant list at Appendix A to 40 CFR Part 423 to reflect the chemical name that it considers to be the original intended name.

Basis for Ecology's Decisions on HHC

Ecology adopted HHC for all Clean Water Act Sec. 307(a) priority toxic pollutants (except mercury/methyl mercury) for which EPA has developed national recommended numeric HHC, regardless of whether the pollutants are known to be present (EPA guidance for option 1, Priority Pollutants Excerpt 2, described previously). This includes criteria for 97 different pollutants. The exception is that Ecology is not proposing new criteria for methyl mercury, therefore it will remain under the NTR. The state water quality standards include a narrative statement for priority pollutants that do not have numeric criteria and for non-priority toxic pollutants. This approach is consistent with Option 1 from EPA's guidance cited previously.

Ecology did not adopt numeric criteria for non-priority pollutants at this time. Ecology will use a narrative statement to protect designated uses from effects of chemicals that do not have numeric criteria. If monitoring or other information indicates that non-priority pollutant sources or concentrations are a concern, Ecology will use the narrative statement to protect designated uses from regulated sources. The ongoing triennial review process for the water quality standards will be used to determine whether there is a need to adopt numeric criteria for additional pollutants in future revisions to the water quality standards.

Ecology added an additional statement on downstream protection to the draft rule in language preceding the toxics table. This language is duplicative of existing implementation language in WAC 173-201A-260(3)(b), requiring that upstream waters be conducted in manners that meet downstream water body criteria and will not change any requirements for implementation of the new HHC criteria. The language was added at EPA's recommendation to states to ensure downstream protection is considered.

Ecology's chemical choice:

- Ensures that Washington will satisfy the intent of the Clean Water Act.
- Is within a state's legal authority under the Clean Water Act to adopt broad water quality standards.

- Is a comprehensive approach to satisfy the statutory requirements because it includes all of the priority toxic pollutants for which EPA has prepared section 304(a) criteria guidance (except mercury/methylmercury).
- Is fairly simple and straightforward to implement (does not require the monitoring needed to support EPA's Option 2 listed previously).
- Contains the same chemical list format (the full priority pollutant list) found in the NTR. Inserting the entire priority pollutant list in the water quality standards (even though not all priority pollutants will have accompanying criteria) makes for an easy comparison of the state's HHC with federally-required NPDES discharge permit application information.
- Relies on an already-existing narrative statement in the standards to protect designated uses from effects of chemicals without adopted numeric criteria.

References

EPA, 1992. U.S. Environmental Protection Agency. Toxics criteria for those states not complying with Clean Water Act section 303(c)(2)(B). 40 CFR Part 131.36. Fed. Register, Vol. 57, No. 246, page 60848. (Also known as the National Toxics Rule.)

EPA, 1999. U.S. Environmental Protection Agency. Toxics criteria for those states not complying with Clean Water Act section 303(c)(2)(B), originally published in 1992, amended in 1999 for PCBs. 40 CFR Part 131.36. Fed. Register, Vol. 64, No. 216, page 61182. http://www.ecfr.gov/cgi-bin/text-idx?SID=76816a2f92256bf94a548ed3115cee23&node=40:23.0.1.1.18.4.16.6&rgn=div8

EPA, 2012. U.S. Environmental Protection Agency. Water Quality Standards Handbook: Second Edition (EPA-823-B-12-002; March 2012); *http://water.epa.gov/scitech/swguidance/standards/handbook/index.cfm) (Note: This website was referenced 4/2014)*

EPA, 2015. U.S. Environmental Protection Agency. National Recommended Human Health Criteria list: *http://water.epa.gov/scitech/swguidance/standards/criteria/current/index.cfm (Note: This website was referenced 10/2015)*

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Human Health Criteria Equations and Variables

Decision

Ecology adopted surface water HHC for 97 priority toxic pollutants. Of those chemicals, 94 have criteria calculations associated with them that are reflected in the following discussion. The other three chemicals (arsenic, copper, and asbestos) are based on Safe Drinking Water Act regulatory levels, and thus their criteria do not involve using human health criteria calculations. The following discussion does not apply to these three chemicals, except where arsenic information is discussed below in the section on Cancer Slope Factor (CSF).

Table 1 provides a comparison of the explicit variables that are found in the human health equations for the federal NTR (applied in Washington), and the new criteria in the WQS. Discussion of the new EPA 304(a) guidance values is also included as needed. In almost all cases, values for chemical-specific toxicity factors are taken from EPA's Integrated Risk Information System (IRIS) or from the EPA National Recommended Water Quality Criteria documents, noted in Table 1. There are also implicit variables in the equations that Ecology did not change from the approach used in the NTR. They are further described in the background section of this document. See Appendix A of this document for the individual chemical-specific values used to calculate the new criteria.

Table 1: Comparison of equation variables for Washington's proposed rule

Explicit variables	NTR Criteria	Washington's new rule (2016)
Fish and shellfish consumption rate (FCR)	6.5 grams/day	175 g/day
Risk level (RL)	Additional lifetime risk of 1 in a million ($1x10^{-6}$)	Additional lifetime risk of 1 in one million ($1x10^{-6}$) (no change)
Relative source contribution (RSC)	1	1 (no change)
Body weight (BW)	70 kilograms (154 pounds).	80 kilograms (176 pounds)
Drinking water intake (DI)	2 liters/day	2.4 liters/day
Reference dose (RfD) for specific chemicals	EPA IRIS values and other sources	Updated values in EPA IRIS and EPA NRWQC documents
Cancer slope factor (CSF) for specific chemicals	EPA IRIS values and other sources	Updated values in EPA IRIS and EPA NRWQC documents
Bioconcentration factor (BCF)	BCFs found in the NTR	Values from 1992 NTR and 1999 revision; EPA's 2002 HHC Calculation Matrix (EPA, 2002), and pre-2015 NRWQC. Two additional BCFs calculated based on EPA 1980.

Background

The human health water quality criteria (HHC) are chemical-specific concentrations applied to surface waters. The HHC are developed to protect human populations from undue risks to chemical exposures from drinking untreated surface-water, and eating fish and shellfish that live in those waters.

The criteria are calculated using equations developed by EPA that incorporate information on risk and exposure, and the degree to which the pollutants accumulate in fish and shellfish tissue. EPA has developed equations for both carcinogens and noncarcinogens that apply to exposures from drinking untreated surface water and consuming fish and shellfish, or, consuming fish and shellfish only. *For purposes of simplifying the discussion, these scenarios will be referred to as fresh waters or marine waters, respectively. However, some freshwaters in Washington do not have "domestic water supply" as a designated use, and for these waters, the criteria that address only the consumption of organisms are applied.* This Decision Document provides summary-only information about the equations that are used to develop HHC for Washington; the bulk of the document provides more detailed discussion about the individual variables that go into the equations.

Ecology used best available science in developing this rule. Note that what is considered "best available science" is subjective and changes over time. An assessment of "best" at any specific time includes the perspectives of the evaluators, the context of the evaluation, and other factors important to the specific type of decision. The topic of best available science is comprehensively discussed in Sullivan et al (2006). Ecology used the best available science in developing new HHC applicable to Washington State. The input variables were chosen to provide full protection for the designated uses addressed by the HHC. Ecology's rule process acknowledged scientific uncertainties in the inputs to the criteria equations (e.g., the use of uncertainty factors in reference dose development). Ecology developed clear science and/or policy statements to support the final criteria, and has clearly stated the basis of these in materials supporting the proposed and new rule, in particular where new science is emerging or underway. These are discussed in this document. In particular this has been clarified for arsenic, PCBs, and dioxin, where issues of toxicity factors, alternative approaches to criteria development, and risk levels have been addressed. The use of a bioconcentration-based approach over the EPA-recommended bioaccumulation factors in criteria calculation is also clarified in this document.

References cited in the document are included at the end under the section on Additional Information.

HHC equations and types of variables considered in the equations: In total, four equations are used to calculate HHC. These equations are based on chemical effects (carcinogens or noncarcinogens) and routes of exposure (fresh or marine water):

- *Chemical effects*: HHC equations are used to calculate criteria for both cancer-causing chemicals, called carcinogens, and non-cancer causing chemicals, called noncarcinogens.

The criteria for any one chemical are based on the acceptable level of risk (the effect that would occur at the lowest water concentration).

- *Routes of exposure*: Washington has both marine and fresh waters that are regulated under the Clean Water Act and under state jurisdiction. Therefore, separate equations are needed for each type of water to account for presence or absence of an untreated drinking water exposure route. Marine waters are assumed to include estuarine waters, and both of these do not have the drinking water use applied.

Several different factors, or variables, are included in each equation. The variables help to characterize risk and exposure, including the degree and type of toxicity attributed to specific chemicals, human body weight, human drinking water rates, fish and shellfish consumption rates, and others. These variables are assigned values, which are then used in the equations to derive HHC concentrations. The exposure variables represent a combination of averages and upper percentiles. The choice of variables, and the science policy and risk management decisions that are included in the variables, act together to determine criteria that are estimates of desired levels of protection.

Why are these variables important? Each variable in the equations affects the final calculated HHC concentrations. Some variables make significant differences in the calculated values, while other variables make smaller changes. For instance, the additional lifetime cancer risk level for carcinogens can make a large difference in some criteria concentrations. If the risk level increases, the criteria become less stringent. Fish consumption rates also affect the calculation considerably. Higher fish consumption rates result in lower criteria concentrations. An example of a variable that has much less effect on the calculated value is body weight. Higher body weight results in only slightly higher criteria concentrations.

EPA publishes Clean Water Act Sec. 304(a) national recommended HHC guidance values for approximately 117 chemicals, including priority and non-priority pollutants. The recommended criteria are calculated using a combination of default and chemical-specific pieces of information recommended for state use by EPA. Some of the recommended criteria are based on Safe Drinking Water Act MCLs (maximum contaminant levels). Values for some variables can differ among states, based on location or regional information, science, science policy, and risk management, and can result in criteria that may differ from those recommended by EPA. For other variables, states generally use standard values, supported by national scientific research, that tend to remain constant across states even when developing state-specific criteria. The following variables are explicitly used in the HHC calculation, and are discussed later in this document:

Values for these variables vary among states:
- Fish Consumption Rate (FCR)
- Risk level (RL)
- Relative Source Contribution (RSC)

States generally use the same values for these variables:
- Body Weight (BW)
- Drinking Water Intake (DI)
- Reference Dose (RfD)
- Cancer Slope Factor (CSF)
- Bioconcentration Factor (BCF).

The four equations for developing HHC are summarized in Table 2. The equations shown in the table have been simplified for purposes of this discussion document. Units and correction factors are not presented. The full equations with all units can be found in the EPA (2000) guidance.

Table 2: Summary of HHC equations

Toxicity endpoint	Water type and exposure route	Chemical-specific criterion equation
Cancer	Fresh water: fish/shellfish consumption and drinking untreated surface water	$\frac{RL \times BW}{CSF \times (DI + [FCR \times BCF])}$
Non-Cancer	Fresh water: fish/shellfish consumption and drinking untreated surface water	$\frac{RfD \times RSC \times BW}{DI + (FCR \times BCF)}$
Cancer	Marine and estuarine waters: fish and shellfish consumption	$\frac{RL \times BW}{CSF \times FCR \times BCF}$
Non-Cancer	Marine and estuarine waters: fish and shellfish consumption	$\frac{RfD \times RSC \times BW}{FCR \times BCF}$

In addition to the variables described in the table, which are used explicitly in the equations, certain other factors are considered *implicitly* (i.e., they are not part of the written equation but are assumed during calculation). Some of these will be discussed briefly later in this document, including lifespan, duration of exposure, and hazard quotient for non-cancer effects.

Basis for Ecology's new criteria:

Variables in the equation
A more detailed description of the variables in the equation will be presented in the following order:

Variables where the values vary among states:

1. Fish Consumption Rate (FCR)
2. Risk level (RL)
3. Relative Source Contribution (RSC)

Variables where the values generally do not vary among states:

4. Body Weight (BW)
5. Drinking Water Intake (DI)
6. Reference Dose (RfD)
7. Cancer Slope Factor (CSF)
8. Bioconcentration Factor (BCF)

Variables implicit in the HHC equations:

9. Lifespan and duration of exposure
10. Hazard quotient for non-cancer effects

1. Fish Consumption Rate (FCR)
Application: *This explicit variable* ***applies to all four equations****: carcinogen/fresh water; carcinogen/marine water; noncarcinogen/fresh water; and noncarcinogen/marine water.*

Ecology used a fish consumption rate of 175 g/day in the HHC equation, based on a Washington-specific risk management decision to use a value that: (1) is representative of state-specific information; and (2) was determined through a process that included consideration of EPA guidance and precedent, and input from multiple groups of stakeholders.

General information: The fish consumption rate (FCR) used in the equations usually refers to a statistic that describes a set of data from surveys of people based on the amount of fish and shellfish they eat. The data are represented as daily intake rates using the units of grams per day (g/day). When calculating HHC, the statistic used to describe the data set is a risk management decision made by states and tribes, and can be an average, a median, an upper percentile, or some other statistic. A state should also consider what target population to base the FCR on, and use survey data that represent that population of users. For example, the FCR could be based on survey data from the general population, or from high-consuming populations in the state.

The statistic used by the EPA and states has historically been an *average of a national general population data set (including consumers and non-consumers*), *freshwater and estuarine aquatic species only* (salmon excluded because of its marine life history). This is the origin of the 6.5 g/day fish consumption rate that is incorporated into the 1992 NTR. In 2000 EPA updated that

national general population average value to 7.5 g/day, based on new science, and changed its guidance on the use of national general population data to recommend using a 90th percentile value (rather than an average) for freshwater and estuarine species only (EPA, 2000). That new 90th percentile recommended value was 17.5 g/day, and has been used by many states in criteria calculation.

EPA makes the following specific recommendation for protection of the general population for purposes of HHC development in the EPA 2000 guidance:

> *"EPA recommends a default fish intake rate of 17.5 grams/day to adequately protect the general population of fish consumers, based on the 1994 to 1996 data from the USDA's CSFII Survey. EPA will use this value when deriving or revising its national 304(a) criteria. This value represents the 90th percentile of the 1994-96 CSFII data. This value also represents the uncooked weight estimated from the CSFII data, and represents intake of freshwater and estuarine finfish and shellfish only."* (EPA, 2000, page 4-24)

In 2015 EPA published revised National Recommended Water Quality Criteria (NRWQC) for human health and included a new 90th percentile FCR for the national general population of 22 g/day, based on newer national survey data.

EPA 2000 makes the following specific recommendation for protection of highly exposed populations:

> *"EPA recommends default fish intake rates for recreational and subsistence fishers of 17.5grams/day and 142.4 grams/day, respectively. These rates are also based on uncooked weights for fresh/estuarine finfish and shellfish only. However, because the level of fish intake in highly exposed populations varies by geographical location, EPA suggests a four preference hierarchy for States and authorized Tribes to follow when deriving consumption rates that encourages use of the best local, State, or regional data available…* ***EPA strongly emphasizes that States and authorized Tribes should consider developing criteria to protect highly exposed population groups and use local or regional data over the default values as more representative of their target population group(s)****. The four preference hierarchy is: (1) use of local data; (2) use of data reflecting similar geography/population groups; (3) use of data from national surveys; and (4) use of EPA's default intake rates."* (EPA, 2000, pages 4-24 to 4-25, emphasis added)

Since Washington has a strong tradition of fish and shellfish harvest and consumption from local waters, and within-state survey information indicates that different groups of people harvest fish both recreationally and for subsistence (Ecology, 2013), *Ecology has made the risk management decision to base the fish consumption rate used in the HHC equation on "highly exposed populations,"* which include, among other groups, the following: tribes, Asian Pacific Islanders (API), recreational and subsistence fishers, immigrant populations. Fish consumption rates developed in several surveys around the Pacific Northwest are summarized and discussed in a recent Ecology publication (Ecology, 2013).

The choice of a FCR is a risk management decision made by states: The choice of an FCR that represents a specific population, and the statistic (e.g., average, median, or other percentile) representing the distribution of individual FCRs from that specific population, is a risk management decision made by states. EPA provides language on this risk management decision in EPA 2000:

> *"Risk management is the process of selecting the most appropriate guidance or regulatory actions by integrating the results of risk assessment with engineering data and with social, economic, and political concerns to reach a decision. In this Methodology, the choice of a default fish consumption rate which is protective of 90 percent of the general population is a risk management decision. The choice of an acceptable cancer risk by a State or Tribe is a risk management decision."* (Section 2.2)

As previously discussed, the statistic used by the EPA and states has historically been an *average of a national general population data set.* The FCR incorporated into the NTR is an average. Ecology is continuing use of the average statistic as described.

The new state FCR of 175 g/day: A FCR of 175 g/day is representative of average FCRs ("all fish and shellfish," including all salmon, restaurant, locally caught, imported, and from other sources) for highly exposed populations that consume both fish and shellfish from Puget Sound waters. This numeric value was used by the Oregon Department of Environmental Quality to calculate HHC in a 2011 rulemaking. A FCR of 175 g/day is considered an "endorsed" value. Groups endorsing the use of this numeric value, at different times in the process, include EPA and several tribes. Average FCR values for various highly exposed groups that harvest both fish and shellfish from Puget Sound waters are found in FCR Technical Support Document (Ecology, 2013).

The range of average values for the three highest Puget Sound tribal average values are in the Table 3, copied from Table 1 of the FCR Technical Support Document (Ecology, 2013):

Table 3: Fish consumption data from Table 1 FCR Technical Support Document

Population	Source of Fish	Number of Adults Surveyed	Mean	Percentiles		
				50th	90th	95th
General population (consumers only)	All sources: EPA method	2,853	56	38	128	168
	All sources: NCI method	6,465	19	13	43	57
Columbia River Tribes	All sources	464	63	41	130	194
	Columbia River	–	56	36	114	171
Tulalip Tribes	All sources	73	82	45	193	268
	Puget Sound	71	60	30	139	237
Squaxin Island Tribe	All sources	117	84	45	206	280
	Puget Sound	–	56	30	139	189
Suquamish Tribe	All sources	92	214	132	489	797
	Puget Sound	91	165	58	397	767
Recreational Fishers (compilation of multiple studies)	Marine waters, WA State	–	11–53	1.0–21	13–246	
	Freshwater, WA State	–	6.0–22	–	42–67	

Sources: Adapted from Polissar et al., 2012, Table E-1. Data for recreational fishers is from Table 3, Technical Issue Paper: *Recreational Fish Consumption Rates* (Ecology, 2012). General population data are for consumers only, as opposed to per capita. See Chapters 4 and 6.

The three highest average (mean) values are from the Tulalip, Squaxin Island, and Suquamish tribal surveys (average FCRs are, respectively, 82 g/day, 84 g/day, 214 g/day). The mean of the three tribal studies combined is 127 g/day. The FCR value of 175 g/day is not a calculated value. It was chosen as part of the risk management process for this rule and is based on the best available science for purposes of this rulemaking and is representative of the average value/values of these surveys.

Ecology compared the Asian Pacific-Islander (API) FCRs from Puget Sound, as summarized in Table 4, to the three tribal studies identified previously. The percentile information from the API survey is comparatively lower than the percentile information for the Suquamish study (the tribe with the highest consumption rates). For example, a median equal to 74 g/day was from the API study, while a median equal to 132 g/day was from the Suquamish study. Average (mean) values were not reported for the API study, but because the mid and upper percentiles are all lower than the Suquamish study, it is reasonable to infer that this population is consuming amounts of fish and shellfish that, at the average, are not greater than the tribal studies used to develop the value of 175 g/day, and are therefore encompassed by the value of 175 g/day.

Table 4: API Consumption rates from Table 30 FCR Technical Support Document (Ecology, 2013)

Population API	Species Group	Source of Fish	Descriptive Statistics (g/day)		
			50th Percentile	90th Percentile	95th Percentile
Asian-Pacific Islander (API)	Total seafood consumption	All sources	74.0	227	286
	All species	Harvested anywhere	6.5	25.9	58.8
	All species	Harvested from King County	5.7	22.2	48.4
	Non-anadromous species	Harvested anywhere	6.2	37.9	54.1
	Non-anadromous species	Harvested from King County	6.0	20.1	45.5

Sources: Adapted from Kissinger, 2005, Table 5. See also Polissar et al., 2012.

Decision for the rule:

Ecology used a FCR of 175 g/day to calculate the HHC, based on a state-specific risk management decision. (http://www.governor.wa.gov/news-media/inslee-announces-new-path-water-quality-rule-continues-work-broader-toxics-reduction).

2. Risk level (RL)

Application: This explicit variable applies ***only to equations for carcinogens****: carcinogen/fresh water and carcinogen/marine water.*

Ecology continued use of the risk level of one-in-one-million (10^{-6}) as specified in 173-201A-240 WAC, except for the chemical-specific risk level for PCBs (discussed later in this document). The new criteria for carcinogens using the risk level are identified in the newly formatted toxics criteria table at 173-201A-240 WAC.

Background: The risk level used in the HHC equations for carcinogens is defined as the "upper bound estimate of excess lifetime cancer risk" (EPA, 2000). The risk level value is only used when calculating criteria for pollutants that may cause cancer. Applying the risk level to the equations results in HHC concentrations that would hypothetically be expected to increase an individual's lifetime risk of cancer by no more than the assigned risk level, regardless of the cancer risk that may come from exposure to the chemical from sources other than surface water.

EPA 2000 guidance recommends that states and tribes set HHC risk levels for the general population at either one additional occurrence of cancer, after 70 years of daily exposure, in 100,000 people (1×10^{-5}) or one in 1,000,000 people (1×10^{-6}). EPA 2000 guidance also recommends that for states with high fish consuming populations, the most highly exposed populations should not exceed a risk level of one additional occurrence of cancer in 10,000 people (1×10^{-4}). Washington's current HHC from the NTR apply a risk level of one additional occurrence of cancer in 1,000,000 (1×10^{-6}).

The choice of an acceptable additional lifetime cancer risk level is a risk management decision made by states. EPA provides specific language on this in EPA 2000:

> *"Risk management is the process of selecting the most appropriate guidance or regulatory actions by integrating the results of risk assessment with engineering data and with social, economic, and political concerns to reach a decision. In this Methodology, the choice of a default fish consumption rate which is protective of 90 percent of the general population is a risk management decision. The choice of an acceptable cancer risk by a State or Tribe is a risk management decision."* (Section 2.2)

General information: The choice of risk level is a policy decision by the state. Nationwide, states (including Washington) and tribes, have typically chosen to use a risk level of one additional occurrence of cancer in 100,000 people (1×10^{-5}) or one in 1,000,000 people (1×10^{-6}) for HHC. This is demonstrated in a list of state and tribal risk levels provided to Ecology by EPA Region 10 (see http://www.ecy.wa.gov/programs/wq/swqs/RiskLevelCarcinogens.pdf). This list was presented as part of Ecology's Policy Forum #3, held February 8, 2013 (http://www.ecy.wa.gov/programs/wq/swqs/hhcpolicyforum.html). EPA guidance advises that states and tribes using these risk levels must ensure that the risk level for the most highly exposed subpopulations does not exceed one additional occurrence of cancer in 10,000 people (1×10^{-4}), (EPA, 2000). Section 303(c) of the Clean Water Act directs the requirements for setting and revising water quality standards, but does not specify risk levels.

It should be noted that it is not possible to assume that an equal amount of risk will be realized by the entire population of a state. All other factors being equal, people and groups who consume more fish and shellfish are inherently at greater risk from those contaminants than those who do not (assuming that contaminants are present in these items and that equal concentrations of contaminants are present in the consumed items). Regardless of the specific fish consumption rate used in the criteria calculations, or the final water quality criteria that are applied to waters, unequal risk among groups and individuals will always exist because of differences in fish consumption habits. This difference would exist even if criteria were not present. Therefore it is not reasonable to assume that a given risk level chosen by a state reflects the actual risk across all populations or among all individuals in the entire state.

How well do the criteria equations characterize actual risk? Even though the HHC equations appear to directly stipulate risk, other factors (those within the HHC equations and those not included in the HHC equations) complicate the ability to gauge an individual's or population's actual risk level.

Direct quantification of risk for populations is described in EPA guidance (EPA, 2000) as follows:

> *"EPA's Guidelines For Exposure Assessment (USEPA, 1992) describes the extreme difficulty in making accurate estimates of exposures and indicates that uncertainties at the more extreme ends of the distribution increase greatly. On quantifying population exposures/risks, the guidelines specifically state:*

In practice, it is difficult even to establish an accurate mean health effect risk for a population. This is due to many complications, including uncertainties in using animal data for human dose-response relationships, nonlinearities in the dose response curve, projecting incidence data from one group to another dissimilar group, etc. Although it has been common practice to estimate the number of cases of disease, especially cancer, for populations exposed to chemicals, it should be understood that these estimates are not meant to be accurate estimates of real (or actuarial) cases of disease. The estimate's value lies in framing hypothetical risk in an understandable way rather than in any literal interpretation of the term 'cases.'"(EPA 2000, pages 2-1 to 2-1)

Washington's current risk level and information on changing the risk level: On December 18, 1991, in its official comments on EPA's proposed NTR the Department of Ecology (Ecology) directed EPA to promulgate HHC for the state at $1x10^{-6}$. At the time, Ecology understood that the $1x10^{-6}$ risk level would be applied with a 6.5 grams/day fish consumption rate of freshwater and estuarine fish, and that higher consumption rates would still be protective, but at a different risk level (for example, a 65 grams/day fish consumption rate would have an estimated $1x10^{-5}$ risk level) as this was clearly described by EPA in the November 19, 1991 proposed NTR. During the summer of 1992, the state formally proposed and held public hearings on revisions to its water quality standards. The standards, which were scheduled for adoption in late November 1992, included a risk level of $1x10^{-6}$ which remain unchanged in the current approved standards.

In the 1992 NTR (EPA, 1992) the following excerpt provided information to states planning to adopt their own criteria in order to be removed from the NTR *(#3. Approach for States that Fully Comply Subsequent to Issuance of this Final Rule)*:

As discussed in prior Sections of this Preamble, the water quality standards program has been established with an emphasis on State primacy. Although this rule was developed to Federally promulgate toxics criteria for States, EPA prefers that States maintain primacy, revise their own standards, and achieve full compliance. EPA is hopeful this rule will provide additional impetus for non-complying States to adopt the criteria for priority toxic pollutants necessary to comply with section 303(c)(2)(B).

Removal of a State from the rule will require another rulemaking by EPA according to the requirements of the Administrative Procedure Act (5 U.S.C. 551 et seq.). EPA will withdraw the Federal rule without a notice and comment rulemaking when the State adopts standards no less stringent than the Federal rule (i.e., standards which provide, at least, equivalent environmental and human health protection). For example, see 51 FR 11580, April 4, 1986, which finalized EPA's removal of a Federal rule for the State of Mississippi.

However, if a State adopts standards for toxics which are less stringent than the Federal rule but, in the Agency's judgment, fully meet the requirements of the Act, EPA will propose to withdraw the rule with a Notice of proposed rulemaking and provide for

*public participation. This procedure would be required for partial or complete removal of a State from this rulemaking. An exception to this requirement would be when a State adopts a human health criterion for a carcinogen at a 10^{-5} risk level where the Agency has promulgated at a 10^{-6} risk level. In such a case, the Agency believes it would be appropriate to withdraw the Federal criterion without notice and comment because the Agency has considered in this rule that criteria based on either 10^{-5} or 10^{-6} risk levels meet the requirements of the Act. A State covered by this final rule could adopt the necessary criteria using any of the three Options or combinations of those Options described in EPA's 1989 guidance." (*1992 NTR*)*

How risk was applied in this new rule: The approach Ecology used to calculate the new HHC is very similar to that used by EPA to calculate their Clean Water Act 304(a) national recommended criteria. EPA's method, however, focuses on providing protection to the general population, while the Ecology approach focuses on protection of highly exposed populations, which in Washington are assumed to include (among others) tribes, API populations, immigrant populations, recreational, and subsistence fishers. Washington implemented this change of focus in the proposed criteria equations by changing the FCR variable from a statistic (the average) that represents the general population FCR distribution to an equivalent statistic (the average) representative of FCR distributions of highly exposed populations. The body weight input to the equations is representative of average adults of both the national general population, for the adult average of at least three tribes in Washington, and is used by EPA in its 2015 NRWQC (see Body Weight (BW) discussion later in this document). The Drinking Water Intake (DI) input to the equations is representative of average adults and the national general population, and is used by EPA in its 2015 NRWQC. (see Drinking Water Intake (DI) discussion later in this document). The risk level used in the HHC equations is one to one million (10^{-6}), the risk level currently in Washington's water quality standards (see Overview section of this document for a description of this risk management decision). However, a state-specific risk level was chosen for PCBs (see section on Challenging Chemicals: PCBs.).

Washington applied the risk framework, developed by EPA for the current federal HHC rule (the 1992 NTR), to highly exposed populations in Washington in the following manner:

- Washington is currently under the federal NTR for HHC. Those criteria are set at a 10^{-6} risk level and the risk level is applied to the arithmetic mean (average) of the *general population.*
- For this new rule, the Washington risk level of 10^{-6} is applied to a FCR of 175 g/day that is representative of the arithmetic means (averages) of *highly exposed populations* instead of the general population. (Note: the risk level used for total PCBs is different from 10^{-6}. Please see section on Challenging Chemicals: PCBs.).

Most states follow EPA's approach and apply the state's default risk level to a general population (as EPA also does in its Clean Water Act §304(a) national recommended criteria) and then ensure that highly exposed populations do not exceed EPA's upper levels of allowed risk. In this new rule Washington has taken the extra protective measure of basing the FCR on

Washington's most highly exposed populations, and the important local food sources of "all fish and shellfish" (which includes the additional protective step of including local and non-local sources, such as all salmon, restaurant, locally caught, imported, and from other sources). The new rule also includes the additional protective step of applying the more broadly protective FCR to a risk level most frequently applied to the general population. The Washington approach ensures that highly exposed populations in Washington will be protected by HHC calculated using the same risk level and FCR statistic (representative of the arithmetic mean) that is currently applied to the NTR HHC calculated for the general population.

Decision for proposed rule: Ecology continued use of the risk of *one-in-one-million or* 10^{-6}. This risk management decision is described in the Overview section of this Decision Document.

3. Relative Source Contribution (RSC)

Application: This explicit variable applies ***only to equations for noncarcinogens****: noncarcinogen/fresh water and noncarcinogen/marine water.*

Ecology applied a relative source contribution value of one (1), which is the same value used to calculate the criteria in the NTR.

Background: The Relative Source Contribution (RSC) is a variable in the HHC equation that represents the portion of an individual's daily exposure to a contaminant that is attributed to exposure sources regulated by the Clean Water Act as opposed to exposure sources of toxic chemicals that are not regulated by the Clean Water Act. The RSC only applies to the equations for noncarcinogens.

The HHC are used to regulate pollution sources that discharge to waters of the state and are under the authority of the Clean Water Act, in order to control chemical exposure from untreated surface-water used for drinking water, and eating fish and shellfish that live in those waters. The RSC is intended to account for secondary sources of pollutants, outside of the authority of the Clean Water Act, such as atmospheric deposition or marine fish sources (e.g., mercury in tuna).

Relative source contributions (RSCs) are used in the criteria equation only for non-carcinogens and non-linear carcinogens. Non-carcinogenic chemicals that express their toxicity through threshold effects are more likely to express effects when a specific dose – the reference dose (RfD) – is surpassed. The RSC, as applied in the HHC equations, assumes that exposure of a particular chemical through surface water (i.e., drinking water and fish/shellfish consumption) contributes a portion of the RfD, with the remaining portion from exposure to other sources (such as dietary intake other than non-local fish and shellfish). The portion of RfD exposure through surface water is the RSC, expressed as a decimal fraction. For example, an RSC of 0.4 indicates 40% of the RfD is due to exposure through surface waters and 60% is due to other sources.

The 1980 EPA guidance for HHC (EPA 1980), used to develop the pre-2000 HHC, included the alternative of considering total exposure from all sources in the criteria calculations, but the Clean Water Act 304(a) HHC, developed following these guidelines, assumed an RSC of 1.0

(EPA, 2002). The 1992 NTR HHC applied a RSC of 1.0 (100% allocation of exposure given to sources regulated by the Clean Water Act). In 2015, EPA published revised NRWQC for a large number of pollutants using RSCs based on EPA 2000 guidance. These RSCs are largely limited to RSC = 0.2.

The EPA 2000 guidance and follow-up clarifications from EPA (2013 and 2015), recommend new default values for the RSC to be used in the HHC equations for noncarcinogens:

> *"In the absence of scientific data, the application of the EPA's default value of 20 percent RSC in calculating 304(a) criteria or establishing State or Tribal water quality standards under Section 303(c) will ensure that the designated use for a water body is protected. This 20 percent default for RSC can only be replaced where sufficient data are available to develop a scientifically defensible alternative value. If appropriate scientific data demonstrating that other sources and routes of exposure besides water and freshwater/estuarine fish are not anticipated for the pollutant in question, then the RSC may be raised to the appropriate level, based on the data, but not to exceed 80 percent. The 80 percent ceiling accounts for the fact that some sources of exposure may be unknown."*

In the simplest terms, EPA's latest RSC guidance recommends two conservative default approaches:

- If sources of exposure to a chemical are not known, then a default RSC of 0.2 is included in the equation.
- If sources of exposure to a chemical are well known and documented, then a calculated RSC is included in the equation. This calculated RSC gives the HHC the remainder of the reference dose or allowable daily exposure that is not accounted for by other non-Clean Water Act sources. EPA guidance suggests that the RSC value should not be greater than 0.8.

An inherent assumption in how the RSC for HHC is developed is that all other sources of the contaminant are required to be accounted for in the exposure scenario, and the HHC get the remainder of the reference dose or allowable daily exposure that is assumed to come from sources under the authority of the Clean Water Act. The resulting situation seems contradictory; as the contribution of a contaminant from water sources becomes smaller, the HHC becomes more stringent and in effect becomes a larger driver for more restrictive limits.

The use of an RSC affects criteria calculation results as follows:

- If the RSC is 1.0, then it does not change the resulting criteria calculation.
- If the RSC is 0.8, then the criterion becomes more stringent by 20%.
- If the RSC is 0.5, then the criterion becomes more stringent by 50%.
- If the RSC is 0.2, then the criterion becomes more stringent by 80%.

The RSC can drive, very directly, the resulting human health water quality criteria and related regulatory and permit levels. Using an RSC of 0.2, for example, means that an ambient water

quality criterion that would otherwise be 10 units would be reduced by 80% to 2 units, thus becoming lower, or more stringent, in order to compensate for sources that are outside of the sources regulated by the Clean Water Act. Many other programs that address toxics, such as the Safe Drinking Water Act and the Superfund Clean-up Program, also establish similar concentration goals but then use a risk management approach that allows for consideration of other factors, such as cost and feasibility, in establishing actual compliance levels that have to be achieved. Conversely, the ambient water quality criteria under the Clean Water Act set direct regulatory levels that are enforced as both ambient concentrations in the water body (through the Clean Water Act 303(d) program with subsequent load allocation requirements [40CFR130]), as well as through NPDES permit levels (criteria applied at end-of-pipe or with use of a dilution zone, depending on the specific circumstances).

EPA's Water Quality Standards Handbook: Second Edition (EPA, 2012) provides additional guidance on this subject. This guidance is different from the EPA 2000 guidance, and indicates that in practice criteria may be based on risk from only the surface water exposure routes:

"Human Exposure Considerations: *A complete human exposure evaluation for toxic pollutants of concern for bioaccumulation would encompass not only estimates of exposures due to fish consumption but also exposure from background concentrations and other exposure routes. The more important of these include recreational and occupational contact, dietary intake from other than fish, intake from air inhalation, and drinking water consumption. For section 304(a) criteria development, EPA typically considers only exposures to a pollutant that occur through the ingestion of water and contaminated fish and shellfish. This is the exposure default assumption, although the human health guidelines provide for considering other sources where data are available (see 45 F.R. 79354). Thus the criteria are based on an assessment of risks related to the surface water exposure route only (57 F.R. 60862-3)." (text copied from EPA web site on 11/10/2015):*

http://www2.epa.gov/sites/production/files/2014-10/documents/handbook-chapter3.pdf

The use of an RSC to compensate for sources of exposure outside the scope of the Clean Water Act when establishing HHC is a risk management decision that states need to carefully weigh. If the scope of the Clean Water Act is limited to addressing potential exposures from NPDES- or other Clean Water Act regulated discharges to surface water, it could be argued that an RSC of less than 1.0 inappropriately expands of the scope of what the Clean Water Act would be expected to control. On the other hand, if it is assumed that the scope of the Clean Water Act includes consideration and protection from other sources of toxics not regulated by the Clean Water Act, such as atmospheric deposition or marine fish sources (e.g., mercury in tuna), one could argue for an RSC of less than 1.0. The role of the RSC and how to calculate it is an issue that must be carefully considered by a state when establishing HHC.

Decision for new rule: Because the geographic and regulatory scope of the Clean Water Act addresses contaminant discharge directly to waters of the state (not other sources or areas), Ecology made a risk management decision that the human health criteria in the new rule be

based on a relative source contribution of one (RSC = 1). Given the limited ability of the Clean Water Act to control sources outside its jurisdiction, Ecology firmly believes that this is a prudent decision.

4. Body Weight (BW)

*Application: This explicit variable **applies to all four equations**: carcinogen/fresh water; carcinogen/marine water; noncarcinogen/fresh water; and noncarcinogen/marine water.*

Ecology updated the BW value used in the equations, based on new science and local data, from 70 kg to 80 kg.

Background: The BW approach included in the 1992 NTR, EPA's 2000 guidance, and EPA's published recommended national Clean Water Act 304(a) criteria values is to use an average adult BW in the HHC calculation. The BW historically used in EPA guidance and regulation is 70 kilograms (154 pounds). EPA's revised NRWQC from 2015 use a BW of 80 kg. (176 pounds). EPA's most recent Exposure Factors Handbook (EPA, 2011) provides an updated average BW of 80 kilograms, which also closely aligns with the tribal average adult BWs of the Tulalip and Suquamish tribes (EPA, 2007) of 81.8 and 79 kilograms, respectively. This newer science and local data compelled Ecology to use the updated BW value in the HHC equations. Table 5 provides HHC-relevant information on use of the body weight exposure factor.

Table 5: Summary of guidance and studies on body weight

Date	Source	BW input
1992	National Toxics Rule (40CFR131.36)	70 kg = average adult body weight
2000	EPA 2000 HHC Methodology (EPA -822-B-00-004)	EPA recommends using 70 kg = average adult body weight as "a representative average value for both male and female adults:" "EPA recommends maintaining the default body weight of 70 kg for calculating AWQC as a representative average value for both male and female adults."
2007	Tribal FCR studies – as summarized in: US EPA Reg. 10, Framework for Selecting and Using Tribal Fish and Shellfish Consumption Rates for Risk-Based Decision Making at CERCLA and RCRA Cleanup Sites in Puget Sound and the Strait of Georgia, Working Document, To Be Applied in Consultation with Tribal Governments on a Site-specific Basis, Revision 00.2007 (EPA, 2007, Tables B-1 and B-2 in Appendix B).	Tulalip Tribe = 81.8 kg average adult Suquamish Tribe = 79 kg average adult
2011	EPA Exposure Factors Handbook - 2011 edition. EPA 600/R-090/052F. (EPA, 2011)	EPA recommends 80 kg for average adult body weight
2015	EPA revised NRWQC for human health	EPA revisions used 80 kg. average adult body weight

Decision for new rule: Based on this information Ecology updated the body weight value used in the equations for the new HHC, based on new science and local data, from 70 kg to 80 kg.

5. Drinking Water Intake (DI)

*Application: This explicit variable **applies only to equations for fresh waters**: carcinogen/fresh water and noncarcinogen/fresh water.*

Ecology used the new EPA-recommended drinking water intake (as per revised 2015 EPA NRWQC) value of 2.4 L/day to calculate criteria in the new rule.

Background: The drinking water intake approach included in the 1992 NTR, EPA's 2000 guidance, and EPA's published recommended Clean Water Act 304(a) national criteria values is to use an approximate 90th percentile adult exposure value in the HHC calculation. The drinking water intake historically used in EPA guidance and regulation is 2 liters/day.

An excerpt from the EPA 2000 guidance that recommends using 2 liters/day states:

> *"EPA recommends maintaining the default drinking water intake rate of 2 L/day to protect most consumers from contaminants in drinking water. EPA believes that the 2 L/day assumption is representative of a majority of the population over the course of a lifetime. EPA also notes that there is comparatively little variability in water intake within the population compared with fish intake (i.e., drinking water intake varies, by and large, by about a three-fold range, whereas fish intake can vary by 100-fold). EPA believes that the 2 L/day assumption continues to represent an appropriate risk management decision…" (EPA, 2000,* (pages 4-22 to 4-23)

EPA's most recent Exposure Factors Handbook (EPA, 2011, Tables 3-10, 3-26, and 3-27) provides examples of updated 90th percentile adult (ages 18-65) drinking water intake values between 2.1 and 3.1 liters/day, based on national data. These values are for direct and indirect (water added in the preparation of a food or beverage) consumption of water, and are further explained in the previous tables. EPA released new *Supplemental Guidance for Superfund* on February 6, 2014 (memo from Dana Stalcup, USEPA to Superfund National Policy Managers, Regions 1-10; OSWER Directive 9200.1-120) that incorporates and adopts updates to *Risk Assessment Guidance for Superfund(RAGS): Human Health Evaluation Manual, Part A through E,* based on data in the 2011 Exposure Factors Handbook. This includes a recommended 90th percentile adult drinking water intake value of 2.5 L/day. EPA's revised 2015 NRWQC for human health use a 90th percentile drinking water intake of 2.4 L/day.

Table 6 is information on the drinking water exposure factor:

Table 6: Drinking water exposure factor

Date	Source	Drinking Water Intake (DI) input
1992	National Toxics Rule, 40CFR131.36 (EPA 1992)	2 L/day = approximate 90th percentile
2000	EPA 2000 HHC Methodology, EPA -822-B-00-004 (EPA, 2000)	EPA recommends using 2 L/day: "EPA recommends maintaining the default drinking water intake rate of 2 L/day to protect most consumers from contaminants in drinking water. EPA believes that the 2 L/day assumption is representative of a majority of the population over the course of a lifetime. EPA also notes that there is comparatively little variability in water intake within the population compared with fish intake (i.e., drinking water intake varies, by and large, by about a three-fold range, whereas fish intake can vary by 100-fold). EPA believes that the 2 L/day assumption continues to represent an appropriate risk management decision…" (pages 4-22 to 4-23)
2011	EPA Exposure Factors Handbook - 2011 edition. EPA 600/R-090/052F (EPA 2011)	The Exposure Factors Handbook contains new information on drinking water intake for various ages, groups, consumer types, and water sources. It provides updated 90th percentile adult drinking water intake values, based on national data, See Chapter 3.
2014	EPA 2014; OSWER Directive 9200.1-120.	Previous default value was 2 L/day. Currently recommended value is 2.5 L/day, which is the 90th percentile of consumer-only ingestion of drinking water (≥ 21 years of age)
2015	EPA, 2015: FR V80, Number 124 (Monday, June 29, 2015)Pages 36986-36989	Previous default value (EPA 2000) was 2 L/day. The updated drinking water intake is 2.4 L/day for consumer-only water ingestion at the 90th percentile for adults (≥21 years of age)

Decision for new rule: Ecology used the EPA 2015 recommended drinking water intake value of 2.4 liters/day to calculate criteria for the proposed rule.

6. Reference Dose (RfD)

Application: This explicit variable ***applies only to noncarcinogens****: noncarcinogen/fresh water; and noncarcinogen/marine water.*

Background: The reference dose is an estimate of the daily exposure to the human population (including sensitive subgroups) via ingestion to a chemical that is likely to be without appreciable risk of deleterious health effects during a lifetime. The reference dose applies only to non-carcinogens. EPA has developed chronic reference doses for use in regulatory programs. These can be found in EPA's Integrated Risk Information System (IRIS) and in EPA's NRWQC documents (EPA, 2015).

Decision for new rule: Ecology used reference doses found in either EPA's IRIS or NRWQC documents to calculate the criteria for non-carcinogens for the new rule.

7. Cancer Slope Factor (CSF)

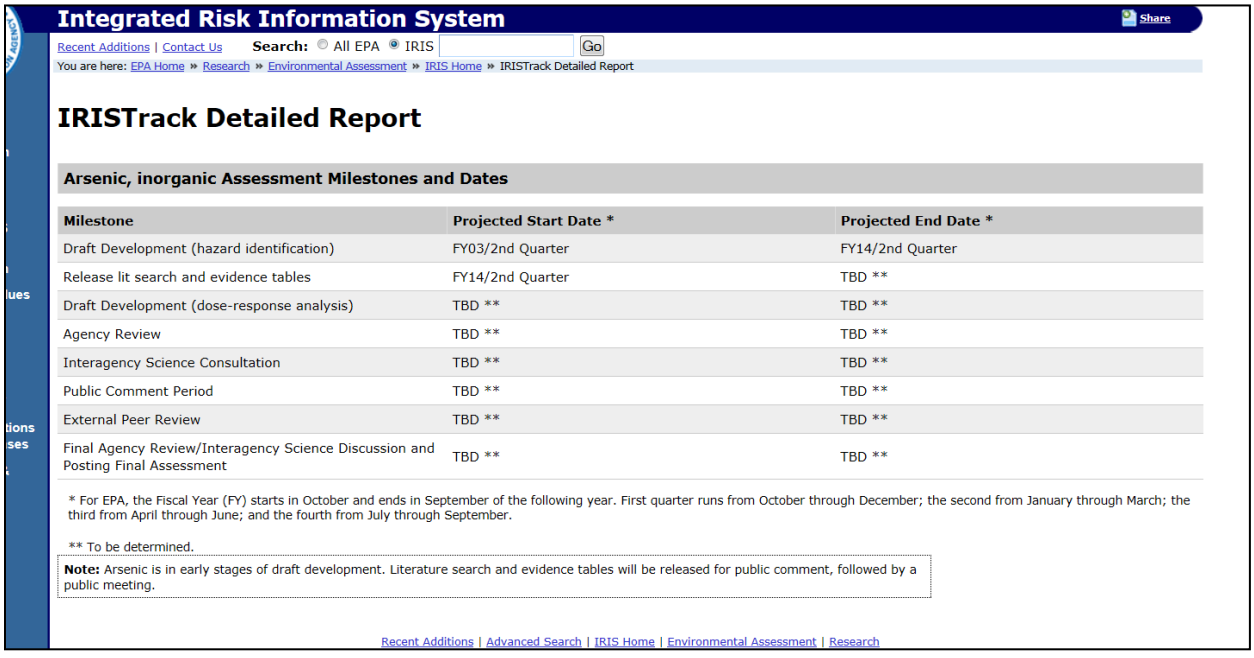
*Application: This explicit variable **applies only to carcinogens**: carcinogen/fresh water and carcinogen/marine water.*

Ecology used EPA 2015 cancer slope factors (most from IRIS) for carcinogens to calculate the criteria in the proposed rule.

Background: The ***cancer slope factor (CSF)*** provides a measure of the toxicity of an identified carcinogen. This slope factor is used for chemicals where the carcinogenic risk is assumed to decrease linearly as the chemical dose decreases. The CSF is specific to each chemical and can be found in the EPA IRIS (EPA, 2014) and in EPA 2015 individual criteria documents.

Ecology used, with few exceptions, the EPA 2015 CSFs for carcinogens to calculate the criteria in the new rule. Ecology made the decision not to use the CSFs in HHC calculations for inorganic arsenic and 2,3,7,8-TCDD based on recent scientific information and uncertainty surrounding assessment of carcinogenicity. Rationale for each of these chemicals varies. The explanation follows:

At any given time, there will be some IRIS toxicity factors undergoing review. In these cases, EPA has a specific process that is followed to review and develop revised factors. At present, several toxicity factors are under review, two of which have been under review for many years: the carcinogenicity reviews of inorganic arsenic and 2,3,7,8-TCDD. Information of the status of the reviews (copied from the EPA IRIS website March 2014) is in Figures 3 and 4. The uncertainty around agreed-upon cancer slope factors for these chemicals is considerable, as evidenced by the long history of the review processes as well as the lack of a prospective date for completion.



Integrated Risk Information System

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IRISTrack Detailed Report

Arsenic, inorganic Assessment Milestones and Dates

Milestone	Projected Start Date *	Projected End Date *
Draft Development (hazard identification)	FY03/2nd Quarter	FY14/2nd Quarter
Release lit search and evidence tables	FY14/2nd Quarter	TBD **
Draft Development (dose-response analysis)	TBD **	TBD **
Agency Review	TBD **	TBD **
Interagency Science Consultation	TBD **	TBD **
Public Comment Period	TBD **	TBD **
External Peer Review	TBD **	TBD **
Final Agency Review/Interagency Science Discussion and Posting Final Assessment	TBD **	TBD **

* For EPA, the Fiscal Year (FY) starts in October and ends in September of the following year. First quarter runs from October through December; the second from January through March; the third from April through June; and the fourth from July through September.

** To be determined.

Note: Arsenic is in early stages of draft development. Literature search and evidence tables will be released for public comment, followed by a public meeting.

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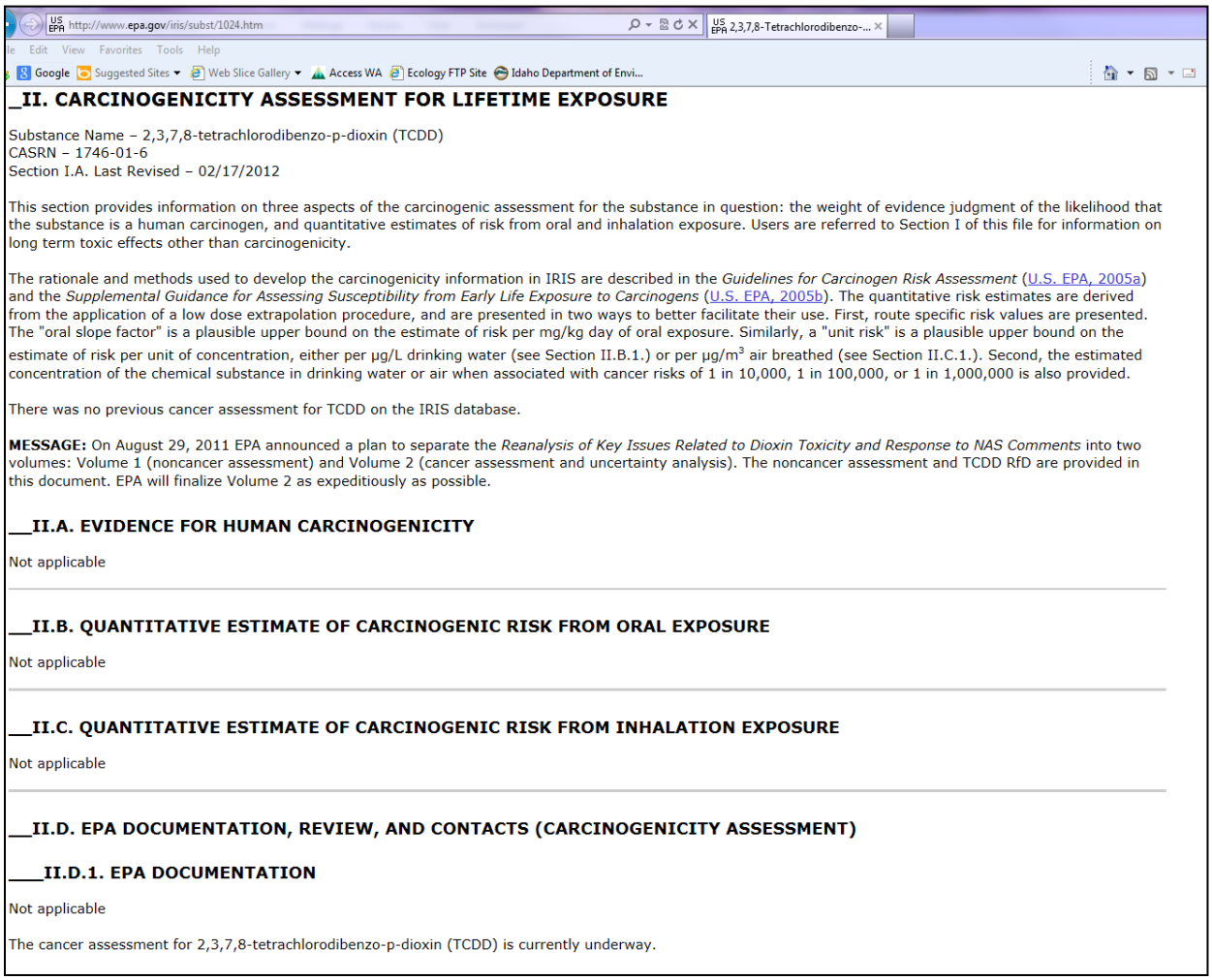
Figure 3: Integrated Risk Information System report for arsenic

Without a reliable toxicity factor for cancer, Ecology cannot calculate arsenic criteria based on cancer. EPA agrees that new cancer-based criteria for arsenic cannot be calculated at this time. In a May 6, 2016 filing with the United States District Court for the Western District of Washington, EPA stated that it will withdraw its proposed arsenic criteria for Washington because "extensive additional scientific analysis is necessary before revised criteria" for arsenic can be promulgated. *Puget Soundkeeper Alliance et. al. V. U.S.E.P.A.*, Case No. 2:16-cv-00293-JLR, EPA's Motion for Summary Judgment (May 6, 2016) at 13. As EPA explained in the Declaration of Elizabeth Southerland, Director of the Office of Science and Technology with EPA's Office of Water, "EPA did not update its CWA section 304(a) recommended criteria" for arsenic in 2015, and "EPA recognizes that there is substantial uncertainty surrounding the toxicological assessment of arsenic with respect to human health effects." Declaration of Elizabeth Southerland (May 5, 2016).



_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name – 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)
CASRN – 1746-01-6
Section I.A. Last Revised – 02/17/2012

This section provides information on three aspects of the carcinogenic assessment for the substance in question: the weight of evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral and inhalation exposure. Users are referred to Section I of this file for information on long term toxic effects other than carcinogenicity.

The rationale and methods used to develop the carcinogenicity information in IRIS are described in the *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a) and the *Supplemental Guidance for Assessing Susceptibility from Early Life Exposure to Carcinogens* (U.S. EPA, 2005b). The quantitative risk estimates are derived from the application of a low dose extrapolation procedure, and are presented in two ways to better facilitate their use. First, route specific risk values are presented. The "oral slope factor" is a plausible upper bound on the estimate of risk per mg/kg day of oral exposure. Similarly, a "unit risk" is a plausible upper bound on the estimate of risk per unit of concentration, either per µg/L drinking water (see Section II.B.1.) or per µg/m^3 air breathed (see Section II.C.1.). Second, the estimated concentration of the chemical substance in drinking water or air when associated with cancer risks of 1 in 10,000, 1 in 100,000, or 1 in 1,000,000 is also provided.

There was no previous cancer assessment for TCDD on the IRIS database.

MESSAGE: On August 29, 2011 EPA announced a plan to separate the *Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments* into two volumes: Volume 1 (noncancer assessment) and Volume 2 (cancer assessment and uncertainty analysis). The noncancer assessment and TCDD RfD are provided in this document. EPA will finalize Volume 2 as expeditiously as possible.

__II.A. EVIDENCE FOR HUMAN CARCINOGENICITY

Not applicable

__II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSURE

Not applicable

__II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION EXPOSURE

Not applicable

__II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS (CARCINOGENICITY ASSESSMENT)

___II.D.1. EPA DOCUMENTATION

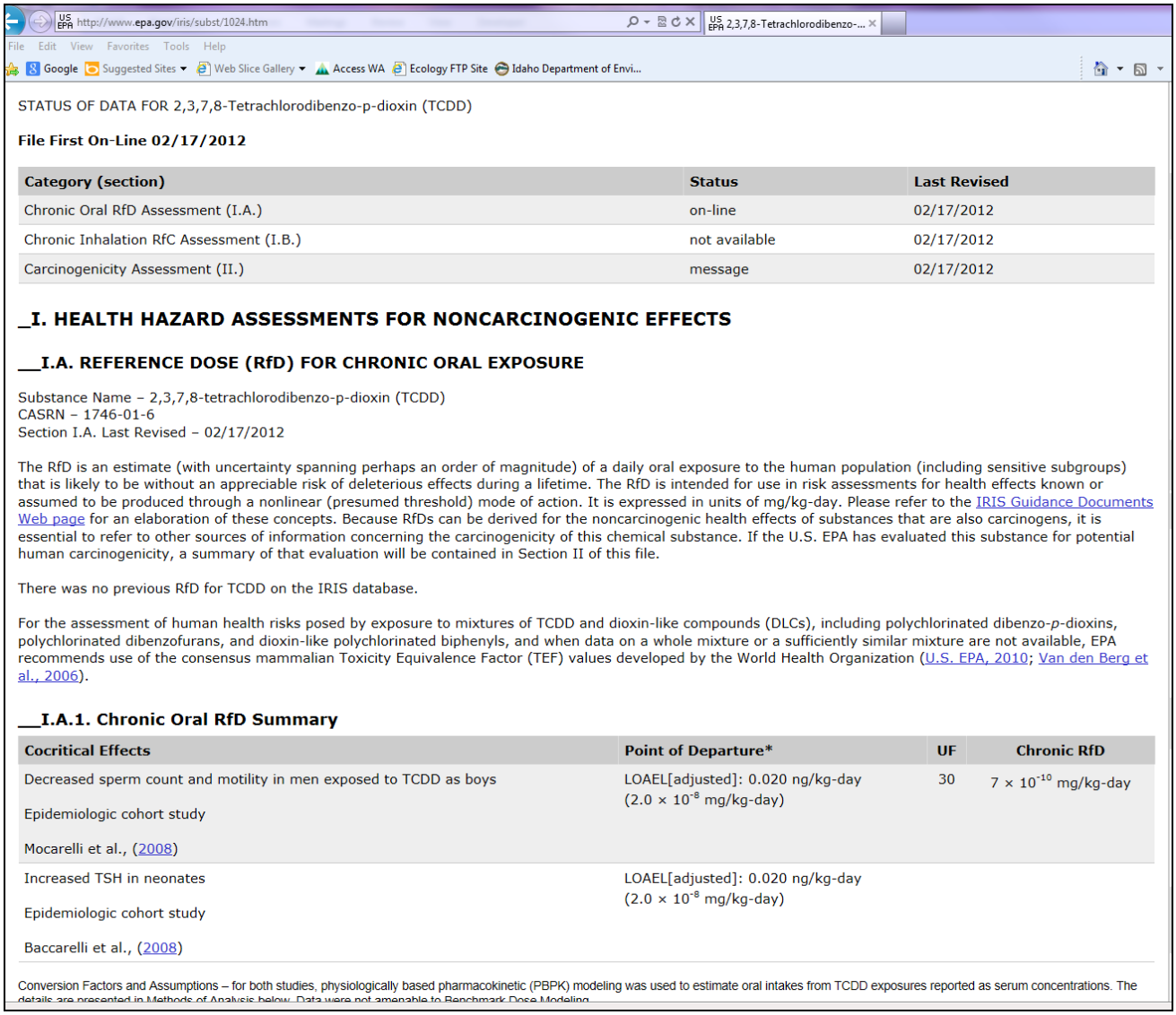
Not applicable

The cancer assessment for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is currently underway.

Figure 4: Carcinogenicity assessment for 2,3,7,8-TCDD

Without a reliable toxicity factor for cancer, Ecology cannot calculate dioxin criteria based on cancer. EPA agrees that new cancer-based criteria for dioxin cannot be calculated at this time. In a May 6, 2016 filing with the United States District Court for the Western District of Washington, EPA stated that it will withdraw its propose dioxin criteria for Washington because "extensive additional scientific analysis is necessary before revised criteria" for dioxin can be promulgated. *Puget Soundkeeper Alliance et. al. V. U.S.E.P.A.*, Case No. 2:16-cv-00293-JLR, EPA's Motion for Summary Judgment (May 6, 2016) at 13. As EPA explained in the Declaration of Elizabeth Southerland, Director of the Office of Science and Technology with EPA's Office of Water, "EPA did not update its CWA section 304(a) recommended criteria" for dioxin in 2015, and "IRIS does not currently contain a quantitative carcinogenicity assessment" for dioxin. Declaration of Elizabeth Southerland (May 5, 2016). These statements indicate that the existing science does not allow either Ecology or EPA to adopt new cancer-based dioxin criteria for Washington.

Based on these uncertainties, Ecology decided not to use CSFs in HHC calculations for these two chemicals. The approach taken for arsenic is described in the section on Challenging chemicals: Arsenic. The approach taken for 2,3,7,8-TCDD is to use the most recent IRIS non-cancer reference dose for HHC calculation. This reference dose was finalized in 2012. The IRIS information (copied from the IRIS website March 2014) follows:



STATUS OF DATA FOR 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)

File First On-Line 02/17/2012

Category (section)	Status	Last Revised
Chronic Oral RfD Assessment (I.A.)	on-line	02/17/2012
Chronic Inhalation RfC Assessment (I.B.)	not available	02/17/2012
Carcinogenicity Assessment (II.)	message	02/17/2012

_I. HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

__I.A. REFERENCE DOSE (RfD) FOR CHRONIC ORAL EXPOSURE

Substance Name – 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)
CASRN – 1746-01-6
Section I.A. Last Revised – 02/17/2012

The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfD is intended for use in risk assessments for health effects known or assumed to be produced through a nonlinear (presumed threshold) mode of action. It is expressed in units of mg/kg-day. Please refer to the IRIS Guidance Documents Web page for an elaboration of these concepts. Because RfDs can be derived for the noncarcinogenic health effects of substances that are also carcinogens, it is essential to refer to other sources of information concerning the carcinogenicity of this chemical substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

There was no previous RfD for TCDD on the IRIS database.

For the assessment of human health risks posed by exposure to mixtures of TCDD and dioxin-like compounds (DLCs), including polychlorinated dibenzo-*p*-dioxins, polychlorinated dibenzofurans, and dioxin-like polychlorinated biphenyls, and when data on a whole mixture or a sufficiently similar mixture are not available, EPA recommends use of the consensus mammalian Toxicity Equivalence Factor (TEF) values developed by the World Health Organization (U.S. EPA, 2010; Van den Berg et al., 2006).

__I.A.1. Chronic Oral RfD Summary

Cocritical Effects	Point of Departure*	UF	Chronic RfD
Decreased sperm count and motility in men exposed to TCDD as boys Epidemiologic cohort study Mocarelli et al., (2008)	LOAEL[adjusted]: 0.020 ng/kg-day (2.0×10^{-8} mg/kg-day)	30	7×10^{-10} mg/kg-day
Increased TSH in neonates Epidemiologic cohort study Baccarelli et al., (2008)	LOAEL[adjusted]: 0.020 ng/kg-day (2.0×10^{-8} mg/kg-day)		

Conversion Factors and Assumptions – for both studies, physiologically based pharmacokinetic (PBPK) modeling was used to estimate oral intakes from TCDD exposures reported as serum concentrations. The details are presented in Methods of Analysis below. Data were not amenable to Benchmark Dose Modeling

Figure 5: Health hazard assessments for noncarcinogenic effects for 2,3,7,8 TCDD

Decision for new rule: Ecology used, with few exceptions, the EPA NRWQC cancer slope factors for carcinogens to calculate the criteria in the proposed rule. Ecology decided, based on scientific information and/or uncertainty, not to use cancer slope factors (either in IRIS or outside of IRIS) in HHC calculations for arsenic and 2,3,7,8-TCDD.

8. Bioconcentration Factor (BCF)

*Application: This explicit variable **applies to all four equations**: carcinogen/fresh water; carcinogen/marine water; noncarcinogen/fresh water; and noncarcinogen/marine water.*

Ecology used a bioconcentration factor-based approach for criteria calculation.

Background: The HHC are expressed as chemical concentrations in water, but are based on information and assumptions about how those chemicals move from water into edible tissues of

aquatic organisms and then into consumers of those tissues. This section addresses the factor in the HHC equations that is used to describe how chemicals accumulate from water into aquatic organisms.

Predicting the accumulation of toxics into aquatic organisms from the surrounding water media is a complex task. Accumulation into aquatic organisms can be affected on a site-specific basis by many factors, some of which are discussed in the following paragraph. The HHC equations depend on a single variable to account for the accumulation step: either the bioconcentration factor (BCF) or the bioaccumulation factor (BAF). This variable in the equations is likely more affected by site-specific waterbody factors than any other variable used in the HHC calculations.

Osterberg and Pelletier, 2015. *Puget Sound Regional Toxics Model…; Page* 94, (for PCBs and PBDEs)
https://fortress.wa.gov/ecy/publications/documents/1503025.pdf
"In sum, the sensitivity tests showed that in relatively uncontaminated areas where contaminant concentrations in the sediments were low, predicted concentrations of contaminants in biota were more strongly influenced by changes to contaminant concentrations in the water column than by comparable changes in sediment concentrations. Although the majority of PCB and PBDE mass in the Sound is stored in the sediments, these results indicate the importance of contaminants in water as an exposure route and driver of bioaccumulation in many areas. Efforts to decrease contaminant concentrations in Puget Sound marine waters (e.g., by actions to reduce loads or prevent releases) may therefore be a critical component of strategies to achieve ecosystem health goals. Sensitivity analyses also indicated that the influence of sediments was greater in areas where sediment concentrations were elevated. These results underscore the importance of sediment cleanup activities for reducing contaminant uptake and bioaccumulation in the urban bays and at regional contaminant "hot spots."

Bioconcentration is the process of absorption of chemicals into an organism only through respiratory and dermal surfaces (Arnot and Gobas, 2006). For purposes of the HHC equations, bioconcentration refers to the accumulation of a chemical directly from the water by fish and shellfish. Using a bioconcentration factor (BCF) accounts for any pollution uptake fish or shellfish are exposed to in their surrounding water. Because BCFs look at a specific portion (water only) of the total uptake of a chemical, the BCFs are generally laboratory-derived or modeled values. Bioaccumulation is a broader term that refers to the accumulation of chemicals from all sources, including water, food, and sediment. Bioconcentration is a subset of bioaccumulation. Models to describe both bioconcentration and bioaccumulation have evolved over the past several decades (e.g., see Arnot and Gobas, 2004 and 2006, Gobas 2001, and Veith 1979) and have been used for many purposes, including risk assessment, chemical prioritization for toxics control strategies, and for HHC development.

The amount of accumulation tied directly to water or to sediments is unknown in most waterbodies, and pathways vary based on many factors, including waterbody-specific physical

characteristics, properties of the chemical of concern, and biota. For instance, Puget Sound-specific modelling (Osterberg and Pelletier, 2015; see text box) for open waters indicates that PCBs and PBDEs accumulation is more closely tied to water concentrations than to sediment concentration. In more contaminated embayments around Puget Sound the sediments are a larger driver for accumulation.

EPA Guidance and use of accumulation factors. EPA HHC guidance on how to describe and predict accumulation into aquatic organisms has changed throughout the years. For example, the 1980 guidance includes use of a BCF-based approach and the 2000 guidance modifies that earlier guidance to use a BAF-based approach. Both older and newer guidance recommend use of steady state accumulation factors.

EPA and states have generally defaulted to the use of EPA's older lipid-normalized BCFs when calculating criteria. These values were used in the 1992 NTR. The majority of BCFs used in the calculation of NRWQC (as listed in EPA 2002 and prior to the 2015 EPA 304(a) guideline updates) were carried over from 1980 criteria documents. BCFs reported in the 1980 criteria documents were generally determined by laboratory experiments, except when field data (e.g., "Practical BCFs (PBCFs)" for mercury (USEPA 1980); in effect, a field derived BAF) contradicted laboratory BCFs. If both laboratory and field data were lacking, the BCFs for lipid soluble compounds used to calculate the 1980 criteria were based on chemical specific octanol-water partition coefficients (K_{ow}'s; the K_{ow} is correlated with the potential for a chemical to bioconcentrate in organisms). In summary, the 1980 BCFs reflect a combination of laboratory measured BCFs, modeled BCFs, and field-measured BAFs. In this discussion all these values are generally referred to as BCFs or as a "BCF-based approach." The approaches for lipid soluble and for non-lipid soluble compounds (USEPA 1980) used to develop the early BCFs follow.

> "*For lipid-soluble compounds, when a measured BCF is available and corresponding lipid content is known* the equation below is used to estimate the weighted average BCF for an average diet.
>
> $$Weighted\ average\ BCF\ for\ average\ diet = Measured\ BCF\ x\ \frac{Weighted\ average\ percent\ lipids\ for\ average\ diet}{Species\ specific\ lipid\ content}$$
>
> *For lipid-soluble compounds, when measured BCF and corresponding lipid content is unknown* the equation below is used to estimate the BCF for aquatic organisms containing about 7.6 percent lipids (Veith 1979; USEPA 1980). This includes an adjustment for 3% lipids in the average diet versus 7.6% in order to derive the weighted average BCF.
>
> $$Log\ BCF = (0.85\ Log\ Kow) - 0.70$$
>
> *For non-lipid soluble compounds*, the available BCFs for the edible portion of consumed freshwater and estuarine fish and shellfish are weighted according to consumption factors to determine a weighted BCF representative of the average diet." (EPA 1980)

Subsequent to the EPA 1980 approach, EPA 2000 guidance recommends the use of a BAF in criteria calculation, and recommends that states and tribes use the methodology outlined in EPA 2000 to develop locally appropriate BAFs. Figure 6 shows the process as summarized by EPA (EPA 2000, page 5-13) in its Figure 5-1):

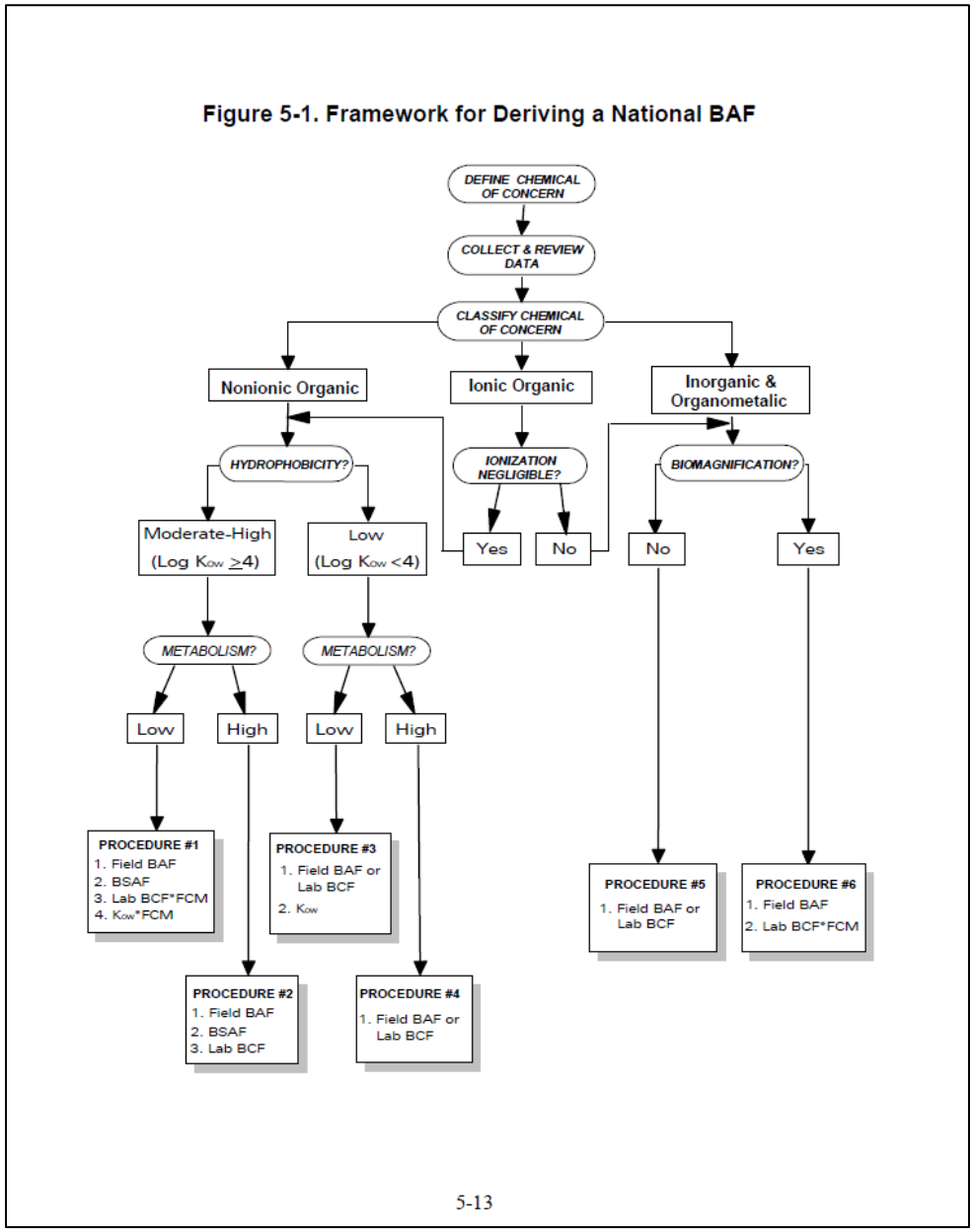


Figure 6: Framework for deriving BAF taken from EPA 2000, Figure 5-1

Subsequent to the 2000 guidance, EPA (2014, 2015) developed Clean Water Act 304(a) draft and final guidance criteria that were calculated using BAFs:

- In May 2014 EPA published 94 draft 304(a) nationally recommended HHC that included use of model-derived BAFs. These BAFs were developed using EPA's EPI Suite™ of models.
- In June 2015 EPA published final 304(a) criteria documents that used the BAF development approach described in EPA 2000 (see Figure 6), which includes use of lipid normalized BCFs in some cases.
- In September 2015, EPA published a new draft regulation for Washington and a revision to the NTR that included draft criteria that were calculated using chemical-specific trophic level 4 BAFs for the majority of the chemicals. The draft federal regulation also includes draft criteria that were developed using new BCFs and the older 1980 (NTR) BCFs (e.g., the draft criteria for metals other than mercury and copper; see following text box).

Washington Chemicals of Concern: PCBs, Arsenic, and Mercury

The accumulation factors used by EPA for some of the chemicals of greatest concern in Washington have not changed since the 1992 NTR, or, have been removed from the HHC equation entirely:

PCBs and arsenic: Older NTR BCFs are still used for the current 304(a) national recommended criteria and for the 2015 EPA proposed Washington regulation to calculate criteria for total PCBs, arsenic, and dioxin . Ecology used these BCFs for calculating the criteria for total PCBs and for dioxin in the draft rule . The criteria for arsenic are discussed later in this document.

Mercury: The methylmercury tissue residue criterion (part of the current 304(a) national recommended criteria and the 2015 EPA proposed regulation for Washington) does not include either a BAF or a BCF in the criterion equation, and instead accumulation is addressed as part of the implementation approaches that states will determine as they adopt and implement methylmercury criteria . Ecology did not adopt the methylmercury criterion in this rulemaking . This decision is discussed later in this document.

Lipid content affects the applicability of calculated BAFs and BCFs: A chemical's tendency to accumulate in lipids is driven by its hydrophobicity and lipophilicity. BAFs and BCFs for lipophilic chemicals are generally lipid normalized from a modeled or measured value to reflect the average percent lipids for aquatic organisms consumed by people.

Most of the BCFs historically used by EPA in NRWQC development, and by most states in HHC development, are lipid-normalized to an average lipid content of 3% for edible tissues and species (see equations earlier in this section) as consumed in national surveys (see Veith 1980; EPA 1980). The percent lipid of individual species consumed from Washington waters (Osterberg and Pelletier, 2015) are both lower and higher (e.g., spot prawn 1.5%; English sole

1.6%; Chinook salmon (immigrant) 5.4%) than the 3% average used by EPA. Attempting to calculate the average % lipid content of the amount of tissues of species consumed in Washington (as reflected by the proportion of different types of organisms consumed as described in the FCR surveys used to develop the proposed FCR of 175 g/day) would likely result in an estimated value with a large margin of uncertainty because the surveys do not all contain detailed information on the amounts of all specific species consumed. However, even if this information was readily available, it would not necessarily reflect the average lipid content of organisms grown in Washington waters because the proposed FCR includes all fish and shellfish including market, imported, restaurant, ocean-caught, etc.

EPA 2000 recommends that BAFs be used in criteria development to more accurately reflect the total uptake of a chemical into aquatic biota and thus more fully account for consumers' exposure to chemicals. EPA 2000 and EPA 2003 provide detailed information on the theory and methods supporting chemical-specific development of national BAFs, including calculation paths to address chemical-specific factors such as tendency to metabolize, Kow, applicability of biota sediment accumulation factor (BSAF) pathways, assumptions about chemical and physical parameters in ambient waters, food web structure, and many other factors. The EPA guidance is too extensive to present here (refer to EPA (2000, 2003) for more information). The national guidance was used by EPA to develop BAFs for the new EPA 2015 NRWQC, mainly for nonionic organic chemicals (these make up a large number of the new 2015 criteria). The EPA 2015 BAFs for these chemicals include trophic level-specific information on lipids, and incorporate this information in calculated baseline BAFs that can be applied across waterbodies. The baseline BAFs are adjusted to reflect the lipid content of commonly consumed aquatic biota. The default lipid fraction for commonly consumed fish and shellfish is derived from national survey information: 0.019 for trophic level 2 organisms, 0.026 for trophic level 3 organisms, and 0.030 for trophic level 4 organisms. Whether these default values are representative of an average lipid value(s) that would be appropriately representative of Washington is confounded by the same sources of uncertainty as discussed above for BCFs.

Dissolved organic carbon (DOC) and particulate organic carbon (POC) affect accumulation: Chemical sorption to POC and DOC in the water column can substantially reduce the fraction of the chemical in water that can actually be absorbed by aquatic organisms (Gobas 2001). Because of this BCFs and BAFs are frequently expressed in terms of the freely dissolved chemical concentration. EPA's 2000 guidance and the new BAFs in EPA's 2015 criteria documents are based on use of the freely dissolved concentration. The EPA 2000 methodology depends on median DOC (2.9 mg/L) and POC (0.5 mg/L) concentrations developed from a national dataset to develop national BAFs. DOC and POC concentrations can vary widely among waterbodies. DOC and POC data from Washington waters show a wide range of values (0.2 to 81.6 mg/L DOC and 0.028 to 1.78 mg/L POC; see Table 7) that differ among marine and estuarine waters, streams, and lakes and reservoirs

Table 7 shows dissolved organic carbon (DOC) and particulate organic carbon (POC) data from surface water sampling in Washington waters. Data is from Ecology's Environmental Management System (EIM) Database, accessed November 18, 2015.

Table 7: DOC and POC data from Washington surface water

Parameter	Statistic	Freshwater streams	Freshwater lakes and reservoirs	Marine and estuarine waters
DOC (mg/L)	min	0.2	0.5	0.611
	max	81.6	22.2	64.9
	median	2.1	2.6	1.805
	mean	3.230	2.514	3.718
	n	6871	1193	204
POC (mg/L)	min			0.028
	max			1.78
	median			0.0545
	mean			0.123
	n			32

EPA encourages states to use local DOC and POC information for water quality standards (EPA 2000):

> *"Although national default values of POC and DOC concentrations are used by EPA to set national 304(a) criteria as described by this document, EPA encourages States and authorized Tribes to use local or regional data on POC and DOC when adopting criteria into their water quality standards. EPA encourages States and Tribes to consider local or regional data on POC and DOC because local or regional conditions may result in differences in POC or DOC concentrations compared with the values used as national defaults."*

Because Washington waters have a wide range of DOC and POC concentrations, the national BAFs that were calculated using national default POCs and DOCs likely are not reflective of BAFs in many of Washington's waters. Site-specific DOC and POC can also affect BCFs, and, how or if these parameters are accounted for in BCF development also introduces uncertainty around the applicability of a single chemical-specific BCF across different waterbodies in Washington. The 1980 BCFs are based on total concentrations (not freely dissolved fractions), and do not incorporate DOC and /or POC into the equations).

There are many site-specific sources of variability in accumulation factors that affect their applicability to specific waterbodies: EPA (2009) describes sources of variability in BAFs:

> *"The bioaccumulation methodology used in the 2000 Human Health Methodology encourages developing site-specific BAFs because EPA recognizes that BAFs vary not*

only between chemicals and trophic levels, but also among different ecosystems and waterbodies; that is, among sites. The bioaccumulation potential of a chemical can be affected by various site-specific physical, biological, and chemical factors:

- *water temperature and dissolved oxygen concentration;*
- *sediment-water disequilibria;*
- *organism health, physiology and growth rate;*
- *food chain structure;*
- *food quality; and*
- *organic carbon composition.*

National average BAF value for a given chemical and trophic level may not provide the most accurate estimate of bioaccumulation for certain waterbodies in the United States. At a given location, the BAF for a chemical may be higher or lower than the national BAF, depending on the nature and extent of site-specific influences."

These site-specific sources of variability could also apply to many measured and calculated BCFs.

Historic and current use of BCFs and BAFs in HHC development: Both BCFs and BAFs have been, and currently are, used in criteria development. Recent actions where both have been applied include:

- EPA used BCFs and trophic level weighted BAFs (based on EPA 2000 methodology) in its June 2015 final revisions to the Clean Water Act 304(a) national recommended criteria (EPA 2015).
- EPA used BCFs and trophic level 4 BAFs in its proposed September 2015 revision to the NTR for Washington (EPA 2015).
- Oregon used EPA's BCFs in its 2011 adoption of HHC that were subsequently approved by EPA.
- Several states surrounding the Great Lakes have used BAFs in EPA-approved criteria development.
- EPA used the older EPA BCF values in 2000 to promulgate Clean Water Act HHC for states in federal regulation (40CFR131.38; FR Vol. 65, No. 97, May 18, 2000, pages 31710-31719).

Different approaches to BAF development have been used for Clean Water Act criteria: EPA has used different approaches to develop BAFs, and depends on a mix of BAFs and BCFs for current (2015) criteria calculations:

- EPA's final Great Lake's Guidance (Final Water Quality Guidance for the Great Lakes System, Federal Register: March 23, 1995 (Volume 60, Number 56, Page 15365-15425) requires use of BAFs, and presents a hierarchy of methods to develop BAFs based on chemical-specific factors.

- In May 2014 EPA published 94 draft Clean Water Act 304(a) nationally recommended HHC that included use of model-derived BAFs. These BAFs were developed using the BCF BAF module of EPA's EPI Suite™ of models. This module was developed using species from the Great Lakes (USEPA 2014).
- EPA used BCFs and trophic level weighted BAFs (based on EPA 2000 methodology) in its June 2015 final revisions to the Clean Water Act 304(a) national recommended criteria (EPA 2015).
- EPA used BCFs and trophic level 4 BAFs in its proposed September 2015 revision to the NTR for Washington (EPA 2015).

Process used to develop new 304(a) guidance documents and concerns about BAF development: 40CFR131.11 recommends that states consider EPA's Clean Water Act 304(a) guidelines when adopting criteria. As part of that consideration states evaluate the basis of and the process used to develop the criteria guideline documents. States need confidence in the EPA guidelines in order to use them as the basis of state regulations, and depend on the criteria guideline documents to provide a clear and adequately extensive content that supports both review and replication of the EPA results and recommendations. In the case of the new BAFs and BCFs in the 2015 304(a) guideline documents, although many can be replicated with the provided information and using EPA's guidance, we have been unable to evaluate and replicate all of the new BAF/BCF values (e.g., anthracene).

EPA published guidance on development of BAFs in 2000, 2003, and 2009. In EPA's 2014 proposed guideline documents EPA used the EPI Suite™ of models to calculate BAFs. In Ecology's comments on EPA's draft 2014 NRWQC Ecology asked for more details about EPA's use of EPI Suite™ to calculate bioaccumulation factors (BAFs), and expressed reservations about the use of BAFs in criteria development. As a result of public comment EPA changed its BAF approach for the final recommended criteria development documents and based its new BAFs on its 2000 HHC methodology. This change of direction was briefly addressed in EPA's response to comments, but after reviewing the finalized 304(a) guidance documents, the approach used to develop the new 2015 BAFs resulted in as much uncertainty as Ecology had over the initial use of the EPI Suite™ models.

Each of EPA's finalized chemical-specific 304(a) guidance documents contains a specific section on BAF development that uses identical language to describe the 2000 guidance. However, out of approximately 2 pages devoted to BAF development in each chemical-specific document, only approximately 3-5 unique sentences are actually present in each document to address chemical-specific information. In some cases EPA cites multiple sources for inputs to its BAF development, but the sources contain values that do not appear to clearly lead to replication of all of EPA's results. Steps to adjust or combine inputs are not clearly explained to users of the documents. Replicating the steps and the inputs EPA took to develop many of the BAFs/BCFs is not possible with the information provided in the individual criteria documents.

On January 14, 2016, EPA posted at its HHC web site:

(http://www.epa.gov/wqc/national-recommended-water-quality-criteria-human-health-criteria-table) supplemental information to support the calculation of the new BAFs and BCFs used in EPA's new 2015 304(a) criteria guidance documents:

- *National Bioaccumulation Factors – Supplemental Information Document (January 2016)*
- *National Bioaccumulation Factors – Supplemental Information Table (excel) (1 pg., 523 K) (MS Excel Spreadsheet) (January 2016).*

EPA's release of this information, as Ecology was preparing the final proposed rule including determination of costs and benefits in accordance with the state's Administrative Procedures Act, did not allow Ecology time to be able to review the new information prior to development of the proposed rule and supporting documentation. Ecology considered this new information on BAFs provided by EPA as it developed the final rule, including consideration of any comments received on the use of BCFs versus BAFs.

Additional circumstances that add to concern about use of the new 2015 BAFs are:

- In EPA's *Water Quality Criterion for the Protection of Human Health: Methylmercury* (USEPA 2001) substantial coverage is given to the development of BAFs and the rationale for *not* developing national trophic level-specific BAFs for this chemical. In the methylmercury implementation document (EPA 2009), detailed information on alternatives for different BAF development pathways is provided. These documents underwent extensive peer and public review, and because only one chemical was being addressed, a detailed focus on the information and approaches to BAF development was part of the process. EPA's recent 2015 304(a) guidance documents include new chemical-specific BAFs for 73 pollutants and new BCFs for 19 pollutants (the new criteria for cyanide uses the older 1980 BCF, as per 68 FR No. 250, Wednesday, December 31, 2003, 75507-75515), and, as mentioned previously, included virtually no chemical specific information on the inputs used in BAF/BCF derivation. The disparity in the process used to develop new BAFs/BCFs for these pollutants, when compared with the transparency and thoughtful approach used in the methylmercury BAF development, caused concerns about using the new BAFs without additional data and information.
- EPA recently (EPA, 2015) published a new draft 304(a) aquatic life criteria document for cadmium. This document includes 2 pages of discussion on cadmium-specific BAF/BCF information, and 11 pages of tables with cadmium-specific BAF/BCF data. The document does not cite EPA 2000 as a method development approach for BAFs for aquatic life criteria, yet we would expect EPA to depend on its guidance in evaluation of cadmium accumulation for different trophic levels. The draft cadmium document does not directly use a BAF or BCF estimate to calculate the draft criteria, yet the BAF/BCF write-up provides substantial clarity and information. This more informative approach was used in the older chemical-specific criteria guidance documents but appears to have been dropped in the new 2015 HHC 304(a) guidance documents. This brevity of information is likely to affect states for many years to come as they attempt to evaluate

the EPA 304(a) guideline documents, which states will be inclined to do because the 40CFR131.11 recommends it.

- The development of the 2015 304(a) guideline documents appears rushed (drafts proposed in May 2014, finals published in June 2015), and EPA did not take the time for a thoughtful external review of individual BAFs, as was done for the methylmercury criteria document.
- Upon release by EPA of the new 2015 NRWQC, states were not provided with sufficient background information on the new BAFs, so Ecology was not in a position to understand if the 2015 BAF recommendations were appropriate to move forward with under Washington State's Administrative Procedures Act rule process as it was developing the proposed new HHC rule.
- Since the proposed rule was published additional information has come to Ecology's attention that reinforces Ecology's concern with the new 2015 304(a) criteria documents and the equation inputs used in those documents. In particular, EPA published and posted a criteria document for the new, and non-priority pollutant, bis(2-chlkoro-1-methylethyl)ether, as a priority pollutant. EPA then proposed criteria for this chemical in draft regulations for Washington and Maine, asserting in the federal publications that the new criteria were for priority pollutants only. This situation reinforces the skepticism that Ecology has regarding the thoroughness of the process used to develop the new 2015 EPA criteria, and reinforces the concern over the single public review of the new 2015 criteria documents, particularly with regard to the bioaccumulation and bioconcentration factors used in calculating those criteria.
- Concern with the new HHC was expressed to EPA in Ecology's public comment on EPA's draft 304(a) criteria (8/6/2014 letter from Melissa Gildersleeve, Ecology, to EPA Water Docket), on EPA's draft regulation for Washington (12/21/15 letter from Maia Bellon, Ecology, to Gina McCarthy, EPA) and in this Decision Document. A significant part of the rationale has to do with the inapplicability of the new BAFs to Washington and the inadequacy of the public process EPA used in developing them. Ecology continues to assert that the BAFs used in the EPA's final 304(a) criteria should have been considered second draft BAFs because they differed so significantly from the first draft that was commented on by the public, and should have been published in the federal register for a second round of public review before finalization. Ecology continues to be concerned with EPA's apparent urgency in finalizing the 304(a) criteria without a second public review to be able to consider the modified BAF approach, which Ecology believes would have been a better approach and resulted in a more durable product. Ecology's comment letter to EPA on their draft proposed regulation and this Decision Document explains why the BAFs used in that proposal are inappropriate for Washington at this time.

- Florida, which recently released a draft HHC rule, also declined to use the EPA national BAFs and, in order to use BAFs appropriately, found it necessary to develop Florida-specific BAFs. That type of intensive effort in Washington would have necessitated another draft rule to be developed and published, which would have significantly delayed adoption of HHC in Washington.

Protectiveness of the calculated criteria and use of BAFs or BCFs: The criteria equations balance many different factors, such as "more protective" (e.g., uncertainty factors up to the thousands for reference doses, linear-multistage-based CSFs, in Washington's proposal a FCR that includes all fish and shellfish from all sources) and "less-protective" (e.g., not accounting for additive or synergistic effects of chemicals), that are used to develop criteria protective of people who consume fish and shellfish. No one input to the equations alone defines the degree of protection provided by the numeric criterion values (see previous discussion on Risk Level above). Choice of the newer BAF-based approach over the older BCF-based approach does not guarantee higher or lower criteria concentrations. In some cases the newer EPA BAFs are lower than the older EPA BCFs (e.g., acrolein has a BCF of 215 and a newer BAF of 1.0) and in some cases higher (e.g., dieldrin has a BCF = 4,670 and newer trophic level BAFs of TL2 = 14,000, TL3 = 210,000, TL4 = 410,000BAF). In general, for those chemicals that have new BAFs, the new BAFs are higher values than the BCFs for more hydrophobic lipophilic compounds. However, the accumulation factors for some of the chemicals of greatest concern in Washington have not changed. For example, older BCFs for total PCBs, arsenic, and dioxin are still the basis of EPA's national recommended criteria (EPA 2015) and of the proposed criteria in EPA's draft regulation for Washington (EPA 2015). As mentioned previously, the methylmercury tissue residue criterion does not include either a BAF or a BCF, and instead accumulation is addressed as part of the implementation approaches that states will determine as they adopt and implement methylmercury criteria.

Choosing a BCF or a BAF for criteria development: Both BCFs and BAFs as currently developed have uncertainty in their applicability and development. However, only two practical alternatives exist to reflect accumulation of toxics by aquatic organisms:

1. 1980 BCF-based approach (as used in the NTR – note that these BCFs are a combination of measured and modeled BCFs and some BAFs, plus two additional newly calculated BCF values based on EPA 1980 guidance; and
2. 2015 BAF-based approach:
    - the trophic level weighted BAFs and BCFs (the majority are BAFs) used to calculate EPA's 2015 NRWQC, or,
    - the trophic level 4 BAFs and BCFs (the majority are BAFs) used in EPA's 2015 proposed new regulation (proposed 40CFR131.45).

Ecology is eliminating the second 2015 BAF approach described previously (trophic level 4 BAFs and BCFs used in EPA's 2015 proposed new regulation) because the use of trophic level 4 BAFs, based mainly on consideration of salmon and steelhead consumption, is not reflective of the consumption patterns shown in the FCR surveys that were used to develop the proposed

Washington FCR of 175 g/day: Washington-specific information on consumption indicates that different groups of people harvest both fish and shellfish, both recreationally and for subsistence (Ecology, 2013). The FCR of 175 g/day includes "all fish and shellfish," including all salmon, restaurant, locally caught, imported, and from other sources, thus includes trophic levels 2-4.

A BAF-only pathway is not readily available because EPA-developed BAFs for all HHC chemicals are not available for Ecology and the public to consider. Other approaches (e.g., developing Washington-specific development of BAFs or BCFs) would greatly increase the data and analysis needed to support the rulemaking and would cause further delays.

Decision for proposed rule: Ecology is making a risk management decision that this proposed rule use a BCF-based approach (as per EPA, 1980, and as used in the NTR) for criteria calculation for the following reasons:

- BCFs are more closely related to the specific environmental media (water) that is regulated under the Clean Water Act.
- The BCFs do not include as many inputs and predictions that are based on national water, sediment, and biota datasets, while the BAFs are dependent on these inputs. The national datasets supporting the BAFs are not necessarily reflective of Washington waters.
- The BCF-based approach includes far fewer input values. Because of this, the BCFs have far fewer sources of directly introduced uncertainty.
- BCFs are acceptable science for purposes of Clean Water Act criteria development. EPA currently uses a combination of BAFs and BCFs to calculate its NRWQC, and used a combination of BAFs and BCFs for its 2015 proposed new regulation for Washington. Therefore, both BAFs and BCFs could represent acceptable science choices for Clean Water Act purposes.

Based on Ecology's decision to use BCFs, new BCFs were calculated using EPA 1980 guidance. EPA (2015) published BAF-based criteria for two additional priority pollutants (1,1,1-trichloroethane and 3-methyl-4-chlorophenol). These pollutants do not have EPA-calculated BCFs available. Ecology-calculated BCFs for these pollutants using the EPA 1980 guidance to provide consistency among the suite of BCF values used in this rulemaking. Ecology queried the EPA EcoTox database for measured BCFs. Calculations follow:

1,1,1-Trichloroethane. A query of the EPA EcoTox database (accessed 10/16/15) resulted in a single measured BCF of 9 L/kg (BCF from: Barrows et al 1978). A measured lipid content for similar bluegills is 4.8% (Johnson 1980, as cited in EPA 1980). BCF calculations, as per EPA 1980 guidance, are shown below:

$$Weighted\ average\ BCF\ for\ average\ diet =$$

$$Measured\ BCF\ x\ \frac{Weighted\ average\ percent\ lipids\ for\ average\ diet}{Species\ specific\ lipid\ content}$$

$$BCF = 5.6\ L/kg$$

3-Methyl-4-chlorophenol. A query of EPA's EcoTox database (accessed 10/16/15) showed no results for measured BCFs for this pollutant. A BCF based on Kow (EPA 1980) was calculated. Log Kow = 3.1 (EPA 2015) was used in the calculation.

$$Log\ BCF = (0.85\ Log\ Kow) - 0.70$$
$$Log\ BCF = (0.85\ x\ 3.1) - 0.70$$
$$\log \quad BCF = 1.935$$
$$BCF = 1258$$

9. Lifespan and duration of exposure:

*Application: These implicit variables **apply in all four equations**: carcinogen/fresh water; carcinogen/marine water; noncarcinogen/fresh water; and noncarcinogen/marine water.*

Ecology proposes to specifically acknowledge the longer-term durations of exposure that are implicit in the criteria in the proposed rule.

Background: EPA 2000 guidance for HHC development assumes a lifetime exposure of 70 years, and a duration of daily exposures over 70 years. Use of the 70-year lifespan and a duration of daily exposures over 70 years is implicit in the HHC equations. These paired assumptions result in no overall numeric change in the equation's results. However, a change in either one of these could change the calculated results of the equation. A 10-year increase or decrease in lifespan would have little effect on the calculated criteria concentrations. Changing the duration of exposure to less than the total lifespan would increase criterion concentrations, but the magnitude of increase would depend on the ratio between lifespan and duration of exposure. For instance, use of a 30-year duration of exposure (as used in some clean-up risk assessments) with a 70-year life span would increase the criteria concentrations substantially. Because the goal of the criteria is to provide for protection of people throughout their lifetime with an assumption that people could obtain all their fish from Washington waters during that period, reducing the level of protection of the criteria concentrations by assuming a shorter duration of exposure was not considered for these criteria development.

EPA also describes the duration of exposure for the HHC in the Water Quality Standards Handbook, Second Edition (EPA, 2012) as follows:

> **"Magnitude and Duration**
>
> *Water quality criteria for human health contain only a single expression of allowable magnitude; a criterion concentration generally to protect against long-term (chronic) human health effects. Currently, national policy and prevailing opinion in the expert community establish that the duration for HHC for carcinogens should be derived assuming lifetime exposure, taken to be a 70-year time period. The duration of exposure assumed in deriving criteria for noncarcinogens is more complicated owing to a wide variety of endpoints: some developmental (and thus age-specific and perhaps gender-specific), some lifetime, and some, such as organoleptic effects, not duration-related at*

all. Thus, appropriate durations depend on the individual noncarcinogenic pollutants and the endpoints or adverse effects being considered."

Ecology is proposing to adopt HHC based on health effects, but not on organoleptic effects, thus non-duration-related exposures are not applicable to the criteria being considered in this rulemaking.

EPA's Superfund Program provides specific guidance (EPA, 1989; *Risk Assessment Guidance for Superfund, Part A, or RAGSA,* see Section 8), on interpreting the duration of exposure applicable to cancer and non-cancer effects:

Page 8-11, guidance on exposure durations for noncarcinogenic health effects:

"Three exposure durations that will need separate consideration for the possibility of adverse noncarcinogenic health effects are chronic, subchronic, and shorter-term exposures. As guidance for Superfund, chronic exposures for humans range in duration from seven years to a lifetime; such long-term exposures are almost always of concern for Superfund sites (e.g., inhabitants of nearby residences, year-round users of specified drinking water sources). Subchronic human exposures typically range in duration from two weeks to seven years and are often of concern at Superfund sites. For example, children might attend a junior high school near the site for no more than two or three years. Exposures less than two weeks in duration are occasionally of concern at Superfund sites. For example, if chemicals known to be developmental toxicants are present at a site, short-term exposures of only a day or two can be of concern."

RAGSA, Pages 8-4 to 8-5, guidance on exposure durations for carcinogenic and noncarcinogenic health effects:

"Averaging period for exposure. *If the toxicity value is based on average lifetime exposure (e.g., slope factors), then the exposure duration must also be expressed in those terms. For estimating cancer risks, always use average lifetime exposure; i.e., convert less-than-lifetime exposures to equivalent lifetime values (see EPA 1986a, Guidelines for Carcinogen Risk Assessment). On the other hand, for evaluating potential noncarcinogenic effects of less-than lifetime exposures, do not compare chronic RfDs to short-term exposure estimates, and do not convert short-term exposures to equivalent lifetime values to compare with the chronic RfDs. Instead, use subchronic or shorter-term toxicity values to evaluate short-term exposures. Check that the estimated exposure duration is sufficiently similar to the duration of the exposure in the study used to identify the toxicity value to be protective of human health (particularly for subchronic and shorter-term effects). A toxicologist should review the comparisons. In the absence of short-term toxicity values, the chronic RfD may be used as an initial screening value; i.e., if the ratio of the short-term exposure value to the chronic RfD is less than one, concern for potential adverse health effects is low. If this ratio exceeds unity, however, more appropriate short-term toxicity values are needed to confirm the existence of a significant*

health threat. ECAO may be consulted for assistance in finding short-term toxicity values."

The reference doses used to calculate the HHC are the chronic reference doses mentioned previously, as opposed to the subchronic or acute toxicity values also mentioned. Toxicity values for shorter duration exposure periods have been developed (e.g., the Agency for Toxics Substances and Disease Registry's Minimal Risk levels (MRLs) at http://www.atsdr.cdc.gov/mrls/index.asp).

Although the duration of exposure for the HHC can be up to 70 years, the EPA recommended criteria do not contain specific durations of exposure in either a chemical-specific or overall approach. The duration of exposure is an important characteristic needed to most effectively implement the criteria to reflect the variables and assumptions in the criteria. Because the EPA criteria and equations do not *explicitly* include a lifetime value or a duration of exposure factor, and because these factors are needed to effectively implement the criteria in a manner consistent with their implicit presence in the calculation, these implicit factors are acknowledged in the proposed rule language accompanying the numeric criteria values, and will be considered by Ecology in development of permit limits and water quality assessments. The proposed rule includes language that explicitly states that the criteria are calculated using durations of exposure that can be up to 70 years. Ecology will draft implementation guidance to address how this information could be used in permit limit development. This information is most likely to affect discharge limits for episodic discharges where the short term nature of some discharges may make calculation of limits that are based on the longer exposure durations that are in the HHC infeasible. In these cases discharge limits, if needed, could be based on best management practices, as per 40CFR122.44(k).

Decision for proposed rule: Ecology proposes to specifically acknowledge the longer-term durations of exposure that are implicit in the criteria calculation in the proposed rule.

10. Hazard quotient (HQ)

Application: This implicit variable ***applies only in the noncarcinogen equations****: noncarcinogen/fresh water; and noncarcinogen/marine water.*

Ecology applied this implicit variable in the HHC equations.

A hazard quotient equal to one represents a risk level where non-cancer effects should not be present at specified exposure assumptions. This value is implicit in the noncarcinogen HHC equations.

Decision for new rule: Ecology applied this EPA implicit variable in the HHC noncarcinogen equations.

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Challenging Chemicals: Polychlorinated Biphenyls (PCBs)

Decision

Ecology adopted HHC (HHC) for total polychlorinated biphenyls (PCBs) of 0.00017 µg/L for most freshwaters (drinking surface waters and ingesting fish and shellfish) and 0.00017 µg/L for marine and estuarine waters and a limited number of fresh waters (fish and shellfish ingestion only). For ease of reference, these different exposure routes are called fresh and marine for the remainder of this document. This decision on criteria concentrations is based on a chemical-specific state risk management decision and is in conformance with EPA historic and recent HHC development guidance.

A comparison of the NTR HHC with the new state criteria for PCBs is defined in the text below:

National Toxics Rule (NTR) HHC	2016New HHC
Freshwater: 0.00017 µg/L	Freshwater: 0.00017 µg/L
Marine: 0.00017 µg/L	Marine: 0.00017 µg/L

Background

Polychlorinated Biphenyls (PCBs) are a group of man-made chlorinated organic compounds. There are 209 individual PCB compounds, known as congeners. Aroclor is a commonly used trade name for specific PCB mixtures and is often referenced in PCB regulations.

PCBs in the environment are human-caused and there are no known natural sources. Used as coolants and lubricants in electrical equipment because of their insulating properties, manufacturing of PCBs was halted in the United States in 1979 (EPA, 2014) due to evidence that PCBs accumulate and persist in the environment and can cause harmful health effects. From 1929 to 1979 about 600,000 metric tons of PCBs were commercially manufactured in the US. The 1976 *Toxics Substances Control Act* (TSCA) prohibited manufacture, processing, and distribution of PCBs. Products made before 1979 that may contain PCBs include older fluorescent lighting fixtures and electrical devices.

Even though they are “banned,” PCBs are still allowed in many products manufactured and sold in the United States, including many pigments and caulking. The concentrations of PCBs in these products are regulated by the EPA under the Toxic Substances Control Act regulations.

PCBs are also regulated under additional state and federal laws, and they are not always consistent. For example, the level of PCBs that is allowed in products under TSCA is millions of times higher than what is allowed in water under the Clean Water Act. This leads to water permit holders being held responsible at the end of their pipe for PCBs that came from other products.

Back in the late 1970's the total amount seemed small and the amount allowed in each product seemed low, but now we know that it's high compared to levels that impact human health.

Health effects that have been associated with exposure to PCBs include acne-like skin conditions in adults, and neurobehavioral and immunological changes in children. PCBs have been shown to cause cancer in animals (EPA 2014). Studies of exposed workers have shown changes in blood and urine that may indicate liver damage. According to the Agency for Toxics Substances & Disease Registry (ATSDR, 2001), PCB exposures in the general population are not likely to result in skin and liver effects.

According to the ATSDR, exposure routes for PCBs include:

- Leaks from old fluorescent lighting fixtures and electrical devices and appliances, such as television sets and refrigerators, that were made 30 or more years ago and may be a source of skin exposure.
- Eating contaminated food. The main dietary sources of PCBs are fish (especially sport fish caught in contaminated lakes or rivers), meat, and dairy products.
- Breathing air near hazardous waste sites and drinking contaminated well water.
- Hazards in the workplace during repair and maintenance of PCB transformers, such as accidents, fires or spills involving transformers, fluorescent lights, and other old electrical devices; and disposal of PCB materials.

HHC for PCBs: The cancer-based HHC for PCBs that are currently effective in Washington for Clean Water Act purposes are found in the 1999 revisions to the 1992 NTR. The newly adopted criteria will be effective only after EPA reviews and approves them for Clean Water Act use. The 1992 NTR rule included HHC for individual Aroclors that were calculated using a cancer potency factor of 7.7 per mg/kg-day (EPA, 1992). EPA reassessed the cancer potency of PCBs in 1996 (EPA, 1996) and adopted an approach that distinguishes among PCB mixtures by using information on environmental mixtures and different exposure pathways. Based on this reassessment, EPA derived a new cancer potency factor of 2 per mg/kg-day. EPA revised the NTR human health criterion for PCBs in 1999 (EPA, 1999) to incorporate this new science. The newer NTR criterion is 0.00017 µg/L for the protection of human health from consumption of aquatic organisms and water, and the consumption of aquatic organisms only.

PCBs in Washington's surface waters: PCBs are difficult to detect in surface waters. The analytical method required by EPA for compliance purposes (EPA Method 608) does not detect PCBs at the low concentrations in water at which they occur. Because PCBs in waters are difficult to detect, methods that depend on concentration of PCBs in fish and shellfish tissue are frequently used to assess PCB levels across the state. Aquatic biota accumulate PCBs as part of their exposure to the food web, and the PCBs are often detected in fish and shellfish tissue. The use of fish and shellfish tissue monitoring data are used to support development of Washington Department of Health fish advisories (WDOH, 2014) and Clean Water Act Section 303(d) impaired waters lists (Ecology, 2012). Monitoring information demonstrates that PCBs are

widespread in the environment, but have in general been decreasing in concentrations since the 1979 "ban" on use of PCBs was put in place.

PCBs present regulatory challenges for Clean Water Act programs because:

- PCBs were widely used prior to the 1979 "ban".
- PCBs are widespread in the sediments and in biota.
- PCBs are long-lasting and bind readily to fats. Because of this they continue to cycle in the environment and in the food web. PCBs readily accumulate in organisms.
- PCBs are transported through the atmosphere.
- Because PCBs are transported along many pathways, and come from many sources associated with human habitation and use, they are found widely in environments that range from pristine to highly developed.
- Treatment plants are most often not designed to remove these chemicals. However, treatment plants that enhance solids removal will also remove PCBs.

These PCB characteristics make them particularly difficult to control, and efforts to address PCBs are multimedia, including contaminated site clean-up, regulation of PCBs in products, and reductions of PCBs from airborne sources. Disposal of PCBs requires specifically designed equipment. Ecology has developed a Chemical Action Plan for PCBs to address additional multi-media approaches to control PCBs entering the environment (Ecology, 2014).

Basis for Ecology's Decision

Ecology's new HHC for total PCBs are based on an approach that is consistent with EPA's 2000 Human Health Criteria Guidance (EPA, 2000) and that also provides a high level of protection for Washingtonians. Ecology used a state-specific risk level exclusively for PCBs. These calculated criteria concentrations are higher than the prior NTR values, and because PCBs are a chemical of concern in Washington, Ecology made a chemical-specific decision *not to increase the criteria concentrations* above the prior criteria levels, thus the proposed criteria values are the same as the NTR values of 0.00017 µg/L.

State-specific risk management decisions on chemical-specific risk levels are consistent with EPA HHC guidance as well as with precedent from other states. For example, EPA approved inorganic arsenic criteria adopted by the Oregon Department of Environmental Quality (ODEQ) based on $1x10^{-4}$ and $1x10^{-5}$ risk levels, even though risk levels for other chemicals were set to 10^{-6} (ODEQ, 2011). This criteria development approach combines the current cancer-based calculation with a state-specific risk level. All other variables in the HHC equations for PCBs would remain the same. The state-specific risk level is summarized in the following text:

Equation variable	Risk Value	Information
Additional lifetime cancer risk level	4.0×10^{-5} (0.00004) = 4 possible additional cancer occurrences in 100,000 people after 70 years of daily exposure	Choice of a state-specific risk level is a risk management decision made by individual states. EPA 2000 guidance (EPA, 2000) specifies that the maximum risk level for highly exposed populations should not exceed $1x10^{-4}$ (1 possible additional cancer occurrence in 10,000 people after 70 years of daily exposure.) The chemical-specific risk level for PCBs was chosen to be consistent with the level of risk/hazard in the toxicity factor used by the WDOH in developing fish advisories. This is an estimated cancer risk at the corresponding safe dose (RfD) for a chemical. This value was developed as follows: Equation: RfD (mg/kg-day) x cpf $(mg/kg\text{-}day)^{-1}$ = Risk Level Equation with PCB toxicity factors: 2.0×10^{-5} mg/kg-day x 2.0 $mg/kg\text{-}day^{-1} = 4.0 \times 10^{-5}$ This state-specific risk level is a *lower* level of risk (*is more protective*) than the maximum risk recommended in EPA guidance.

Since the bioconcentration factor for PCBs is very large, exposure through drinking water is negligible. The calculated criteria for exposure routes with and without drinking water are virtually the same, as are the calculated criteria values. The calculated total PCB criteria using this approach are 0.00029 µg/L. These calculated values are higher than the current NTR values, and because PCBs are a chemical of concern in Washington Ecology made a chemical-specific risk management decision not to increase the criteria concentrations, thus the proposed criteria values are the same as the NTR values of 0.00017 µg/L. This value is associated with a lower risk level ($2.3 \times 10^{-5)}$ than the calculated criteria. These values are shown below.

Additional lifetime Cancer Risk Level	Average Fish Consumption Rate (g/day)	Calculated HHC concentration (µg/L = parts per billion)
Calculated value:		
4×10^{-5} Four–in-one hundred thousand = 0.00004	175	0.00029
New criteria (= NTR Criteria)		
0.00017		
The risk level associated with the final 0.00017 ppb PCB criteria is 2.3×10^{-5}		

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Challenging Chemicals: Arsenic

Decision

Ecology adopted (1) surface water HHC for arsenic of 10 µg/L (total arsenic) and (2) required arsenic pollution minimization efforts.

These criteria are equivalent to the Safe Drinking Water Act (SDWA), Maximum Contaminant Level (MCL) that applies in Washington for drinking water sources. The decision to use the drinking water MCL is based on scientific information, regulatory precedent by other states and EPA, and acknowledgement of high concentrations of naturally occurring arsenic in Washington surface waters.

A comparison of the NTR HHC with the new HHC for arsenic is shown in the text below:

National Toxics Rule (NTR) HHC	2016 New HHC
Freshwater: 0.018 µg/L (inorganic)	Freshwater and Marine Water: 10 µg/L (total)
Marine: 0.14 µg/L (inorganic)	

Background

Arsenic is a naturally occurring element present in the environment in both inorganic and organic forms. Arsenic is present in rocks, soils, and the waters in contact with them, and concentrations in ground waters in the United States generally are highest in the West, with elevated levels also commonly occurring in the Midwest and Northeast. (USGS, 2000). Inorganic forms of arsenic are considered to be the most toxic, and are found in groundwater and surface water, as well as in many foods. A wide variety of adverse health effects, including skin and internal cancers, and cardiovascular and neurological effects, have been attributed to chronic arsenic exposure, primarily from drinking water (NAS, 1999; CTD, 2013).

There are also anthropogenic sources of arsenic in the environment, which include pesticides and herbicides, pressure treated lumber (this is a legacy source, as production of new pressure treated lumber treated with an arsenic compound has been phased out), fertilizers, pharmaceuticals, electronic semiconductors, automobile lead-acid batteries, lead bullets and shot, and metal smelting.

Arsenic Standards in Washington State: Washington's aquatic life water quality standards for arsenic are contained in the state's water quality standards rule for aquatic life criteria (WAC 173-201A-240). Arsenic HHC are also contained in the United States Environmental Protection Agency (EPA)-promulgated NTR (EPA 1992; 40 CFR 131.36). Both HHC and aquatic life criteria are shown in Table 8 below and are expressed as micrograms per liter (µg/L), which is equivalent to parts per billion (ppb). EPA recently proposed a revision to the NTR for Washington that contains proposed criteria for inorganic arsenic of 0.0045 µg/L (freshwater) and 0.0059 µg/L (marine and estuarine waters). These proposed federal criteria are based on a cancer slope factor of 1.75 mg/kg day.

Table 8: Washington's water quality standards for arsenic prior to the new rule

National Toxics Rule (NTR)- Human Health Criteria (1992)		Washington State Water Quality Standards (WAC 173-201A) for Aquatic Life			
Freshwater-Organism + Water	Marine-Organism Only	Acute Marine	Chronic Marine	Acute Freshwater	Chronic Freshwater
0. 018 µg/L (inorganic)	0.14 µg/L (inorganic)	69 µg/L (dissolved)	36 µg/L (dissolved)	360 µg/L (dissolved)	190 µg/L (dissolved)

In addition to the NTR and the state water quality standards, EPA establishes Maximum Contaminant Levels (MCLs) for arsenic under the federal Safe Drinking Water Act (SDWA). Up until 2001, the drinking water MCL for arsenic was 50 µg/L. EPA lowered the arsenic MCL to 10 µg/L in 2001 (EPA, 2001), following an extensive public process. The new standard went into effect for public supplies of drinking water nationwide in 2006. SDWA standards for arsenic in Washington are under the authority of the Washington Department of Health (WDOH).

EPA is currently in the process of reviewing the toxicity information in the Integrated Risk Information System (IRIS) related to inorganic arsenic, and plans to submit its next draft to the National Research Council for future peer review (EPA, 2014).

HHC for arsenic in other states*:* Nationwide, nearly half of the states use the SDWA MCL value of 10 µg/L for their arsenic HHC (ODEQ, 2011, P. 19). Use of SDWA regulatory levels as HHC is not unusual for both EPA and states. EPA developed Clean Water Act §304(a) national recommended HHC (for freshwater) for asbestos in 1991 and copper in 1998 based on SDWA regulatory levels (EPA 2002). The SDWA-based asbestos criterion (7,000,000 fibers/L) is currently in EPA's NTR and was issued to several states in 1992 and was retained in the 1999 NTR revision, and the copper criterion (1,300 mg/L) was issued by EPA to California in 2000 (40 CFR 131.38 - Establishment of Numeric Criteria for Priority Toxic Pollutants for the State Of California). EPA's 2015 draft HHC regulation for Washington includes retention of the asbestos criterion in the NTR, as well as addition of the SDWA-based copper criterion.

In the west, where naturally high levels of arsenic in groundwater and geology are prevalent, six states have also adopted the SDWA MCL as their HHC for arsenic. Oregon took a different approach and adopted risk-based HHC for arsenic (see Table 9 below).

EPA promulgated HHC for the state of California in 2000, as the California Toxics Rule. However, EPA did not promulgate criteria for arsenic and acknowledged the limitations associated with using the 1988 IRIS cancer slope factor. The following is language from the EPA's 2000 promulgation of the California Toxics Rule (EPA, 2000):

> *"EPA is not promulgating human health criteria for arsenic in today's rule. EPA recognizes that it promulgated human health water quality criteria for arsenic for a number of States in 1992, in the NTR, based on EPA's 1980 section 304(a) criteria guidance for arsenic established, in part, from IRIS values current at that time. However, a number of issues and uncertainties existed at the time of the CTR proposal concerning the health effects of arsenic…."*
>
> *"…Today's rule defers promulgating arsenic criteria based on the Agency's previous risk assessment of skin cancer….."*

Table 9: EPA approved Human Health Criteria for arsenic in western states

State	Arsenic criteria (µg/L)	Basis
Alaska	10 (total arsenic)	Same as SDWA MCL
Idaho	10 (total arsenic)	
Wyoming	10 (total arsenic)	
Nevada	10 (total arsenic)	
Utah	10 (total arsenic)	
New Mexico	10 (total arsenic)	
Oregon	2.1 (drinking surface + fish and shellfish: "fresh waters") (inorganic arsenic)	1 x 10^{-4} cancer risk level
	1.0 (fish and shellfish only: marine and estuarine)(inorganic arsenic)	1 x 10^{-5} cancer risk level
California [(1)]	5.0 Note: California uses the term "objective" , which is comparable to the term "state criteria."	Objectives are found in individual Basin Plans for the California Regional Water Quality Control Boards (see notes below for examples [(1)]– Based on Maximum Contaminant Levels as specified in Table 64431-A (Inorganic Chemicals) of Section 64431, Title 22 of the California Code of Regulations, as of June 3, 2005.

Notes:
[(1)] (California Regional Water Quality Control Board, San Francisco Bay Region, 2013), (Los Angeles Regional Water Quality Control Board, 1994), (North Coast Regional Water Quality Control Board, 2011), (Regional Water Quality Control Board, Central Coast Region, 2011)

The arsenic cancer slope factor (CSF): Without a reliable toxicity factor for cancer Ecology cannot calculate arsenic criteria based on cancer. EPA agrees that new cancer-based criteria for arsenic cannot be calculated at this time. In a May 6, 2016 filing with the United States District Court for the Western District of Washington, EPA stated that it will withdraw its proposed arsenic criteria for Washington because "extensive additional scientific analysis is necessary before revised criteria" for arsenic can be promulgated. *Puget Soundkeeper Alliance et. al. V. U.S.E.P.A.*, Case No. 2:16-cv-00293-JLR, EPA's Motion for Summary Judgment (May 6, 2016) at 13. As EPA explained in the Declaration of Elizabeth Southerland, Director of the Office of Science and Technology with EPA's Office of Water, "EPA did not update its CWA section 304(a) recommended criteria" for arsenic in 2015, and "EPA recognizes that there is substantial uncertainty surrounding the toxicological assessment of arsenic with respect to human health effects." Declaration of Elizabeth Southerland (May 5, 2016) at 7.

Ecology has determined that use of the EPA cancer potency factor would introduce a significant amount of uncertainty if used to develop HHC for arsenic:

- The inorganic arsenic cancer potency factor has been under reassessment for many years, and a date for finalization is not finalized (EPA, 2014). Newer information from EPA indicates that the CSF for arsenic could be finalized in EPA's IRIS in 2017 (see EPA's public comment letter on this proposed rule, included in the Concise Explanatory Statement accompanying this rulemaking).
- EPA did not use the 1998 IRIS cancer potency factor in its development of the new Safe Drinking Water Act (SDWA) MCL of 10 ppb promulgated in 2001, nor did they depend on this value in their promulgation of the HHC for the state of California in 2000. In the 2000 California Toxics Rule, EPA expressed their finding of uncertainty around the effects of arsenic, and did not use the newer 1998 cancer potency factor (EPA 2000). EPA used the older cancer potency factor ((1.75 per (mg/kg)/day) derived from the drinking water unit risk (5E-5 per (μg/L)) that was used to calculate the NTR arsenic criteria in its 1998 and 2002 national recommended guidance criteria calculations, but not as the basis of new regulations in either the 2000 California Toxics Rule or the new 2001 Safe Drinking water Act MCL for arsenic.
- Using either the older cancer potency factor of 1.75 per (mg/kg)/day) derived from the drinking water unit risk that was used to calculate the NTR arsenic criteria, or, the 1998 cancer potency factor of 1.5E+0 per (mg/kg)/day), injects a high degree of uncertainty into the criteria calculation for a regulatory level, especially given that EPA has not relied on either of these as the basis of more final recent regulations.

The arsenic BCF: In addition to an uncertain cancer slope factor, the accumulation factor used in the development of EPA's current 304(a) criteria is based on total arsenic, and will need to be modified in order to accurately address accumulation of inorganic arsenic into tissues. The bioconcentration factor (BCF) of 44 L/kg used in EPA's 304(a) criteria is based on total arsenic. This value does not accurately reflect the uptake of inorganic arsenic, the most toxic form of arsenic and the form to which EPA applies it's 304(a) criteria. Most of the arsenic in fish and

shellfish tissues is in the organic form, which is much less toxic than the inorganic form (EPA 1997). EPA (1997; page 10) estimated the percentage of inorganic arsenic in tissue*: "the maximum inorganic arsenic in fish and shellfish used for this estimate is 4% …The median inorganic arsenic value for the fish and shellfish data… is 0.4%. No inorganic arsenic was detected in 23 of 42 fish samples and 18 of 50 shellfish samples. Therefore, the median value reflects the higher inorganic arsenic concentrations found in shellfish and is a conservative value."* A BCF specific to inorganic arsenic is not available in EPA's criteria documents, but applying the data above to the current BCF of 44 indicates that the BCF of 44 could be adjusted downward by a large amount if inorganic arsenic only were considered. A new BCF for arsenic, as well as a new CSF, will be required for in order to calculate criteria for arsenic using the HHC equations.

The arsenic Safe Drinking Water Act (SDWA) MCL: The SDWA is based on science and feasibility. This does not invalidate use of a SDWA MCL for use in Clean Water Act programs. EPA uses SDWA values as 304(a) criteria for both asbestos and copper, and has approved use of the arsenic SDWA MCL as a Clean Water Act criterion for many states. Nothing in the Clean Water Act prohibits use of SDWA regulatory values, or of cost, in the state adoption of standards. In fact, the Clean Water Act and the Code of Federal Regulations explicitly direct states to adopt standards taking into account "use and value" of the resource. EPA's 2000 guidance (page 2-4) specifies that many factors apart from science can be taken into consideration in state risk management decisions: *"Risk management is the process of selecting the most appropriate guidance or regulatory actions by integrating the results of risk assessment with engineering data and with social, economic, and political concerns to reach a decision."*

The EPA went through an extensive process to evaluate science and feasibility to derive and finalize the SDWA arsenic MCL, and that MCL development is based on consideration of newer science than the older CSF included in EPA's 304(a) criteria for arsenic.

Arsenic exposures through tissue: Although Ecology acknowledges the large amount of uncertainty in the CSF and the BCF, using the CSFs and BCF in comparative criteria calculations helps to illustrate why the organism ingestion exposure route is largely irrelevant when considering risk levels between 10^{-4} and 10^{-6}, and why the only relevant exposure routes for those waters with drinking water as a designated use (most freshwaters in the state) is the drinking water exposure route.

The same inputs to the organism + water criteria equation for carcinogens that EPA used in its draft rule for Washington results in the hypothetical criterion (0.0045 µg/L) with the hypothetical 10^{-6} risk level in the table below. If that criterion concentration is held constant, but the risk level is increased due to changes in the FCR, the small effect of the FCR on the criteria can be seen. Using the EPA inputs and holding all variables other than FCR and risk level constant, it takes 2,240 g/day of fish + 2.4 L/day of drinking water to raise the risk level to 10^{-5} while staying at the same hypothetical water concentration. It takes 22,900 g/day of fish + 2.4 L/day of drinking water to raise the risk level to 10^{-4} while staying at the same hypothetical water concentration.

FCR survey data from Washington indicates that no one, even high consuming individuals from the surveys of the highest consuming populations, eat this much fish and shellfish on average on a daily basis over a lifetime. These increases in FCR are possible because the BCF for arsenic is low, and most of the risk is conferred by the exposure to 2.4 L/day of drinking water. In addition, the use of a BCF that was calculated for total arsenic instead of inorganic arsenic provides a large and unaccounted for protective factor in this example. Since virtually no risk is associated with the exposure to organisms, a criterion based on drinking water protection is appropriate and protective for waters with designated uses of drinking water supply.

Table 10 : Hypothetical criterion resulting from draft EPA criteria for Arsenic

Hypothetical criteria value (µg/L)[1]	Risk level	Fish consumption rate (g/day)	Fish consumption rate (pounds/day	Body weight (kg)	Cancer slope factor[3]	Drinking water intake (L/day)	BCF for total arsenic (not inorganic) (L/kg)[4]
0.0045[2]	10^{-6}	175	0.39	80	1.75	2.4	44
0.0045	10^{-5}	2,240	4.94	80	1.75	2.4	44
0.0045	10^{-4}	22,900	50.49	80	1.75	2.4	44

Footnotes:

[1] Criteria values were held constant, only the FCR and risk levels were changed in the calculations.

[2] This is EPA's proposed criteria in its proposed regulation for Washington, which was calculated with the variables shown in this row of the table.

[3] This CSF was used for illustrative purposes only. Scientific uncertainty precludes its use in criteria development.

[4] This is the BCF for total arsenic in tissues from EPA's most recent Clean Water Act 304(a) criteria document for arsenic. Most arsenic in tissues is in the organic form (see: EPA 1997. *Arsenic and fish consumption*. EPA 822-R-97-003.) A BCF (or BAF) that expresses total or inorganic arsenic in water to inorganic arsenic in tissue would be much lower than the 44 L/kg used here. In that case the possible FCRs in the table would be even greater. Uncertainty in this value precludes its use in criteria development.

Concentrations of arsenic in surface waters of Washington: In Washington, natural levels of inorganic arsenic in surface freshwaters are most frequently below the SDWA MCL of 10 µg/L total arsenic, but are frequently higher than the NTR HHC inorganic arsenic concentration of 0.018 µg/L. In situations where natural conditions result in ambient concentrations that are greater than the NTR criteria concentrations, Ecology uses the "natural conditions" provision in the water quality standards at WAC 173-201A-260 rather than the numeric criteria to implement the arsenic criteria.

The following provides one example of a total maximum daily load (TMDL) study that demonstrates natural concentrations of arsenic from the Similkameen River in Okanogan County:

The Similkameen River "TMDL Evaluation for Arsenic" (Ecology, 2002) noted that "EPA human health criteria of 0.018 and 0.14 µg/L are, however, consistently exceeded by an order of magnitude or more." Ecology's TMDL demonstrated that natural background arsenic levels in the Similkameen River are greater the NTR human health criteria. The TMDL determined that the Similkameen River naturally exceeds the EPA arsenic criteria upstream of the areas disturbed by mining. It was determined that natural conditions constitute the water quality criteria. Because arsenic levels naturally exceed criteria, the loading capacity for the river was set equal to the natural background concentration of arsenic. The TMDL was approved by EPA in 2004.

Basis for Ecology's decision

Ecology made two specific rule changes for arsenic:

- Surface water HHC for total arsenic at the SDWA MCL of 10 µg/L, based on a consideration of the continuing uncertainty around the long-term reassessment of the EPA IRIS cancer potency factor for arsenic, the need for a BCF specific to inorganic arsenic, EPA's Clean Water Act-approval of the of the SDWA MCL for arsenic for other states, and presence of naturally occurring arsenic in Washington. The criterion of 10 µg/L is being applied to both marine and freshwater scenarios. The MCL was developed for drinking waters. Because calculation of new criteria for arsenic is not possible with current information, Ecology also chose to apply the criterion of 10 µg/L to marine and estuarine waters in lieu of not adopting a criterion value for these waters.
- Pollution minimization requirements to reduce anthropogenic inputs of arsenic in discharges to surface waters.

Ecology has determined that use of the EPA cancer potency factor and BCF would introduce a significant amount of uncertainty if used to develop HHC for arsenic.

After review of what other states have done in setting HHC for arsenic, with subsequent approval by EPA, consideration of naturally high concentrations of arsenic in Washington, the scientific uncertainty in assessing risk from exposures to arsenic from tissue ingestion (no CSF for inorganic arsenic) and also with translating that to a water criterion value (no accumulation translator (BCF) for inorganic arsenic), and given the extensive process carried out by EPA to develop a protective MCL appropriate for drinking water exposures, Ecology has determined that use of the SDWA MCL for arsenic, coupled with pollution prevention requirements for industrial dischargers, is appropriate for Washington:

- ***Use of SDWA MCL for Arsenic:*** Use of the MCL has been approved by EPA widely across the nation. In particular, several other western states that have high levels of natural arsenic in the environment have adopted the SDWA MCL and are successfully applying it for protection of human health (Table 2). The SDWA is based on science and feasibility. This does not invalidate use of a SDWA MCL for use in Clean Water Act programs. EPA uses SDWA values as 304(a) criteria for both asbestos and copper, and has approved use of the

arsenic SDWA MCL as a Clean Water Act criterion for many states. Nothing in the Clean Water Act prohibits use of SDWA regulatory values in the state adoption of standards.

- ***Pollution prevention requirements:*** Adopting new arsenic criteria that reflect both a change in the chemical form (a change from inorganic arsenic to total arsenic) and a higher concentration has prompted Ecology to address implementation of the arsenic criteria to ensure that unforeseen industrial discharges of arsenic are controlled and reduced. The following rule language was adopted to address discharges of arsenic, from industrial sources, to waters with the designated use of domestic water supply:

  "When Ecology determines that an indirect or direct industrial discharge to surface waters designated for domestic water supply may be adding arsenic to its wastewater, Ecology will require the discharger to develop and implement a pollution prevention plan to reduce arsenic through the use of AKART (All Known and Reasonable Treatment). Indirect discharges are industries that discharge wastewater to a privately or publicly owned wastewater treatment facility."

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Challenging Chemicals: Methylmercury

Decision

Ecology decided to defer state adoption of HHC for methylmercury at this time, and plans to schedule adoption of methylmercury criteria and develop a comprehensive implementation plan after the current rulemaking is completed and has received EPA Clean Water Act approval. This decision means that Washington's HHC for total mercury will remain in the NTR until new methylmercury criteria are adopted by the state. The decision allows time for Ecology to gather more information to make an informed decision on how the new methylmercury criteria will be implemented.

Background

Mercury is a toxic metal that is released to the environment through natural and human processes. Most commonly, the gaseous form is released to the atmosphere, which is then deposited onto land and water from rain and snow. Once in the water, mercury can convert to its most toxic form, methylmercury, which accumulates in fish and aquatic organisms. Humans are exposed to methylmercury and its associated health problems by consuming contaminated fish. As of 2008, all 50 states had issued fish consumption advisories due to mercury contamination (EPA, 2010). Washington currently has Clean Water Act Section 303(d) listings based on the current mercury HHC, and the Washington Department of Health has issued statewide fish advisories for mercury for different fish species.

Washington's criteria for mercury: Washington's HHC and aquatic life criteria for mercury are shown in Table 11 below. The HHC for total mercury were issued to Washington in the 1992 NTR (40 CFR 131.36). Washington's current aquatic life criteria for total mercury are contained in the state's water quality standards rule for aquatic life criteria (WAC 173-201A-240). The HHC are based on non-cancer effects to human health. The acute aquatic life criteria are based on aquatic life effects, and the chronic aquatic life criteria are based on human health protection. The chronic marine and freshwater numeric criteria and the chronic criteria provision of "edible tissue concentrations shall not be allowed to exceed 1.0 mg/kg of methylmercury" are all based on the federal Food and Drug Administration's action level of 1 parts per million (ppm) for methylmercury in commercial fish.

Table 11: Washington's current water quality standards for mercury

National Toxics Rule (NTR)-Human Health Criteria (1992)		Washington State water quality standards (WAC 173-201A) Aquatic Life Criteria			
Organism + Water (µg/L)	Organism Only (µg/L)	Acute Marine (µg/L)	Chronic Marine (µg/L)	Acute Freshwater (µg/L)	Chronic Freshwater (µg/L)
0. 14 (total)	0. 15 (total)	1.8 (dissolved)	[(1)] 0.025 (total)	2.1 (dissolved)	[(1)] 0.012 (total)

Footnote 1. Edible fish tissue concentrations shall not be allowed to exceed 1.0 mg/kg of methylmercury.

EPA national recommended 304(a) guidance criterion for methylmercury: Prior to 2001 the U.S. Environmental Protection Agency (EPA) recommended that states adopt mercury HHC as "total mercury" measured in surface waters. In January 2001, EPA published a new recommended Clean Water Act section 304(a) water quality criterion for methylmercury based on fish tissue residues. This new criterion replaced the prior total mercury recommended criteria. The new recommended water quality criterion, 0.3 milligram (mg) methylmercury per kilogram (kg) fish tissue wet weight, describes the concentration of methylmercury in freshwater and estuarine fish and shellfish tissue that EPA recommends not be exceeded in order to protect consumers of fish and shellfish. The new EPA 2001 recommended national criterion (0.3 mg/kg) was calculated using a fish consumption rate of 17.5 g fish/day of freshwater and estuarine fish. The older total mercury HHC (the 1992 NTR criteria) were calculated using a fish consumption rate of 18.7 g/day, as opposed to the 6.5 g/day fish consumption rate incorporated in other HHC published by EPA prior to 2001 (EPA 2001) and 2002 (US EPA 2002).

EPA draft federal criterion for methylmercury for Washington: In September 2015 EPA proposed a regulatory change that would revise the current federal human health criteria applicable to Washington's waters (the NTR; 40CFR131.36). In 1992 EPA promulgated HHC for Washington State in the NTR, and this regulation contains the state's current HHC for mercury. EPA's newest proposal for Washington contains updates for 99 priority pollutants, including an "organisms-only" criterion for methylmercury of 0.033 mg/kg in tissue. If EPA approves criteria submitted by the state, Ecology assumes the corresponding federal criteria for mercury would remain in the NTR.

Implementation considerations: Washington currently implements the HHC and aquatic life criteria for total and dissolved mercury in discharge permits, in water quality assessments, and in Section 401 water quality certifications. In discharge permitting, the chronic aquatic life criteria are most likely to result in effluent limits because they are set at lower concentrations than the NTR criteria. EPA has published sensitive analytical methods for total mercury that are used in NPDES permitting as required in 40 CFR Part 136.

The 2001 methylmercury criterion was the first EPA-developed HHC expressed as a fish and shellfish *tissue* value rather than as a water column value. EPA recognized that this approach differed from traditional water column criteria and might pose implementation challenges. Therefore, in April 2010, EPA issued *Guidance for Implementing the January 2001*

Methylmercury Water Quality Criterion to provide direction to states and tribes on how to use the new fish tissue-based criterion recommendation in developing water quality standards for methylmercury and in implementing those standards in total maximum daily loads (TMDLs) and National Pollutant Discharge Elimination System (NPDES) permits. This guidance would also be applicable to EPA's 2015 proposed federal NTR criterion for Washington. However, even with guidance from EPA, questions around the following exist and will require development of a Washington specific approach:

- Mixing zones
- Variances
- Field sampling recommendations
- Assessing non-attainment of fish tissue criterion
- Developing TMDLs for water bodies impaired by mercury
- Incorporating methylmercury limits into NPDES permits

Controlling sources of mercury: Controlling the sources of mercury entering the aquatic environment is a complex issue. Complications include:

- There are many sources and pathways for mercury to enter Washington's environment (atmospheric transport from local areas and from other areas of the world, direct discharges, pharmaceuticals, food supplies, contaminated sites, etc.) - see Ecology's Mercury Chemical Action Plan information at http://www.ecy.wa.gov/mercury/.).
- Many of these mercury sources cannot be addressed using Clean Water Act laws and implementing regulations.
- There are existing levels of mercury in fish sampled throughout the state that have prompted the WDOH to issue statewide fish advisories for selected species of fish.
- Developing NPDES discharge limits for permits based on a form of mercury (methylmercury criterion) that is created after mercury enters the environment is not straightforward.

Developing an implementation process that effectively addresses mercury controls and also delineates between Clean Water Act and non-Clean Water Act responsibilities will take considerable time and resources, as well as considerable public input.

Basis for Ecology's decision

Ecology has decided to defer state adoption of HHC for methylmercury at this time, and plans to schedule adoption of methylmercury criteria and develop a comprehensive implementation plan after the current rulemaking is completed and has received Clean Water Act approval. This decision means that Washington's HHC for total mercury will remain in the NTR until new methylmercury criteria are adopted by the state or are updated by EPA.

Ecology based this decision on the following factors:

- Implementation and control strategies to reduce methylmercury concentrations in fish and shellfish tissue need an integrated approach that uses available Clean Water Act tools and also other non-Clean Water Act actions (Ecology 2003).
- Taking time to develop an integrated approach now would slow the progress of the adoption of the other proposed HHC and implementation tools. Ecology thinks continued progress on the main rule adoption is important to maintain.
- The state currently has criteria for mercury that address human health protection (the NTR criteria and the marine and freshwater chronic aquatic life criteria).

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Implementation Tools: Intake Credits

Decision

Ecology added a new definition for "intake credits" and a new section to the water quality standards rule at WAC 173-201A-460 that addresses situations where facilities bring in and discharge levels of background pollutants contained in the intake water, referred to as intake credits (see Figure 7 below for implementation of the new language). Intake credits have typically been allowed for technology based effluent limits (TBELs). The new rule language is applicable to the granting of intake credits for use with water quality-based effluent limits (WQBELs). The new language clarifies the conditions where intake credits would be allowed for determining reasonable potential and WQBELs. The procedure accounts for pollutants already present in the intake water, and would only be allowed when the mass and concentration of effluent is the same or less than intake water, and there is "no net addition" of the pollutant.

Background

An intake credit is a tool intended to be used primarily in the National Pollutant Discharge Elimination System (NPDES) Permit Program, in specific circumstances where the discharger is not contributing any additional mass of the identified intake pollutant in its wastewater, thereby having a "no net addition" of the pollutant. Examples of a pollutant already found in the intake water could be from naturally-occurring or legacy pollutants that are outside of the control of the facility. This implementation tool will not impact Washington's water quality and public health because it will not be granted unless the facility meets the requirements for "no net additions" of the pollutant.

The following conditions must be met for an intake credit to apply:

- The facility must not contribute any additional mass of the identified intake pollutant to its wastewater unless an equal or greater mass is removed prior to discharge.
- Intake water must come from the same body of water to which the discharge is made.
- The facility must not alter the identified intake pollutant chemically or physically in a manner that would cause adverse water quality impacts to occur that would not occur if the pollutants were left in-stream.
- The facility must not increase the identified intake pollutant concentration at the point of compliance as compared to the pollutant concentration in the intake water.
- The timing and location of the discharge must not cause adverse water quality impacts to occur that would not occur if the identified intake pollutant were left in-stream.

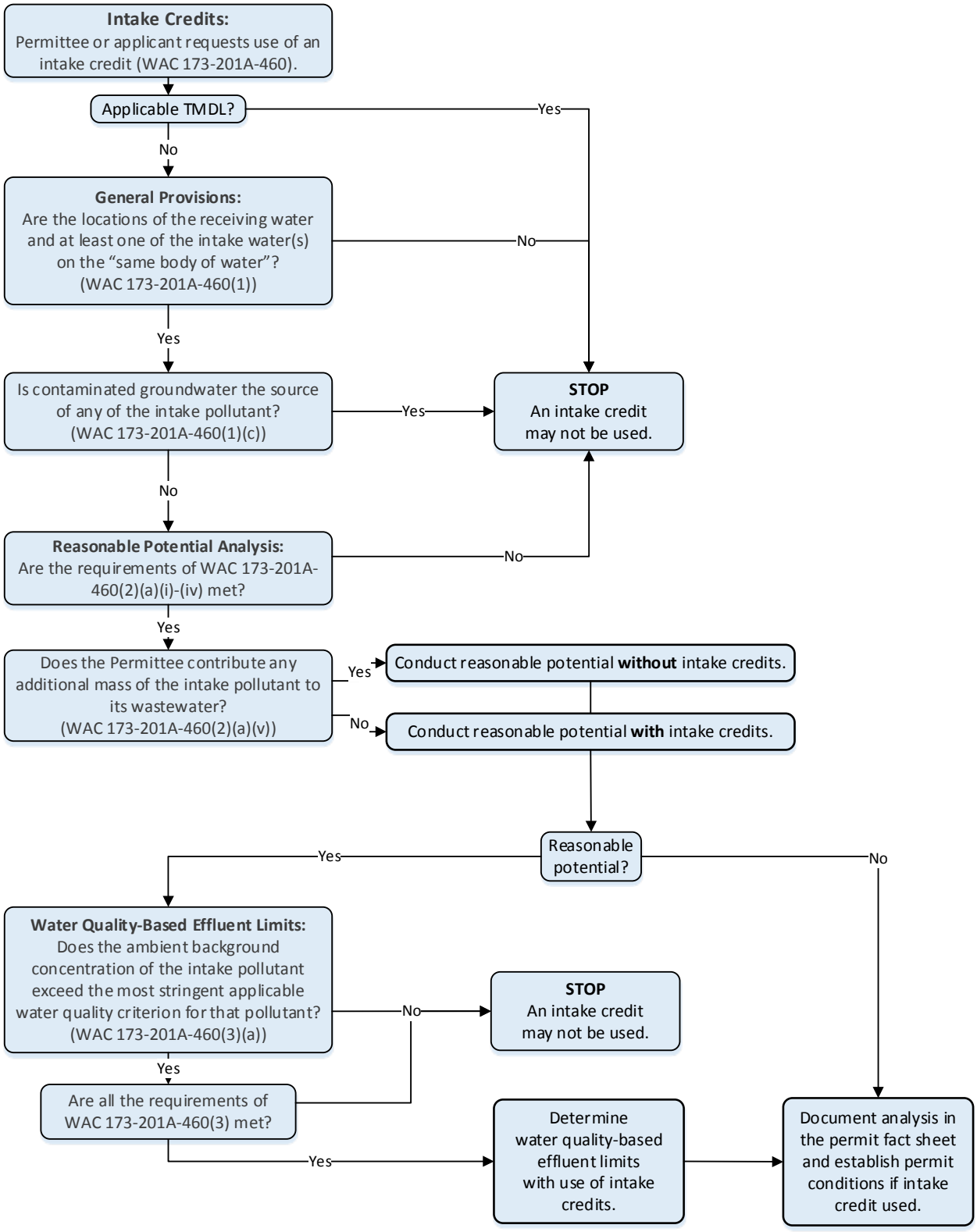

Figure 7: Flowchart for implementation of intake credit language at WAC 173-201A-460

Basis for Ecology's decision

The new language in WAC 173-201A-460 closely follows the directives for allowing intake credits for determining reasonable potential and WQBELs outlined in EPA's Great Lakes Initiative, and in the recently adopted and EPA-approved Oregon water quality standards.

Federal regulations at 40 CFR 122.45(g) allow for adjustment of (TBELs) to reflect credit for pollutants in the discharge's intake water. Therefore, the permittee is only responsible for treating the portion of the pollutant load generated or concentrated as part of their process. The credits are commonly referred to as "intake credits." Although intake credits are commonly used by states for TBELs, states have only recently begun to use intake credits for WQBELs. The most developed of these is contained in the *Great Lakes Water Quality Guidance*, which offers a process for doing an alternative reasonable potential analysis for WQBELs that incorporates the concept of intake credits.

Intake credit language has been adopted into the water quality administrative rules of a number of states including California, Ohio, Indiana, Michigan, Wisconsin, Illinois, Minnesota, Pennsylvania, and New York, although they are only included in a limited number of actual permits due to the inherent limitations of the Intake Credit procedure and the availability of other implementation procedures.

In Region 10, Oregon recently revised its intake credits provisions as part of their rulemaking for HHC and modeled their revisions after the language approved by the EPA for the Great Lakes Initiative. This language can be found in OAR 340-045-0105, and includes the general requirements listed above. The Oregon regulations provide facilities the ability to gain credit for pollutants in their intake water when there is "*no net addition*" of pollution, or when the facility removes any additional mass of a pollutant that might have been added during production, prior to discharging.

References

EPA, 1995. Federal Register, Volume 60, Number 56, "Final Water Quality Guidance for the Great Lakes System", Appendix F, Procedure 5; Reasonable Potential to Exceed Water Quality Standards, Part D. Available online at: http://www.federalregister.gov/articles/1995/03/23/95-6671/final-water-quality-guidance-for-the-great-lakes-system.

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Implementation Tools: Compliance Schedules

Decision

Ecology added a new definition in WAC 173-201A-020 to define “Compliance Schedule” or “Schedule of Compliance.” Ecology deleted the specific period of time for a compliance schedule and added language to describe circumstances when a compliance schedule can go beyond the term of a permit, and ensure that compliance is achieved as soon as possible. Language has been added to authorize compliance schedules for longer periods of time in accordance with RCW 90.48.605, where a total maximum daily load (TMDL) exists. Language has also been added for circumstances when more time is needed and a TMDL does not exist.

Background

A compliance schedule is a tool that is intended to be used in the National Pollutant Discharge Elimination System (NPDES) Permit Program, in specific circumstances where an individual discharger requires additional time to comply with NPDES permit limits based on new or revised criteria in a state’s water quality standards. The compliance schedule allows the particular discharger time to meet permit's limit while taking steps to eventually achieve compliance. Typically, the compliance schedule is included as part of the Terms and Conditions in an NPDES permit and includes interim requirements. A key point in a compliance schedule is that the discharger is required to achieve the final water quality-based effluent limit as soon as possible.

A compliance schedule is an enforceable tool used as part of a permit, order, or directive to achieve compliance with applicable effluent standards and limitations, water quality standards, or other legally applicable requirements. Compliance schedules include a sequence of interim requirements such as actions, operations, or milestone events to achieve the stated goals. Compliance schedules are a broadly used tool for achieving state and federal regulations; compliance schedules under the Clean Water Act are defined federally at Clean Water Act 502(17) and 40 CFR Section 122.2.

Schedules of compliance have existed in Ecology regulations at WAC 173-220-140 and WAC 173-226-180 for the NPDES permit program since 1974. These regulations require that compliance schedules set forth the shortest, reasonable period of time to achieve the specified requirements, and require that such period to be consistent with federal guidelines and requirements of the Clean Water Act. Compliance schedules become an enforceable part of the permit. If a permittee fails or refuses to comply with interim or final requirements of a compliance schedule in a permit, such noncompliance constitutes a violation of the permit. Compliance schedules were incorporated into the state water quality standards in 1992 to ensure continued use in the permitting program, and can be found at WAC 173-210A-510(4).

The use and limitations of compliance schedules for NPDES permits in Washington are described at WAC 173-220-140 and WAC 173-226-180. For purposes of water quality

standards, compliance schedules may be used only where there is a finding that a permittee cannot immediately comply with a new, or newly revised, water-quality based effluent limit (WQBEL). Compliance schedules lasting longer than one year must include interim milestones, along with dates for their achievement, with no more than one year between dates. Interim milestones might relate, for example, to purchase and installation of new equipment, modification of existing facilities, construction of new facilities, and/or development of new programs. Compliance schedules also must include specific numeric or narrative effluent limits that will be met during the compliance schedule period.

Compliance schedules are not allowed for new or expanded facilities.

Compliance schedules must require a permittee to meet the applicable WQBEL "as soon as possible." The determination of what constitutes "as soon as possible" is made on a permit-by-permit basis considering the specific steps a permittee must take to achieve compliance. A compliance schedule typically is short-term in duration and includes a schedule of actions (investigations such as source identification studies, treatment feasibility studies) to meet the final effluent limitation. A compliance schedule differs from a variance in that a discharge may need more time to meet a final effluent limitation, but it has identified specific actions that will attain water quality effluent limits. In other words, the discharger knows they can achieve the water quality standard but they need more time.

The prior Washington State regulations limited compliance schedules to no more than ten years. However, Ecology was been directed by the Legislature to extend the maximum length of compliance schedules to more than ten years when a compliance schedule is appropriate, the base requirements for compliance schedules are met (i.e., compliance "as soon as possible"), and a permittee is not able to meet its total maximum daily load (TMDL) waste load allocations only by controlling and treating its own effluent. Statutory language can be found at RCW 90.48.605 - Amending state water quality standards — Compliance schedules in excess of ten years authorized. Available online: http://apps.leg.wa.gov/rcw/default.aspx?cite=90.48.605.

Basis for Ecology's Decision

The main basis for Ecology's proposal is state legislation in 2009 that recognized there are circumstances where extending a compliance schedule would be appropriate. Compliance schedules must still meet requirements in state NPDES regulations at WAC 173-220-140 and WAC 173-226-180, which includes specific timeframes within the schedule of compliance and enforceable provisions. RCW 90.48.605 focuses on instances when a TMDL exists on the receiving water, and describes a four part test that must be established:

1. The permittee is meeting its requirements under the total maximum daily load as soon as possible.
2. The actions proposed in the compliance schedule are sufficient to achieve water quality standards as soon as possible.
3. A compliance schedule is appropriate.

4. The permittee is not able to meet its waste load allocation solely by controlling and treating its own effluent.

Ecology has also added language that takes into consideration circumstances where a TMDL does not exist, but a compliance schedule would be the most appropriate tool to bring the permittee into compliance with the standard in the shortest timeframe possible. In this case, the actions must be identified that will bring the discharger into compliance with the effluent limits, but more time is needed than the term of the permit.

Revised language for compliance schedules emphasizes that compliance schedules must be completed as soon as possible and should generally not exceed the term of the permit. The revisions remove the ten-year limit for compliance schedules to allow flexibility on a permit by permit basis.

In considering a longer time period than ten years under certain circumstances, the use of compliance schedules in other states was reviewed. As an example, in Idaho, the town of Smelterville wastewater treatment plant draft permit includes a compliance schedule of "twenty years plus five months" for dissolved metals. Smelterville is located within the Bunker Hill Mining and Metallurgical Complex Superfund Site that has a current clean-up schedule of thirty years. This schedule, along with the need for additional data collection to determine the source of continued elevated metal levels in the new treatment plant effluent, was part of the justification for the twenty-year compliance schedule. EPA has approved this schedule as meeting the "as soon as possible" requirement.

In summary, the following apply as a basis for the use of the new rule language for the general allowance for compliance schedules in Washington:

- They are a part of a permit and do not require a rule change.
- They are allowed when the facility can achieve water quality standards but needs more time.
- The discharger must meet water quality standards or compliance "as soon as possible."
- They must contain an enforceable sequence of actions and final limit.
- They must make progress towards the final limit or water quality standards by requiring interim actions with milestones if the schedule is longer than one year.
- They are not allowed for new dischargers.
- They cannot be renewed.

References

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Implementation Tools: Variances

Decision

Ecology added a new definition in WAC 173-201A-020 to define "Variance." Ecology revised language in WAC 173-201A-420 that establishes minimum qualifications for granting variances for individual dischargers, stretches of waters, or application to multiple dischargers. Language was adopted to establish a process for considering a variance that includes:

- A public process, including tribal notification, rulemaking, and EPA approval.
- The time period for when a variance would be in effect, generally not to exceed the term of the permit but under certain circumstances can be longer, as long as the time is as short a duration as possible.
- Requirements for a pollutant reduction plan that identifies specific schedule of actions that are set forth to achieve compliance with the original criteria.
- Requirements for interim numeric and narrative requirements that reflect the highest achievable water quality, within the shortest time possible, during the term of the variance.
- Requirements for a mandatory five-year review if the variance extends beyond the term of a permit.
- For variances that apply more broadly than individual variances, require a watershed assessment or total maximum daily load (TMDL) to identify responsible sources.
- Conditions under which a variance would be shortened or terminated, and when renewal would be considered.

Background

A variance is a time-limited designated use and criterion for a specific pollutant(s) or water quality parameter(s) for a single discharger, a group of dischargers, or stretch of waters. Variances establish a set of temporary requirements that apply instead of the otherwise applicable water quality standards and related water quality criteria. A variance may be considered when the standards are expected to be attained by the end of the variance period or the attainable use cannot be reliably determined. Variances can be targeted to specific pollutants, sources, and/or stretches of waters. Variances are not allowed for new or expanded facilities.

EPA's recent revision to the federal water quality standards regulations (40CFR131) added new regulatory requirements for variances (40CFR131.14), as well as the ability to use variances for restoration activities. The new federal regulation defines a variance as

> *"131.3(o) A water quality standards variance is a time-limited designated use and criterion for a specific pollutant(s) or water quality parameter(s) that reflect the highest attainable condition during the term of the water quality standards variance."*

The US Environmental Protection Agency (EPA) has dictated that state variance procedures, as part of state water quality standards, must be consistent with the substantive requirements of 40 CFR 131.14. EPA has approved state-adopted variances in the past and has indicated that it will continue to do so if:

- Each variance is adopted into rule as part of the water quality standard.
- The state demonstrates that meeting the standard is unattainable based on one or more of the grounds outlined in 40 CFR 13 1.10(g) for removing a designated use. Note: EPA's new water quality standards regulation makes this requirement only applicable to Clean Water Act 101(1)(2) uses (the "fishable/swimmable" uses of the Clean Water Act), which is Ecology's intent also. Variances for other uses must include consideration of the "use and value" of the water. (see 40CFR131.14 for new federal requirements).
- The justification submitted by the state includes documentation that treatment more advanced than that required by sections 303(c)(2)(A) and (B) has been carefully considered, and that alternative effluent control strategies have been evaluated.
- The more stringent state criterion is maintained and is binding upon all other dischargers on the stream or stream segment.
- The discharger who is given a variance for one particular constituent is required to meet the applicable criteria for other constituents.
- The variance is granted for a specific period of time and can be renewed upon expiration.
- The discharger either must meet the standard upon the expiration of this time period or must make a new demonstration of "unattainability."
- Reasonable progress is being made toward meeting the standards.
- The variance was subjected to public notice, opportunity for comment, and public hearing. The public notice should contain a clear description of the impact of the variance upon achieving water quality standards in the affected stretch of waters.

The temporary requirements established through a variance are only effective for the life of the variance. Because a variance establishes a temporary set of requirements that apply instead of the underlying water quality criteria, EPA has specified that variances for the Clean Water Act 101(a)(2) fishable/swimmable uses are appropriate only under the same circumstances required in federal rule to undertake a Use Attainability Analysis (UAA), used to change a designated use for a water body. Also, variances can be granted when they are needed to undertake restoration activities:

40CFRE131.14(b)(2)(i)(A)

"…the State must demonstrate that attaining the designated use and criterion is not feasible throughout the term of the water quality standards variance because:

(1) One of the factors listed in § 131.10(g) is met, or

(2) Actions necessary to facilitate lake, wetland, or stream restoration through dam removal or other significant reconfiguration activities preclude attainment of the designated use and criterion while the actions are being implemented.".

Regulations found in 40 CFR 131.10(g) establish six circumstances under which a UAA, or a variance, might be appropriate. They are:

1. Naturally occurring pollutant concentrations prevent attainment of the use.
2. Natural, ephemeral, intermittent or low flow conditions or water levels prevent attainment of the use, unless these conditions may be compensated for by discharge of sufficient volume of effluent discharges without violating state water conservation requirements to enable uses to be met.
3. Human caused conditions or sources of pollution prevent attainment of the use and cannot be remedied or would cause more environmental damage to correct than to leave in place.
4. Dams, diversions, or other types of hydrologic modifications preclude attainment of the use, and it is not feasible to restore the water body to its original condition or to operate such modification in a way that would result in attainment of the use.
5. Physical conditions related to the natural features of the water body, such as the lack of a proper substrate, cover, flow, depth, pools, riffles, and the like, unrelated to water quality, preclude attainment of aquatic life protection uses.
6. Controls more stringent than those required by Sections 301(b) and 306 of the Clean Water Act would result in substantial and widespread economic and social impact.

Recent EPA guidance offered two examples of the circumstances under which variances may be particularly appropriate to consider:

- When attaining the designated use and criteria is not feasible under current conditions (e.g., water quality-based controls required to meet the numeric nutrient criterion would result in substantial and widespread social and economic impact) but achieving the standards could be feasible in the future if circumstances related to the attainability determination change (e.g., development of less expensive pollution control technology or a change in local economic conditions).
- When it is not known whether the designated use and criteria may ultimately be attainable, but feasible progress toward attaining the designated use and criteria can be made by implementing known controls and tracking environmental improvements (e.g., complex use attainability challenges involving legacy pollutants).

Federal regulations (40CFR131.14) require that the term of the variance can only be as long as necessary to achieve the highest attainable condition.

Variances have not been issued in Washington to date but are allowed under WAC 173-201A-420. The new language states that a variance is subject to a public and intergovernmental involvement process, and a variance does not go into effect until it is incorporated into WAC 173-201A and approved by EPA. The new duration of a variance is not specified and variances may be renewed after providing another opportunity for public and intergovernmental involvement and review.

Basis for Ecology's decision

Ecology adopted HHC for Washington's water quality standards. Changes to the variables that go into the HHC equation, such as an updated fish consumption rate, generally result in more protective criteria. Ecology recognizes that these new, more protective criteria may be difficult to meet in situations where technology is not yet available or feasible to remove the pollutant, or in cases where either (1) a persistent pollutant resides and is cycling within the aquatic ecosystem of the water body and cannot be removed without degrading the system, or (2) when the main sources of the pollutant are not within the scope of the state's jurisdiction to control through water quality protection. In addition, other criteria and uses may not be possible to attain in the short term and variances could be applicable to these circumstances as well. An example of this is the time needed to improve temperature in streams where the only feasible cooling method is shade via streamside tree planting and subsequent tree canopy maturation.

EPA has advised states that a variance should be used instead of removal of a use where the state believes the standard can or might ultimately be attained. By maintaining the beneficial use rather than changing it, the state will ensure that further progress is made in improving water quality and attaining the standard. With a variance, NPDES permits may be written such that reasonable progress is made toward attaining the standards without violating section 402(a)(l) of the Clean Water Act, which requires that NPDES permits must meet the applicable water quality standards.

With these factors in mind, Ecology revised the variance section of the water quality standards at WAC 173-201A-420, as part of the rulemaking for developing HHC. The key goals of these revisions are:

- ***Provide accountability*** that the discharger cannot feasibly meet the original criteria and that they continually strive to make reasonable progress to meet the original criteria and highest attainable condition during the life of the variance. Build in checks and balances to ensure that variance information is reviewed on a regular basis, new technology and science is taken into account, and benchmarks are required to ensure that implementation of the variance is occurring and that the variance continues to be necessary.
- ***Extend timeframe*** of a variance where necessary to allow time to deal with difficult, complex toxics compounds, such as legacy pollutants or those that come from sources outside of Clean Water Act jurisdiction. Include mandatory reviews to ensure that the variance is still necessary. Provide framework for renewing, shortening, and revoking a variance.
- ***Efficiency of Resources*** where possible, reduce resource intensity of regulating agencies in issuing variances.

The new language at WAC 173-201A-420 includes general provisions, and specific requirements that would apply for variances for individual dischargers, stretches of waters, and multiple dischargers. Requirements are intended to be consistent with federal guidance and also provide the necessary tools for implementing state water quality standards.

Besides requirements for issuing an individual variance, new rule language also provides requirements for issuing a variance to multiple dischargers for circumstances where multiple permittees cannot attain a designated use or criteria for the same pollutant(s) for the same reason, regardless of whether or not they are located on the same water body. In these cases, the new rule language streamlines the variance process by adopting one variance that applies to all the permittees. These are generally known as "multiple discharger variances." Multiple discharger variances may be considered under the same circumstances, and must meet the same standards, as single discharger variances. A permittee that could not qualify for an individual variance should not qualify for a multiple discharger variance. Ecology is following EPA guidance, which recommends that justifications for multiple discharger variances should:

1. Apply only to permittees experiencing the same challenges in meeting water quality based effluent limits for the same pollutant(s), criteria, and designated uses.
2. Group permittees based on specific characteristics or technical and economic scenarios that they share, and conduct a separate analysis for each group. The more homogenous a group is in terms of factors affecting attainability of the designated use and criteria, the more credible a multiple discharger variance will be. For example: type of discharger (public or private); industrial classification; permittee size and/or effluent quality; pollutant treatability; whether or not the permittee can achieve a level of effluent quality comparable to the other permittees in the group; and water body or watershed characteristics.
3. Collect sufficient information from each individual permittee to support the assignment of each individual permittee to the designated group of multiple dischargers. The justification for a multiple discharger variance should account for as much individual permittee information as possible. When a permittee does not fit with any of the group characteristics, an individual variance should instead be considered.

Ecology is adopted new language that will allow a variance for stretches of waters, such that the variance would apply to an entire stretch of water or portions of water body segments. Other states have used water body variances where the problems in a stretch of waters are significantly impacting water quality and habitat, are widespread, and involve numerous sources of point and nonpoint pollution; that is, where waters are significantly impaired by multiple sources, not just a few point sources. For example, where historic mining practices have impaired both water quality and habitat throughout a headwater basin, states have applied temporary standards with specific expiration dates for certain pollutants related to the historic mining practices rather than downgrading these waters through a use change. In this way, states have maintained designated uses and underlying criteria for other pollutants, while recognizing that existing ambient conditions for certain pollutants are not correctable in the short-term.

The temporary standards provide a basis for permit limits in the shorter term that will in turn lead to remediation of damaged water resources to the point that they will once again provide protection for the underlying designated use and criteria. By issuing a variance instead of a use change, the underlying use and criteria are preserved, allowing them to actively drive water

quality improvements in the longer-term. A water body variance provides time for the state to work with both point and nonpoint sources to determine and implement adaptive management approaches on a water body or watershed scale to achieve pollutant reductions and strive toward attaining the water body's designated use and associated criteria.

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Implementation Clarification for Combined Sewer Overflows (CSO) Treatment Plants

Decision

Ecology added a new definition to WAC 173-201A-020 to define CSO Treatment Plants and new language to WAC 173-201A-510 *Means of Implementation*, to clarify implementation of HHC in NPDES permits for CSO Treatment Plants. This new rule language provides clarification but does not change any current practices with regard to permit requirements.

Background

The following description of CSO's is taken from EPA 2004.

"Two types of public sewer systems predominate in the United States: combined sewer systems (CSSs), and sanitary sewer systems (SSSs). CSSs were among the earliest sewer systems constructed in the United States and were built until the first part of the 20th century. As defined in the 1994 CSO Control Policy (EPA 1994a), a CSS is:

> *A wastewater collection system owned by a state or municipality (as defined by Section 502(4) of the Clean Water Act) that conveys domestic, commercial, and industrial wastewaters and storm water runoff through a single pipe system to a publicly-owned treatment works (POTW).*

During wet weather events (e.g., rainfall or snowmelt), the combined volume of wastewater and storm water runoff entering CSSs often exceeds conveyance capacity. Most CSSs are designed to discharge flows that exceed conveyance capacity directly to surface waters, such as rivers, streams, estuaries, and coastal waters. Such events are called CSOs. A CSO is defined as:

> *The discharge from a CSS at a point prior to the POTW treatment plant.*
>
> *Some CSO outfalls discharge infrequently, while others discharge every time it rains. Overflow frequency and duration varies from system to system and from outfall to outfall within a single CSS. Because CSOs contain untreated wastewater and storm water, they contribute microbial pathogens and other pollutants to surface waters. CSOs can impact the environment and human health. Specifically, CSOs can cause or contribute to water quality impairments, beach closures, shellfish bed closures, contamination of drinking water supplies, and other environmental and human health problems."*

CSOs are driven by influxes of stormwater into combined sanitary and stormwater collection systems. Because of the episodic and short-term nature of CSO discharges it is infeasible to calculate effluent limits that are based on criteria with durations of exposure up to 70 years. The federal regulations (40CFR122.44(k)) allow use of best management practices (BMP)-based limits in NPDES permits if it is infeasible to calculate numeric limits:

"§ 122.44 Establishing limitations, standards, and other permit conditions (applicable to State NPDES programs, see § 123.25).

In addition to the conditions established under § 122.43(a), each NPDES permit shall include conditions meeting the following requirements when applicable.

***(k)** Best management practices (BMPs) to control or abate the discharge of pollutants when:*

***(1)** Authorized under section 304(e) of the Clean Water Act for the control of toxic pollutants and hazardous substances from ancillary industrial activities;*
***(2)** Authorized under section 402(p) of the Clean Water Act for the control of storm water discharges;*
***(3)** Numeric effluent limitations are infeasible; or*
***(4)** The practices are reasonably necessary to achieve effluent limitations and standards or to carry out the purposes and intent of the Clean Water Act."*

In Washington CSO control strategies are implemented through methods and approaches specified in chapter 173 of the Washington Administrative Code (WAC 173), 40CFR122, and the *Water Quality Program Permit Writer's Manual* (Ecology 2015). Chapter 173-245 WAC establishes procedures for CSO reduction. One reduction strategy available is treatment at the CSO site. Discharges from these CSO Treatment Plants are typically more frequent than once per year though still relatively infrequent and typically of short duration. Ecology adopted the additional CSO treatment plant implementation language in the water quality standards in order to provide clarity to the implementation of HHC in permits for CSO Treatment Plants.

Basis for Ecology's decision

Ecology adopted CSO treatment plant implementation language in the water quality standards in order to provide clarity to the implementation of HHC in permits for CSO Treatment Plants. The new rule language is below:

173-201A-020 Definitions.
Combined Sewer Overflow (CSO) Treatment Plant – is a facility that provides At-Site treatment as provided for in chapter 173-245 WAC. A CSO Treatment plant is a specific facility identified in a department-approved CSO Reduction Plan (Long-term Control Plan) that is designed, operated and controlled by a municipal utility to capture and treat excess combined sanitary sewage and stormwater from a combined sewer system.

173-201A-510 Means of Implementation
(6) *Combined Sewer Overflow Treatment Plant*

The influent to these facilities is highly variable in frequency, volume, duration, and pollutant concentration. The primary means to be used for requiring compliance with the human health criteria shall be through the application of narrative limitations, which

includes but is not limited to best management practices required in waste discharge permits, rules, orders and directives issued by the department.

References

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Appendix A. Input Values to Calculate New HHC Criteria

The table below contains the input values used by Ecology to calculate the new 2016 human health criteria found in WAC 173-201A-240, as adopted on August 1, 2016. Risk levels and hazard quotients are not shown. The risk level used with the cancer slope factors was 1×10^{-6}, except for PCBs, which was 4×10^{-5}. The hazard quotient used with the reference doses was 1. For further information see the following sections in this document:

- Human Health Criteria Equations and Variables
- Challenging Chemicals: Arsenic
- Challenging Chemicals: PCBs, for the bases of the input values.

Notes:
1. RfDs in orange are in the EPA 2015 final criteria documents and have corresponding CSFs which are the basis of the EPA proposed Rule for Washington. These RfDs were not the basis of the proposed EPA rule.
2. Safe Drinking Water Act criteria bases are indicated in blue rows.

Column headings:
PP# = Priority pollutant number (Appendix A to 40 CFR Part 423)
NTR Chem # = Chemical number in the National Toxics Rule (40CFR131.36)
CAS # = Chemical Abstract Service number
RSC = Relative source contribution
RfD = Reference dose (mg/kg-day)
BW = Body weight (kg)
DWI = Drinking water intake (L/day)
FCR = Fish consumption rate (kg/day)
BCF = bioconcentration factor (L/kg)
CSF = Cancer slope factor (mg/kg-day)

PP #	NTR Chem #	Chemical Name	CAS # - 1	CAS # -2	RSC	RfD	BW	DWI	FCR	BCF	CSF
11	41	1,1,1-Trichloroethane	71556	71-55-6	1	2	80	2.4	0.175	5.6	-
15	37	1,1,2,2-Tetrachloroethane	79345	79-34-5	1	0.02	80	2.4	0.175	5	0.2
14	42	1,1,2-Trichloroethane	79005	79-00-5	1	0.004	80	2.4	0.175	4.5	0.057
29	30	1,1-Dichloroethylene	75354	75-35-4	1	0.05	80	2.4	0.175	5.6	-
8	101	1,2,4-Trichlorobenzene	120821	120-82-1	1	0.01	80	2.4	0.175	114	0.029
25	75	1,2-Dichlorobenzene	95501	95-50-1	1	0.3	80	2.4	0.175	55.6	-
10	29	1,2-Dichloroethane	107062	107-06-2	1	0.078	80	2.4	0.175	1.2	0.0033
32	31	1,2-Dichloropropane	78875	78-87-5	1	0.0893	80	2.4	0.175	4.1	0.036
37	85	1,2-Diphenylhydrazine	122667	122-66-7	1	-	80	2.4	0.175	24.9	0.8
30	40	1,2-Trans-Dichloroethylene	156605	156-60-5	1	0.02	80	2.4	0.175	1.58	-
26	76	1,3-Dichlorobenzene	541731	541-73-1	1	0.002	80	2.4	0.175	55.6	-
33	32	1,3-Dichloropropene	542756	542-75-6	1	0.025	80	2.4	0.175	1.91	0.122
27	77	1,4-Dichlorobenzene	106467	106-46-7	1	0.07	80	2.4	0.175	55.6	-
129	16	2,3,7,8-TCDD (Dioxin)	1746016	1746-01-6	1	7E-10	80	2.4	0.175	5,000	-
21	55	2,4,6-Trichlorophenol	88062	88-06-2	1	0.001	80	2.4	0.175	150	0.011
31	46	2,4-Dichlorophenol	120832	120-83-2	1	0.003	80	2.4	0.175	40.7	-
34	47	2,4-Dimethylphenol	105679	105-67-9	1	0.02	80	2.4	0.175	93.8	-
59	49	2,4-Dinitrophenol	51285	51-28-5	1	0.002	80	2.4	0.175	1.5	-
35	82	2,4-Dinitrotoluene	121142	121-14-2	1	0.002	80	2.4	0.175	3.8	0.667
20	71	2-Chloronaphthalene	91587	91-58-7	1	0.08	80	2.4	0.175	202	-
24	45	2-Chlorophenol	95578	95-57-8	1	0.005	80	2.4	0.175	134	-
60	48	2-Methyl-4,6-Dinitrophenol	534521	534-52-1	1	0.0003	80	2.4	0.175	5.5	-
28	78	3,3'-Dichlorobenzidine	91941	91-94-1	1	-	80	2.4	0.175	312	0.45
22	52	3-Methyl-4-Chlorophenol	59507	59-50-7	1	0.1	80	2.4	0.175	1258	-
94	110	4,4'-DDD	72548	72-54-8	1	0.0005	80	2.4	0.175	53,600	0.24

PP #	NTR Chem #	Chemical Name	CAS # - 1	CAS # -2	RSC	RfD	BW	DWI	FCR	BCF	CSF
93	109	4,4'-DDE	72559	72-55-9	1	0.0005	80	2.4	0.175	53,600	0.167
92	108	4,4'-DDT	50293	50-29-3	1	0.0005	80	2.4	0.175	53,600	0.34
1	56	Acenaphthene	83329	83-32-9	1	0.06	80	2.4	0.175	242	-
2	17	Acrolein	107028	107-02-8	1	0.0005	80	2.4	0.175	215	-
3	18	Acrylonitrile	107131	107-13-1	1	-	80	2.4	0.175	30	0.54
89	102	Aldrin	309002	309-00-2	1	0.00003	80	2.4	0.175	4,670	17
102	103	alpha-BHC	319846	319-84-6	1	0.008	80	2.4	0.175	130	6.3
95	112	alpha-Endosulfan	959988	959-98-8	1	0.006	80	2.4	0.175	270	-
78	58	Anthracene	120127	120-12-7	1	0.3	80	2.4	0.175	30	-
114	1	Antimony	7440360	7440-36-0	1	0.0004	80	2.4	0.175	1	-
115	2	Arsenic	7440382	7440-38-2	Based on Safe Drinking Water Act, see sections in this document: Human Health Criteria Equations and Variables, and, Challenging Chemicals: Arsenic						
116	15	Asbestos	1332214	1332-21-4	Based on Safe Drinking Water Act, as per EPA 304(a) criteria documents.						
4	19	Benzene	71432	71-43-2	1	0.0005	80	2.4	0.175	5.2	0.055
5	59	Benzidine	92875	92-87-5	1	0.003	80	2.4	0.175	87.5	230
72	60	Benzo(a)Anthracene	56553	56-55-3	1	-	80	2.4	0.175	30	0.73
73	61	Benzo(a)Pyrene	50328	50-32-8	1	-	80	2.4	0.175	30	7.3
74	62	Benzo(b)Fluoranthene	205992	205-99-2	1	-	80	2.4	0.175	30	0.73
75	64	Benzo(k)Fluoranthene	207089	207-08-9	1	-	80	2.4	0.175	30	0.073
103	104	beta-BHC	319857	319-85-7	1	-	80	2.4	0.175	130	1.8
96	113	beta-Endosulfan	33213659	33213-65-9	1	0.006	80	2.4	0.175	270	-
18	66	Bis(2-Chloroethyl)Ether	111444	111-44-4	1	-	80	2.4	0.175	6.9	1.1
66	68	Bis(2-Ethylhexyl) Phthalate	117817	117-81-7	1	0.06	80	2.4	0.175	130	0.014
47	20	Bromoform	75252	75-25-2	1	0.03	80	2.4	0.175	3.75	0.0045
67	70	Butylbenzyl Phthalate	85687	85-68-7	1	1.3	80	2.4	0.175	414	0.0019
6	21	Carbon Tetrachloride	56235	56-23-5	1	0.004	80	2.4	0.175	18.75	0.07

PP #	NTR Chem #	Chemical Name	CAS # - 1	CAS # -2	RSC	RfD	BW	DWI	FCR	BCF	CSF
91	107	Chlordane	57749	57-74-9	1	0.0005	80	2.4	0.175	14,100	0.35
7	22	Chlorobenzene	108907	108-90-7	1	0.02	80	2.4	0.175	10.3	-
51	23	Chlorodibromomethane	124481	124-48-1	1	0.02	80	2.4	0.175	3.75	0.04
23	26	Chloroform	67663	67-66-3	1	0.01	80	2.4	0.175	3.75	-
76	73	Chrysene	218019	218-01-9	1	-	80	2.4	0.175	30	0.0073
120	6	Copper	7440508	7440-50-8	Based on Safe Drinking Water Act, as per EPA 304(a) criteria documents.						
121	14	Cyanide	57125	57-12-5	1	0.0006	80	2.4	0.175	1	-
82	74	Dibenzo (a,h) Anthracene	53703	53-70-3	1	-	80	2.4	0.175	30	7.3
48	27	Dichlorobromomethane	75274	75-27-4	1	0.003	80	2.4	0.175	3.75	0.034
90	111	Dieldrin	60571	60-57-1	1	0.00005	80	2.4	0.175	4,670	16
70	79	Diethyl Phthalate	84662	84-66-2	1	0.8	80	2.4	0.175	73	-
71	80	Dimethyl Phthalate	131113	131-11-3	1	10	80	2.4	0.175	36	-
68	81	Di-n-Butyl Phthalate	84742	84-74-2	1	0.1	80	2.4	0.175	89	-
97	114	Endosulfan Sulfate	1031078	1031-07-8	1	0.006	80	2.4	0.175	270	-
98	115	Endrin	72208	72-20-8	1	0.0003	80	2.4	0.175	3,970	-
99	116	Endrin Aldehyde	7421934	7421-93-4	1	0.0003	80	2.4	0.175	3,970	-
38	33	Ethylbenzene	100414	100-41-4	1	0.022	80	2.4	0.175	37.5	-
39	86	Fluoranthene	206440	206-44-0	1	0.04	80	2.4	0.175	1,150	-
80	87	Fluorene	86737	86-73-7	1	0.04	80	2.4	0.175	30	-
104	105	gamma-BHC (Lindane)	58899	58-89-9	1	0.0047	80	2.4	0.175	130	-
100	117	Heptachlor	76448	76-44-8	1	0.0001	80	2.4	0.175	11,200	4.1
101	118	Heptachlor Epoxide	1024573	1024-57-3	1	0.000013	80	2.4	0.175	11,200	5.5
9	88	Hexachlorobenzene	118741	118-74-1	1	0.0008	80	2.4	0.175	8,690	1.02
52	89	Hexachlorobutadiene	87683	87-68-3	1	0.0003	80	2.4	0.175	2.78	0.04
53	90	Hexachloro-cyclopentadiene	77474	77-47-4	1	0.006	80	2.4	0.175	4.34	-
12	91	Hexachloroethane	67721	67-72-1	1	0.0007	80	2.4	0.175	86.9	0.04

PP #	NTR Chem #	Chemical Name	CAS # - 1	CAS # -2	RSC	RfD	BW	DWI	FCR	BCF	CSF
83	92	Indeno (1,2,3-cd) Pyrene	193395	193-39-5	1	-	80	2.4	0.175	30	0.73
54	93	Isophorone	78591	78-59-1	1	0.2	80	2.4	0.175	4.38	0.00095
46	34	Methyl Bromide	74839	74-83-9	1	0.02	80	2.4	0.175	3.75	-
44	36	Methylene Chloride	75092	75-09-2	1	0.006	80	2.4	0.175	0.9	0.002
	8b	Methylmercury	22967926	22967-92-6	1	0.0001	80	2.4	0.175	NA	-
124	9	Nickel	7440020	7440-02-0	1	0.02	80	2.4	0.175	47	-
56	95	Nitrobenzene	98953	98-95-3	1	0.002	80	2.4	0.175	2.89	-
61	96	N-Nitrosodimethylamine	62759	62-75-9	1	-	80	2.4	0.175	0.026	51
63	97	N-Nitrosodi-n-Propylamine	621647	621-64-7	1	-	80	2.4	0.175	1.13	7
62	98	N-Nitrosodiphenylamine	86306	86-30-6	1	-	80	2.4	0.175	136	0.0049
64	53	Pentachlorophenol	87865	87-86-5	1	0.005	80	2.4	0.175	11	0.4
65	54	Phenol	108952	108-95-2	1	0.6	80	2.4	0.175	1.4	-
106-112	119	Polychlorinated Biphenyls (PCBs)	n	1336-36-3	1	-	80	2.4	0.175	31,200	2
84	100	Pyrene	129000	129-00-0	1	0.03	80	2.4	0.175	30	-
125	10	Selenium	7782492	7782-49-2	1	0.005	80	2.4	0.175	4.8	-
85	38	Tetrachloroethylene	127184	127-18-4	1	0.006	80	2.4	0.175	30.6	0.0021
127	12	Thallium	7440280	7440-28-0	1	0.000068	80	2.4	0.175	116	-
86	39	Toluene	108883	108-88-3	1	0.0097	80	2.4	0.175	10.7	-
113	120	Toxaphene	8001352	8001-35-2	1	0.00035	80	2.4	0.175	13,100	1.1
87	43	Trichloroethylene	79016	79-01-6	1	0.005	80	2.4	0.175	10.6	0.05
88	44	Vinyl Chloride	75014	75-01-4	1	0.003	80	2.4	0.175	1.17	1.5
128	13	Zinc	7440666	7440-66-6	1	0.3	80	2.4	0.175	47	-

IDAHO HUMAN HEALTH CRITERIA UPDATE JUSTIFICATION AND COMPLIANCE WITH THE CLEAN WATER ACT

I. Requirements Under the Clean Water Act and Federal Regulations

Idaho DEQ developed the human health criteria for toxic pollutants in accordance with Section 303(c) of the Clean Water Act (CWA) and the federal regulations implementing the CWA, 40 CFR Part 131.

Section 303(c)(2)(A) of the Clean Water Act (CWA) provides that state water quality standards (WQS) must consist of designated uses of navigable waters in the State and water quality criteria for such waters based upon the designated uses. The WQS must protect the public health or welfare, enhance the quality of water and serve the purposes of the CWA. In establishing WQS, States must take into consideration their use and value for public water supplies, propagation of fish and wildlife, recreational purposes and agricultural, industrial and other purposes.

Section 303(c)(2)(B) of the CWA requires States to adopt, as part of the WQS, criteria for all toxic pollutants that EPA has identified under section 307 of the CWA, and for which EPA has published recommended criteria under section 304(a), the discharge or presence of which in the affected waters could reasonably be expected to interfere with designated uses adopted by the State.

Under section 303(c)(3) of the CWA, if WQS are consistent with the minimum requirements in the CWA EPA must, within 60 days of the date of submission, approve the WQS.

The federal regulations provide more detail regarding the minimum requirements for WQS. 40 CFR 131.11 sets forth the requirements for criteria, such as the human health criteria submitted by DEQ. 40 CFR 131.11(a)(1) provides that criteria must protect the designated use, and must be based on sound science. 40 CFR 131.11(a)(2) specifically provides that criteria for toxic pollutants must be sufficient to protect designated uses.

40 CFR 131.11(b) explains that when establishing criteria, States should base numeric values on 304(a) Guidance, 304(a) Guidance modified to reflect site-specific conditions, or other scientifically defensible methods.

II. 304(a) Guidance and Supporting Documents

In 2002, EPA updated its national recommended water quality criteria, published under Section 304(a) of the CWA. The update included revised human health criteria based upon an updated national default fish consumption rate of 17.5 g/day. The 2002 revised recommended human health criteria were based upon EPA's 2000 Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (EPA-822-B-00-004, October 2000) (hereafter "2000 Methodology"). On June 29, 2015, EPA again updated recommended human health criteria based upon a number of updated exposure inputs, including an updated national default fish consumption rate of 22 g/day. The 2015 updated criteria are also based upon the 2000 Methodology.

The 2000 Methodology is intended to provide States flexibility in establishing human health criteria, and EPA strongly encourages States to use the Methodology. The 2000 Methodology also defines the factors EPA intends to use in evaluating and determining consistency of State WQS with the requirements of the CWA. (2000 Methodology p.1-1 to 1-2).

Thus, while there are other EPA publications which are relevant to the evaluation of DEQ's submission of human health criteria (some of which are cited to in this submission) the 2000 Methodology continues to be the principal basis for the 304(a) recommended criteria and EPA's review of State human health criteria submissions.

According to the 2000 Methodology, many of the decisions States must make with respect to the human health criteria are not science based decisions, but rather risk management decisions, which EPA defines as "the process of selecting the most appropriate guidance or regulatory actions by integrating the results of risk assessment with engineering data and with social, economic, and political concerns to reach a decision." (2000 Methodology p. 2-4). EPA recognizes that such risk management decisions are in many cases better made by States. (2000 Methodology p. iii).

Several of the critical decisions in deriving Idaho's human health criteria are risk management decisions, including the choice of cancer risk level and the percentage of the population's fish consumption rate to use. (2000 Methodology p. 2-4).

III. Idaho's Human Health Criteria Rulemaking

A. EPA's 2012 Disapproval

The criteria submitted to EPA today are a result of EPA's 2012 disapproval of criteria DEQ submitted to EPA for review in 2006. EPA's disapproval was based upon the assertion that DEQ did not consider several sources of information regarding local and regional fish consumption before using the national default fish consumption rate of 17.5g/day to set criteria. In its disapproval, EPA stated that in order to meet applicable requirements of the CWA, DEQ must "evaluate local and regional fish consumption information to determine

whether its statewide criteria are protective of designated uses." (May 10, 2012 EPA letter p. 3). EPA also suggested that Idaho consider undertaking a fish consumption survey. (May 10, 2012 letter p. 5).

B. DEQ's Rulemaking Process

In response to EPA's disapproval, DEQ took the actions EPA specified were needed to remedy the disapproval. DEQ evaluated existing fish consumption data, including all the data referenced by EPA in its disapproval letter. DEQ found that the existing data suggested there are likely fish consuming populations in Idaho that consume more than the national default consumption rate. DEQ also found, however, that the existing data was limited in scope for Idaho residents, old and of questionable quality. Therefore, DEQ determined, as suggested by EPA, to conduct its own fish consumption survey of Idaho residents.

In fall 2012, DEQ began a series of public meetings with stakeholders, including EPA, Idaho Tribes, industry representatives and conservation and environmental groups, to address the human health criteria. With the input from stakeholders, DEQ and its contractor designed the fish consumption survey that was then implemented with the results becoming available in June 2015.

During the period in which the data was being collected through the survey, DEQ continued to meet with stakeholders to discuss important policy decisions regarding the development of human health criteria. In all, 18 meetings were conducted between 2012 and 2015. (The DEQ human health criteria rulemaking record can be viewed at http://www.deq.idaho.gov/laws-rules-etc/deq-rulemakings/docket-no-58-0102-1201/. In addition, all rulemaking records are a part of this submission and provided on a CD.)

In addition to the Idaho fish consumption survey, EPA sponsored fish consumption surveys of the Nez Perce and Shoshone-Bannock Tribes, as well at "heritage" studies involving the Kootenai, Coeur d'Alene, Nez Perce and Shoshone-Bannock Tribes. DEQ considered the results of both the Idaho survey and the EPA surveys of the current fish consumption rate (FCR) of the Nez Perce and Shoshone-Bannock Tribes and the heritage studies in calculating human health criteria.

The human health criteria rule was adopted by the DEQ Board on December 10, 2015, and approved by the Idaho legislature during the 2016 legislative session. The rule became effective on March 25, 2016. The rule was adopted in accordance with applicable law. (Letter dated December 12, 2016 to Dan Opalski from Idaho Deputy Attorney General Douglas Conde).

IV. DEQ's Human Health Criteria and Compliance with the CWA

A. Equations Used in Calculating Criteria

The equations used by DEQ to derive the human health criteria (Idaho Human Health Criteria, Technical Support Document, December 2015, hereafter "Idaho HHC TSD") are identical to those proposed by EPA in its 2000 Methodology, and used in the 2002 and 2015 national recommended criteria. (2000 Methodology p.1-9). The equations are:

Noncancer Effects:

$$\mathbf{AWQC} = \mathbf{RfD} * \mathbf{RSC} * \left(\frac{\mathbf{BW}}{\mathbf{DI} + (\mathbf{FI} * \mathbf{BAF})}\right)$$

Cancer Effects: Linear Low-Dose Extrapolation:

$$\mathbf{AWQC} = \mathbf{RSD} * \left(\frac{\mathbf{BW}}{\mathbf{DI} + (\mathbf{FI} * \mathbf{BAF}}\right)$$

Where $\boldsymbol{RSD} = \frac{\textbf{Target Incremental Cancer Risk}}{\textbf{Cancer Potency Factor}}$

As outlined below, DEQ followed EPA's 2000 Methodology with respect to each of the inputs used in this equation.

B. Fish Consumption Rate

One of the inputs to the equations used to derive human health criteria is the FCR, which is referred to as FI in the equations. There are a number of decisions States must make with respect to the FCR. These include: use of the national default FCR or local data; what fish to include in the FCR; do you use the fish consumption data for the general population, the fish consumption data for higher consuming sub-populations, or both; and what percentile of the distribution of FCRs in the target population should be used.

1. National Default v. Local FCR Survey Data.

In the 2000 Methodology, EPA suggests a hierarchy of preference with respect to fish consumption data: (1) local data; (2) data reflecting similar geography/population groups; (3) data from national surveys; and (4) EPA's default intake rates.

In accordance with the 2000 Methodology, and as suggested by EPA in its disapproval letter, DEQ used local fish consumption data in the development of the human health criteria. DEQ used both the survey it conducted of the Idaho general population and Idaho resident anglers, and the EPA sponsored tribal surveys.

The fish consumption surveys relied upon by DEQ were peer reviewed and are scientifically and technically supported. (Idaho Fish Consumption Survey, Northwest Research Group (March 31, 2016); NCI Method Estimates of Usual Intake Distributions for Fish Consumption in Idaho (March 31, 2016). EPA has congratulated Idaho "for using state of the

art survey methodology" in its development of the human health criteria. (November 6, 2015 letter from Angela Chung to Don Essig RE: EPA Comments on Idaho's Revised Human Health Toxic Criteria, Proposed rule, Docket No.: 58-0102-1201 p. 1).

2. What Fish to Include

a. Marine Species

EPA's 2002 national recommended human health criteria were based upon a default fish consumption rate of fresh and estuarine species only; marine species of fish were not included. (2000 Methodology p. 4-25 to 4-26.) In its 2015 recommended criteria, EPA modified this approach slightly to include freshwater and nearshore (estuarine and a fraction of marine fish caught in near shore areas). (EPA Response to Scientific Views from the Public on Draft Updated National Recommended Water Quality Criteria for the Protection of Human Health (June 2015) p.17). EPA's exclusion of marine species appears to be based on the fact marine species are not within Waters of the U.S., and therefore, do not pick up pollutants from waters regulated under the CWA. (Estimated Fish Consumption Rate for the U.S. Population and Selected Subpopulations (NHANES 2003-2010) p. 13: "As marine fish are not harvested from U.S. waters for which states would be developing water quality standards, the issue of importation for these species is not relevant."; EPA Response to Comments, Revision of Certain Federal Water Quality Criteria Applicable to Washington (Docket ID: EPA-HQ-OW-2015-0174) p. 147: "A key consideration in including certain fish species in the FCR used to set water quality criteria is whether they acquire contaminants from waters under CWA jurisdiction."))

EPA treats salmon as a marine species, and therefore, in the development of its national recommended criteria, EPA largely excluded the consumption of salmon. (EPA included 4% of

salmon consumption based on data showing that 4% of salmon consumed was caught in fresh and estuarine waters.) (2000 Methodology p. 4-28 to 4-29; NHANES 2003-2010 at page 9). EPA provides, however, that States may choose to include marine species, but EPA cautions that in doing so States must adjust the relative source contribution (RSC), which takes into account exposure through consumption of marine species, so that marine species are not double counted. (2000 Methodology p. 4-25; 2013 Human Health Water Quality Criteria and Fish Consumption Rates, Frequently Asked Questions—hereafter "2013 FAQ").

In the DEQ rulemaking, EPA commented that DEQ should include salmon in the fish consumption rate because of information that, according to EPA, suggests salmon consumed in Idaho pick up some pollutant load in regional waters within the jurisdiction of the CWA and even in Idaho waters. (EPA Comments on IDEQ October 7, 2015 Proposed Rule Revisions to Idaho's Human Health Criteria for Toxics (November 6, 2015) p. 3 to 6).

In setting human health criteria, DEQ used the reported consumption of tribal group 2 fish from the Nez Perce fish consumption survey. Group 2 fish include near coastal, estuarine, freshwater and anadromous fish. This means DEQ included all salmon species, as well as tilapia and several species of marine shellfish that are not found in Idaho waters. And, DEQ used the marine species in the fish consumption rate without adjusting the RSC. DEQ also reviewed and compared the tribal group 2 fish consumption to the Idaho general population's FCR of all fish, which was the closest comparable fish group from the general population survey and includes anadromous fish. The inclusion of salmon without any adjustment to the RSC results in DEQ being more protective or conservative than the approach to the fish consumption data EPA recommends in its 2000 Methodology and other national guidance.

As explained in its Response to Comments document, DEQ used the tribal group 2 fish because of the uncertainties, raised by EPA, regarding the source of pollutants in Idaho fish[1]; because of the desire to consider local information regarding the importance of salmon consumption among Idaho tribes; and because using this more inclusive range of fish, and thus higher consumption rate, along with other conservative factors, while using a 10-5 cancer risk level, helps to ensure that DEQ criteria remain protective. (Public Comment Summary p. 10-11).

b. Market Fish

Both the 2002 and the 2015 national recommended human health criteria use the consumption of all freshwater and estuarine (and in 2015 nearshore marine) fish regardless of the source, including fish purchased at the market. EPA included market fish despite the reality that most market fish are not caught in local waters and therefore would not be affected by an individual State's human health criteria. EPA's inclusion of market fish is based upon EPA's belief that WQS should allow residents to safely consume from local waters the amount of fish they would normally consume from all fresh and estuarine (including nearshore) waters. (NHANES 2003-2010 p. 9).

DEQ used the Nez Perce FCR of tribal group 2 fish that includes near coastal, estuarine, freshwater and anadromous fish, regardless of the source. DEQ also took into consideration how this fish consumption rate compares to the general population survey results of all fish, which again includes all fish consumed regardless of the source. Therefore, in this respect, DEQ's fish consumption rate exceeds the approach recommended by EPA.

[1] DEQ believes there are remaining questions regarding the extent anadromous fish obtain pollutants within CWA jurisdictional waters, including Idaho waters.

3. What Population's Fish Consumption Data to Consider

EPA's 304(a) national recommended human health criteria are aimed at protecting the majority of the population. EPA uses a mix of median, mean and percentile estimates for the human exposure factors in the equation for deriving human health criteria, including using the 90th percentile of fish consumption of the general population. (2000 Methodology p. 2-1, 2-2). EPA also, however, encourages States to ensure that the criteria protect highly exposed populations, with the understanding that the level of consumption and therefore the level of risk will differ among populations. (2000 Methodology p. 4-25). To do so, EPA recommends States use local fish consumption data that includes both high-end consumers and the general population: "If a State or Tribe chooses values (whether the central tendency or high-end values) from studies that particularly target high-end consumers, these values should be compared to high-end fish intake rates for the general population to make sure that the high-end consumers within the general population would be protected by the chosen intake rates." (2000 Methodology p. 4-26; see also 2013 FAQ: "An analysis of protectiveness of the criteria for the general population, recreational fishers and subsistence fishers should be included in the criteria documentation.").

DEQ followed the 2000 Methodology. DEQ used Idaho specific survey results. DEQ considered the survey results for the general population in Idaho. DEQ also considered survey results for the three higher consuming subpopulations for which recent data were available: the Nez Perce Tribe, the Shoshone-Bannock Tribe and Idaho adult anglers. DEQ chose a FCR that reflects the mean FCR from the survey of Nez Perce tribal survey results (the Nez Perc tribe is the highest of the higher consuming Idaho subpopulations for which data was available) and

the 95th percentile of the general population survey results. In short, DEQ has developed criteria that take into account and protect the general population as well as high-consuming subpopulations in the State, which is exactly what the 2000 Methodology recommends.

It is important to note that DEQ has developed state-wide criteria that apply to all State waters outside tribal jurisdiction, and the Idaho population that uses those waters. For waters outside tribal jurisdiction, the tribal treaty reserved right to take fish at all usual and accustomed places is one shared in common with the rest of Idaho's population. The tribal population that has the opportunity to fish in such waters is a small part of the total population of Idaho to whom the criteria apply. (U.S. Census information for Idaho indicates American Indian and Alaska Natives represent 1.7% of the Idaho population. http://www.census.gov/quickfacts/table/PST045215/16.) [2] Therefore, in developing Idaho criteria, tribal members are clearly a subpopulation of the general population of the State of Idaho targeted by the human health criteria.

4. What Percentile of the Fish Consumption Data to Use

Choosing the percentage of the population to apply the chosen level of protection to is a risk management decision as opposed to a science-based decision. EPA in its 2000 Methodology provides States the flexibility to choose among a range of fish consumption values for a given population, from high-end values (such as the 90th or 95th percentile) to average values. (2000 Methodology p. 1-9; 2-4 and 4-26). In developing the 2002 national recommended criteria, EPA used 17.5 g/day which represents the 90th percentile of the general

[2] At the time the Idaho fish consumption survey was conducted, the Idaho adult population was 1,141,984. In contrast, according to the tribal fish consumption surveys, there were 2,727 adult Nez Perce tribal members (1,574 adult tribal members qualified to participate in the survey) and 3,242 adult Shoshone-Bannock tribal members qualified to participate in the survey.

population's fish consumption data. EPA also recognized that some States may need to consider highly exposed populations, and provided default values for sport fishers and subsistence fishers which represent the average or 50 percentile consumption values for these groups. (2000 Methodology p. 1-12, 1-13; 4-27). EPA used this same approach with respect to the 2015 national recommended criteria. (2015 EPA Response to Scientific Views from the Public p. 16). In sum, EPA in its national recommended criteria uses the 90th percentile of the general population FCR, and the 50th percentile or average for high-consuming groups such as sport and subsistence fishers.

DEQ used 66.5 g/day as the fish consumption rate. This value represents the mean (70th percentile) of the Nez Perce group 2 fish consumption rate, and approximately the 95th percentile of the Idaho general population consumption rate of all fish.[3] Thus, DEQ's fish consumption rate exceeds, i.e., is more protective than, EPA's recommended FCR because DEQ used what is comparable to the 95th percentile rather than EPA's 90th percentile of the general population FCR, and DEQ used the 70th percentile rather than EPA's average or 50th percentile of the high consumer FCR. DEQ is also 10 times more protective than EPA guidance by virtue of the fact DEQ applied a 10-5 cancer risk level for the 70th percentile of the FCR of the Nez Perce tribe rather than the 10-4 level of protection EPA allows.

As noted, EPA's national recommended criteria use the average FCR to develop default criteria for high consuming subpopulations. In developing the national recommended criteria, EPA treated subsistence fishers, such as tribal groups, as high consuming subpopulations. (2000 Methodology p. 4-25 to 4-28). EPA noted in the 2000 Methodology that its approach to

[3] The "all fish"' category is broader than the group 2 tribal fish, and therefore likely overstates the general population's consumption of group 2 fish. It was, however, the closest category of fish to the tribal group 2 fish.

high consuming subpopulations was consistent with the approach used for the Great Lakes. With respect to the Great Lakes, EPA treated high consuming tribal groups as a subpopulation of the region. Therefore, according to EPA, the tribal subpopulations were adequately protected by the mean of the high consuming population's FCR—15 g/day-- because the criteria would protect tribal members eating up to 150 g/day at a 10-4 cancer risk rate. (Water Quality Guidance for the Great Lakes System: Supplementary Information Document, EPA-820-B-95-001 (March 1995) p. 163).[4]

DEQ's treatment of Idaho Tribes is consistent with EPA's national guidance and reflects the reality that Idaho tribal members are a subpopulation of the State. DEQ's criteria do not apply to waters within tribal jurisdiction. For waters within tribal jurisdiction, tribes can obtain treatment as a State status under the CWA and develop their own WQS to protect those tribal members who harvest and consume fish from such waters. The Idaho human health criteria are aimed at protecting all residents of the State who use waters outside tribal reservations, including those tribal members who have a right in common with other Idaho residents to fish in such waters. In the context of state-wide criteria that are applied outside tribal reservations, DEQ's has correctly treated the Tribes as a higher consuming subpopulation of the State.

5. Suppression

In EPA's comments regarding DEQ's proposed human health criteria, EPA argues FCRs used by DEQ "must reasonably represent tribal subsistence consumers' practices that reflect

[4] EPA recently issued final human health criteria for the State of Washington in which EPA deviated from its own national guidance by treating Washington's tribes as the general population. EPA explained its position in a conclusory fashion by stating that because tribal members have a right in common with others in Washington to harvest fish they must be treated as something factually they are not—the general population of the State of Washington. DEQ disagrees with EPA's treatment of the tribes as reflected in the Washington rulemaking.

consumption unsuppressed by fish availability or concerns about the safety of available fish." (EPA Comments on Idaho Department of Environmental Quality's (DEQ) October 7, 2015 Proposed Rule Revisions to Idaho's Human Health Criteria for Toxics, November 6, 2015 p. 6 to7). In other words, EPA argues DEQ must predict the amount of fish Idaho residents might consume for subsistence purposes if there were more fish available, they had no concerns about the safety of fish, or other factors that currently suppress fish consumption were not present. EPA's comments in Idaho and actions in Maine and Washington indicate EPA believes States must adopt a designated use that reflects this unsuppressed level of subsistence fish harvest and consumption and then adopt criteria to protect such a use.

The CWA and EPA's implementing regulations contain nothing to suggest that States must adopt a designated use reflecting an unsuppressed fish harvest and consumption use and adopt criteria to protect such a use. Instead, States are given the choice to determine appropriate uses, as long as they protect for section 101(a) uses that include propagation of fish, shellfish and wildlife and recreation in and on the water.

Idaho WQS meet the requirements set forth in the CWA. All waters in Idaho are protected for aquatic life and recreational uses. (IDAPA 58.01.02.100). The recreational use includes fishing on or about the water. (IDAPA 58.01.02.100.02). The human health criteria based on exposure to toxins through fish consumption alone apply to waters designated for a recreation use, while criteria based on exposure to toxins through both fish consumption and drinking water intake apply to waters additionally designated for domestic water supply. (IDAPA 58.01.02.210.01).

DEQ has not adopted, and is not required to adopt, a use that is intended to protect subsistence harvest and consumption of fish at a level that existed historically before dams, population increases and other factors reduced the numbers of fish available for harvest. DEQ's recreation use is defined to include water quality appropriate for recreational uses on or about the water, including fishing. (IDAPA 58.01.02.100.03.b). No reasonable interpretation of this language suggests that Idaho has adopted a use intended to support or restore historic subsistence fish harvest levels. EPA has approved Idaho's designated uses, finding them to be consistent with the CWA and federal regulations. Therefore, DEQ has no obligation to adopt criteria to protect for some kind of unsuppressed subsistence level of fish harvest and consumption.

While States and Tribes are not required to adopt a use that reflects the return to a historic fish consumption rate, the CWA allows the States and Tribes the discretion to do more than the CWA requires. This is what the Spokane Tribe did by adopting a traditional lifestyle use and criteria to support that use. When EPA approved the Spokane Tribe's criteria, it made a point in emphasizing how this use and criteria were beyond the minimum requirements of the CWA, and therefore, needed to be judged by a different standard. (Technical Support Document for Action on the Revised Surface Water Quality Standards of the Spokane Tribes of Indians (December 11, 2013) p. 20 to 22). Thus, EPA has recognized there is no requirement under the CWA for States to adopt a use that reflects an unsuppressed or historic FCR, rather this is something a State or Tribe may choose to do.

As noted, federal law does not require DEQ adopt human health criteria based upon unsuppressed fish harvest and consumption use. In addition, the 304(a) national

recommended criteria published by EPA in 2002 and updated in 2015 are not based upon an unsuppressed fish consumption rate, but instead are based upon actual fish consumption data taken from national surveys. DEQ's development of human health criteria followed EPA's national guidance. DEQ used the best fish consumption data available based on current Idaho-specific surveys of the general population, anglers, and Idaho tribal members.

The federal regulations require criteria to be based on sound science, and in its national guidance EPA emphasizes the use of local data collected through surveys using appropriate survey methodology. Even if DEQ desired to base its human health criteria on an unsuppressed FCR it has no data that it could use. In fact, EPA has never defined what an "unsuppressed" FCR is, or how a State should determine such a FCR. EPA refers to the unsuppressed FCR as an "evolving concept."[5]

EPA did sponsor studies of Idaho tribal "heritage fish consumption" which is defined as "estimates of Tribal fish consumption during the period when Tribes had full access to their traditional fisheries". (A Fish Consumption Survey of the Nez Perce Tribe, Volume I: Heritage Fish Consumption Rates of the Nez Perce Tribe p. 7). But, the reported heritage levels do not provide a valid basis for a FCR in Idaho. First, the decline in fish consumption from the reported heritage rate is caused by a number of factors, most of which have nothing to do with water quality and can not be remedied by Idaho's human health water quality criteria. One of the principal factors contributing to a decline in tribal fish consumption is the decline of the fish population. According to the Nez Perce Heritage Study, the decline is due to commercial, recreational and subsistence fishing; habitat alteration due to urbanization, farming, logging,

[5] . Since DEQ adopted its human health criteria, EPA has proposed several methods of measuring suppression. See EPA Draft Guidance for Conducting Fish Consumption Surveys (June 2016).

and ranching; dams ; water withdrawals; hatchery production; predation by marine mammals, birds and other fish species; competition with other fish species; diseases and parasites and reduction in annual nutrient distribution. (Nez Perce Heritage Study p. 7). In addition, tribal consumption has changed because of changes in cultural practices, including changes in dietary preferences. (Nez Perce Heritage Study at page 1). The majority of these factors are unrelated to water quality.

It must also be emphasized that to the extent fish populations are reduced by poor water quality, the Idaho WQS contain separate criteria to protect aquatic life, which are not at issue here. EPA has approved DEQ's aquatic life criteria, finding them to adequately protect the aquatic life, including fish, in Idaho.

Adopting an unsuppressed FCR would conceivably protect for a future rate of fish consumption that might occur if the factors that are suppressing consumption are remedied. But, many of factors that are suppressing fish consumption from heritage levels can not reasonably be expected to change in the foreseeable future, if ever. For example, the biggest factor in a decline from heritage levels of consumption is the presence of dams that block fish migration. (Nez Perce Heritage Study p.6 to 8). It is unlikely that all the federal dams on the Columbia River system will be removed. In addition, cultural changes have occurred that are not likely to be altered going forward. In short, not only are many of the factors that affect current fish consumption unrelated to and can not be altered by water quality human health criteria, they are also things that will not likely change in the future. Therefore, heritage rates of fish consumption do not reflect any realistic projection of future consumption.

The bottom line is even if the CWA required DEQ to set human health criteria based upon an unsuppressed FCR, DEQ has no data upon which it could accurately quantify such a FCR.

While DEQ was not required to and did not attempt to calculate an unsuppressed subsistence level of fish consumption, DEQ did take into consideration the entire range of fish consumption data, that captures current subsistence fishing if any exists in Idaho. If tribal members are currently subsistence fishers, then their consumption rates were reflected in the Nez Perce and Shoshone-Bannocks surveys. As noted below in the section on cancer risk levels, DEQ's criteria adequately protects tribal consumers even at the highest levels of consumption recorded in the survey, and therefore, current subsistence fishers are also protected.

EPA should consider several other factors in connection with Idaho's human health criteria and the concept of suppression. First, DEQ does not agree that its failure to consider suppression will lead to a downward spiral wherein less stringent criteria leads to greater fish contamination and then less consumption which then triggers even less stringent criteria. History in Idaho has shown the opposite. That is, here in Idaho over the past twenty years the FCR used in criteria has actually increased three times, from 6.5 g/day in 1992 NTR, to 17.5 g/day in Idaho's 2005 update, to 66.5 g/day in the current update. This increase is consistent with national trends that show an increase in fish consumption. This nation-wide increase is reflected in EPA's increase in the national default FCR based upon nation-wide surveys as well as data compiled by the U.S. Department of Agriculture. (US Census Bureau, Statistical Abstract of the United States: 2012, 131st ed. Washington DC). To the extent criteria values are

dependent on FCRs there is no evidence a downward spiral is about to commence, in fact the evidence is quite the contrary in so far as the human health criteria are concerned.

Second, there is no basis to believe that DEQ's failure to use some kind of unsuppressed FCR will leave higher consumers at too high a risk should they ultimately be able to realize unsuppressed rates of consumption. Idaho's criteria provide a 10-5 incremental risk of cancer for someone consuming 66.5 g/day of fish. This means someone eating 665g/day would have a 10-4 incremental increase in risk. This is a level of risk that EPA considers protective. (See discussion below regarding the cancer risk rate). 665g/day greatly exceeds even the 99th percentile of current tribal fish consumption rates. DEQ has built into the criteria a margin of safety that allows for much greater fish consumption, at levels approximating heritage rates, without incurring unacceptable risk. In addition, should this future be realized, based on past criteria revision history, there is no reason to believe that criteria would not again be revised taking into account higher future consumption rates such as might result from increased availability of fish to be harvested and consumed. Indeed, Idaho is required by the CWA to review its WQS every three years and therefore will have an opportunity to update criteria as necessary.

In summary, Idaho's FCR of 66.5 g/day based on current fish consumption rates is protective today, and into the future. No downward spiral in human health criteria is evident; in fact quite the opposite is true, as the FCR factor used to derive Idaho's human health criteria has increased each time DEQ has revised the criteria.

C. Cancer Risk Level

For pollutants that are carcinogens, the equation for developing human health criteria includes the increased likelihood of developing cancer. This likelihood is expressed as a probability, such as one in one million (1x10-6).

In the 2000 Methodology, EPA provides that States have the choice of using a cancer risk level of either 10-6 or 10-5 for the general population as long as highly exposed populations do not exceed a 10-4 risk level. (2000 Methodology at page 2-6).

The acceptance of this range of cancer risk is a long-standing EPA policy. See, e.g., National Toxics Rule, 57 FR 60848-01 (1992); Final Water Quality Guidance for the Great Lakes System, 60 FR 15366 (1995). See also, Idaho Fish Consumption Rate and Human Health Water Quality Criteria—Discussion Paper#7, Risk Management and Protection of Human Health and the material cited therein. As EPA explained with respect to its guidance for the Great Lakes: "The choice of 10-5 risk level was recommended by the Initiative Committees and is within a range of risk levels (i.e., 10-4 to 10-6) that EPA considers to be adequately protective and which EPA has historically considered acceptable in making regulatory decisions. The majority of the Great Lakes States traditionally have used 10-5 risk level in setting their water quality criteria." (Water Quality Guidance for the Great Lakes System: Supplementary Information Document, EPA-820-B-95-001 (March 1995) at page 151).

As reflected in EPA's policy, the risk among population groups that consume different amounts of fish will always vary and can never be equalized. EPA explains this in the 2000 Methodology at page 2-7: "When these exposure parameter values change, so does the relative risk. For a criterion derived on the basis of a cancer risk level of 10^{-6}, individuals

consuming up to 10 times the assumed fish intake rate would not exceed a 10^{-5} risk level. Similarly, individuals consuming up to 100 times the assumed rate would not exceed a 10^{-4} risk level. Thus, for a criterion based on EPA's default fish intake rate (17.5 gm/day) and a risk level of 10^{-6}, those consuming a pound per day (i.e., 454 grams/day) would potentially experience between a 10^{-5} and a 10^{-4} risk level (closer to a 10^{-5} risk level). (Note: Fish consumers of up to 1,750 gm/day would not exceed the 10^{-4} risk level). If a criterion were based on high-end intake rates and the relative risk of 10^{-6}, then an average fish consumer would be protected at a cancer risk level of approximately 10^{-8}. **The point is that the risks for different population groups are not the same.**" (emphasis added).

The inherent variation in risk associated with different fish consumption patterns is also emphasized by EPA with respect to the Great Lakes guidance: "Obviously, as long as there is variability in fish consumption patterns among various segments of the population, it would be impossible for EPA to ensure that all groups would face identical risk from consuming fish. Therefore, EPA has sought to ensure that, after attainment of water quality criteria in ambient waters, no group is subject to increased cancer risks greater than the risk range that the EPA has long considered protective." (Water Quality Guidance for the Great Lakes System: Supplementary Information Document, EPA-820-B-95-001 (March 1995) at page 164).

EPA guidance allows States flexibility in choosing a CRL, and ultimately EPA recognizes that "[t]he choice of an acceptable cancer risk by a State or Tribe is a risk management decision." (2000 Methodology at page 2-4).

DEQ made the risk management decision to use a cancer risk level of 10-5, along with a FCR of 66.5 g/day. This choice was based upon (1) the risk level being within the range that is

considered protective of both the general population and more highly exposed subpopulations; (2) an assessment of the overall protectiveness provided by the criteria, taking into account all the inputs; (3) a view towards developing criteria that are not only protective, but reasonably achievable; and (4) consistency with longstanding EPA guidance. As EPA did with respect to its national recommended criteria, DEQ "has selected parameter values using its best judgment regarding the overall protection afforded by the resulting AWQC when all parameters are combined." (2000 Methodology p. 1-9). DEQ took into consideration the protective nature--in many instances more protective than EPA guidance suggests--of including anadromous fish in the FCR, including market fish in the FCR, not adjusting the RSC, using the 95 percentile of general population and 70th percentile of the highest consuming population's fish consumption data, using the latest bioaccumulation factors (BAFs) and toxicological information, using only consumers of fish in the FCR distribution and employing EPA's recommended drinking water intake and body weight inputs. Given the very conservative nature of all of these inputs, it was reasonable, as a risk management decision, to choose a cancer risk level which is still protective but which is somewhat higher than what was used in the past by DEQ in its human health criteria.[6]

This risk management decision is consistent with EPA policy. First, the general population is protected at a 10-5 risk level. The 66.5 g/day FCR used is approximately the 95th percentile of the general population's consumption of all fish, and therefore, protects a higher percentage of the Idaho general population at the 10-5 level than EPA recommends in its

[6] DEQ's prior human health criteria used a CRL of 10-6. At the time the prior criteria were adopted, DEQ did not have sufficient Idaho specific fish consumption information and used the national default fish consumption rate that largely excluded the consumption of salmon. Idaho has now included salmon in its FCR, calculated using Idaho-specific fish consumption information, without adjusting the RSC and has used other very conservative inputs that warrant the CRL currently used.

national guidance (EPA recommends using either 10-6 or 10-5 and the 90th percentile of the general population FCR. 2000 Methodology p. 2-6; 4-25 to 4-28).

Second, survey results indicate the Nez Perce Tribe FCR is the highest of the higher consuming populations in Idaho for which data is available. Under the criteria DEQ has developed, the Nez Perce Tribe is protected at a 10-5 level using their mean FCR that reflects about the 70th percentile of tribal fish consumption. This means that 70% of tribal fish consumers are protected at this risk level or better. In order to exceed the 10-4 risk level, a tribal member would have to consume more than 665 g/day of fish, all at criteria level of contamination. The Nez Perce survey indicates that the 95th percentile of fish consumption is 234 g/day. While the survey did not report percentiles for higher fish consumption rates, given the numbers reported, DEQ estimates that the 99th percentile of tribal fish consumption is approximately 360 g/day. Thus, it is reasonable to conclude that 99 percent of the higher consuming population in Idaho consumes considerably less fish than the amount that would expose them to an unacceptable risk. EPA conducts an identical comparison of risks and consumption rates to justify using 10-5 cancer risk level in its guidance for the Great Lakes. (Water Quality Guidance for the Great Lakes System: Supplementary Information Document, EPA-820-B-95-001 (March 1995) p. 163).

In sum, DEQ's cancer risk level protects the general population and more highly exposed subpopulations within Idaho at acceptable levels. It is consistent with longstanding EPA 304(a) guidance, and in conjunction with the other exposure factors, results in criteria protective of Idaho's designated uses and meets the requirements of the CWA.

D. Body Weight and Drinking Water Intake

In its 2015 national recommended human health criteria, EPA used a body weight of 80 kg, and a drinking water intake of 2.4 L/day.

DEQ used the EPA drinking water intake value of 2.4 L/day. The Idaho fish consumption survey indicated a mean body weight of 80 kg. As this closely matched the value used by EPA in its national recommended criteria, this is the value DEQ used. (Idaho Human Health Criteria, Technical Support Document p. 4).

E. Bioaccumulation Rate

In its 2015 national recommended human health criteria, EPA used BAFs which account for chemical accumulation in aquatic organisms from all potential exposure routes.

Where available, DEQ used BAFs derived by EPA for its 2015 national recommended criteria. (Idaho Human Health Criteria, Technical Support Document at p. 2 to 4).

F. Toxicity Values

DEQ used the toxicity values, reference dose and risk-specific dose, recommended by EPA in its 2015 national recommended criteria. (Idaho Human Health Criteria, Technical Support Document).

G. Downstream Protection

40 CFR 131.10(b) provides: "In designating uses of a water body and the appropriate criteria for those uses, the State shall take into consideration the water quality standards of downstream waters and shall ensure that its water quality standards provide for the attainment and maintenance of the water quality standards of downstream waters."

According to EPA, this language does not require States adopt identical or uniform criteria: "The regulations do not compel states to adopt the same criteria and uses, nor do they suggest that this is the only way a state can meet these requirements. The water quality program is structured to provide state with flexibility to determine the best way to meet their obligations under 131.10(b)." (Letter from EPA to Maxine Lipeles, J.D. dated June 25, 2004; EPA Response to Comments, Revision of Certain Federal Water Quality Criteria Applicable to Washington (Docket ID: EPA-HQ-OW-2015-0174) p. 254).

Consistent with EPA's interpretation of 40 CFR 131.10(b), EPA has recommended States include a narrative downstream protection provision in the WQS, and has provided templates for such narrative provisions. (Templates for Narrative Downstream Protection Criteria in State Water Quality Standards (EPA Publication No. 820-F-14-002).

DEQ used one of the templates recommended by EPA. This can be found in the Idaho WQS at 58.01.02.070.08. This section reads as follows: "All waters shall maintain a level of water quality at their pour point into downstream waters that provides for the attainment and maintenance of water quality standards of those downstream waters, including water of another state or tribe." Therefore, DEQ has met its obligation under the federal regulations with respect to downstream protection.

Notwithstanding the fact that DEQ has followed EPA's national guidance, and in fact has used EPA's suggested language in its WQS, EPA urges Idaho to adopt human health criteria based on the same FCR used in Oregon and Washington, which EPA argues is necessary to afford protection to downstream waters. DEQ does not agree that using a FCR identical to

Oregon and Washington is required or would even ensure attainment of downstream standards. A uniform FCR alone does not guarantee uniform criteria.

First, the FCR is just one of a number of input values used in determining human health criteria. Therefore, using the same FCR alone does not necessarily result in identical criteria or ensure compliance with downstream human health criteria.

Second, EPA emphasizes in its national guidance the need to use local fish consumption data. More specifically, EPA in its 2012 disapproval directed DEQ consider local data in order to remedy the disapproval. Idaho used Idaho-specific data from surveys of the general population, anglers and Idaho tribes. Idaho as an inland State presents different fish harvest and consumption opportunities and patterns than Washington and Oregon, both coastal states, and the Idaho data reflect the differences. Simply picking the FCR used in Washington or Oregon would mean ignoring the Idaho specific data and differences in fishery resources.

Third, attempting to adopt criteria identical to Washington and Oregon was and is impossible. Washington's human health criteria were in a state of flux at the time DEQ adopted its human health criteria in December of 2015. Oregon's human health criteria are based on a different set of inputs than the inputs used in Idaho's current proposal. Idaho used EPA's latest national recommendations for bioaccumulation, relative source contribution, toxicity, body weight, drinking water intake, whereas Oregon's criteria are not based on these latest EPA recommendations. Unless Idaho ignores EPA's latest recommendations, it could not have identical criteria to Oregon.

Fourth, rather than focusing on the FCR alone, it is more important to look at the protectiveness of the actual criteria. A comparison of actual criteria (rather than just one of the

input factors) reveals some of Idaho's proposed criteria are lower in value than Oregon's, while others are higher. This mismatch is likely to always be the case, or at least often so, as adjacent sates update their criteria on different schedules and with different information and policy decisions each time.

Figures x1 and X2 compare the Idaho and Oregon criteria for fish + water exposure and fish only exposure respectively. In these figures the diagonal lines represents unity, criteria that are the same value in both states would fall on this line. Points above the line reflect a criterion that is higher (less stringent) in Oregon than in Idaho, below the line vice versa. Two things are immediately apparent. First, despite Idaho's FCR of 66.5 g/day being little more than one third of Oregon's 175g/day, many of the Oregon Criteria are less stringent than in Idaho. Second, there is also quite a spread in the criteria values about and below the line, orders of magnitude differences in criteria between the two states, cutting both ways.

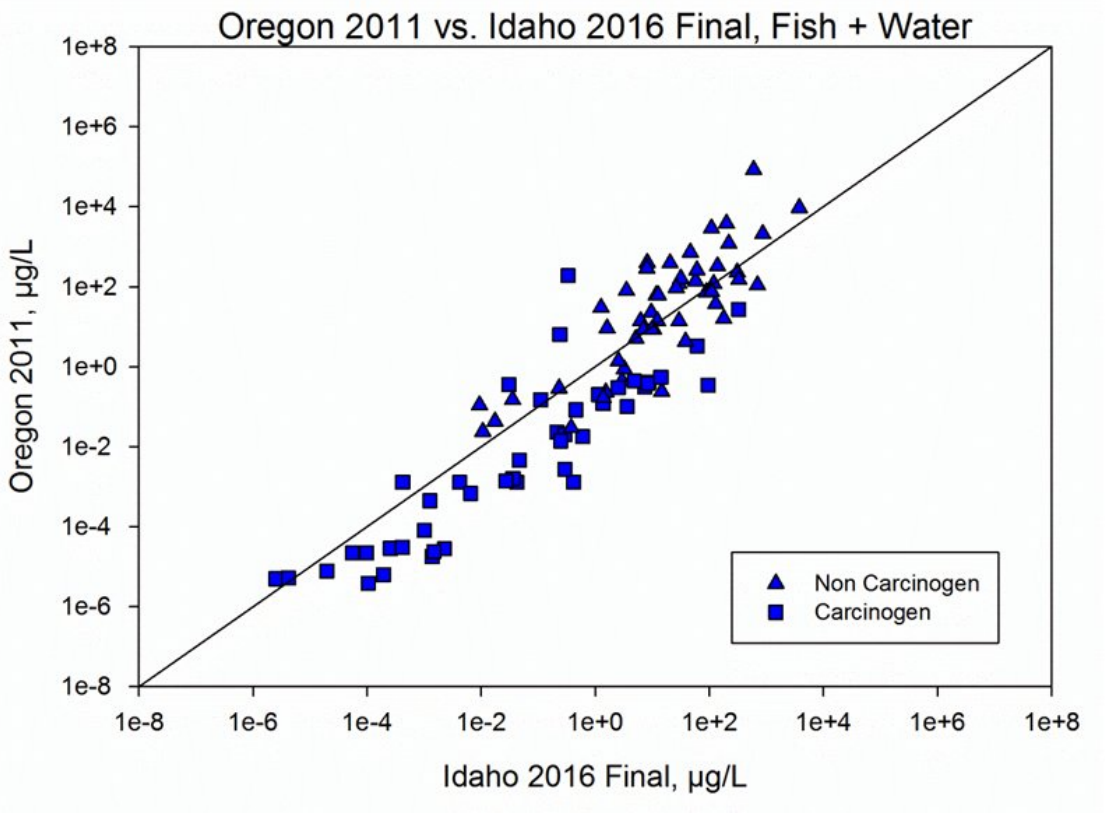

Figure x1. Comparison of Idaho's 2016 human health criteria to Oregon's 2011 criteria for exposure due to fish consumption and drinking water intake.

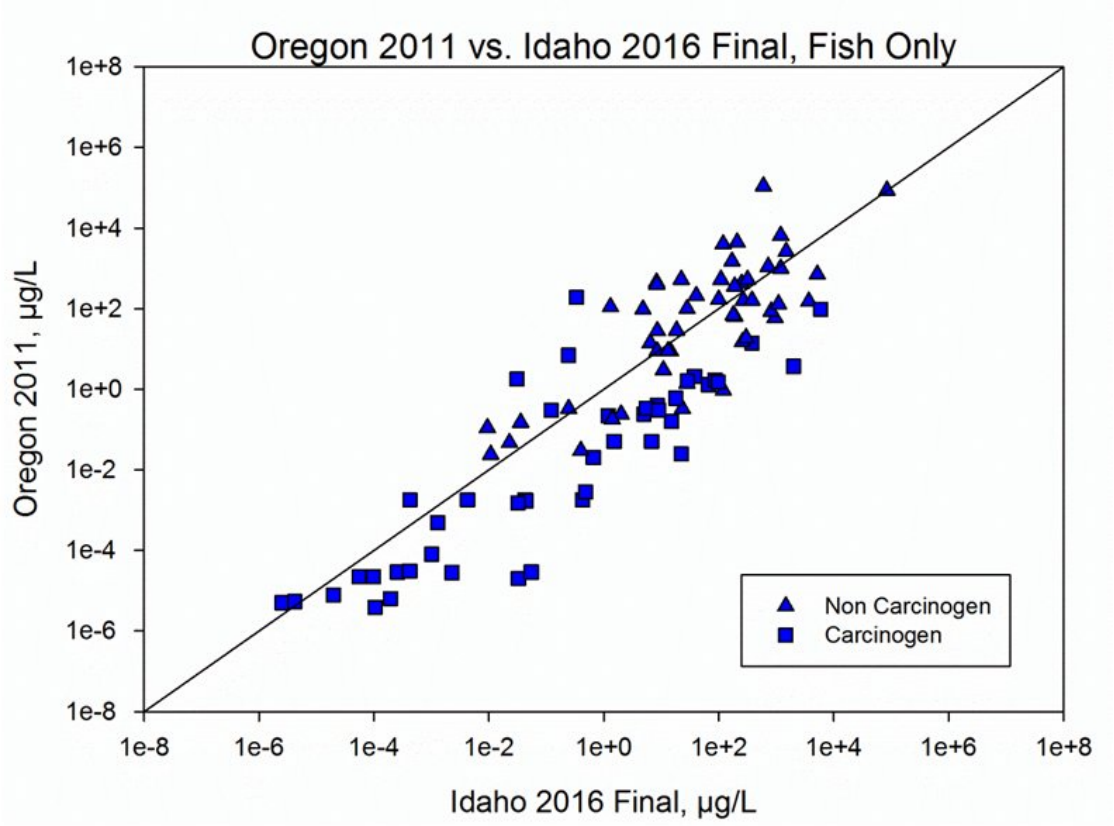

Figure x2. Comparison of Idaho's 2016 human health criteria to Oregon's 2011 for exposure due to fish consumption only.

Fifth, as EPA has provided in its national guidance, uniform criteria across jurisdictional boundaries is not needed to provide downstream protection. Implementing Idaho's narrative downstream protection provision through discharge permits and TMDLs is a more direct and effective means of ensuring downstream protection.

H. Tribal Treaties

EPA in its comments on Idaho's proposed human health criteria states that tribal treaty provisions that reserve to the tribes the right to take fish at all usual and accustomed places in common with Idaho citizens require that Idaho's criteria protect tribal subsistence consumption unsuppressed by fish availability or concerns about the safety of available fish. According to

EPA the treaty reserved fishing rights also require DEQ treat the tribes as the general population of Idaho.

DEQ disagrees with EPA's interpretation of the treaties and the manner in which EPA reads the treaties in conjunction with the requirements of the CWA. In this regard, DEQ requests EPA consider DEQ's response to comments set forth in DEQ's Public Comment Summary.

DEQ particularly disagrees with EPA's view that tribal reserved fishing rights require Idaho to do more than what is already required by the CWA. Under the CWA, human health criteria must protect designated uses. In Idaho, this includes recreational uses that include fishing. This means the criteria must provide a level of water quality that allows the safe consumption of fish taken in Idaho waters. DEQ met the CWA requirements. DEQ specifically considered and used Idaho tribal fish consumption data, and set criteria that ensure tribal consumers, even those consuming fish at the highest levels reported by the tribal surveys, are protected within the range EPA considers safe.

As set out in DEQ's response to comments during the rulemaking, there is no legal basis for EPA's position with respect to tribal treaties. To the extent, however, that the treaties include an implied right to water quality that is relevant to setting human health criteria, any such right would be satisfied by ensuring tribal fish consumers taking fish pursuant to reserved treaty rights are adequately protected. DEQ has done just that.

V. Conclusion

DEQ's human health criteria meet the requirements of the CWA and federal implementing regulations and must be approved by EPA. The criteria protect designated uses

and are based on sound science. DEQ used 304(a) guidance modified to reflect site-specific conditions. The criteria are consistent with EPA national guidance as reflected in the 2000 Methodology and other national guidance documents. DEQ also took those actions EPA specified were needed to remedy the 2012 disapproval of DEQ's criteria.

The 2000 Methodology defines the factors that will produce human health criteria that meet the requirements of the CWA and federal implementing regulations. Therefore, EPA uses the 2000 Methodology in its review of State human health criteria. (2000 Methodology p. 1-1 to 1-2). Each factor DEQ used in developing its human health criteria meets or exceeds the recommendations set out in the 2000 Methodology.

1. DEQ used the equations to develop the human health criteria set out in the 2000 Methodology and used by EPA in developing its 304(a) national recommended criteria.
2. In accordance with the actions EPA specified were needed to remedy its 2012 disapproval of Idaho's human health criteria, and consistent with EPA's 2000 Methodology, DEQ used local fish consumption information. DEQ used fish consumption information from surveys, conducted using state-of-the-art methodology, of the Idaho general population, Idaho anglers and tribal populations. DEQ also considered heritage studies funded by EPA.
3. DEQ included marine species and market fish in its FCR without adjusting the RSC. Therefore, DEQ was more protective than the approach recommended by EPA in the 2000 Methodology and other national guidance.

4. DEQ considered the FCR of both the general population and higher consuming populations as recommended by EPA in its 2000 Methodology and other national guidance.
5. DEQ used a FCR that reflects at least the 95th percentile of the general population's fish consumption and the 70th percentile of the highest consuming subpopulation's fish consumption. The use of these values is more protective than the values recommended in the 2000 Methodology and used in the development of EPA's 304(a) national recommended criteria.
6. DEQ used an incremental cancer risk level (CRL) of 10-5, which is within the risk range recommended by EPA in its 2000 Methodology and other national guidance. Also consistent with EPA recommendations, DEQ's human health criteria protects the highest consuming subpopulation at better than a 10-4 CRL.
7. The body weight, drinking water intake, bioaccumulation rate and toxicity factors all reflect EPA's latest recommended values from the 2015 EPA 304(a) national recommended criteria.
8. DEQ included a downstream protection provision that mirrors language recommended by EPA.

As outlined above, DEQ used each of the factors EPA has determined are based on sound science and will produce criteria that are protective of human health and meet the requirements of the CWA. Therefore, the DEQ criteria must be approved. DEQ did not, however, adjust the criteria to reflect the concept of an historic subsistence harvest and consumption use. Such a use, and criteria to protect such a use, are not required by the CWA,

implementing federal regulations or the 2000 Methodology. In addition, to the extent the Idaho tribal treaties include an implied right to water quality that is relevant to human health criteria (which DEQ does not believe exists) that right to water quality is satisfied by the Idaho human health criteria because the criteria ensure tribal consumers, even those consuming fish at the highest levels reported by the tribal surveys, are protected within the range EPA considers safe.

VI. Documents to be Considered

All documents listed below are hereby incorporated by reference as a part of DEQ's submission of its revised Water Quality Standards and must be considered by EPA in its review of the revised standards. Links to documents are provided where available. The documents are also provided on a CD.

(1) All documents included on DEQ's website for this rulemaking docket. The documents are available at http://www.deq.idaho.gov/laws-rules-etc/deq-rulemakings/docket-no-58-0102-1201/.

(2) Joint Stipulations and Agreement Regarding Certain Documents, Maine v. McCarthy, Civil Action No: 1:14-cv-264-JDL, May 18, 2016.

(3) Proposal of Certain Federal Water Quality Standards Applicable to Maine, 81 FR 23239, April 20, 2016.

(4) Memorandum from Gina McCarthy to All EPA Employees, Subject: Commemorating the 30th Anniversary of the EPA's Indian Policy, December 1, 2014.

(5) Letter to Erica Fleisig, Office of Water, Standard and Health Protection Division, United States Environmental Protection Agency, with comments submitted on behalf of the Northwest Pulp & Paper Association and other entities re: Revision of Certain Federal Water Quality Criteria Applicable to Washington, dated December 18, 2015, and all attachments to these comments, EPA Docket ID No.: EPA-HQ-OW-2015-0174.

(6) *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)*, United States Environmental Protection Agency, EPA-822-B-00-004, October 2000.

(7) Letter from Michael Bussell, Director Office of Water and Watersheds, United States Environmental Protection Agency, Region 10 to Barry Burnell, Water Quality Division Administrator, Department of Environmental Quality, May 10, 2012.

(8) *Idaho Human Health Criteria*, Technical Support Document, State of Idaho, Department of Environmental Quality, December 2015.

(9) Dennis W. Buckman, PhD, Ruth Parsons, BA and Lisa Kahle, *NCI Method Estimates of Usual Intake Distributions for Fish Consumption in Idaho*, Information Management Services, Inc., March 31, 2016.

(10) Letter from Angela Chung, United States Environmental Protection Agency to Don Essig, Idaho Department of Environmental Quality, re EPA Comments on Idaho's Revised Human Health Toxic Criteria, Proposed rule, Docket No. 58-0102-1201, November 6, 2015.

(11) *EPA Response to Scientific Views from the Public on Draft Updated National Recommended Water Quality Criteria for the Protection of Human Health*, Docket ID No. EPA-HQ-OW-2014-0135, United States Environmental Protection Agency, June 2015.

(12) *Estimated Fish Consumption Rate for the U.S. Population and Selected Subpopulations (NHANES 2003-2010)*, EPA-820-R-14-002, United States Environmental Protection Agency, April 2014.

(13) *Human Health Ambient Water Quality Criteria and Fish Consumption Rates: Frequently Asked Questions,* United States Environmental Protection Agency, January 18, 2013.

(14) Letter to The Honorable Rudy Peone, Spokane Tribe of Indians from Daniel D. Opalski, Director, Office of Water and Watersheds, United States Environmental Protection Agency dated December 19 2013 re attached *Technical Support Document for Action on the Revised Surface Water Quality Standards of the Spokane Tribe of Indians Submitted April 2010*, December 11, 2013.

(15) Nayak L. Polissar, PhD, Anthony Salisbury, Callie Ridolfi, MS, MBA, Kristin Callahan, MS, Moni Neradilek, MS, Daniel S. Hippe, MS and William H. Beckley, MS, *A Fish Consumption Survey of the Nez Perce Tribe,* The Mountain-Whisper-Light Statistics Pacific Market Research Ridolfi, Inc., September 30, 2015.

(16) *Water Quality Guidance for the Great Lakes System: Supplementary Information Document (SID)*, United States Environmental Protection Agency, EPA-820-B-95-001, March 1995.

(17) *Idaho Fish Consumption Rate and human Health Water Quality Criteria – Discussion Paper #7*, Idaho Department of Environmental Quality, December 2014.

(18) Letter from Benjamin H. Grumbles, Acting Assistant Administrator, United States Environmental Protection Agency to Maxine I. Lipeles, J.D., Director, Interdisciplinary Environmental Clinic re letter of February 25, 2003,dated June 25, 2004.

(19) *Templates for Narrative Downstream Protection Criteria in State Water Quality Standards*, EPA Publication No. 820-F-14-002, United States Environmental Protection Agency

(20) West, J.E., S.M. O'Neill, and G.M. Ylitalo. 2008. *Spatial extent, magnitude, and patterns of persistent organochlorine pollutants in Pacific herring (Clupea pallasi) populations in the Puget Sound (USA) and the Strait of Georgia (Canada)*. Science of The Total Environment 394:369-378.

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(25) Letter from Paul Wiegand, Vice President, Water Resources & Director, Northern and Western Regions, NCASI to Alex LaBeau, President, Idaho Association of Commerce and Industry (November 2, 2016).

(26) *Life History Factors for Pacific Salmon* (02-13-2015).

(27) *Preliminary Evaluation of the Lo and GOBAS (2015) In-Migration Model*, Arcadis Design & Consultancy, November 2016.

(28) *An Evaluation of the Protectiveness of Idaho's December 2015 Proposed Surface Water Quality Criteria*, Arcadis Design & Consultancy, November 2016.

(29) Jeff Louch, Vickie Tatum & Paul Wiegand, NCASI, Inc. Ellen Ebert, Integral Corp., and Kevin Connor & Paul Anderson, ARCADIS-US, *A Review of Methods for Deriving Human Health-Based Water Quality Criteria with Consideration of Protectiveness*, ARCADIS-US, August 2012.

(30) Vickie Tatum, Paul Wiegand, Steve Stratton, Jeffrey Louch, Ellen Ebert & Paul Anderson, *Derivation of Human Health-Based Ambient Water Quality Criteria: A Consideration of Conservatism and Protectiveness Goals*, Integr Environ Assess Manag, 9999; 1-8 (2014).

(31) *Treatment Technology Review and Assessment*, HDR, Inc., December 4, 2013.

(32) National Center for Health Statistics, *Your Chances of Dying*.

(33) Paul Anderson, Michele Buonanduci & Kate Sellers, *Acceptable Risk: Who are we protecting and did we mean to?*, Arcadis Design & Consultancy, October 20, 2015.

(34) Norman D. Forsberg, Dave Stone, Anna Harding, Barbara Harper, Stuart Harris, Melissa M. Matzke, Andres Cardenas, Katrina M. Waters, and Kim A. Anderson, *Effect of Native*

American Fish Smoking Methods on Dietary Exposure to Polycyclic Aromatic Hydrocarbons and Possible Risks to Human Health, Journal of Agricultural and Food Chemistry, 2012 at A-H.

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(36) *Comparative Risks of Multiple Chemical Exposures, Final Report for the Legislative Commission on Minnesota Resources*, Minnesota Department of Health, July 2000.

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(41) *Fish Consumption Rates Used in Human Health Criteria Calculations*, Washington State Department of Ecology, September 9, 2013.

(42) James Tupper and Bradford Doll, *Water Quality Risk Policy for the Protection of Human Health*, Tupper Mack Wells PLLC, September 18, 2013.

(43) *Draft Guidance for Conducting Fish Consumption Surveys,* Environmental Protection Agency, June 2016.

(44) Idaho QuickFacts from the US Census Bureau at: http://www.census.gov/quickfacts/table/PST045215/16.

(45) *Revision of Certain Federal Water Quality Criteria Applicable to Washington*, 81 FR 85417-01 (November 28, 2016).

(46) Water Quality Standards; Establishment of Numeric Criteria for Priority Toxic Pollutants; States' Compliance, 57 FR 60848-01.

(47) *Final Water Quality Guidance for the Great Lakes System*, 60 FR 15366 (1995).

(48) Response to Comments, Revision of Certain Federal Water Quality Criteria Applicable to Washington, United States Environmental Protection Agecy, Docket ID No.: EPA-HQ-OW-2015-0174.

(49) *Idaho Fish Consumption Survey,* Northwest Research Group, LLC, March 31, 2016.

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