NATURAL RESOURCES DEFENSE COUNCIL
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ENVIRONMENTAL WORKING GROUP
IMPROVING KIDS' ENVIRONMENT

October 17, 2014 (REVISED FROM VERSION FILED October 16, 2014)

Dr. Dennis Keefe
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Re: Petition seeking amended food additive regulation to remove FDA's approval at 21 C.F.R. § 176.170 of the use of long-chain perfluorocarboxylate oil and grease repellents in paper and paperboard - Pre-Notification Consultation 1417 (PNC 1417)

Dear Dr. Keefe:

In 2010, the U.S. Food and Drug Administration's (FDA) food additives toxicologists concluded that, in animal studies, long-chain perfluorinated compounds adversely affect fetal and newborn development and that one group of these compounds, long-chain perfluorocarboxylates[1], adversely affect the male, and, possibly the female, reproductive systems.[2] A 'long-chain' means the compound has eight or more carbons ("≥ C8") connected together and the carbons are saturated with fluorine atoms. As the chain lengthens, FDA's toxicologists noted that the chemical's biopersistence, and hence potency, in the human body increases.[3] These findings on long-chain perfluorocarboxylates expand on the toxicologist's 2007 conclusion that carcinogenicity was a concern for chemicals that were structurally similar to the perfluorooctanoic acid (PFOA).[4]

The agency's food additive toxicologists stated that "[d]ue to the considerable uncertainties remaining regarding the toxic effects of perfluorinated compounds as a class in humans, significant questions remain regarding the safe levels of dietary exposure to ≥ C8 perfluorinated

[1] Including chemicals that may be converted to perfluorocarboxylates.
[2] FDA Memo from Toxicology Group I to Regulatory Group 2 on September 30, 2010 at page 34-35.
[3] *Ibid*., p. 34-35.
[4] *Ibid*., p. 1.

compound such that additional testing is recommended to ensure safety."[5] In other words, without additional testing, there was no longer a reasonable certainty of no harm from the intended uses of the long-chain perfluorinated compounds.

Based on this conclusion, FDA took the unprecedented step of asking three companies with effective Food Contact Substance notifications (FCN) for perfluorocarboxylates to cease their sale and distribution in the United States.[6] In 2011, all three voluntarily agreed.[7]

Despite this important step, three classes of long-chain chemicals that are likely to be converted to perfluorocarboxylates[8] continue to be allowed to be used in paper and paperboard under FDA's indirect food additive regulations at 21 C.F.R. § 176.170(a)(5). Table 1 and Appendix 2 provide details for each class.

Table 1: Three classes of long-chain perfluorocarboxylates that NRDC is requesting FDA to remove from 21 C.F.R. § 176.170

Class	Description of indirect additive[a]	Company Requesting Approval	Year Approved	Max. Estimated Exposure[b]
1	Diethanolamine salts of mono- and bis (1*H*,1*H*,2*H*,2*H* perfluoroalkyl) phosphates where the alkyl group is even-numbered in the range C8-C18 and the salts have a fluorine content of 52.4% to 54.4% as determined on a solids basis	DuPont	1967	0.013 mg / person / day
2	Pentanoic acid, 4,4-bis [(*gamma-omega*-perfluoro-C8-20-alkyl)thio] derivatives, compounds with diethanolamine (CAS Reg. No. 71608-61-2)	Ciba-Geigy[c] (now BASF)	1983	0.05 mg / person / day
3	Perfluoroalkyl substituted phosphate ester acids, ammonium salts formed by the reaction of 2,2-bis[([gamma], [omega]-perfluoro C4-20 alkylthio) methyl]-1,3-propanediol, polyphosphoric acid and ammonium hydroxide	Ciba-Geigy[c] (now BASF)	1996 & 1997	0.13 mg / person / day

[a] See Appendix 2 for details on each class.
[b] See Appendix 3.
[c] Ciba-Geigy transferred this business to Ciba Specialty Chemicals in 1996. BASF purchased it in 2008.

Because the agency did not follow-up its initiative on the above mentioned FCNs by taking the critical next step of revoking these approvals made decades earlier, any company, even those not

[5] *Ibid*., p. 36.
[6] See Appendix 6 for a description of the seven FCNs.
[7] *Ibid*.
[8] For convenience, we refer to chemicals that are likely to be converted to perfluorocarboxylates as part of the class of perfluorocarboxylates.

requesting FDA's approval, can continue using the chemicals listed on Table 1in pizza boxes, sandwich wrappers, and other food packaging without FDA's or the public's knowledge. While the shutdown of domestic production of these chemicals has minimized their use and most food product manufacturers may no longer rely on them, new overseas production in China and India could easily fill the void without FDA's knowledge.

After reviewing the literature[9] published since FDA reached its conclusions that there was insufficient scientific data supporting the safety of long-chain perfluorocarboxylates, the Natural Resources Defense Council (NRDC) found that the evidence of adverse health effects caused by these chemicals has only strengthened since 2010. We identified 10 additional animal studies, an epidemiological study and three systematic reviews that were published between 2009 and 2014. All supported FDA's toxicology conclusions that significant gaps remain in our knowledge of the safety of long-chain perfluorocarboxylates regarding pre-natal and post-natal developmental toxicity endpoints, reproductive health and function in males, and reproductive health in females. Particularly compelling were
1) A systematic, objective and transparent review of the scientific literature on PFOA concluding that there is sufficient human evidence that developmental exposure to PFOA reduces fetal growth;[10] and
2) The U.S. Environmental Protection Agency's (EPA) draft comprehensive analysis[11] of the health effects of PFOA released in February 2014. EPA's draft report established a reference dose[12] of 0.00002 mg PFOA per kg of body weight per day (mg/kg-bw/day). For comparison, a 60 kg adult consuming 3 kg of food a day and the maximum exposure estimates listed in Table 1 would have an Estimated Daily Intake (EDI) for the three classes of additives would range from 0.00022 to 0.0022 mg/kg-bw/day – 10 to 100 times greater than EPA's draft Reference Dose for PFOA.

We understand that PFOA may be only a small component in the three classes of perfluorocarboxylates in Table 1 and the chemicals may not be readily metabolized to PFOA in the body. However, they are structurally similar, leading us to conclude that the FDA's concerns about the health effects of PFOA in 2010 also apply to the three classes of chemicals mentioned above. Therefore, perfluorocarboxylates are:

- Likely to adversely affect fetal and neonatal development;
- Likely to adversely affect the male, and, possibly the female, reproductive systems; and
- Likely to cause cancer.

[9] See Appendix 4 and 5 for review.
[10] Johnson PI et al. The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Systematic Review of Human Evidence for PFOA Effects on Fetal Growth. 2014. *Environmental Health Perspectives* 122:1028-1039. http://dx.doi.org/10.1289/ehp.1307893
[11] EPA, External Peer Review of EPA's Draft Health Effects Documents for Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS), http://peerreview.versar.com/epa/pfoa/. (Accessed March 17, 2014). The two documents are "Health Effects Document for Perfluorooctanoic Acid (PFOA)" (EPA Doc. No. 822R14001) and "Health Effects Document for Perfluorooctane Sulfonate (PFOS)" (EPA Doc No. 822R14002) (2014).
[12] For dietary exposures, a reference dose is developed in a manner consistent with FDA's Acceptable Daily Intake or ADI.

These effects are even more significant because these chemicals, like PFOA, are likely to persist in the human body in ways not fully understood decades ago when FDA made its original safety decisions to approve the use of these chemicals.

Given the dearth of toxicology studies on these three classes of chemicals, without evidence showing that these chemicals impact the human body differently than PFOA, there is no longer "a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use" as required by the FFDCA and 21 C.F.R. Parts 170 and 171. In other words, the uses allowed by the rule are not safe per 21 C.F.R. § 170.3(i).

Therefore, the Natural Resources Defense Council (NRDC) submits this food additive petition, pursuant to section 409(b)(l) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 C.F.R. § 171.130, requesting that FDA revoke the approved uses of the perfluorocarboxylates in 21 C.F.R. § 176.170 as described in Table 1.[13]

By making this change, any company seeking to use long-chain perfluorocarboxylates would need to notify FDA by submitting a FCN or food additive petition before commencing the use.

Acceptance of this petition would complement actions taken by the U.S. Environmental Protection Agency (EPA) pursuant to the Toxic Substance Control Act (TSCA).[14] Using Section 5 of TSCA, EPA has issued Significant New Use Restrictions (SNURs) under 40 C.F.R. §§ 721.982 and 721.10536 from 2000 to 2013 that today require the agency be notified of new uses of various long-chain perfluorinated compounds.[15] If a chemical's use is subject to a SNUR, the importer or manufacturer must notify the EPA 90 days before commencing import or manufacture.

In addition, in 2006 EPA prohibited the use of Class 2 perfluorcarboxylate in Table 1 as an inert ingredient in pesticides applied to food because the potential risks meant the agency was unable to determine that the use met the safety requirements of the Section 408(c)(2) of the Federal Food Drug and Cosmetic Act.[16] The reasonable certainty of no harm safety standard used by EPA to make it decision is essentially the same as the one FDA must use for food additives.

Therefore, we request that FDA revoke the approvals it granted decades ago for the three classes of long-chain perfluorocarboxylates listed in Table 1 from 21 C.F.R. § 176.170. See Appendix 1 for additional details on the petition and Appendix 7 for the specific changes we seek in the regulation. This letter and all appendices constitute our complete petition. Please note that this is NOT a citizens petition. We have enclosed three copies per 21 C.F.R. § 171.1.

If you have questions or comments, please contact Erik D. Olson at eolson@nrdc.org.

[13] See Appendix 1 for the information requested by FDA at 21 C.F.R. § 171.130.
[14] Because TSCA exempts chemicals used to make food, drugs, medical devices, and cosmetics regulated by FDA at 15 U.S.C. § 2602(2)(B)(vi), EPA's SNURs do not apply to long-chain perfluorinated compounds used in as food additives including food contact substances.
[15] 78 Fed. Reg. 62,451 (Oct. 22, 2013).
[16] 72 Fed. Reg. 45,409 (August 9, 2006).

Sincerely,

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- Appendix 1: Responses to Elements Required by 21 C.F.R. § 171.1
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Appendix 1
Responses to Elements Required by 21 C.F.R. § 171.1

Per 21 C.F.R. § 171.1, we provide responses to the requested elements of a food additive petition with one element per page.

Name and Pertinent Information Concerning Food Additive

The identity of the food additive is as follows:

1.	Name:	Long-chain perfluorocarboxylates listed in 21 C.F.R. § 176.170 and described in detail in Appendix 2.
2.	Chemical formula:	Not applicable. Multiple chemicals
3.	Formula weight:	Not applicable. Multiple chemicals
4.	Chemical Abstract Service No.:	Not applicable. Multiple chemicals
5.	INS No.:	Not applicable. Multiple chemicals
6.	UNI No.:	Not applicable. Multiple chemicals

Any chemical listed in 21 C.F.R. § 176.170 and described in detail in Appendix 2 that meets the descriptions for long-chain perfluorocarboxylates.

The composition, raw materials, and manufacturing method are described in the food additive petitions that FDA approved as follows:

- For FAP 5B1747 accepted pursuant to Federal Register Docket No. 67-10113 on August 28, 1967 for "Diethanolamine salts of mono- and bis (1*H*,1*H*,2*H*,2*H* perfluoroalkyl) phosphates where the alkyl group is even-numbered in the range C8-C18 and the salts have a fluorine content of 52.4% to 54.4% as determined on a solids basis."
- For FAP 3B3700 accepted pursuant to Federal Register Docket No. 83F-0043 on March 4, 1983 and amended on October 26, 1983 for "Pentanoic acid, 4,4-bis [(*gamma-omega*-perfluoro-C8-20-alkyl)thio] derivatives, compounds with diethanolamine (CAS Reg. No. 71608-61-2)."
- For FAP 3B4353 accepted pursuant to Federal Register Docket No. 92F-0504 on January 26, 1993 and amended on July 22, 1995 for "Perfluoroalkyl substituted phosphate ester acids, ammonium salts formed by the reaction of 2,2-bis[([gamma], [omega]-perfluoroC4-20alkylthio) methyl]-1,3-propanediol, polyphosphoric acid and ammonium hydroxide."

Directions, Recommendations, and Suggestions Regarding Proposed Use
We are asking FDA to revoke the approvals for the long-chain perfluorocarboxylates as described in the section above.

Data establishing that food additive will have intended physical or other technical effect.
We are asking FDA to revoke the approvals for the long-chain perfluorocarboxylates as described in the section above. As a result, there is no intended physical or technical effect.

Description of practicable methods to determine the amount of the food additive in the food
We are asking FDA to revoke the approvals for the long-chain perfluorocarboxylates. As a result, there should be no amount of the food additive in the food.

Full reports of investigations made with respect to the safety of the food additive
See Appendices 4 and 5.

Proposed tolerances for the food additive
We are asking FDA to revoke the approvals for the long-chain perfluorocarboxylates as described in the section above. As a result, no tolerance is needed. Appendix 3 describes current estimated exposures for these chemicals.

Full information on each proposed change to the original regulation
See Appendix 7 for the specific changes requested to 21 CFR §176.170. Text in strikethrough font is to be deleted.

Environmental impact statement
This food additive petition is categorically excluded from the need to prepare an Environmental Assessment under 21 CFR 25.32(m) for actions to prohibit or otherwise restrict or reduce the use of a substance in in food, food packaging, or cosmetics. The proposed action complies with the categorical exclusion criteria. No extraordinary circumstances exist which would require the submission of an Environmental Assessment or Environmental Impact Statement.

Appendix 2
Description of each of the three classes of long-chain perfluorocarboxylates

We reviewed 21 C.F.R. § 176.170 and identified three classes of compounds that include chemicals that met this definition. They are as follows:

1. Diethanolamine salts of mono- and bis (1*H*,1*H*,2*H*,2*H* perfluoroalkyl) phosphates where the alkyl group is even-numbered in the range C8-C18 and the salts have a fluorine content of 52.4% to 54.4% as determined on a solids basis

This class meets the definition of a long-chain perfluorocarboxylates because the perfluoroalkyl group is defined as having a chain with between 8 and 18 carbons. At least some of the chemicals appear to be a precursor of perfluorocarboxylic acid.

In 1967, FDA approved the use of this class of chemicals in response to a food additive petition by E.I. du Pont de Nemours & Company (DuPont).[17] Three years later, the company submitted a food additive petition to reduce these levels by 18% but FDA does not appear to have accepted it.[18]

The regulation allows chemicals that meet this description to be used "only as an oil and water repellant at a level not to exceed 0.17 pound (0.09 pound of fluorine) per 1,000 square feet of treated paper or paperboard, as determined by analysis for total fluorine in the treated paper or paperboard without correction for any fluorine which might be present in the untreated paper or paperboard, when such paper or paperboard is used in contact with nonalcoholic foods . . . ."[19] It may be used in a wide range of conditions excluding only high temperature heat sterilized.

To provide context on these limits, consider the FDA approved maximum application rate of 0.17 pound of the chemical per 1000 ft^2. This corresponds to 77 mg/ft^2. A square foot is a little smaller than a 14" pizza, a sandwich wrapper, or 6" carryout box: common uses for greaseproofing paper and paperboard. Not all of these chemicals in the paperboard would likely get into the food. FDA's regulation sets an upper limit of how much of the chemical may be getting into food at 0.5 mg/in^2.[20] For one square foot, this limit corresponds to 72 mg.

Migration tests conducted by the company demonstrated that the chemical was not likely to migrate into food at levels anywhere near the allowed amount. Based on these tests, FDA concluded that aqueous foods in contact with the treated paper under the range of conditions of use would be below 0.51 ppm.[21] After DuPont submitted additional tests, FDA agreed the rates would be 0.07 ppm for fatty foods and 0.09 for aqueous foods. Since only 5 percent of all food consumed would be in contact with treated paper, the combined impact on diet of 0.0044 ppm.[22]

[17] 32 Fed. Reg. 12,474 (Aug. 29, 1967).
[18] 35 Fed. Reg. 13,323 (Aug. 20, 1970).
[19] 21 C.F.R. § 176.170(b).
[20] 21 C.F.R. § 176.170(c).
[21] FDA Memo dated October 6, 1970.
[22] FDA Memo dated December 8, 1971.

Using FDA's standard assumption of a 3 kg diet, an adult's estimated exposure to the Class 1 perfluorocarboxylates would be 0.013 mg/day.

2. Pentanoic acid, 4,4-bis [(*gamma-omega*-perfluoro-C8-20-alkyl)thio] derivatives, chemicals with diethanolamine (CAS Reg. No. 71608-61-2)

This class meets the definition of a long-chain perfluorocarboxylates because the perfluoroalkyl group is defined as having a chain with between 8 and 18 carbons. At least some of the chemicals appear to be a precursor of perfluorocarboxylic acid.

In 1983, FDA approved the use of this class of chemicals in response to a food additive petition by Ciba-Geigy Corporation.[23]

The regulation allows chemicals that meet this description to be used "only as an oil and water repellent and used at a level not to exceed 8 pounds per ton of the finished paper or paperboard when such paper or paperboard is used in contact with nonalcoholic foods"[24] at room temperature or below or for reheating frozen food.

To provide context on these limits, consider the FDA approved maximum application rate of 8 pounds of the chemical per ton of typical paperboard with a weight of 50 pound per 1000 square foot. This corresponds to 91 mg/ft^2. A square foot is a little smaller than a 14" pizza, a sandwich wrapper, or 6" carryout box: common uses for greaseproofing paper and paperboard. Not all of these chemicals in the paperboard would likely get into the food. FDA's regulation sets an upper limit of how much of the chemical may be getting into food at 0.5 mg/in^2.[25] For one square foot, this limit corresponds to 72 mg.

Migration tests conducted by the company demonstrated that the chemical was not likely to migrate into food at levels anywhere near the allowed amount. Based on these tests, FDA concluded that food in contact with the treated paper under the range of conditions of use would be as below 1.5 ppm.[26] After narrowing the range of allowed uses, with only 10 percent of all food consumed would be in contact with treated paper, the combined impact on diet of 0.018 ppm.[27] Using FDA's standard assumption of a 3 kg diet, an adult's estimated exposure to the Class 1 perfluorocarboxylates would be 0.05 mg/day.[28]

The agency based its decision on two toxicology studies: an oral study designed to determine the dose necessary to kill half the animals and a 30-day, subacute oral study in rats.[29]

[23] 48 Fed. Reg. 51,770 (Nov. 14, 1983).
[24] 21 C.F.R. § 176.170(b).
[25] 21 C.F.R. § 176.170(c).
[26] FDA memo dated February 10, 1983
[27] Ciba Geigy memo to FDA dated September 29, 1983.
[28] FDA Memo dated August 2, 1983
[29] FDA Memo dated August 2, 1983

3. Perfluoroalkyl substituted phosphate ester acids, ammonium salts formed by the reaction of 2,2-bis[([gamma], [omega]-perfluoroC4-20alkylthio) methyl]-1,3-propanediol, polyphosphoric acid and ammonium hydroxide

This class meets the definition of a long-chain perfluorinated compound because the perfluoroalkyl group is defined as having a chain with between 4 and 20 carbons. Because the chemicals in this class contain a thio group and are phosphate ester acids, they are likely a precursor of a PFHxS or a perfluorocarboxylic acid. Chemicals with a perfluoroalkyl group of only 4 or 5 carbons are unlikely to be qualify but given the likelihood that the products of a mixture of different carbon chain lengths, we do not believe it is appropriate to consider them to be short-chain perfluorinated compounds.
In 1995, FDA approved the use of this class of chemicals in response to a food additive petition by Ciba-Geigy Corporation.[30] The company submitted a food additive petition to expand the allowed used in 1996[31] and FDA approved that petition in 1997.[32]

The regulation allows chemicals that meet this description to be used "only as an oil and water repellant at a level not to exceed 0.44 percent perfluoroalkyl actives by weight of the finished paper and paperboard in contact with non-alcoholic foods"[33] for frozen or refrigerated storage.

To provide context on these limits, consider the FDA approved maximum application rate of 8 pounds of the chemical per ton of typical paperboard with a weight of 50 pound per 1000 square foot. This corresponds to 100 mg/ft^2. A square foot is a little smaller than a 14" pizza, a sandwich wrapper, or 6" carryout box: common uses for greaseproofing paper and paperboard. Not all of these chemicals in the paperboard would likely get into the food. FDA's regulation sets an upper limit of how much of the chemical may be getting into food at 0.5 mg/in^2.[34] For one square foot, this limit corresponds to 72 mg.

Migration tests conducted by the company demonstrated that the chemical was not likely to migrate into food at levels anywhere near the allowed amount. Based on these tests in Ciba-Geigy's petition to expand the uses, FDA concluded that food in contact with the treated paper under the range of conditions of use would be as below 0.52 ppm. [35] With only 8 percent of all food consumed would be in contact with treated paper, the combined impact on diet of 0.04 ppm.[36] Using FDA's standard assumption of a 3 kg diet, an adult's estimated exposure to the Class 1 perfluorocarboxylates would be 0.13 mg/day.[37]

[30] 60 Fed. Reg. 39,645 (Aug. 3, 1995).
[31] 61 Fed. Reg. 37,483 (July 18, 1996).
[32] 62 Fed. Reg. 10,452 (Mar. 7, 1997).
[33] 21 C.F.R. § 176.170(b).
[34] 21 C.F.R. § 176.170(c).
[35] FDA Memo dated August 30, 1996.
[36] FDA memo dated January 14, 1997.
[37] Ibid.

Appendix 3
FDA's related estimated daily intakes for perfluorocarboxylates

According to FDA's "List of Indirect Additives Used in Food Contact Substances" database, of the 3,237 chemicals in the database, 1000 are authorized by 21 C.F.R. § 176.170 to be used to treat paper and paperboard in contact with aqueous and fatty foods.[38] From this list of 1000, we identified 9 that were perfluorocarboxylates. See Table A3-1.

For several of the chemicals, we were not able to determine the class as described in Appendix 2 since the number provided in the database was not an actual CAS number but instead was assigned by FDA and the names were difficult to match. Where we could make the connection based on name or CAS number, we designated the class in the third column.

When we look at the carbon chain lists for the first four (FDA Doc. No. 7100, 7101, 7102, and 7088), they include chains as short as two carbons. Nowhere in 21 C.F.R. § 176.170 can we see where these are allowed. It appears that FDA's publicly available database identified chemicals as authorized by that section when in fact they are not covered. We do not know how to resolve this contradiction.

Table A3-1: Long-chain perfluorocarboxylates in FDA's Indirect Additives Database

Chemical Name*	CAS No. or FDA ID No.**	Class (from Appendix 2)
TETRAAMMONIUM2,2-BIS(**PERFLUOROALKYL(C2-18)**ETHYL)THIOMETHYL)-1,3-BIS(DIHYDROGENPHOSPHATE)PROPANE	977169-41-7 FDA Doc No. 7100	Unknown
DIAMMONIUM2,2-BIS((**PERFLUOROALKYL(C2-18)**ETHYL)THIOMETHYL)-3-HYDROXYPROPYL PHOSPHATE	977169-40-6 FDA Doc No. 7101	Unknown
AMMONIUMBIS(2,2-BIS((**PERFLUOROALKYL(C2-18)**ETHYL)THIOMETHYL)-3 HYDROXYPROPYL)PHOSPHATE	977169-39-3 FDA Doc No. 7102	Unknown
AMMONIUM5,5-BIS((**PERFLUOROALKYL(C2-18)**ETHYL)THIOMETHYL)-2-HYDROXY-2-OXO-1,3,2-DIOXAPHOSPHORINANE	977169-38-2 FDA Doc No. 7088	Unknown
DIETHANOLAMINEMONO- AND BIS(1H,1H,2H,2H-**PERFLUOROALKYL**) PHOSPHATE	977042-24-2 FDA Doc No. 5436	1
PENTANOICACID, 4,4-BIS ((GAMMA-OMEGA-**PERFLUORO-C8-20-ALKYL)**THIO) DERIVATIVES,COMPOUNDS WITH DIETHANOLAMINE	71608-61-2 FDA Doc No. 5171	2
* Portions of the chemical name indicating it is a long-chain perfluorinated chemical in bold typeface. **Numbers that begin with 977 were assigned by FDA and are not Chemical Abstract Service (CAS) numbers.		

[38] FDA, List of Indirect Additives Used in Food Contact Substances, http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?filter=176.170&sortColumn=&rpt=iaListing (accessed March 11, 2014).

In FDA's Cumulative Estimated Daily Intake (CEDI) Database,[39] we found exposure estimates for long-chain perfluorocarboxylates. See Table A3-2. We sorted them by decreasing estimated daily intake. Because of differences in FDA's naming chemicals and FDA assignment of its own numbers instead of proper CAS numbers, it is difficult to connect these chemicals to the three classes in Table 1 that are described in 21 C.F.R. § 176.170. Where we could make the connection based on name or CAS number, we designated the class after the C.F.R section number cited (last column).

FDA's publicly accessible resources regarding the database do not explain specifically how the agency developed its estimates.

Table A3-2: Long-chain perfluorocarboxylates in FDA's Cumulative Estimated Daily Intake (CEDI) database

Chemical Name in FDA's Database[1]	CAS No. or FDA ID No.[2]	CUM DC (ppb)[3]	CEDI (mg/kg-bw/day)[4]	21 CFR Section Cited[5]
PENTANOIC ACID, 4,4-BIS ((GAMMA-OMEGA-**PERFLUORO-C8-20-ALKYL**)THIO) DERIVATIVES, COMPOUNDS WITH DIETHANOLAMINE	71608-61-2	18	0.0009	176.170 Class 1
PERFLUOROALKYL SUBSTITUTED PHOSPHATE ESTER ACIDS, AMMONIUM SALTS FORMED BY REACTION OF 2,2-BIS[(GAMMA,OMEGA-**PERFLUORO-C(4-20)**-ALKYLTHIO)METHYL]-1,3-PROPANEDIOL, POLYPHOSPHORIC ACID AND AMMONIUM HYDROXIDE	None provided by FDA	15.5	0.000775	176.170 Class 3
AMMONIUM BIS(2,2-BIS((**PERFLUOROALKYL**(C2-18)ETHYL)THIOMETHYL)-3 HYDROXYPROPYL) PHOSPHATE	977169-39-3	8	0.0004	176.170 Class 3
COPOLYMERS OF 2-**PERFLUOROALKYL**ETHYLACRYLATE, 2-N,N-DIETHYLAMINOETHYL METHACRYLATE, AND GLYCIDYL METHACRYLATE	None provided by FDA	7	0.00035	None Listed
2-**PERFLUOROALKYL**ETHYL ACRYLATE	65605-70-1	1.4	0.00007	None Listed
COPOLYMERS OF 2-**PERFLUOROALKYL**ETHYLACRYLATE, 2-N,N-DIETHYLAMINOETHYL METHACRYLATE, AND GLYCIDYL METHACRYALTE	247047-61-6	1.1	0.000055	None Listed
BIS(1,1,2,2-TETRAHYDRO**PERFLUOROOCTYL**) ETHER	78522-74-4	0.58	0.000029	None Listed

[39] FDA, CEDI Database, http://www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/CEDI/default.htm (accessed March 2, 2014)

2-PROPENOIC ACID, 2-METHYL-, 2-(DIMETHYLAMINO)ETHYL ESTER, POLYMERS WITH 2-GAMMA-OMEGA-**PERFLUORO-C(8-14)**-ALKYL ACRYLATE, ACETATES, N-OXIDES	479029-28-2	0.5	0.000025	None Listed
PERFLUOROOCTANOIC ACID	335-67-1	0.12	0.000006	None Listed
TERPOLYMER OF TETRAFLUOROETHYLENE, **PERFLUORO(2,5-DIMETHYL-3,6-3,6-DIOXANONANE** VINYL ETHER, AND PERFLUORO(6,6-DIHYDRO-6-IODO-3-OXA-1-HEXENE)	106108-23-0	0.05	0.0000025	None Listed

[1] Portions of the chemical name indicating it is a long-chain perfluorocarboxylate in bold typeface.
[2] Numbers that begin with 977 were assigned by FDA and are not Chemical Abstract Service (CAS) numbers.
[3] CUM DC = Dietary concentration in the food expressed in parts per billion (pbb)
[4] CEDI = Cumulative estimated daily intake determined by FDA's Office of Food Additive Safety (OFAS) for the food contact substance in mg of chemical per kilogram of body weight per day (mg/kg bw/d).
[5] Where we could match the chemical named in CEDI with one of the three classes in Table 1, we noted the match.

We also evaluated four additional resources for exposure information on long-chain perfluorinated compounds. First, in 2009, the Centers for Disease Control and Prevention (CDC) released its Fourth National Report on Human Exposure to Environmental Chemicals.[40] CDC has updated the information with more recent test results at http://www.cdc.gov/exposurereport/. The report describes serum test results from the National Health and Nutrition Examination Survey's (NHANES) biomonitoring for the following long- and short-chain perfluorochemicals:

- Perfluorobutane Sulfonic Acid (PFBuS)
- Perfluorodecanoic Acid (CAS. No. 335-76-2) (PFDeA)
- Perfluorododecanoic Acid (CAS No. 307-55-1) (PFDoA)
- Perfluoroheptanoic Acid (CAS No. 375-85-9) (PFHpA)
- Perfluorohexane Sulfonic Acid (CAS No. 355-46-4) (PFHxS)
- Perfluorononanoic Acid (CAS No.375-95-1) (PFNA)
- Perfluorooctanoic Acid (CAS No. 335-67-1) (PFOA)
- Perfluorooctane Sulfonic Acid (CAS No. 1763-23-1) (PFOS)
- Perfluorooctane Sulfonamide (CAS No. 754-91-6) (PFOSA)
- 2-(*N*-Ethyl-Perfluorooctane sulfonamide) Acetic Acid (Et-PFOSA-AcOH)
- 2-(*N*-Methyl-perfluorooctane sulfonamido) Acetic Acid (Me-PFOSA-AcOH)
- Perfluoroundecanoic Acid (CAS No. 2058-94-8) (PFUA)

The monitoring results show that many Americans have been exposed to at least one of these 12 chemicals or one of the chemical's precursors.

Perfluorocarboxylates approved by FDA in 21 C.F.R. § 176.170 (the three classes described in Table 1) may be metabolized into some of the chemicals monitored by NHANES. More

[40] CDC, Fourth National Report on Human Exposure to Environmental Chemicals, 2009. See http://www.cdc.gov/exposurereport/ started at page 247.

information would be needed about the specific chemicals used and how they are metabolized to make a firm determination.

Second, the European Food Safety Authority (EFSA) also has conducted a series of progressively more detailed exposure studies for long-chain perfluorinated compounds. In 2008, it published a preliminary evaluation and developed a tolerable daily intake.[41] In 2012, it issued a more detailed examination of the levels in food.[42]

Third, in 2013, the European Commission's Community Research and Development Information Service published its final report for its project titled PERFluorinated Organics in Our Diet (PERFOOD).[43] This report describes tools to monitor the chemicals in food and drinking water. It also provides the results of studies looking at the impact of food contact materials and process technologies including some migration studies.

These European studies may be difficult to connect to FDA's CEDI because Europe's allowed uses of long-chain perfluorocarboxylates cannot be easily compared to those allowed by FDA pursuant to 21 C.F.R. § 176.170 or the chemicals named in CEDI.

Fourth, in 2010 Schecter et al. reported on the presence of perfluorocarboxylates in composite food samples.[44] The study showed perfluorooctanoic acid (PFOA) was measured in 17 of 31 samples, ranging from 0.07 ng/g in potatoes to 1.80 ng/g in olive oil. Two years later, the same lead author found that perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorohexane sulfonic acid (PFHxS), and perfluorooctane sulfonic acid (PFOS), were detected in the blood of > 92% of 300 participating children; the other PFCs measured were detected less frequently. Overall median serum concentrations of PFOS (4.1 ng/mL) were higher than those for PFOA (2.85 ng/mL), PFNA (1.2 ng/mL), and PFHxS (1.2 ng/mL).[45]

[41] EFSA, Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and their salts: Scientific Opinion of the Panel on Contaminants in the Food chain (Question No EFSA-Q-2004-163), 2008, The EFSA Journal, (2008) 653, 1-131

[42] EFSA, Scientific Report of EFSA, Perfluoroalkylated substances in food: occurrence and dietary exposure, 2012, EFSA Journal 2012:10(6):2743.

[43] CORDIS, PERFOOD Scientific and Technological Results, 2013. See http://cordis.europa.eu/publication/rcn/15158_en.html.

[44] Schecter et al., Perfluorinated Compounds, Polychlorinated Biphenyls, and Organochlorine Pesticide Contamination in Composite Food Samples from Dallas, Texas, USA, 2010, *Environ Health Perspect* 118:796-802 (2010). http://dx.doi.org/10.1289/ehp.0901347.

[45] Schecter et al., Polyfluoroalkyl Compounds in Texas Children from Birth through 12 Years of Age, 2012, *Environ Health Perspect*; DOI:10.1289/ehp.1104325.

Appendix 4
Toxicology assessment for three classes of long-chain perfluorocarboxylates

FDA's 2010 toxicological assessment of long-chain perfluorocarboxylates[46] is incorporated by reference. To update that assessment, the Natural Resources Defense Council (NRDC) took a five-step approach to identifying the available toxicology literature relevant to the three classes of long-chain perfluorocarboxylates whose approval at 21 CFR 176.170 NRDC seeks to have the Food and Drug Administration (FDA) revoke. The three classes are described in Table 1 and listed below for convenience:

Class 1: Diethanolamine salts of mono- and bis (1*H*,1*H*,2*H*,2*H* perfluoroalkyl) phosphates where the alkyl group is even-numbered in the range C8-C18 and the salts have a fluorine content of 52.4% to 54.4% as determined on a solids basis

Class 2: Pentanoic acid, 4,4-bis [(*gamma*-*omega*-perfluoro-C8-20-alkyl)thio] derivatives, chemicals with diethanolamine (CAS Reg. No. 71608-61-2)

Class 3: Perfluoroalkyl substituted phosphate ester acids, ammonium salts formed by the reaction of 2,2-bis[([gamma], [omega]-perfluoroC4-20alkylthio) methyl]-1,3-propanediol, polyphosphoric acid and ammonium hydroxide

NRDC took a five-step approach to review information available to us for the three classes.

Step 1: *Review food additive petition documents.* We reviewed the *Federal Register* notices for the food additive petitions addressing the three classes of long-chain perfluorocarboxylates as well as documents developed by FDA as part of its review of the petitions that the agency provided to us.

Step 2: *Review published literature for the three classes of long-chain perfluorocarboxylates.* We conducted a comprehensive review of the literature to identify toxicology studies for the three classes of chemicals.

Step 3: *Review FDA's 2010 toxicology assessment of long-chain perfluorocarboxylates.* We reviewed the toxicology assessment[47] provided by FDA conducted in 2010 by its food additive toxicologists. The analysis concluded that until additional data gaps are filled, long-chain perfluorocarboxylates should be considered as a class of chemicals associated with cancer and adverse effects on pre- and post-natal development and on reproductive health and function. The three classes of chemicals addressed in this food additive petition would qualify in the broader class of long-chain perfluorocarboxylates.

Step 4: *Review EPA's 2014 draft health assessment of PFOA and its precursors*. In February, 2014, the Environmental Protection Agency's drinking water

[46] FDA Memo from Toxicology Group I to Regulatory Group 2 on September 30, 2010 at page 34-35.
[47] *Ibid.*

program released a comprehensive health assessment of PFOA and its precursors. These precursors included the three classes of long-chain perfluorocarboxylates addressed in this food additive petition. The agency sought public comment on the report and solicited nominations for an external peer review panel that will review the report in detail. We reviewed EPA's assessment and identified studies referenced by EPA and published after 2009 and not included in the FDA's analysis.

Step 5: *Review public comments on EPA's draft health assessment of PFOA and its precursors.* As part of its request for public comments on its February 2014 health assessment, EPA also asked for suggestions on additional studies that it and the external peer review panel should consider. When the comment period closed and the comments were posted at www.regulations.gov, we reviewed them to identify issues and identified additional studies not referenced by FDA in 2010 or by EPA in 2014.

Appendix 5 describes our analysis of the 10 animal studies and includes the latest published scientific evidence that PFOA is "known to be toxic" to human reproduction and development we identified through this process published after 2009 that were not considered in FDA's 2010 toxicological assessment of long-chain perfluorocarboxylates.

Step 1: Review food additive petition documents.
We reviewed the following *Federal Register* notices related to the food additive petitions for the three classes:

- Class 1
  - 32 Fed. Reg. 12474 (August 29, 1967)
  - 35 Fed. Reg. 13323 (August 20, 1970)
- Class 2
  - 48 Fed. Reg. 11513 (March 18, 1983)
  - 48 FedReg 51770 (November 14, 1983)
- Class 3
  - 58 Fed. Reg. 8289 (February 12, 1993)
  - 60 Fed. Reg. 39625 (August 3, 1995)
  - 61 Fed. Reg. 37351 (July 18, 1996)
  - 62 Fed. Reg. 10411 (March 7, 1997)

None of the notices referred to any hazard characterization, hazard identification or toxicology studies.

Of the redacted documents that FDA provided NRDC for each of the three classes, we identified the following references to hazard characterization, hazard identification or toxicology studies:

- Class 2: FDA said that "This conclusion is based on 'virtually nil' migration, oral LD50 studies in animals, and a 30-day subacute oral study in rats."[48]

[48] FDA Memo from Quinn to Director of Foods on August 2, 1983 recommending approval of additive.

- Class 3: FDA said that "The DHEE representative concludes that based on the 'virtually nil' dietary exposure to the additive, the proposed use of the subject additive is supported by the available toxicity data presented in the petition."[49]

In summary, it is unlikely that the studies would be sufficient to determine whether the adverse effects described in FDA's 2010 assessment of long-chain perfluorocarboxylates were occurring with these classes of chemicals.

Step 2: Review published literature for the three classes of long-chain perfluorocarboxylates

While FDA's 2010 assessment[50] consider long-chain perfluorocarboxylates as a class, it is not clear from the documentation whether the agency specifically searched for the three classes of perfluorocarboxylates covered by this petition and described in Table 1. Therefore, NRDC conducted a literature search for the three classes following FDA's format and using the same resources listed by the agency: the U.S. EPA's website, the Agency for Toxic Substances and Disease Registry (ATSDR)'s website, PubMed, Google Scholar, ToxNet, ChemIDplus advanced, Scirus, and IPCS Inchem. Our objective was to identify relevant animal studies whether published before or after 2010. Because FDA's description of the classes at 21 CFR § 176.170 contain descriptive words in addition to chemical terms, we distilled the classes into the following search terms to help ensure our review was broad:

- Class 1:
  - Diethanolamine salts of mono- and bis(1*H*,1*H*,2*H*,2*H* perfluoroalkyl) phosphates
  - 1H,1H,2H,2H perfluoroalkyl phosphates
- Class 2:
  - 71608-61-2
  - Pentanoic acid, 4,4-bis [(*gamma-omega*-perfluoro-C8-20-alkyl)thio]
  - 4,4-bis [(gamma-omega-perfluoro-C8-20-alkyl)thio]
- Class 3:
  - 2,2-bis[([gamma], [omega]-perfluoroC4-20alkylthio) methyl]-1,3-propanediol
  - Perfluoroalkyl substituted phosphate ester acids, ammonium salts formed by the reaction of 2,2-bis[([gamma], [omega]-perfluoroC4-20alkylthio) methyl]-1,3-propanediol, polyphosphoric acid and ammonium hydroxide

a. **U.S. EPA's website**: We found that in 2006 the agency revoked a tolerance exemption for chemicals similar to Class 1[51] as part of its systematic review of active and 'inert' ingredients in pesticides pursuant to the Food Quality Protection Act of 1996. The class was described as "Mono- and Bis-(1*H*, 1*H*, 2*H*, 2*H*-perfluoroalkyl) Phosphates Where the Alkyl Group is Even Numbered and in the C6-C12 Range." The only difference from Class 1 is in the carbon chain length: Class 1 includes C8 to C18 while EPA considered C6 to C12. In light of FDA's conclusion that longer chain lengths are more likely to persist in the human body, they may be more potent that the ones revoked by EPA.

[49] FDA Memo from Rulis to Director of Center for Food Safety and Applied Nutrition on January 14, 1997 recommending approval of additive.
[50] FDA Memo from Toxicology Group I to Regulatory Group 2 on September 30, 2010 at page 34-35.
[51] 71 *Fed.Reg.* 45408 (August 9, 2006).

By revoking the tolerance exemption, EPA concluded that it could not be reasonably certain that the intended use would cause no harm and prohibited the use of the chemicals in pesticides. Three companies commented on EPA's notice. None challenged EPA's conclusions on the chemical described under the current tolerance exemption. The agency concluded that:

> "EPA determined that there were potential risks of concern associated with the use of these perfluoroalkyl phosphates. EPA concluded that it was unable to determine that the tolerance exemption met the safety requirements of FFDCA section 408(c)(2) and proposed the revocation of the tolerance exemption in the **Federal Register** on April 19, 2006 (71 FR 20048) (FRL–8058–3).

b. **National Institute of Health's ChemID*plus***: We only found information for Class 2 search terms.[52] It was described in three EPA databases: TSCA Inventory, ACToR, and SRS. We checked each of those databases and found only descriptions of the chemicals and no evidence of toxicology studies.

c. **National Library of Medicine's PubMed**: We found four studies for perfluorinated compounds: three systematic reviews on PFOA and a cross-sectional study using NHANES data from 1999-2008. The systematic reviews were:

- To determine whether developmental exposure to PFOA affects fetal growth hormone.[53] After applying a rigorous and transparent method to evaluate epidemiological data, the authors reviewed 18 human studies and found that a 1 ng/ml increase in serum or plasma PFOA was associated with a -18.9 g difference in birth weight. They concluded that "there is "sufficient" human evidence that developmental exposure to PFOA reduces fetal growth."
- To answer whether fetal developmental exposure to PFOA or its salts affect fetal growth in animals.[54] After applying a rigorous and transparent method to evaluate animal data, the authors reviewed 21 studies that met their criteria. They found that increased dams exposure concentration of PFOA was associated with decreased pup birth weight (-0.023 g per 1-unit increase in dose (milligram/kilogram body weight-day)). They concluded that there was sufficient evidence that fetal developmental exposure to PFOA reduces fetal growth in animals.
- To integrate scientific findings from human and animal studies to determine the overall strength of the evidence to answer the question: does developmental

[52] http://chem.sis.nlm.nih.gov/chemidplus/rn/71608-61-2.

[53] Johnson PI et al. The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Systematic Review of Human Evidence for PFOA Effects on Fetal Growth. 2014. *Environmental Health Perspectives* 122:1028-1039. http://dx.doi.org/10.1289/ehp.1307893

[54] Koustas E et al. The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Systematic Review of Nonhuman Evidence for PFOA Effects on Fetal Growth. 2014. *Environmental Health Perspectives* 122:1015-1027. http://dx.doi.org/10.1289/ehp.1307177

> exposure to PFOA affect fetal growth in humans.[55] The integration of human and animal data "produced a final strength of evidence rating in which the review authors concluded that PFOA is "known to be toxic" to human reproduction and development." The authors concluded that "developmental exposure to PFOA adversely affects human health."

The cross sectional study evaluated the association between serum concentration of eight PFCs, including PFOA, PFOS, PFNA and PFHxS, with self-reported lifetime asthma, wheezing and current asthma among 12-19 years of age NHANES participants.[56] They concluded that the study "provides some evidence for associations between exposure to PFCs and asthma-related outcomes in children."

Summarizing Step 2, only one of the resources used by FDA (PubMed) revealed studies for a handful of perfluorinated carboxylates; none of the resources revealed any studies for the three classes of chemicals. Abstracts of the studies are included in Appendix 5.

Step 3: Review FDA's 2010 toxicology assessment of long-chain perfluorcarboxylates

In 2010, the U.S. Food and Drug Administration's (FDA) food additives toxicologists updated a series of reviews they had conducted of long-chain perfluorinated compounds.[57] A 2002 review had set a unit risk cancer value for perfluorooctanoic acid (PFOA).[58] A 2007 review found that "carcinogenicity was considered to be the most sensitive and relevant endpoint for PFOA in particular."[59] The 2010 review focused on three non-cancer endpoints: pre- and post-natal development; reproductive health and function; and thyroid gland.

Much of the toxicology and epidemiology research has focused on PFOA because long-chain perfluorinated chemicals may be degraded into PFOA in the environment. However FDA's scientists concluded that they are not metabolized to PFOA in the body.[60] Because PFOA is structurally similar to many types of long-chain perfluorinated compounds, especially carboxylates, the agency used evidence of PFOA and other similar chemicals to identify similar data gaps for those it reviewed for safety.

In sum, the agency's food additive toxicologists reached the following conclusions for perfluorinated compound with long chains (e.g. chains of at least eight carbons saturated with fluorine).

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[55] Robinson KA et al. The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Integration of Animal and Human Evidence for PFOA Effects on Fetal Growth. 2014. *Environmental Health Perspectives* 122:1040-1051. http://dx.doi.org/10.1289/ehp.1307923

[56] Humblet O et al. Perfluoroalkyl Chemicals and Asthma among Children 12–19 Years of Age: NHANES (1999–2008). 2014. *Environmental Health Perspectives* 122:1129-1133. http://dx.doi.org/10.1289/ehp.1306606

[57] FDA Memo from Toxicology Group I to Regulatory Group 2 on September 30, 2010 at page 34-35.

[58] *Ibid*., p. 1 citing Twaroski/Gilliam, 10/1/02.

[59] *Ibid*., citing McDougal/Honigfort, 6/13/07.

[60] *Ibid.*, p. 4. Note that this conclusion is inconsistent with statements by the Agency for Toxic Substances and Disease Registry in 2009 as part of its draft toxicological profile on perfluoroalkyls. ATSDR stated that "[e]xposure of mice to 8– 2 telomer alcohol also generated PFNA [perfluorononanoic acid] as a metabolite (Kudo et al. 2005)." [ATSDR 2009 page 226]

- **Cancer:** "In the absence of data to suggest otherwise, carcinogenicity was also considered to be the most sensitive endpoint for structurally-similar perfluorinated compounds, such as ≥ C8 perfluorinated telomer alcohols, based on the available data for PFOA. . . ."[61]
- **Pre- and post-natal development:** The toxicologists found perfluorocarboxylic acids and perfluorotelomer alcohols have adverse effects for the following parameters:
    - Pregnancy maintenance/fetal loss;
    - Reduced skeletal ossification and/or skeletal variations;
    - Decreased fetal body weight;
    - Neonatal survival;
    - Decreased post-natal bodyweight gain prior to weaning;
    - Delayed attainment of eye-opening and hair growth; and
    - Stunted mammary gland development in animals exposed during gestation.[62]
- **Reproductive health and function:** The toxicologists found perfluorocarboxylates have adverse effects for the following parameters:
    - Fertility and estrous cycle parameters;
    - Ovarian and accessory sex organ weight parameters;
    - Ovarian and/or accessory sex organ histopathology; and
    - Serum hormones.[63]
- **Thyroid gland:** The toxicologists found that the reviewed evidence for perfluorinated compounds on thyroid function was mixed.[64]

The scientists noted that "[w]hile the available data on the developmental effects of ≥C8 perfluorinated compounds is scarce, the known increase in biopersistence, and hence potency, supports the generalization of the results from the C8 homologues to the entire class."[65]

The scientists made clear that there is considerable uncertainty with regard to the effects of long-chain perfluorinated compounds as a class due to factors that include:

- Almost all of the available data are from studies conducted with PFOA; lack of information on the pharmacokinetics of long-chain perfluorocarboxylic acids and the eight-carbon, telomer-based perfluorinated alcohols in species other than rats;
- Lack of information on the pharmacokinetics of the telomer-based perfluorinated alcohols longer than eight carbons; and
- Paucity of toxicity data appropriate for use in human health risk assessment for perfluorocarboxylic acids and perfluorinated telomer alcohols with more than eight carbons.[66]

Based on its analysis, FDA's food additive toxicologists recommended "a full, Redbook-compliant, one-year study with an *in utero* phase, as this study design will provide the most comprehensive assessment of the endpoints of concern. This study design will assess chronic toxicity and the possibility of delayed toxicity in adulthood derived from developmental

[61] *Ibid.*, p. 1 citing McDougal/Honigfort, 6/13/07.
[62] *Ibid.*, p. 16-17.
[63] *Ibid.*, p. 30-31.
[64] *Ibid.*, p. 33.
[65] *Ibid.*, p. 34-35.
[66] *Ibid.*, p. 35.

exposure, as well as assessing effects on the developing and mature endocrine system. Moreover, as per the discussion above regarding the appropriate model for use in risk assessment of these compounds, Toxicology recommends that the one-year study with *in utero* phase be conducted in mice, due to pharmacokinetic considerations."[67]

Summarizing Step 3, NRDC believes that the three classes of perfluorocarboxylates in Table 1 should be treated as a class with other perfluorocarboxylates including PFOA.

Step 4: Review EPA's 2014 draft health assessment of PFOA and its precursors

In February 2014, the U.S. Environmental Protection Agency's (EPA) Drinking Water Program released its draft comprehensive assessment of the health effects of PFOA.[68] Because carboxylates degrade in the environment into PFOA, the analysis considered the science involving those chemicals as well. The agency stated that "PFOA is not readily eliminated from humans as evidenced by the half-life of 2.3 years. In contrast, half-life values for the monkey, rat, and mouse are 20.8 days, 11.5 days, and 15.6 days, respectively. Differences in transporters may explain species differences in elimination."[69] It found a positive association between:

- Serum PFOA concentrations and:
    - Increased liver enzymes and/or decreased bilirubin in both worker and general populations;
    - Chronic kidney disease in the general population, and
    - Odds of experiencing early menopause.
- Maternal or child plasma levels of PFOA and:
    - Decreased antibody titers in children after vaccination;
    - Obesogenic effects in female children at 20 years of age; and
    - Parent reported Attention Deficit Hyperactivity Disorders.[70]

Based on this data, EPA selected a draft ingestion reference dose (RfD) for PFOA of 0.00002 mg/kg-bw/day (equivalent to 20 nanograms/kg-bw/day).[71]

If, as FDA concluded in 2010, perfluorocarboxylates are a class that includes PFOA, then this RfD should be applied to all perfluorocarboxylates including the three classes in Table 1. Since the longer chain perfluorocarboxylates are likely to be retained in the body at greater levels than PFOA, the RfD may need to be lower. Only additional toxicology data from the type of study FDA's toxicologists called for in 2010, would be able to rebut this presumption.

EPA developed potential RfDs ranging from 0.000003 to 0.00002 mg/kg-bw/day after systematically examining the toxicology and applying appropriate uncertainty factors using:

- No Observed Adverse Effect Level (NOAEL) and Lowest Observed Adverse Effect Level (LOAEL) values;
- Lower 90% confidence bounds on the Benchmark Dose Level ($BMDL_{10}$); and

[67] *Ibid.*
[68] EPA, DRAFT Health Effects Documents for Perfluorooctanoic Acid (PFOA), EPA Doc. No. 822R14001, 2014.
[69] *Ibid.*, p. 1-1.
[70] *Ibid.*
[71] *Ibid.*, p. 1-2.

- Human Equivalent Dose (HED) based on the NOAEL and LOAEL.[72]

The agency selected 0.00002 mg/kg-bw/day as the draft RfD because it was the most commonly occurring RfD; however, it was almost 7 times greater than the lowest one calculated. The agency reasoned that:

> "This value is the outcome for all modeled rat and mouse serum values except for the Dewitt et al. (2008) 15-day study with an impact on liver weight but not the co-monitored immunological effects. The liver endpoint in the Lau et al. (2006) and York et al. (2002) studies were accompanied by developmental effects and effects on kidney weights, respectively. The modeled serum value from Thumford (2001) based on liver effects in the monkey, also strongly supports the chosen RfD." [73]

EPA's evaluation builds on three other evaluations. In an October 28, 2009 memo, EPA's Office of Emergency Management and its Office of Superfund Remediation and Technology Innovation jointly developed RfDs for PFOA and PFOS for use in clean-up situations.[74] This document was based on January 2009 provisional health advisories (PHAs) developed by EPA's Office of Water. The PHAs relied heavily on the European Food Safety Authority's (EFSA) 2008 evaluation developing a Tolerable Daily Intake (TDI).[75] The process to develop a TDI is comparable to both EPA's RfD and FDA's ADI.

Natural Resources Defense Council (NRDC) reviewed the bibliography listed in EPA's draft assessment and found 56 references not included in FDA's analysis that were published in 2010 or later. Of these 56 references, we found:

- 26 described epidemiology studies;
- 10 described *in vivo* animal studies with 3 on rats and 8 on mice;
- 8 described *in vitro* studies;
- 3 were reviews;
- 2 described human clinical studies;
- 2 described measurement methods;
- 4 described models; and
- 1 described water treatment methods.

We reviewed the 10 *in vivo* animal studies. These are described and discussed in Appendix 5. In summary, NRDC did not find anything in the 10 *in vivo* animal studies that contradicted FDA's conclusions, especially that perfluorocarboxylates should be treated as a class. On the contrary, we found additional evidence supporting FDA's conclusion that these chemicals cause adverse health effects in animals.

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[72] *Ibid.*, p. 5-19-20. See Table 5-11 and 5-12.
[73] *Ibid.*
[74] EPA, The Toxicity of Perfluorooctanic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS), October 28, 2009. See http://www.epa.gov/opptintr/pfoa/pubs/Final%20PFOA%20PFOS%20RfD%20memo%2010-28-09.pdf.
[75] EFSA, Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and their salts: Scientific Opinion of the Panel on Contaminants in the Food chain (Question No EFSA-Q-2004-163), 2008, The EFSA Journal, (2008) 653, 1-131.

Step 5: Review public comments on EPA's draft health assessment of PFOA and its precursors

When EPA released its draft health assessment for PFOA in February 2014, it sought public comments on the document seeking, in particular, information on additional studies it should consider.[76] It also asked for nominations for an external peer review panel.[77] Two months later, the agency posted the responses to its request for comments[78] and announced its interim list of potential peer reviewers and sought comments on the list.[79]

NRDC reviewed the 19 comments EPA received in response to its request. Nine were from industry, five from a state agency, two from academia, and one each from Department of Defense, a law firm representing concerned citizens, and an anonymous individual.

The public comments to EPA identified 89 additional studies addressing PFOA or its precursors not included in EPA 2014 assessment or FDA's 2010 assessment. Of these 89 references, we found:

- 58 described epidemiology studies;
- 14 were reviews;
- 6 described human clinical studies;
- 5 described *in vitro* studies;
- 4 described models.
- 2 described measurement methods;
- 4 described models;
- 0 described *in vivo* animal studies.

Therefore, in Step 5 we identified no additional *in vivo* animal studies conducted on PFOA or perfluorocarboxylates through our review of responses to EPA's request for comments on its health assessment of PFOA or its precursors.

Summary

Overall, after completing the five steps and reviewing the literature[80] published since FDA reached its conclusions that there was insufficient scientific data supporting the safety of long-chain perfluorocarboxylates, the Natural Resources Defense Council (NRDC) found that the evidence of adverse health effects caused by these chemicals has only strengthened since 2010. Although this is a positive finding, a significant gap remains in the toxicology data for the three chemical classes. Therefore, there is no reasonable certainty that the intended uses cause no harm.

[76] 79 Fed.Reg 11429 (February 28, 2014). See also http://peerreview.versar.com/epa/pfoa/.
[77] *Ibid.*
[78] EPA, Docket No. EPA–HQ–OW–2014–0138. See www.regulations.gov.
[79] 79 Fed.Reg. 24419 (April 30, 2014).
[80] See Appendix 4 and 5 for review.

Appendix 5

Review of animal studies published since FDA's 2010 assessment of long-chain perfluorocarboxylates

The following is the Natural Resources Defense Council's analysis of the 10 animal studies, eight on mice and three on rats, not included in FDA's 2010 assessment of perfluorocarboxylates. All 10 studies were located in Step 4 of our analysis where we reviewed EPA's 2014 assessment of PFOA and its precursors.

Mice Toxicology Studies

1. Albrecht, P.P., N.E. Torsell, P. Krishnan, D.J. Ehresman, S.R. Frame, S.-C. Chang, J.L. Butenhoff, G.L. Kennedy, F.J. Gonzalex, and J.M. Peters. 2013. A species difference in the peroxisome proliferator-activated receptor α-dependent response to the developmental effects of perfluorooctanoic acid. Toxicol. Sci. 131: 568-582.
    a. ABSTRACT: This study examined the effect of prenatal perfluorooctanoic acid (PFOA) administration on pre- and postnatal development using peroxisome proliferator-activated receptor α (PPARα)-humanized mice to determine if species differences in receptor activity might influence the developmental effects induced by PFOA. Pregnant mice were treated daily with water or PFOA (3mg/kg) by po gavage from gestation day 1 (GD1) until GD17 and then either euthanized on GD18 or allowed to give birth and then euthanized on postnatal day 20 (PND20). No changes in average fetal weight, crown-to-rump length, or placental weight were observed on GD18. Expression of mRNA encoding the PPARα target genes acyl CoA oxidase (Acox1) and cytochrome P450 4a10 (Cyp4a10) in maternal and fetal liver was increased on GD18 in wild-type and PPARα-humanized mice but not in Pparα-null mice. On PND20, relative liver weight was higher in wild-type mice but not in Pparα-null mice or PPARα-humanized mice. Hepatic expression of Acox1 and Cyp4a10 mRNA was higher in wild-type mice but not in Pparα-null mice or PPARα-humanized mice on PND20. The percentage of mice surviving postnatally was lower in wild-type litters but not in litters from Pparα-null mice or PPARα-humanized mice. No changes in pup weight gain, onset of eye opening, or mammary gland development were found in any genotype. Results from these studies demonstrate that the developmental/postnatal effects resulting from prenatal PFOA exposure in mice are differentially mediated by mouse and human PPARα.
    b. ANALYSIS: This study was conducted in mice using a single dose of PFOA (3mg/kg/day) administered to dams via gavage. Exposure occurred during gestation days (GD) 1 to 17; offspring were evaluated before birth (GD18) or on postnatal day (PND) 20. The study aimed at evaluating whether PPAR alpha may influence the developmental effects induced by PFOA. The study used three different mice: wild type, PPAR alpha-humanized mice and PPAR alpha null mice. Changes in liver gene expression and postnatal survival seem to be differentially mediated by mouse and human PPAR alpha.
    c. CONCLUSION: Unlike the studies cited in FDA's toxicology analysis, this study did not report effects on the mammary gland. This difference is likely due to differences

in doses and age of the offspring. In sum, this study does not contradict FDA's toxicology conclusions regarding prenatal and postnatal endpoints.

2. Li, Y., D.H. Ramdhan, H. Naito, N. Yamagishi, Y. Ito, Y. Hayashi, Y. Yanagiba, A. Okamura, H. Tamada, F.J. Gonzalez, and T. Nakajima. 2011. Ammonium perfluorooctanoate may cause testosterone reduction by adversely affecting testis in relation to PPARα. Toxicol. Lett. 205:265-272.
    a. ABSRACT: Perfluorooctanoate, a peroxisome proliferator-activated receptor alpha (PPARα) agonist, has the potential to lower testosterone levels as a result of testicular toxicity. To elucidate the mechanism and impact of PPARα on this reproductive toxicity, ammonium perfluorooctanoate (APFO) at doses of 0, 1.0 (low) mg/kg/day, or 5.0 (high) mg/kg/day was orally given daily to 129/sv wild-type (*mPPARα*), *Pparα*-null and PPARα-humanized (*hPPARα*) mice for 6 weeks. Both low- and high-dose APFO significantly reduced plasma testosterone concentrations in *mPPARα* and *hPPARα* mice, respectively. These decreases may, in part, be associated with decreased expression of mitochondrial cytochrome P450 side-chain cleavage enzyme, steroidogenic acute regulatory protein or peripheral benzodiazepine receptor as well as microsomal cytochrome $P450_{17\alpha}$ involved in the steroidogenesis. Additionally, both doses increased abnormalities in sperm morphology and vacuolated cells in the seminiferous tubules of both mouse lines. In contrast, APFO caused only a marginal effect either on the testosterone synthesis system or sperm and testis morphology in *Pparα*-null mice. These results suggest that APFO may disrupt testosterone biosynthesis by lowering the delivery of cholesterol into the mitochondria and decreasing the conversion of cholesterol to pregnenolone and androstandione in the testis of *mPPARα* and *hPPARα* mice, which may, in part, be related to APFO-induced mitochondrial damage.
    b. ANALYSIS: This mouse study used two doses of ammonium perfluorooctanoate (APFO), 1 and 5mg/kg/d administered orally to wild type, PPAR-alpha humanized and PPAR-alpha null mice for 6 weeks. The study looked at the effect of APFO on testosterone production. The data showed that both doses of APFO significantly reduced plasma testosterone levels, decreased expression of mitochondrial and microsomal cytochrome P450-related molecules associated with steroidogenesis. The treated animals also had abnormal sperm morphology and vacuolated cells in the seminiferous tubules. These effects were observed in the wild-type and humanized PPAR-alpha mice but were not that profound in the PPAR-alpha null mice.
    c. CONCLUSIONS: This study supports FDA's toxicology conclusion that "≥ C8 perfluorinated carboxylic acids appear to have direct adverse effects on reproductive hormone homeostasis" and "may therefore be considered as endocrine disruptors in male rats". This study provides further evidence of endocrine disruption in a different species, mouse, and at doses lower than previously assessed by FDA. Also, it adds a new finding: sperm and seminiferous tubules morphology is altered.

3. Macon, M.B., L.R. Villanueva, K. Tatum-gibbs, R.D. Zehr, M.J. Strynar, J.P. Stanko, S.S. White, L. Helfant, and S.E. Fenton. 2011. Prenatal perfluorooctanoic acid exposure in CD-1 mice: low dose developmental effects and internal dosimetry. Toxicol.Sci. doi:10.1093/toxcie/kfr076

a. ABSTRACT: Perfluorooctanoic acid (PFOA) is an environmental contaminant that causes adverse developmental effects in laboratory animals. To investigate the low-dose effects of PFOA on offspring, timed-pregnant CD-1 mice were gavage dosed with PFOA for all or half of gestation. In the full-gestation study, mice were administered 0, 0.3, 1.0, and 3.0 mg PFOA/kg body weight (BW)/day from gestation days (GD) 1–17. In the late-gestation study, mice were administered 0, 0.01, 0.1, and 1.0 mg PFOA/kg BW/day from GD 10–17. Exposure to PFOA significantly ($p < 0.05$) increased offspring relative liver weights in all treatment groups in the full-gestation study and in the 1.0 mg PFOA/kg group in the late-gestation study. In both studies, the offspring of all PFOA-treated dams exhibited significantly stunted mammary epithelial growth as assessed by developmental scoring. At postnatal day 21, mammary glands from the 1.0 mg/kg GD 10–17 group had significantly less longitudinal epithelial growth and fewer terminal end buds compared with controls ($p < 0.05$). Evaluation of internal dosimetry in offspring revealed that PFOA concentrations remained elevated in liver and serum for up to 6 weeks and that brain concentrations were low and undetectable after 4 weeks. These data indicate that PFOA-induced effects on mammary tissue (1) occur at lower doses than effects on liver weight in CD-1 mice, an observation that may be strain specific, and (2) persist until 12 weeks of age following full-gestational exposure. Due to the low-dose sensitivity of mammary glands to PFOA in CD-1 mice, a no observable adverse effect level for mammary developmental delays was not identified in these studies.
b. ANALYSIS: In this study, gavaged pregnant mice were treated with one of three doses of PFOA (0.3, 1 and 3mg/kg/day) from GD1-17 or GD10-17. The offspring were studied for up to 12 weeks after birth. Regardless of the starting time of prenatal exposure, the offspring of all treated dams showed significant developmental delay in mammary gland development that persisted for three months after birth. Liver weight was increased in all offspring exposed during the full length of gestation regardless of the dose. PFOA serum and liver levels remained high measureable for up to six weeks after birth, while brain levels were lower and undetectable after 4 weeks.
c. CONCLUSION: This study supports FDA's analysis that the mammary gland is altered by PFOA; that the doses that cause mammary gland delay are lower than those inducing an increase in liver weight; adds information on PFOA accumulating in liver and found in offspring brains up to a month after birth. In sum, this study does not contradict FDA's toxicology conclusions regarding prenatal and postnatal endpoints.

4. Minata, M., K.H. Harada, A. Kärrman, T. Hitomi, M. Hirosawa, F.J. Gonzales, and A. Koizumi. 2010. Role of peroxisome proliferator-activated receptor-α in hepatobiliary injury induced by ammonium perfluorooctanoate in mouse liver. Ind. Health 48: 96-107.
    a. ABSTRACT: Peroxisome proliferator-activated receptor-alpha (PPAR alpha) has been suggested to protect against chemically induced hepatobiliary injuries in rodents. This function could mask the potential toxicities of perfluorooctanoic acid (PFOA) that is an emerging environmental contaminant and a weak ligand of PPAR alpha. However its function has not been clarified. In this study, PFOA was found to elicit hepatocyte and bile duct injuries in Ppar alpha-null mice after 4 wk treatment with PFOA ammonium salt (0, 12.5, 25, 50 micromol/kg/d, gavage). In wild-type mice, PFOA caused major hepatocellular damage dose-dependently and minor

cholangiopathy observed only at 25 and 50 micromol/kg. In treated Ppar alpha-null mice, PFOA produced marked fat accumulation, severe cholangiopathy, hepatocellular damage and apoptotic cells especially in bile ducts. Oxidative stress was also increased 4-fold at 50 micromol/kg and TNF-alpha mRNA was upregulated more than 3-fold at 25 micromol/kg in Ppar alpha-null mice. Biliary bile acid/phospholipid ratios were higher in Ppar alpha-null mice than in wild-type mice. Results from these studies suggest that PPAR alpha is protective against PFOA and have a critical role in drug induced hepatobiliary injury.

b. ANALYSIS: This is a mouse study evaluating the role of PPAR alpha in liver toxicity. The study used wild-type and PPAR alpha null mice exposed to three doses of PFOA (12.5, 25 and 50 micromol/kg/d) by gavage. After four weeks of treatment the PPAR alpha null animals developed liver and bile duct injuries, fat accumulation and cholangiopathy. These animals also showed increased oxidative stress and altered bile chemistry.

c. CONCLUSION: These findings argue against the long-held theory that, in mice, liver toxicity is mediated by PPAR alpha mediated mechanism and therefore this endpoint is irrelevant to human health effects. In sum, this study does not contradict FDA's toxicology conclusions regarding any of the evaluated endpoints.

5. Onishchenko, N., C Fischer, W.N.W. Ibrahim, S. Negri, S. Spulbur, S. Cottica, and S. Ceccatelli. 2011. Prenatal exposure to PFOS or PFOA alters motor function in mice in a sex-related manner. Neurotox. Res. 19:452-461. http://www.ncbi.nlm.nih.gov/pubmed/20512442

   a. ABSTRACT: Perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) are organic surfactants widely used in various industrial and consumer applications. Due to their chemical properties, these perfluorinated compounds (PFCs) have also become persistent contaminants. The risk of possible intrauterine and lactational exposure to these chemicals poses a significant health concern for potential developmental effects. In the present study we have found that dietary exposure of mice to 0.3 mg/kg of PFOS or PFOA throughout pregnancy results in different distribution pattern in the offspring brain and liver. In particular, exposure to PFOS led to four times higher accumulation of the chemical in the brains of newborn mice than PFOA. We have used a battery of behavioral tests to evaluate motor function, circadian activity, and emotion-related behavior in the exposed offspring. Exposure to PFOS resulted in decreased locomotion in a novel environment and reduced muscle strength only in male offspring. Prenatal exposure to PFOA was associated with changes in exploratory behavior in male and female offspring, as well as with increased global activity in males in their home cage. The neurobehavioral outcome of prenatal exposure to PFCs in mice is characterized by mild alterations in motor function and it appears to be sex-related.

   b. ANALYSIS: This is a mouse study with two groups, one control and one treated with PFOA at 0.3mg/kg/d in the diet; the dams were exposed through gestation and the offspring were tested at ages 5-8 weeks and 3-4 months old. Measurements included a battery of behavioral tests including motor function, circadian activity and emotion-related behavior. The findings include PFOA measurement in the newborns' brains and altered behavioral and motor activities in the offspring exposed in utero to PFOA.

c. CONCLUSION: These data supports FDA's toxicology report on prenatal and postnatal endpoints regarding "brief in utero exposure alone is sufficient to induce postnatal toxicity into adulthood."

6. Suh, C.H., N.K. Cho, C.K. Lee, C.H. Lee, D.W. Kim, J.H. Kim, B.C. Son, and J.T. Lee. 2011. Perfluorooctanoic acid-induced inhibition of placental-family hormone and fetal growth retardation in mice. Mol. Cell. Endocrinol. Doi:10.1016/j.mce.2011.01.009. http://www.ncbi.nlm.nih.gov/pubmed/21241770
    a. ABSTRACT: Perfluorooctanoic acid (PFOA) is a persistent pollutant worldwide and even found in human cord blood and breast milk. Some animal studies have reported that PFOA causes developmental toxicity such as fetal weight loss, but the mechanism is still unclear. This study focused on developmental toxicity of PFOA, particularly impacts of PFOA on placental endocrine function such as placental prolactin (PRL)-family hormone gene expression and fetal growth in mouse. Time-mated CD-1 mice were dosed by gavage with 0, 2, 10 and 25 mg/kg B.W/day of PFOA (n-10) dissolved with de-ionized water from gestational day (GD) 11-16. During treatment, body weight of each pregnant mouse was measured daily. On day 16, caesarean sections were performed and developmental data were observed. Three placentas from three different pregnant mice were assigned to each of the following experiments. The mRNA levels of mouse placental lactogen (mPL)-II, prolactin like protein (mPLP)-E, -F and Pit-1α and β isotype mRNAs, a transacting factor of mPLs and mPLPs genes, were analyzed using northern blot, in situ hybridization and RT-PCR, respectively. Maternal body weight gain was significantly declined from GD 13 in the PFOA treated groups compared to control. Developmental data such as fetal and placental weights were significantly decreased in accordance with PFOA dosage. Number of dead fetuses and post-implantation losses were significantly increased in the PFOA-exposed groups. In addition, placental efficiency (fetal weight/placental weight) was significantly reduced in PFOA treated groups in accordance with PFOA dosage. Histopathologic changes were observed in placenta. Dose dependent necrotic changes were observed in both 10 mg and 25 mg PFOA treated groups. Cell frequency of glycogen trophoblast cell and parietal trophoblast giant cell were decreased dose dependently in the junctional zone. In the labyrinth zone, sinusoidal trophoblast giant cell frequency was decreased in the 25 mg PFOA treated group. Also, morphological change such as crushed nuclear (atrophy) of trophoblast cells was observed in 25 mg PFOA treated group. Finally, mRNA levels of the mPL-II, mPLP-E, -F and Pit-1α and β were significantly reduced in the PFOA treated groups dose dependently. In addition, the changing pattern between mPL-II, mPLP-E, -F mRNA levels and fetal body weight showed positive relationship. In conclusion, the inhibitory effects of PFOA on the placental prolactin-family hormone genes expression may be secondary effects to insufficient trophoblast cell type differentiation and/or increased trophoblast cell necrosis. The impacts of PFOA on placental development and endocrine function reduced the placental efficiency and partly contributed to the fetal growth retardation in the mouse.
    b. ANALYSIS: This mouse study used three doses of PFOA (2, 10 and 25mg/kg/d) administered to dams from GD11-16 via gavage. The study looked at placental health and fetal development endpoints. The data showed that placental morphology

(including necrosis), cell differentiation and gene expression were altered in a dose-dependent manner. Placental and fetal weights were significantly reduced in all treated groups. The expression of genes related to the placental prolactin family was reduced likely due to the effect on placental development and functionality, which may have also delayed fetal growth.

c. CONCLUSION: These findings support FDA's toxicology conclusion that perfluoroalkyl compounds affect prenatal endpoints.

7. White, S.S., J.P. Stanko, K. Kato, A.M. Calafat, E.P. Hines, and S.E. Fenton. 2011. Gestional and chronic low-dose PFOA exposures and mammary gland growth and differentiation in three generations of CD-1 mice. Environ. Health Perspect. Doi:10.1289/ehp.1002741
    a. ABSTRACT: We treated P0 dams with 0, 1, or 5 mg PFOA/kg/day on gestation days 1-17. In addition, a second group of P0 dams treated with 0 or 1 mg/kg/day during gestation and their F1 and F2 offspring received continuous PFOA exposure (5 ppb) in drinking water. Resulting adult F1 females were bred to generate F2 offspring, whose development was monitored over postnatal days (PNDs) 1-63. F1 gland function was assessed on PND10 by timed-lactation experiments. Mammary tissue was isolated from P0, F1, and F2 females throughout the study and histologically assessed for age-appropriate development. PFOA-exposed F1 dams exhibited diminished lactational morphology, although F1 maternal behavior and F2 offspring body weights were not significantly affected by P0 treatment. In addition to reduced gland development in F1 females under all exposures, F2 females with chronic low-dose drinking-water exposures exhibited visibly slowed mammary gland differentiation from weaning onward. F2 females derived from 5 mg/kg PFOA-treated P0 dams displayed gland morphology similar to F2 chronic water exposure groups on PNDs 22-63. Gestational PFOA exposure induced delays in mammary gland development and/or lactational differentiation across three generations. Chronic, low-dose PFOA exposure in drinking water was also sufficient to alter mammary morphological development in mice, at concentrations approximating those found in contaminated human water supplies.
    b. ANALYSIS: This mouse study looked at effects of PFOA on the development of the mammary gland over two generations of females exposed at two different developmental times: 1) gestation only (from GD1-17) with doses of 1 and 5 mg/kg/d, and 2) gestation plus continuous postnatal exposure via drinking water at a 1mg/kg/d dose. The findings included: gestational exposure to PFOA delays mammary gland development and differentiation during lactation in parental, F1 and F2 generation of female mice. Chronic exposure to PFOA through drinking water also altered the mammary gland development across generations.
    c. CONCLUSION: This study supports FDA's toxicology conclusion that "brief in utero exposure alone is sufficient to induce postnatal toxicity into adulthood" and expands it to include long lasting effects through generations. In additions, it shows that continuous exposure to low doses starting *in utero* also have significant effects on the mammary gland.

8. Yahia, D., M.A. El-Nasser, M. Abedel-Latif, C. Tsukuba, M. Yoshida, I. Sato, and S. Tsuda. 2010. Effects of perfluorooctanoic acid (PFOA) exposure to pregnant mice on reproduction. J. Toxicol. Sci. 35: 527-533.
    a. ABSTRACT: Perfluorooctanoic acid (PFOA) has similar characteristics to perfluorooctane sulfonate (PFOS) in reproduction toxicity featured by neonatal death. We found that PFOS exposure to mice during pregnancy led to intracranial blood vessel dilatation of fetuses accompanied by severe lung collapse which caused neonatal mortality. Thus, we adopted the corresponding experimental design to PFOS in order to characterize the neonatal death by PFOA. Pregnant ICR mice were given 1, 5 and 10 mg/kg PFOA daily by gavage from gestational day (GD) 0 to 17 and 18 for prenatal and postnatal evaluations, respectively. Five to nine dams per group were sacrificed on GD 18 for prenatal evaluation; other 10 dams were left to give birth. No maternal death was observed. The liver weight increased dose-dependently, with hepatocellular hypertrophy, necrosis, increased mitosis and mild calcification at 10 mg/kg. PFOA at 10 mg/kg increased serum enzyme activities (GGT, ALT, AST and ALP) with hypoproteinemia and hypolipidemia. PFOA treatment reduced the fetal body weight at 5 and 10 mg/kg. Teratological evaluation showed delayed ossification of the sternum and phalanges and delayed eruption of incisors at 10 mg/kg, but did not show intracranial blood vessel dilatation. Postnatal evaluation revealed that PFOA reduced the neonatal survival rate at 5 and 10 mg/kg. At 5 mg/kg pups were born alive and active and 16% died within 4 days observation, while all died within 6 hr after birth at 10 mg/kg without showing intracranial blood vessel dilatation. The cause of neonatal death by PFOA may be different from PFOS.
    b. ANALYSIS: This mouse study uses three doses of PFOA (1, 5 and 10mg/kg/d) administered to dams by gavage from GD 0-17 and 18. Prenatal and postnatal endpoints were evaluated. The findings included: fetal evaluation at GD17 showed reduced body weight, delayed ossification of the sternum and phalanges and delayed tooth eruption. At postnatal day 4 there was a 16% pup death in the middle dose group; all pups died hours after birth in the high dose group.
    c. CONCLUSION: This study supports FDA's toxicology assessment of similar prenatal and postnatal endpoints. In addition it also shows that the dam's liver and kidney weights increased in all doses, and brain weight was increased at the highest dose.

Rat Toxicology Studies

9. Butenhoff, J.L., G.L. Kennedy, Jr., S.-C. Chang, and G.W. Olsen. 2012. Chronic dietary toxicity and carcinogenicity study with ammonium perfluorooctanoate in Sprague-Dawley rats. Toxicol. 298:1-13. http://www.sciencedirect.com/science/article/pii/S0300483X12001151
    a. ABSTRACT: In order to assess the potential chronic toxicity and tumorigenicity of ammonium perfluorooctanoate (APFO), a 2-year dietary study was conducted with male and female rats fed 30 ppm or 300 ppm (approximately 1.5 and 15 mg/kg). In males fed 300 ppm, mean body weights were lower across most of the test period and survival in these rats was greater than that seen either in the 30 ppm or the control group. Non-neoplastic effects were observed in liver in rats fed 300 ppm and included elevated liver weight, an increase in the incidence of diffuse hepatocellular hypertrophy, portal mononuclear cell infiltration, and mild hepatocellular vacuolation without an increase in hepatocellular necrosis. Mean serum activities of alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase were elevated up to three times the control means, primarily at the 300 ppm dose. A significant increase in Leydig cell tumors of the testes was seen in the males fed 300 ppm, and tumors of the liver and acinar pancreas, which are often observed in rats from chronic exposure to peroxisome proliferating agents, were not observed in this study. All other tumor types were those seen spontaneously in rats of this stock and age and were not associated with feeding of APFO.
    b. ANALYSIS: This is a 2-year chronic and carcinogenesis study; rats were exposed to two doses of ammonium perfluorooctanoate (APFO) in the diet (1.5 and 15 mg/kg/day). The data showed a significant increase in testicular cancer in the high dose treatment. The liver also showed significant toxicity including increased weight, cell hypertrophy and vacualization and white blood cell infiltration; serum liver enzyme levels were also higher compared to untreated animals.
    c. CONCLUSION: This study supports FDA's toxicology evaluation regarding liver toxicity and carcinogenicity of perfluorocarboxylic compounds.

10. Cui, L., C. Liao, Q. Zhou, T. Xia, Z. Yun, and G. Jiang. 2010. Excretion of PFOA and PFOS in male rats during a subchronic exposure. Arch. Environ. Contam. Toxicol. 58: 205-213.
    a. ABSTRACT: Perfluorinated compounds (PFCs), a class of synthetic surfactants that are widely used, have become global environmental contaminants because of their high persistence and bioaccumulation. An increasing number of studies have described the pharmacokinetics of PFCs following in vivo exposure, however, few papers have focused on the excretion of these compounds during a period of consecutive exposure. In this study, the excretions of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) in male Sprague-Dawley rats gavaged consecutively for 28 days were investigated and compared. The faster elimination rate in urine compared to feces indicated that urinary excretion is the primary clearance route in rats for either PFOA or PFOS. During the first 24 h after administration of PFOA (5 and 20 mg/kg body weight/day), about 24.7-29.6% of the oral dose was excreted through urine and feces, while for PFOS, the excretion amounts were only 2.6-2.8% of the total gavaged doses (5 and 20 mg/kg body weight/day). The excretion

rates of both PFCs increased with increasing exposure doses. The higher elimination rate of PFOA through excretion indicated its lower accumulation in rats, thus inducing possible lower toxicities compared to PFOS.

b. ANALYSIS: This rat study used two doses of PFOA (5 and 20 mg/kg/d) administered to male rats for 28 consecutive days by gavage. It assessed the rate and route of excretion. The authors found that less than 30% of the oral dose was eliminated in feces and urine during the first 24 hours after administration of PFOA and the rate of elimination increased with time.
c. CONCLUSION: This study adds supporting data on excretion of PFOA and it does not contradict FDA's toxicology conclusions regarding any of the evaluated endpoints.

In summary, NRDC did not find anything in the 10 *in vivo* animal studies that contradicted FDA's conclusions, especially that perfluorocarboxylates should be treated as a class. On the contrary, we found additional evidence supporting FDA's conclusion that these chemicals cause adverse health effects in animals.

Recent publications on systematic reviews of PFOA exposure including human and animal data, and epidemiological study using biomonitoring NHANES data.

The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Systematic Review of Human Evidence for PFOA Effects on Fetal Growth
Paula I. Johnson, Patrice Sutton, Dylan S. Atchley, Erica Koustas, Juleen Lam, Saunak Sen, Karen A. Robinson, Daniel A. Axelrad, and Tracey J. Woodruff. Environ Health Perspect 122:1028–1039; http://dx.doi.org/10.1289/ehp.1307893

Background: The Navigation Guide methodology was developed to meet the need for a robust method of systematic and transparent research synthesis in environmental health science. We conducted a case study systematic review to support proof of concept of the method.
Objective: We applied the Navigation Guide systematic review methodology to determine whether developmental exposure to perfluorooctanoic acid (PFOA) affects fetal growth in humans.
Methods: We applied the first 3 steps of the Navigation Guide methodology to human epidemiological data: 1) specify the study question, 2) select the evidence, and 3) rate the quality and strength of the evidence. We developed a protocol, conducted a comprehensive search of the literature, and identified relevant studies using prespecified criteria. We evaluated each study for risk of bias and conducted meta-analyses on a subset of studies. We rated quality and strength of the entire body of human evidence.
Results: We identified 18 human studies that met our inclusion criteria, and 9 of these were combined through meta-analysis. Through meta-analysis, we estimated that a 1‑ng/mL increase in serum or plasma PFOA was associated with a –18.9 g (95% CI: –29.8, –7.9) difference in birth weight. We concluded that the risk of bias across studies was low, and we assigned a "moderate" quality rating to the overall body of human evidence.

Conclusion: On the basis of this first application of the Navigation Guide systematic review methodology, we concluded that there is "sufficient" human evidence that developmental exposure to PFOA reduces fetal growth.

The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Systematic Review of Nonhuman Evidence for PFOA Effects on Fetal Growth.
Erica Koustas, Juleen Lam, Patrice Sutton, Paula I. Johnson, Dylan S. Atchley, Saunak Sen, Karen A. Robinson, Daniel A. Axelrad, and Tracey J. Woodruff. Environ Health Perspect 122:1015–1027; http://dx.doi.org/10.1289/ehp.1307177

Background: In contrast to current methods of expert-based narrative review, the Navigation Guide is a systematic and transparent method for synthesizing environmental health research from multiple evidence streams. The Navigation Guide was developed to effectively and efficiently translate the available scientific evidence into timely prevention-oriented action.
Objectives: We applied the Navigation Guide systematic review method to answer the question "Does fetal developmental exposure to perfluorooctanoic acid (PFOA) or its salts affect fetal growth in animals ?" and to rate the strength of the experimental animal evidence.
Methods: We conducted a comprehensive search of the literature, applied prespecified criteria to the search results to identify relevant studies, extracted data from studies, obtained additional information from study authors, conducted meta-analyses, and rated the overall quality and strength of the evidence.
Results: Twenty-one studies met the inclusion criteria. From the meta-analysis of eight mouse gavage data sets, we estimated that exposure of pregnant mice to increasing concentrations of PFOA was associated with a change in mean pup birth weight of –0.023 g (95% CI: –0.029, –0.016) per 1-unit increase in dose (milligrams per kilogram body weight per day). The evidence, consisting of 15 mammalian and 6 nonmammalian studies, was rated as "moderate" and "low" quality, respectively.
Conclusion: Based on this first application of the Navigation Guide methodology, we found sufficient evidence that fetal developmental exposure to PFOA reduces fetal growth in animals.

The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Integration of Animal and Human Evidence for PFOA Effects on Fetal Growth
Juleen Lam, Erica Koustas, Patrice Sutton, Paula I. Johnson, Dylan S. Atchley, Saunak Sen, Karen A. Robinson, Daniel A. Axelrad, and Tracey J. Woodruff. Environ Health Perspect 122:1040–1051; http://dx.doi.org/10.1289/ehp.1307923

Background: The Navigation Guide is a novel systematic review method to synthesize scientific evidence and reach strength of evidence conclusions for environmental health decision making.
Objective: Our aim was to integrate scientific findings from human and nonhuman studies to determine the overall strength of evidence for the question "Does developmental exposure to

perfluorooctanoic acid (PFOA) affect fetal growth in humans?"
Methods: We developed and applied prespecified criteria to systematically and transparently a) rate the quality of the scientific evidence as "high," "moderate," or "low"; b) rate the strength of the human and nonhuman evidence separately as "sufficient," "limited," "moderate," or evidence of lack of toxicity"; and c) integrate the strength of the human and nonhuman evidence ratings into a strength of the evidence conclusion.
Results: We identified 18 epidemiology studies and 21 animal toxicology studies relevant to our study question. We rated both the human and nonhuman mammalian evidence as "moderate" quality and "sufficient" strength. Integration of these evidence ratings produced a final strength of evidence rating in which review authors concluded that PFOA is "known to be toxic" to human reproduction and development based on sufficient evidence of decreased fetal growth in both human and nonhuman mammalian species.
Conclusion: We concluded that developmental exposure to PFOA adversely affects human health based on sufficient evidence of decreased fetal growth in both human and nonhuman mammalian species. The results of this case study demonstrate the application of a systematic and transparent methodology, via the Navigation Guide, for reaching strength of evidence conclusions in environmental health.

Perfluoroalkyl Chemicals and Asthma among Children 12–19 Years of Age: NHANES (1999–2008)
Olivier Humblet, Ledif Grisell Diaz-Ramirez, John R. Balmes, Susan M. Pinney, and Robert A. Hiatt. Environ Health Perspect 122:1129–1133; http://dx.doi.org/10.1289/ehp.1306606

Background: Perfluoroalkyl chemicals (PFCs) are a family of commonly used industrial chemicals whose persistence and ubiquity in human blood samples has led to concern about possible toxicity. Several animal studies and one recent human study have suggested a link between exposure to PFCs and asthma, although few epidemiologic studies have been conducted.
Objectives: We investigated children's PFC serum concentrations and their associations with asthma-related outcomes.
Methods: We evaluated the association between serum concentrations of eight PFCs, including perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), perfluorononanoic acid (PFNA), and perfluorohexane sulfonic acid (PFHxS), with self-reported lifetime asthma, recent wheezing, and current asthma using data from participants 12–19 years of age from the 1999–2000 and 2003–2008 National Health and Nutrition Examination Surveys.
Results: In multivariable-adjusted models, PFOA was associated with higher odds of ever having received a diagnosis of asthma [odds ratio (OR) = 1.18; 95% CI: 1.01, 1.39 for a doubling in PFOA], whereas for PFOS there were inverse relationships with both asthma and wheezing (OR = 0.88; 95% CI: 0.74, 1.04, and OR = 0.83; 95% CI: 0.67, 1.02, respectively). The associations were attenuated after accounting for sampling weights. No associations were seen between the other PFCs and any outcome.

Conclusions: This cross-sectional study provides some evidence for associations between exposure to PFCs and asthma-related outcomes in children. The evidence is inconsistent, however, and prospective studies are needed.

Appendix 6
Long-Chain Perfluorocarboxylates Removed from Commerce in 2011.

Table A-1: Effective Food Contact Substance Notifications for Long-Chain Perfluorocarboxylates for which the manufacturer voluntarily ceased introduction into interstate commerce in 2011 in response to FDA's 2010 request.

FCN No.	Manufacturer	Description of Food Contact Substance (FCS) covered by the effective FCS Notification (FCN)	Intended Use	Effective Date (before cessation)
59	BASF Corp.	Glycine, N,N-bis[2-hydroxy-3-(2-propenyloxy)propyl]-, monosodium salt, reaction products with ammonium hydroxide and pentafluoroiodoethane-tetrafluoroethylene telomer (CAS Reg. No. 220459-70-1).	As a component of paper and paperboard in contact with nonalcoholic food.	August 16, 2000
206	DuPont Chemical Solutions Enterprise	Copolymer of 2-perfluoroalkylethyl acrylate, 2-N,N-diethylaminoethyl methacrylate, and glycidyl methacrylate.	As an oil and grease-resistant treatment for paper and paperboard intended for food-contact use.	June 12, 2002
255	BASF Corp.	3-cyclohexane-1-carboxylic acid, 6-((di-2-propenylamino)carbonyl)-,(1R,6R), reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, ammonium salts.	As an oil repellent sizing agent in the production of paper and paperboard.	September 5, 2002
311	DuPont Chemical Solutions Enterprise	Copolymers of 2-perfluoroalkylethyl acrylate, 2-N,N-diethylaminoethyl methacrylate, and glycidyl methacrylate.	As an oil or grease resistant treatment for paper and paperboard intended for single service use in microwave heat-susceptor packaging; the food-contact substance is intended to contact all food types.	April 15, 2003
338	DuPont Chemical Solutions Enterprise	Copolymers of 2-perfluoroalkylethyl acrylate, 2-N,N-diethylaminoethyl methacrylate, and glycidyl methacrylate.	As an oil or grease resistant treatment for paper and paperboard intended for food-contact use.	August 19, 2003

628	Clariant Corp.	Copolymer of 2-perfluoroalkylethyl acrylate, 2-(dimethylamino)ethyl methacrylate, and oxidized 2-(dimethylamino)ethyl methacrylate (CAS Reg. No. 479029-28-2).	As an oil and grease repellent in the manufacture of paper and paperboard.	October 10, 2006
646	DuPont Chemical Solutions Enterprise	Copolymers of 2-perfluoroalkylethyl acrylate, 2-N,N-diethylaminoethyl methacrylate, glycidyl methacrylate, acrylic acid, and methacrylic acid (CAS Reg. No. 870465-08-0).	As an oil and grease resistant treatment for paper and paperboard employed either prior to the sheet forming operation or at the size press.	September 30, 2006
See http://www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/Notifications/ucm308462.htm.				

Appendix 7
Requested Changes to 21 C.F.R. § 176.170

[Code of Federal Regulations]
[Title 21, Volume 3]
[Revised as of April 1, 2013]
[CITE: 21CFR176.170]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER B--FOOD FOR HUMAN CONSUMPTION (CONTINUED)
PART 176 -- INDIRECT FOOD ADDITIVES: PAPER AND PAPERBOARD COMPONENTS
Subpart B--Substances for Use Only as Components of Paper and Paperboard

Sec. 176.170 Components of paper and paperboard in contact with aqueous and fatty foods.

Substances identified in this section may be safely used as components of the uncoated or coated food-contact surface of paper and paperboard intended for use in producing, manufacturing, packaging, processing, preparing, treating, packing, transporting, or holding aqueous and fatty foods, subject to the provisions of this section. Components of paper and paperboard in contact with dry food of the type identified under Type VIII of table 1 in paragraph (c) of this section are subject to the provisions of 176.180.
(a) Substances identified in paragraph (a) (1) through (5) of this section may be used as components of the food-contact surface of paper and paperboard. Paper and paperboard products shall be exempted from compliance with the extractives limitations prescribed in paragraph (c) of this section:*Provided,* That the components of the food-contact surface consist entirely of one or more of the substances identified in this paragraph:*And provided further,* That if the paper or paperboard when extracted under the conditions prescribed in paragraph (c) of this section exceeds the limitations on extractives contained in paragraph (c) of this section, information shall be available from manufacturing records from which it is possible to determine that only substances identified in this paragraph (a) are present in the food-contact surface of such paper or paperboard.
(1) Substances generally recognized as safe in food.
(2) Substances generally recognized as safe for their intended use in paper and paperboard products used in food packaging.
(3) Substances used in accordance with a prior sanction or approval.
(4) Substances that by regulation in parts 170 through 189 of this chapter may be safely used without extractives limitations as components of the uncoated or coated food-contact surface of paper and paperboard in contact with aqueous or fatty food, subject to the provisions of such regulation.
(5) Substances identified in this paragraph, as follows:

List of Substances	**Limitations**
Acetyl peroxide	For use only as polymerization catalyst.
Acrylamide-methacrylic acid-maleic anhydride copolymers containing not more than 0.2 percent of	For use only as a retention aid employed prior to t

residual acrylamide monomer and having an average nitrogen content of 14.9 percent such that a 1 percent by weight aqueous solution has a minimum viscosity of 600 centipoises at 75 deg. F, as determined by LVG-series Brookfield viscometer (or equivalent) using a No. 2 spindle at 30 r.p.m	sheet-forming operation in the manufacture of paper and paperboard in such an amount that the finished paper and paperboard will contain the additive at a level not in excess of 0.05 percent by weight of dry fibers in the finished paper and paperboard.
Acrylamide-[beta]-methacrylyloxyethyltrimethylammonium methyl sulfate copolymer resins containing not more than 10 molar percent of [beta]-methacrylyloxyethyltrimethylammonium methyl sulfate and containing less than 0.2% of residual acrylamide monomer	For use only as a retention aid and flocculant employed prior to the sheet-forming operation in the manufacture of paper and paperboard.
Acrylic acid, sodium salt copolymer with polyethyleneglycol allyl ether (CAS Reg. No. 86830-15-1)	For use only in paper mill boilers.
Acrylic acid copolymer with 2-acrylamido-2-methylpropane-sulfonic acid (CAS Reg. No. 40623-75-4) and/or its ammonium/alkali metal mixed salts. The copolymer is produced by poly-merization of acrylic acid and 2-acrylamido-2-methylpropane-sulfonic acid in a weight ratio of 60/40, such that a 28 percent by weight aqueous solution of the polymer has a viscosity of 75-150 centipoises at 25 deg. C as determined by LV-series Brookfield viscometer (or equivalent) using a No. 2 spindle at 60 r.p.m	For use only as a scale inhibitor prior to the sheet-forming operation in the manufacture of paper and paperboard and used at a level not to exceed 1.0 kilogram (2.2 pounds) of copolymer per 907 kilograms (1 ton) of dry paper and paperboard fibers.
Acrylonitrile polymer, reaction product with ethylenediamine sulfate having a nitrogen content of 22.5-25.0 percent (Kjeldahl dry basis) and containing no more than 0.075 percent monomer as ethylenediamine. The finished resin in a 24 percent by weight aqueous solution has a viscosity of 1,000-2,000 centipoises at 25 deg. C as determined by LVT-series Brookfield viscometer using a No. 4 spindle at 50 r.p.m. (or by other equivalent method)	For use only as a size promoter and retention aid at a level not to exceed 0.5 percent by weight of the dry paper and paperboard.
Acrylonitrile polymer with styrene, reaction product with ethylenediamine acetate, having a nitrogen content of 7.4-8.3 percent (Kjeldahl dry basis) and containing no more than 0.25 percent monomer as ethylenediamine	1. For use only as a sizing material applied after the sheet-forming operation in the manufacture of paper and paperboard in such amount that the paper and paperboard will contain the additive at a level not in excess of 0.25 percent by weight of the dry paper and paperboard.2. For use only as a sizing material applied prior to the sheet-forming operation in the manufacture of paper and paperboard in such amount that the paper and paperboard will contain the additive at a level not in excess of 1.0 percent by weight of the dry paper and paperboard.
1-Alkenyl olefins, containing not less than 72 percent of $C_{30}$and higher olefins	For use only under the following conditions:1. In coatings for paper and paperboard with food of Types I, II, IV-B, and VII-B described in table 1 of paragraph (c) of this section under conditions of use E, F, and G described in table 2 of paragraph (c) of this section.2. In coatings for paper and paperboard

	with food of Type VIII described in table I of paragraph (c) of this section under conditions of use A through H described in table 2 of paragraph (c) of this section.
(2-Alkenyl) succinic anhydrides mixture, in which the alkenyl groups are derived from olefins which contain not less than 95 percent of C_{15}-C_{21}groups	For use only as a sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard and limited to use at a level not to exceed 1 percent by weight of the finished dry paper and paperboard fibers.
Alkyl(C_{12}-C_{20})methacrylatemethacrylic acid copolymers (CAS Reg. No. 27401-06-5)	For use only as stabilizers employed prior to the sheet-forming operation in the manufacture of paper and paperboard.
tert-Alkyl(C_8-C_{16})mercaptans	For use only as polymerization-control agent.
Aluminum acetate	
2-Amino-2-methyl-1-propanol (CAS Reg. No. 124-68-5)	For use as a dispersant for pigment suspension at a level not to exceed 0.25 percent by weight of pigment. The suspension is used as a component of coatings for paper and paperboard under conditions of use described in paragraph (c) of this section, table 2, conditions of use E through G.
Ammonium bis(*N*-ethyl-2-perfluoroalkylsulfonamido ethyl) phosphates, containing not more than 15% ammonium mono (*N*-ethyl-2-perfluoroalkylsulfonamido ethyl) phosphates, where the alkyl group is more than 95% $C_8$and the salts have a fluorine content of 50.2% to 52.8% as determined on a solids basis	For use only as an oil and water repellant at a level not to exceed 0.17 pound (0.09 pound of fluorine) per 1,000 square feet of treated paper or paperboard of a sheet basis weight of 100 pounds or less per 3,000 square feet of paper or paperboard, and at a level not to exceed 0.5 pound (0.26 pound of fluorine) per 1,000 square feet of treated paper or paperboard having a sheet basis weight greater than 100 lb. per 3,000 square feet as determined by analysis for total fluorine in the treated paper or paperboard without correction for any fluorine that might be present in the untreated paper or paperboard, when such paper or paperboard is used as follows:1. In contact, under conditions of use C, D, E, F, G, or H described in table 2 of paragraph (c) of this section, with nonalcoholic food.2. In contact with bakery products

	of Type VII, VIII, and IX described in table I of paragraph (c) of this section under good manufacturing practices of commercial and institutional baking.
Ammonium persulfate	
Ammonium thiosulfate	
Ammonium zirconium carbonate (CAS Reg. No. 32535-84-5) and its tartaric acid adduct	For use only as an insolubilizer for binders used in coatings for paper and paperboard, and limited to use at a level not to exceed 2.5 percent by weight of coating solids.
Ammonium zirconium citrate (CAS Reg. No. 149564-62-5), ammonium zirconium lactate-citrate (CAS Reg. No. 149564-64-7), ammonium zirconium lactate (CAS Reg. No. 149564-63-6)	For use as insolubilizers with protein binders in coatings for paper and paperboard, at a level not to exceed 1.4 percent by weight of coating solids.
Anionic polyurethane, produced by reacting the preliminary adduct formed from the reaction of glyceryl monostearate and 2,4-toluenediisocyanate with not more than 10 mole percent*N*-methyldiethanolamine and not less than 90 mole percent dimethylolpropionic acid. The final product is a 15 to 20 percent by weight aqueous solution, having a Brookfield viscosity of 25 to 100 centipoises at 24 deg. C (75 deg. F)	For use only as a surface sizing agent at a level not to exceed 0.1 percent by weight of dry paper and paperboard.
9,10-Anthraquinone (Chemical Abstracts Service Registry No. 84-65-1) which has a purity of not less than 98 percent	For use only as a pulping aid in the alkaline pulping of lignocellulosic material at levels not to exceed 0.1 percent by weight of the raw lignocellulosic material.
Aromatic petroleum hydrocarbon resin, hydrogenated (CAS Reg. No. 88526-47-0), produced by the catalytic polymerization of aromatic substituted olefins from low boiling distillates of cracked petroleum stocks with a boiling point no greater than 220 deg. C (428 deg. F), and the subsequent catalytic reduction of the resulting aromatic petroleum hydrocarbon resin. The resin meets the following specifications: softening point 85 deg. C (185 deg. F) minimum, as determined by ASTM Method E 28-67 (Reapproved 1982), "Standard Test Method for Softening Point by Ring-and-Ball Apparatus," and aniline point 70 deg. C (158 deg. F) minimum, as determined by ASTM Method D 611-82, "Standard Test Methods for Aniline Point and Mixed Aniline Point of Petroleum Products and Hydrocarbon Solvents," which are incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from the American Society for Testing and Materials, 100 Barr Harbor Dr., West Conshohocken, Philadelphia, PA 19428-2959, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*	For use only as modifiers in wax polymer blend coatings for paper and paperboard at a level not to exceed 50 weight-percent of the coating solids under conditions of use E, F, and G identified in table 2 of paragraph (c) of this section.
Azo-bisisobutyronitrile	For use only as polymerization catalyst.

1,2-Benzisothiazolin-3-one (CAS Registry No. 2634-33-5)	For use only as a preservative in paper coating compositions and limited to use at a level not to exceed 0.01 mg/in^2(0.0016 mg/cm^2) of the finished paper and paperboard.
Benzoyl peroxide	Do.
N,*N*-Bis(2-hydroxyethyl)alkyl (C_{12}-C_{18})amide	For use only as an adjuvant to control pulp absorbency and pitch content in the manufacture of paper and paperboard prior to the sheet forming operation.
Bis(methoxymethyl)tetrakis-[(octadecyloxy)-methyl]melamine resins having a 5.8-6.5 percent nitrogen content (CAS Reg. No. 68412-27-1)	For use only under the following conditions:1. As a water repellant employed prior to the sheet-forming operation in the manufacture of paper and paperboard in such amount that the finished paper and paperboard will contain the additive at a level not in excess of 1.6 percent by weight of the finished dry paper and paperboard fibers.2. The finished paper and paperboard will be used in contact with nonalcoholic foods only.3. As a water repellant employed after the sheet-forming operation in the manufacture of paper and paperboard in such amount that the finished paper and paperboard will contain the additive at a level not to exceed 1.6 percent by weight of the finished dry paper and paperboard fibers. The finished paper and paperboard will be used only in contact with food of Types I, II, IV-B, VI, VII-B, and VIII described in table 1 of paragraph (c) of this section.
2-Bromo-2-nitro-1,3-propanediol (CAS Reg. No. 52-51-7)	For use only as an antimicrobial/preservative in fillers, pigment slurries, starch sizing solutions, and latex coatings at levels not to exceed 0.01 percent by weight of those components.
Butanedioic acid, sulfo-1,4-di-(C_9-C_{11}alkyl) ester, ammonium salt (also known as butanedioic acid, sulfo-1,4-diisodecyl ester, ammonium salt [CAS Reg. No. 144093-88-9]).	For use as a surface active agent in package coating inks at levels not to exceed 3 percent by weight of the coating ink.
tert-Butyl hydroperoxide	For use only as polymerization catalyst.
tert-Butyl peroxide	Do.

Calcium isostearate	For use only with*n*-decyl alcohol as a stabilizing material for aqueous calcium stearate dispersions intended for use as components of coatings for paper and paperboard.
Carrageenan and salts of carrageenan as described in 172.620 and 172.626 of this chapter	
Castor oil, hydrogenated	
Castor oil, sulfated, ammonium, potassium, or sodium salt	
Cellulose, regenerated	
Chloracetamide	For use only as polymerization-control agent.
Cobaltous acetate	For use only as polymerization catalyst.
Cumene hydroperoxide	Do.
Cyanoguanidine	For use only:1. As a modifier for amino resins.2. As a fluidizing agent in starch and protein coatings for paper and paperboard.
n-Decyl alcohol	For use only with calcium isostearate as a stabilizing material for aqueous calcium stearate dispersions intended for use as components of coatings for paper and paperboard.
Dialdehyde guar gum	For use only as a wet-strength agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard and used at a level not to exceed 1% by weight of the finished dry paper and paperboard fibers.
Dialdehyde locust bean gum	Do.
Dialkyl(C_{16}-C_{18})carbamoyl chloride (CAS Reg. No. 41319-54-4) manufactured by the reaction of secondary amines derived from fatty acids of animal or vegetable sources with phosgene	For use as a sizing agent at a level not to exceed 0.2 percent by weight of the dry fiber.

Diallyldimethyl ammonium chloride polymer with acrylamide and potassium acrylate, produced by copolymerizing either (1) diallyldimethyl ammonium chloride and acrylamide in a weight ratio of 50/50, with 4.4 percent of the acrylamide subsequently hydrolyzed to potassium acrylate or (2) polymerized diallyldimethyl ammonium chloride, acrylamide and potassium acrylate (as acrylic acid) in a weight ratio of 50/47.8/2.2, respectively, so that the finished resin in a 1 percent by weight aqueous solution (active polymer) has a viscosity of more than 22 centipoises at 22 deg. C (72 deg. F) as determined by LVF series, Brookfield Viscometer using No. 1 spindle at 60 RPM (or by other equivalent method) (CAS Reg. No. 25136-75-8)	For use only as a retention and/or drainage aid employed prior to the sheet-forming operations in the manufacture of paper and paperboard and limited to use at a level not to exceed 0.05 percent by weight of the finished paper and paperboard.
Diallyldimethylammonium chloride with acrylamide (CAS Reg. No. 26590-05-6). The copolymer is produced by copolymerizing diallyldimethylammonium chloride with acrylamide in a weight ratio of 50-50 so that the finished resin in a 1 percent by weight aqueous solution (active polymer) has a viscosity of more than 22 centipoises at 22 deg. C (71.6 deg. F), as determined by LVF-series Brookfield viscometer using a No. 1 spindle at 60 r.p.m. (or by other equivalent method)	For use only as a drainage and/or retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard and limited to use at a level not to exceed 0.05 percent by weight of the finished paper and paperboard.
Diallyldiethylammonium chloride polymer with acrylamide, and diallyldimethylammonium chloride, produced by copolymerizing acrylamide, diallyldiethylammonium chloride, and diallyldimethylammonium chloride, respectively, in the following weight ratios and having viscosities determined at 22 deg. C, by LVF-series Brookfield viscometer using a No. 1 spindle at 60 r.p.m. (or by other equivalent method), as follows:	
1. Weight ratio: 50-2.5-47.5. The finished resin in a 1 percent by weight aqueous solution has a minimum viscosity of 22 centipoises	For use only as a retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard and limited to use at a level not to exceed 0.05 percent by weight of the finished paper and paperboard.
2. Weight ratio: 25-2.5-72.5. The finished resin in a 0.20 percent by weight aqueous solution has a minimum viscosity of 20 centipoises	For use only as a drainage and/or retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard and limited to use at a level not to exceed 0.075 percent by weight of the finished paper and paperboard.
3. Weight ratio: 80-2.5-17.5. The finished resin in a 0.30 percent by weight aqueous solution has a minimum viscosity of 50 centipoises	For use only as a drainage and/or retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard and limited to use at a level not to exceed 0.075 percent by weight of the finished paper and paperboard.
Diallyldiethylammonium chloride polymer with acrylamide, potassium acrylate, and diallyldimethylammonium chloride. The polymer is produced by copolymerizing either: (1) acrylamide, diallyldiethylammonium chloride, and diallyldimethylammonium chloride in a weight ratio of 50-2.5-	For use only as a retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard and limited to use at a level not to

47.5, respectively, with 4.4 percent of the acrylamide subsequently hydrolyzed to potassium acrylate, or (2) acrylamide, potassium acrylate (as acrylic acid), diallyldiethylammonium chloride, and diallyldimethylammonium chloride in a weight ratio of 47.8-2.2-2.5-47.5, so that the finished resin in a 1 percent by weight aqueous solution has a minimum viscosity of 22 centipoises at 22 deg. C, as determined by LVF-series Brookfield viscometer using a No. 1 spindle at 60 r.p.m. (or by other equivalent method)	exceed 0.05 percent by weight of the finished paper and paperboard.
Diallyldimethylammonium chloride polymer with acrylamide, reaction product with glyoxal, produced by copolymerizing not less than 90 weight percent of acrylamide and not more than 10 weight percent of diallyldimethylammonium chloride, which is then cross-linked with not more than 30 weight percent of glyoxal, such that a 10 percent aqueous solution has a minimum viscosity of 25 centipoises at 25 deg. C as determined by Brookfield viscometer Model RVF, using a No. 1 spindle at 100 r.p.m	For use only as a dry and wet strength agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard in such an amount that the finished paper and paperboard will contain the additive at a level not in excess of 2 percent by weight of the dry fibers in the finished paper and paperboard.
2,2-Dibromo-3-nitrilopropionamide (CAS Reg. No.10222-01-2).	For use as a preservative at a level not to exceed 100 parts per million in coating formulations and in component slurries and emulsions, used in the production of paper and paperboard and coatings for paper and paperboard.
2,5-Di-*tert*-butyl hydroquinone	For use only as an antioxidant for fatty based coating adjuvants provided it is used at a level not to exceed 0.005% by weight of coating solids.
Diethanolamine	For use only:1. As an adjuvant to control pulp absorbency and pitch content in the manufacture of paper and paperboard prior to the sheet-forming operation.2.In paper mill boilers.
~~Diethanolamine salts of mono- and bis (1*H*,1*H*,2*H*,2*H* perfluoroalkyl) phosphates where the alkyl group is even-numbered in the range C_8-$C_{18}$and the salts have a fluorine content of 52.4% to 54.4% as determined on a solids basis~~	~~For use only as an oil and water repellant at a level not to exceed 0.17 pound (0.09 pound of fluorine) per 1,000 square feet of treated paper or paperboard, as determined by analysis for total fluorine in the treated paper or paperboard without correction for any fluorine which might be present in the untreated paper or paperboard, when such paper or paperboard is used in contact with nonalcoholic foods under the conditions of use described in paragraph (c) of this section, table 2, conditions of use (B) through (H).~~
Diethyl(2-hydroxyethyl) methylammonium methyl sulfate, acrylate, polymer with acrylamide, chemical	For use only as a retention aid and drainage aid

abstract service registry No. [26796-75-8] having 90-95 mole pct. acrylamide, a nitrogen content of not more than 19.7 pct. (Kjeldahl, dry basis), and a residual acrylamide monomer content of not more than 0.1 pct. The finished polymer in a 1 pct. by weight aqueous solution has a minimum viscosity of 900 centipoises at 25 deg. C as determined by LVT-series Brookfield viscometer using a No. 2 spindle at 12 r.p.m. (or by equivalent method)	employed prior to the sheet-forming operation in the manufacture of paper and paperboard at a level not to exceed 0.15 pct. by weight of finished dry paper and paperboard fibers.
Diethylenetriamine	For use only as a modifier for amino resins.
N,*N*-Diisopropanolamide of tallow fatty acids	For use only as an adjuvant to control pulp absorbency and pitch content in the manufacture of paper and paperboard prior to the sheet-forming operation.
Dimethylamine-epichlorohydrin copolymer in which not more than 5 mole-percent of dimethylamine may be replaced by an equimolar amount of ethylenediamine and in which the ratio of total amine to epichlorohydrin does not exceed 1:1. The nitrogen content of the copolymer shall be 9.4 to 10.8 weight percent on a dry basis and a 10 percent by weight aqueous solution of the final product has a minimum viscosity of 5.0 centipoises at 25 deg. C, as determined by LVT-series Brookfield viscometer using a No. 1 spindle at 60 r.p.m. (or by other equivalent method)	For use only:1. As a retention aid employed before the sheet-forming operation in the manufacture of paper and paperboard and limited to use at a level not to exceed 1 percent by weight of the finished paper and paperboard.2. At the size press at a level not to exceed 0.017 percent by weight of the finished paper and paperboard.
N-[(Dimethylamino)methyl]-acrylamide polymer with acrylamide and styrene having a nitrogen content of not more than 16.9 percent and a residual acrylamide monomer content of not more than 0.2 percent on a dry basis	For use only as a dry-strength agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard and used at a level not to exceed 1 percent by weight of finished dry paper or paperboard fibers.
N,*N'*-Dioleoylethylenediamine	
Diphenylamine	For use only as an antioxidant for fatty based coating adjuvants provided it is used at a level not to exceed 0.005% by weight of coating solids.
Dipropylene glycol	
Disodium salt of 1,4-dihydro-9,10-dihydroxyanthracene (CAS Reg. No. 73347-80-5)	For use only as a catalyst in the alkaline pulping of lignocellulosic materials at levels not to exceed 0.1 percent by weight of the raw lignocellulosic materials.
N,*N'*-Distearoylethylenediamine	
n-Dodecylguanidine acetate	For use only as an antimicrobial agent in paper and paperboard under the following conditions:
1. For contact only with nonalcoholic food having a pH above 5 and provided it is used at a level not to	

exceed 0.4 percent by weight of the paper and paperboard.2. For use in the outer ply of multiwall paper bags for contact with dry food of Type VIII described in table I of paragraph (c) of this section and provided it is used at a level of 0.8 percent by weight of the paper.	
n-Dodecylguanidine hydrochloride	For use only as an antimicrobial agent in paper and paperboard under the following conditions:1. For contact only with nonalcoholic food having a pH above 5 and provided it is used at a level not to exceed 0.4 percent by weight of the paper and paperboard.2. For use in the outer ply of multiwall paper bags for contact with dry food of Type VIII described in table I of paragraph (c) of this section and provided it is used at a level of 0.8 percent by weight of the paper.
Fatty acids derived from animal and vegetable fats and oils and salts of such acids, single or mixed, as follows:	
Aluminum.	
Ammonium.	
Calcium.	
Magnesium.	
Potassium.	
Sodium.	
Zinc.	
Ferric chloride	
Ferrous ammonium sulfate	
Fish oil, hydrogenated	
Fish oil, hydrogenated, potassium salt	
Furcelleran and salts of furcelleran as described in 172.655 and 172.660 of this chapter	
Glutaraldehyde (CAS Reg. No. 111-30-8)	For use only as an antimicrobial agent in pigment and filler slurries used in the manufacture of paper and paperboard at levels not to exceed 300 parts per million by weight of the slurry solids.
Glyceryl lactostearate	

Glyceryl mono-1,2-hydroxystearate	
Glyceryl monoricinoleate	
Guar gum modified by treatment with [beta]-diethylamino- ethyl chloride hydrochloride	For use only as a retention aid and/or drainage aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard.
Guar gum modified by treatment with not more than 25 weight percent of 2,3-epoxypropyltri-methylammonium chloride such that the finished product has a maximum chlorine content of 4.5 percent, a maximum nitrogen content of 3.0 percent, and a minimum viscosity in 1-percent-by-weight aqueous solution of 1,000 centipoises at 77 deg. F, as determined by RV-series Brookfield viscometer (or equivalent) using a No. 3 spindle at 20 r.p.m	For use only as a retention aid and/or internal size employed prior to the sheet-forming operation in the manufacture of paper and paperboard, and limited to use at a level: (1) Not to exceed 0.15 percent by weight of the finished dry paper and paperboard fibers intended for use in contact with all types of foods, except (2) not to exceed 0.30 pct. by weight of the finished dried paper and paperboard fibers for use with nonalcoholic and nonfatty food of types identified under Types I, II, IV-B, VI-B, VII-B, and VIII of table I in par. (c) of this section.
N,N,N',N',N[Prime],N[Prime]-Hexakis (methoxymethyl)-1,3,5-triazine-2,4,6-triamine polymer with stearyl alcohol, [alpha]-octadecenyl-omega-hydroxypoly(oxy-1,2-ethanediyl), and alkyl (C20+) alcohols (CAS Reg. No. 130328-24-4)	For use only as a water-repellent applied to the surface of paper and paperboard at levels not to exceed 1 percent by weight of the finished dry paperboard fibers. The finished paper and paperboard will be used in contact with aqueous foods under conditions of use B through G as described in table 2 of paragraph (c) of this section.
Hexamethylenetetramine	For use only as polymerization cross-linking agent for protein, including casein.
Hydroquinone and the monomethyl or monoethyl ethers of hydroquinone	For use only as an inhibitor for monomers.
Hydroxymethyl-5,5-dimethylhydantoin (CAS Reg. No. 27636-82-4), mixture with 1,3-bis(hydroxymethyl)-5,5-dimethylhydantoin (CAS Reg. No. 6440-58-0)	For use only as a preservative in clay-type fillers at a level not to exceed a combined total of 1,200 milligrams/kilograms hydroxymethyl-5,5-dimethylhydantoin and 1,3-bis(hydroxymethyl)-5,5-dimethylhydantoin in the filler.
Hydroxypropyl guar gum having a minimum viscosity of 5,000 centipoises at 25 deg. C., as determined by RV-series Brookfield viscometer using a No. 4 spindle at 20 r.p.m. (or other suitable method) and using a test sample prepared by dissolving 5 grams of moisture-free hydroxypropyl guar gum in 495 milliliters of a 70 percent by weight aqueous propylene glycol solution	For use only as a dry strength and formation aid agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard and used at a level not to exceed 1.5 percent by weight of finished

	dry paper or paperboard fibers.
12-Hydroxystearic acid-polyethylene glycol block copolymers (CAS Reg. No. 70142-34-6) produced by the reaction of polyethylene glycol (minimum molecular weight 200) with 12-hydroxystearic acid	For use only as a surfactant for dispersions of polyacrylamide retention and drainage aids employed prior to the sheet forming operation in the manufacture of paper and paperboard.
Imidazolium compounds, 2-($C_{17}$and C_{17}-unsaturated alkyl)-1-[2-($C_{18}$and C_{18}-unsaturated amido)ethyl]-4,5-dihydro-1-methyl, methyl sulfates (CAS Reg. No. 72749-55-4).	For use only at a level not to exceed 0.5 percent by weight of the dry paper and paperboard.
Isopropyl*m*-and*p*-cresols (thymol derived)	For use only as an antioxidant for fatty based coating adjuvants provided it is used as a level not to exceed 0.005% by weight of coating solids.
Isopropyl peroxydicarbonate	For use only as polymerization catalyst.
Japan wax	
Lanolin	
Lauryl peroxide	For use only as polymerization catalyst.
Lauryl sulfate salts:	
Ammonium.	
Magnesium.	
Potassium.	
Sodium.	
Lecithin, hydroxylated	
Lignin sulfonate and its calcium, potassium, and sodium salts	
Maleic anhydride, polymer with ethyl acrylate and vinyl acetate, hydrolyzed (CAS Reg. No. 113221-69-5) and/or its ammonium, potassium, and sodium salts	For use only as a deposit control additive prior to the sheet forming operation to prevent scale buildup in the manufacture of paper and paperboard in contact with food, at a level not to exceed 0.075 percent (as the acid) by weight of the dry paper and paperboard.
Methacrylic acid-acrylic acid copolymer (CAS Reg. No. 25751-21-7)	For use only as a boiler water additive at a level not to exceed 50 parts per million in the boiler water.
N-methyldiallylamine hydrochloride polymer with epichlorohydrin having a nitrogen content of 4.8 to 5.9 percent (Kjeldahl dry basis) such that a 20 percent by weight aqueous solution has a minimum viscosity of 30 centipoises and maximum viscosity of 100 centipoises at 25 deg. C, as determined by LVF Model Brookfield viscometer using a No. 1 spindle at 60 r.p.m. (or equivalent method)	For use only as a retention aid, flocculating agent, and wet-strength agent employed in the manufacture of paper and paperboard prior to the sheet-forming operation and limited to use at a level not to exceed

	1.5 percent by weight of the dry paper and paperboard.
Methyl naphthalene sulfonic acid-formaldehyde condensate, sodium salt	For use only as an adjuvant to control pulp absorbency and pitch content in the manufacture of paper and paperboard prior to the sheet-forming operation.
N-methyl-*N*-(tall oil acyl) taurine, sodium salt (CAS Reg. No. 61791-41-1)	For use only to control scale formation in the manufacture of paper and paperboard prior to the sheetforming operation at a level not to exceed 0.015 percent by weight of the dry paper and paperboard.
Mineral oil, white	
Mono-, di-, tri-(1-methyl-1-phenylethyl)-phenol, ethoxylated, sulfated, ammonium salt with an average of 12 to 16 moles of ethylene oxide (CAS Reg. No. 68130-71-2)	For use only as an emulsifier for rosin based sizing at a level not to exceed 0.03 percent by weight of the finished dry paper and paperboard.
Monoglyceride citrate	
Monoisopropanolamine (CAS Reg. No. 78-96-6)	For use as a dispersant for titanium dioxide suspensions at a level not to exceed 0.68 percent by weight of titanium dioxide. The finished paper and paperboard will be used in contact with all food types under conditions of use E through G described in table 2 of paragraph (c) of this section.
Mustardseed oil, sulfated, ammonium, potassium, or sodium salt	
Naphthalene sulfonic acid-formaldehyde condensate, sodium salt	For use only as an adjuvant to control pulp absorbency and pitch content in the manufacture of paper and paperboard prior to the sheet-forming operation.
Nitrocellulose, 10.9-12.2% nitrogen	
Oleic acid, sulfated, ammonium, potassium, or sodium salt	
N-Oleoyl-*N'*-stearoylethylenediamine	
Oxystearin	
Paraformaldehyde	For use only as setting agent for protein.
~~Pentanoic acid, 4,4-bis [(*gamma-omega* perfluoro-C_{8-20}-alkyl)thio] derivatives, compounds with diethanolamine (CAS Reg. No. 71608-61-2)~~	~~For use only as an oil and water repellent and used at a level not to exceed 8 pounds per ton of the finished~~

	~~paper or paperboard when such paper or paperboard is used in contact with nonalcoholic foods under conditions of use E through H described in table 2 of paragraph (c) of this section.~~
Perfluoroalkyl acrylate copolymer (CAS Reg. No. 92265-81-1) containing 35 to 40 weight percent fluorine, produced by the copolymerization of ethanaminium,*N*,*N*,*N*-trimethyl-2-[(2-methyl-1-oxo-2-propenyl)-oxy]-, chloride; 2-propenoic acid, 2-methyl-, oxiranylmethyl ester; 2-propenoic acid, 2-ethoxyethyl ester; and 2-propenoic acid, 2<(heptadecafluoro- octyl)sulfonyl] methyl amino]ethyl ester	For use only as an oil and water repellent at a level not to exceed 0.5 percent by weight of the finished paper and paperboard in contact with nonalcoholic foods under conditions of use C, D, E, F, G, or H described in table 2 of paragraph (c) of this section.
~~Perfluoroalkyl substituted phosphate ester acids, ammonium salts formed by the reaction of 2,2-bis[([gamma],[omega]-perfluoroC_{4-20}alkylthio) methyl]-1,3-propanediol, polyphosphoric acid and ammonium hydroxide~~	~~For use only as an oil and water repellant at a level not to exceed 0.44 percent perfluoroalkyl actives by weight of the finished paper and paperboard in contact with non-alcoholic foods under condition of use H as described in table 2 of paragraph (c) of this section; and in contact with food of types III, IV-A, V, VII-A, and IX described in table 1 of paragraph (c) of this section under conditions of use C through G as described in table 2 of paragraph (c) of this section.~~
Petrolatum	Complying with 178.3700 of this chapter.
Petroleum asphalt, steam and vacuum refined to meet the following specifications: Softening point 88deg. C to 93deg. C, as determined by ASTM method D36-76, "Standard Test Method for Softening Point of Bitumen (Ring-and-Ball Apparatus);" penetration at 25deg. C not to exceed 0.3 mm, as determined by ASTM method D5-73 (Reapproved 1978), "Standard Test Method for Penetration of Bituminous Materials," which are incorporated by reference (Copies may be obtained from the American Society for Testing Materials, 100 Barr Harbor Dr., West Conshohocken, Philadelphia, PA 19428-2959, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*); and maximum weight loss not to exceed 3% when distilled to 371deg. C, nor to exceed an additional 1.1% when further distilled between 371deg. C and thermal decomposition	For use only as a component of internal sizing of paper and paperboard intended for use in contact only with raw fruits, raw vegetables, and dry food of the type identified under Type VIII of table 1 in paragraph (c) of this section, and provided that the asphalt is used at a level not to exceed 5% by weight of the finished dry paper and paperboard fibers.
Petroleum wax, synthetic	Complying with 178.3720 of this chapter.
Phenothiazine	For use only as antioxidant in dry rosin size.
Phenyl acid phosphate	For use only as polymerization catalyst in melamine-formaldehyde modified alkyd coatings and limited to use at a level not to exceed 2% by weight of the

	coating solids.
Phenyl-[beta]-naphthylamine	For use only as antioxidant in dry rosin size and limited to use at a level not to exceed 0.4% by weight of the dry rosin size.
Phosphoric acid esters and polyesters (and their sodium salts) of triethanolamine formed by the reaction of triethanolamine with polyphosphoric acid to produce a mixture of esters having an average nitrogen content of 1.5 percent and an average phosphorus content of 32 percent (as PO_4)	For use as an adjuvant prior to the sheet forming operation to control pitch and scale formation in the manufacture of paper and paperboard intended for use in contact with food only of the types identified in paragraph (c) of this section, table 1, under Types I, IV, V, VII, VIII, and IX, and used at a level not to exceed 0.075 percent by weight of dry paper or paperboard fibers.
Poly[acrylamide-acrylic acid-*N*-(dimethyl-aminomethyl)acryl- amide], produced by reacting 2.40 to 3.12 parts by weight of polyacrylamide with 1.55 parts dimethylamine and 1 part formaldehyde, and containing no more than 0.2 percent monomer as acrylamide	For use only as a drainage aid and retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard for use in contact with fatty foods under conditions of use described in paragraph (c) of this section, table 2, conditions of use E, F, and G.
Poly(2-aminoethyl acrylate nitrate-*co*-2-hydroxypropyl acrylate) produced when one mole of hydroxypropyl acrylate and three moles of acrylic acid are reacted with three moles of ethylenimine and three moles of nitric acid, such that a 35 percent by weight aqueous solution has a minimum viscosity of 150 centipoises at 72 deg. F., as determined by RVF-series Brookfield viscometer (or equivalent) using a No. 2 spindle at 20 r.p.m	For use only as a retention and drainage aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard at a level not to exceed 0.2 percent by weight of dry paper or paperboard fiber.
Polyacrolein (1 part) -sodium bisulfite (0.7 part) adduct, containing excess bisulfite (ratio of excess bisulfite to adduct not to exceed 1.5 to 1)	For use only as an agent in modifying starches and starch gums used in the production of paper and paperboard and limited to use at a level not to exceed 0.09 mg/in^{2}of the finished paper and paperboard.
Poly[acrylamide-acrylic acid-*N*-(dimethylaminomethyl) acrylamide] (C.A. Registry No. 53800-41-2), produced by reacting 9.6-16.4 parts by weight of polyacrylamide with 1.6 parts dimethylamine and 1 part formaldehyde, and containing no more than 0.2% monomer as acrylamide, such that a 20% aqueous solution has a minimum viscosity of 4,000 cP at 25 deg. C., as determined by Brookfield viscometer model RVT, using a No. 5 spindle at 20 r/min (or equivalent method)	For use only as a drainage aid, retention aid, or dry-strength agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard at a level not to exceed 0.25 percent by weight of finished dry paper and paperboard fibers, when such paper or paperboard is used in contact with fatty foods under conditions of use described in paragraph (c) of this section, table 2, conditions of use E, F, and G.

Polyamide-epichlorohydrin modified resin produced by reacting adipic acid with diethylene triamine to produce a basic polyamide which is modified by reaction with formic acid and formaldehyde and further reacted with epichlorohydrin in the presence of ammonium hydroxide to form a water-soluble cationic resin having a nitrogen content of 13-16 percent (Kjeldahl, dry basis) such that a 35 percent by weight aqueous solution has a minimum viscosity of 75 centipoises at 25 deg. C, as determined by Brookfield viscometer using a No. 1 spindle at 12 r.p.m	For use only as a retention aid and flocculant employed prior to the sheet-forming operation in the manufacture of paper and paperboard and used at a level not to exceed 0.2 percent dry resin by weight of finished dry paper or paperboard fibers.
Polyamide-epichlorohydrin water-soluble thermosetting resins [CAS Reg. No. 68583-79-9] prepared by reacting adipic acid with diethylenetriamine to form a basic polyamide and further reacting the polyamide with an epichlorohydrin and dimethylamine mixture such that the finished resins have a nitrogen content of 17.0 to 18.0 percent of a dry basis, and that a 30-percent-by-weight aqueous solution has a minimum viscosity of 350 centipoises at 20 deg. C, as determined by a Brookfield viscometer using a No. 3 spindle at 30 r.p.m. (or equivalent method)	For use only under the following conditions:1. As a retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard and limited to use at a level not to exceed 0.12 percent by weight of dry paper or paperboard.2. The finished paper or paperboard will be used in contact with food only of the types identified in paragraph (c) of this section, table 1, under types I and IV-B and under conditions of use described in paragraph (c) of this section, table 2, conditions of use F and G.
Polyamide-epichlorohydrin water-soluble thermosetting resin (CAS Reg. No. 96387-48-3) prepared by reacting*N*-methyl-bis(3-aminopropyl) amine with oxalic acid and urea to form a basic polyamide and further reacting the polyamide with epichlorohydrin	For use only as a wet strength agent and/or retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard and used at a level not to exceed 1.5 percent by weight of dry paper and paperboard fibers.
Polyamide-epichlorohydrin water-soluble thermosetting resins prepared by reacting adipic acid, isophthalic acid, itaconic acid or dimethyl glutarate with diethylenetriamine to form a basic polyamide and further reacting the polyamide with one of the following:	For use only in the manufacture of paper and paperboard under conditions such that the resins do not exceed 1.5 percent by weight of the paper or paperboard.
Epichlorohydrin.	
Epichlorohydrin and ammonia mixture.	
Epichlorohydrin and sodium hydrosulfite mixture.	
Polyamidoamine-ethyleneimine-epichlorohydrin resin prepared by reacting hexanedioic acid,*N*-(2-aminoethyl)-1,2-ethanediamine, (chloromethyl)oxirane, ethyleneimine (aziridine), and polyethylene glycol, partly neutralized with sulfuric acid (CAS Reg. No. 167678-45-7)	For use only as a retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard at a level not to exceed 0.12 percent resin by weight of the finished dry paper or paperboard.
Polyamidol-epichlorohydrin modified resin produced by reacting glutaric acid dimethyl ester with diethylene-triamine to produce a basic polyamide which is modified by reaction with formaldehyde and	For use only as a wet strength agent employed prior to the sheet-forming operation in the manufacture of

further reacted with epicholorohydrin to form a water soluble cationic resin having a nitrogen content of 10.9-11.9 percent and a chlorine content of 13.8-14.8 percent, on a dry basis, and a minimum viscosity, in 12.5 percent by weight aqueous solution, of 10 centipoises at 25 deg. C, as determined by a Brookfield Model LVF viscometer using a No. 1 spindle at 60 r.p.m. (or equivalent method)	paper and paperboard, and used at a level not to exceed 2.5 percent by weight of dry paper and paperboard fibers when such paper or paperboard is used in contact with food under conditions of use E through G described in table 2 of paragraph (c) of this section.
Polyamine-epichlorohydrin resin produced by the reaction of epichlorohydrin with monomethylamine to form a prepolymer and further reaction of this prepolymer with*N,N,N',N'*-tetramethylethylenediamine such that the finished resin having a nitrogen content of 11.6 to 14.8 percent and a chlorine content of 20.8 to 26.4 percent and a minimum viscosity, in 25 percent by weight aqueous solution, of 500 centipoises at 25 deg. C, as determined by LV-series Brookfield viscometer using a No. 2 spindle at 12 r.p.m. (or by other equivalent method)	For use only as a flocculant, drainage aid, formation aid, retention aid, or strength additive employed prior to the sheet-forming operation in the manufacture of paper and paperboard, and used at a level not to exceed 0.12 percent by weight of dry paper and paperboard fibers.
Polyamine-epichlorohydrin resin produced by the reaction of*N,N*-dimethyl-1,3-propanediamine with epichlorohydrin and further reacted with sulfuric acid, Chemical Abstracts Service Registry Number [27029-41-0], such that the finished resin has a maximum nitrogen content of 14.4 percent (dry basis) and a minimum viscosity in 30 percent by weight aqueous solution (pH 4-6) of 50 centipoises at 25 deg. C, as determined by Brookfield LVT model viscometer, using a No. 1 spindle at 12 r.p.m. (or equivalent method)	For use only as a clarifier in the treatment of influent water to be used in the manufacture of paper and paperboard, and used at a level not to exceed 20 parts per million of the influent water.
Polyamine-epichlorohydrin water-soluble thermosetting resin produced by reacting epichlorohydrin with: (i) polyamines comprising at least 95 percent by weight $C_4$to C_6aliphatic diamines and/or their self-condensation products, and/or (ii) prepolymers produced by reacting 1,2-dichloroethane with the polyamines in (i). The finished resin has a nitrogen content of 5.0 to 9.0 percent, a chlorine content of 18.0 to 35.0 percent on a dry basis, and a minimum viscosity, in a 25 percent by weight aqueous solution, of 50 centipoises at 20 deg. C (68 deg. F), as determined by Brookfield HAT model viscometer using a No. 1H spindle at 50 r.p.m. (or equivlent method)	For use only as a wetstrength agent and/or retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard, and used at a level not to exceed 1 percent by weight of dry paper and paperboard fibers.
Polyamine-epichlorohydrin water-soluble thermosetting resin produced by reacting epichlorohydrin with: (i) polyamines comprising at least 95 percent by weight $C_4$to C_6aliphatic diamines and/or their seIf-condensation products and/or (ii) hexamethylenediamine, and/or (iii) bis(hexamethylene) triamine and higher homologues, and/or (iv) prepolymers produced by reacting 1,2-dichloroethane with the polyamines in (i) and/or (ii) and/or (iii). The finished resin has a nitrogen content of 5.0 to 9.0 percent, a chlorine content of 18.0 to 35.0 percent on a dry basis, and a minimum viscosity, in a 25 percent by weight aqueous solution, of 50 centipoises at 20 deg. C (68 deg. F), as determined by Brookfield HAT model viscometer using a No. 1H spindle at 50 r.p.m. (or equivalent method)	For use only as a wet-strength agent and/or retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard, and used at a level not to exceed 1 percent by weight of dry paper and paperboard fibers.
Polyamine-epichlorohydrin water soluble thermosetting resin prepared by reacting hexamethylenediamine with 1,2-dichloroethane to form a prepolymer and further reacting this prepolymer with epichlorohydrin. This resin is then reacted with nitrilotris (methylene-phosphonic acid),	For use only as a wet-strength agent and/or retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard, and used at

pentasodium salt, such that the finished resin has a nitrogen content of 5.0-5.3 percent; a chlorine content of 29.7-31.3 percent; and a phosphorus content of 2.0-2.2 percent, on a dry basis, and a minimum viscosity, in 25 percent by weight aqueous solution, of 50 centipoises at 25 deg. C., as determined on a Brookfield HAT model viscometer using a No. 1H spindle at 50 r.p.m. (or equivalent method)	a level not to exceed 1 percent by weight of dry paper and paperboard fibers.
Polyamine resin produced by the reaction of 1,2-dichloroethane with bis(hexamethylene)triamine and higher homologues such that the finished resin has a nitrogen content of 13.0-15.0 percent on a dry basis, and a minimum viscosity in 25-percent-by-weight aqueous solution of 75 centipoises at 25 deg. C., as determined by Brookfield HAT model viscometer using a No. 1 spindle at 50 r.p.m. (or equivalent method)	For use only as a retention aid and/or flocculent employed prior to the sheet-forming operation in the manufacture of paper and paperboard and used at a level not to exceed 0.1 percent by weight of dry paper or paperboard fibers.
Polyaminoamide-epichlorohydrin modified resin produced by reacting adipic acid with diethylenetriamine to produce a polyamide which is modified by reaction with diethylaminopropylamine and further reacted with dichloroethyl ether to form a polyamide intermediate. This polyamide intermediate is then reacted with epichlorohydrin such that the finished resins have a nitrogen content of 10.9-12.4 percent (Kjeldahl, dry basis) and a minimum viscosity in 40 percent-by-weight aqueous solution of 250 centipoises at 22 deg. C, as determined by a Brookfield Model LVT viscometer using a No. 2 spindle at 30 r.p.m. (or equivalent method)	For use only as a wet-strength agent and/or retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard, and used at a level not to exceed 0.5 percent by weight of the finished dry paper and paperboard.
Polybutene, hydrogenated; complying with the identity prescribed under 178.3740(b) of this chapter	For use only as provided in 175.300, 178.3740 and 178.3860 of this chapter.
Poly(diallyldimethylammonium chloride) (CAS Reg. No. 26062-79-3) produced by the polymerization of (diallyldimethylammonium chloride) so that the finished resin has a nitrogen content of 8.66+/-0.4 percent on a dry weight basis and a minimum viscosity in a 40 percent by weight aqueous solution of 1,000 centipoises at 25 deg. C (77 deg. F), determined by LVF Model Brookfield Viscometer using a No. 3 spindle at 30 r.p.m. (or equivalent method). The level of residual monomer is not to exceed 1 percent by weight of the polymer (dry basis)	For use only:1. As a pigment dispersant and/or retention aid prior to the sheet-forming operation in the manufacture of paper and paperboard, and used at a level not to exceed 10 pounds of active polymer per ton of finished paper and paperboard.2. As a pigment dispersant in coatings at a level not to exceed 3.5 pounds of active polymer per ton of finished paper and paperboard.
Poly (diallyldimethylammonium chloride) (CAS Reg. No. 26062-79-3) produced by the polymerization of diallyldimethylammonium chloride so that the finished resin has a nitrogen content of 8.66+/-0.4 percent on a dry basis and a minimum viscosity in a 15 weight-percent aqueous solution of 10 centipoises at 25 deg. C (77 deg. F), as determined by LVF Model Brookfield viscometer using a No. 1 spindle at 60 r/min (or equivalent method). The level of residual monomer is not to exceed 1 weight-percent of the polymer (dry basis)	For use only as a flocculant employed prior to the sheet-forming operation in the manufacture of paper and paperboard, and used at a level not to exceed 10 mg/L (10 parts per million) of influent water.
Poly(1,2-dimethyl-5-vinylpyridinium methyl sulfate) having a nitrogen content of 5.7 to 7.3 percent and a sulfur content of 11.7 to 13.3 percent by weight on a dry basis and having a minimum viscosity in 30-percent-by-weight aqueous solution of 2,000 centipoises at 25 deg. C., as determined by LV-series Brookfield viscometer (or equivalent) using a No. 4 spindle at 60 r.p.m	For use only as an adjuvant employed in the manufacture of paper and paperboard prior to the sheet-forming operation.

Polyester resin produced by reacting dimethylolpropionic acid (CAS Registry No. 4767-03-7) as a comonomer, at no more than 30 percent by weight of total polymer solids in reaction with 2,2-dimethyl-1,3-propanediol, phthalic anhydride and isophthalic acid, such that the polyester resin has a viscosity of 200-600 centipoises at 80 deg. F as determined by a Brookfield RVT viscometer using a number 3 spindle at 50 rpm (or equivalent method)	For use only as a surface-sizing compound applied after the sheet-forming operation in the manufacture of paper and paperboard and limited to use at levels not to exceed 0.1 percent by weight of finished dry paper or paperboard.
Polyethylene, oxidized; complying with the identity prescribed in 177.1620(a) of this chapter	For use only as component of coatings that contact food only of the type identified under Type VII-B of table 1 in paragraph (c) of this section, and limited to use at a level not to exceed 50 percent by weight of the coating solids.
Polyethyleneamine mixture produced when 1 mole of ethylene dichloride, 1.05 moles of ammonia, and 2 moles of sodium hydroxide are made to react so that a 10 percent aqueous solution has a minimum viscosity of 40 centipoises at 77 deg. F, as determined by Brookfield viscometer using a No. 1 spindle at 60 r.p.m	For use only as a retention aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard.
Polyethylene glycol (200) dilaurate	For use only as an adjuvant employed in the manufacture of paper and paperboard prior to the sheet-forming operation.
Polyethylene glycol (400) dioleate	
Polyethylene glycol (400) esters of coconut oil fatty acids	
Polyethylene glycol (600) esters of tall oil fatty acids	
Polyethylene glycol (400) monolaurate	
Polyethylene glycol (600) monolaurate	
Polyethylene glycol (400) monooleate	
Polyethylene glycol (600) monooleate	
Polyethylene glycol (400) monostearate	
Polyethylene glycol (600) monostearate	
Polyethylene glycol (3,000) monostearate	
Polyethylenimine, produced by the polymerization of ethylenimine	For use only as an adjuvant employed prior to sheet formation in paper-making systems operated at a pH of 4.5 or higher, and limited to use at a level not to exceed 5% by weight of finished dry paper or paperboard fibers.
Poly(isobutene)/maleic anhydride adduct, diethanolamine reaction product. The mole ratio of	For use only as a surfactant for dispersions of

poly(isobutene)/maleic anydride adduct to diethanolamine is 1:1	polyacrylamide retention and drainage aids employed prior to the sheet formation operation in the manufacture of paper and paperboard.
Polymethacrylic acid, sodium salt, having a viscosity in 30-percent-by-weight aqueous solution of 125-325 centipoises at 25 deg. C as determined by LV-series Brookfield viscometer (or equivalent) using a No. 2 spindle at 60 r.p.m	For use only as a coating adjuvant for controlling viscosity when used at a level not to exceed 0.3% by weight of coating solids.
Polymethacrylic acid, sodium salt, having a viscosity in 40-percent-by-weight aqueous solution of 400-700 centipoises at 25 deg. C, as determined by LV-series Brookfield viscometer (or equivalent) using a No. 2 spindle at 30 r.p.m	For use only as a coating adjuvant for controlling viscosity when used at a level not to exceed 0.1% by weight of coating solids.
Poly[(methylimino)(2-hydroxytrimethylene)hydrochloride] produced by reaction of 1:1 molar ratio of methylamine and epichlorohydrin so that a 31-percent aqueous solution at 25deg. C has a Stokes viscosity range of 2.5-4.0 as determined by ASTM method D1545-76 (Reapproved; 1981), "Standard Test Method for Viscosity of Transparent Liquids by Bubble Time Method," which is incorporated by reference. Copies may be obtained from the American Society for Testing Materials, 100 Barr Harbor Dr., West Conshohocken, Philadelphia, PA 19428-2959, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*	For use only as a retention aid employed prior to the sheet-forming operation in such an amount that finished paper and paperboard will contain the additive at a level not in excess of 1 percent by weight of the dry paper and paperboard.
Poly[oxyethylene (dimethyliminio) ethylene (dimethyliminio) ethylene dichloride] produced by reacting equimolar quantities of*N,N,N,N*-tetramethylethylene-diamine and dichlorethyl ether to yield a solution of the solid polymer in distilled water at 25deg. C with a reduced viscosity of not less than 0.15 deciliter per gram as determined by ASTM method D1243-79, "Standard Test Method for -Dilute Solution Viscosity of Vinyl Chloride Polymers," which is incorporated by reference. Copies may be obtained from the American Society for Testing Materials, 100 Barr Harbor Dr., West Conshohocken, Philadelphia, PA 19428-2959, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*). The following formula is used for determining reduced viscosity:	For use only to improve dry-strength of paper and paperboard and as a retention and drainage aid employed prior to the sheet-forming operation in the manufacture of paper and paperboard and limited to use at a level not to exceed 0.1 percent by weight of the finished dry paper and paperboard fibers.
Reduced viscosity in terms of deciliters per gram=$(t-t_0)/(t-C)$,	
where:	
t=Solution efflux time	
t_o=Water efflux time	
C=Concentration of solution in terms of grams per deciliter	
Polypropylene glycol (minimum molecular weight 1,000)	

Potassium persulfate	
2-Propenoic acid, telomer with sodium 2-methyl-2-[(1-oxo-2-propenyl)amino]-1-propane sulfonate and sodium phosphinate (CAS Reg. No. 110224-99-2)	For use only as a deposit control additive employed prior to the sheet forming operation in the manufacture of paper and paperboard and at a level not to exceed 0.15 percent by weight of the dry paper and paperboard.
Propylene glycol alginate	
Protein hydrolysate from animal hides or soybean protein condensed with oleic and/or stearic acid	
Rapeseed oil, sulfated ammonium, potassium, or sodium salt	
Ricebran oil, sulfated ammonium, potassium, or sodium salt	
Rosin and rosin derivatives	As provided in 178.3870 of this chapter.
Siloxanes (silicones), dimethyl, isopropyl methyl, methyl 1-methyl-C_{9-49}-alkyl (CAS Reg. No. 144635-08-5)	For use only as a component of polyolefin coatings with 177.1520 of this chapter at a level not to exceed 3 percent by weight. The finished coating will be used only for paper and paperboard that contact food of types VI-A and VI-B of table 1 in paragraph (c) of this section, and under conditions of use C, D, and E, as described in table 2 in paragraph (c) of this section, with a maximum hot fill temperature of 200 deg. F (94 deg. C).
Silver chloride-coated titanium dioxide	For use only as a preservative in polymer latex emulsions at a level not to exceed 2.2 parts per million (based on silver ion concentration) in the dry coating.
Sodium carboxymethyl guar gum having a minimum viscosity of 2,700 centipoises at 25 deg. C after 24 hours as determined by RV-series Brookfield viscometer (or equivalent) using a No. 4 spindle at 20 r.p.m. and using a test sample prepared by dissolving 8 grams of sodium carboxymethyl guar gum in 392 milliliters of 0.2-percent-by-weight aqueous sodium*o*-phenylphenate solution	For use only as a dry-strength and formation-aid agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard and used at a level not to exceed 1% by weight of finished dry paper or paperboard fibers.
Sodium dioctyl sulfosuccinate	
Sodium formaldehyde sulfoxylate	For use only as polymerization catalyst.
Sodium hypochlorite	
Sodium*N*-methyl-*N*-oleyltaurate	For use only as an adjuvant to control pulp

	absorbency and pitch content in the manufacture of paper and paperboard prior to the sheet-forming operation.
Sodium nitrite	For use only:1. At levels not to exceed 0.2% by weight of lubricants or release agents applied at levels not to exceed 1 lb. per ton of finished paper or paperboard.2. As an anticorrosion agent at levels not to exceed 0.2% by weight of wax emulsions used as internal sizing in the manufacture of paper and paperboard prior to the sheet-forming operation.
Sodium persulfate	
Sodium polyacrylate	For use only:1. As a thickening agent for natural rubber latex coatings, provided it is used at a level not to exceed 2 percent by weight of coating solids.2. As a pigment dispersant in coatings at a level not to exceed 0.25 percent by weight of pigment.
Sodium poly(isopropenylphosphonate) (CAS Reg. No. 118632-18-1)	For use only in paper mill boilers.
Sodium zinc potassium polyphosphate (CAS Reg. No. 65997-17-3)	For use only as a pigment dispersant in coatings at a level not to exceed 1 percent by weight of pigment.
Sperm oil, sulfated, ammonium, potassium, or sodium salt	
Stannous oleate	
Stearyl-2-lactylic acid and its calcium salt	
Styrene-butadiene copolymers produced by copolymerizing styrene-butadiene with one or more of the monomers: acrylamide, acrylic acid, fumaric acid, 2-hydroxyethyl acrylate, itaconic acid, methacrylic acid, and*N*-methylolacrylamide (CAS Reg. No. 53504-31-7). The finished copolymers shall contain not more than 10 weight percent of total polymer units derived from acrylic acid, fumaric acid, 2-hydroxyethyl acrylate, itaconic acid, and methacrylic acid, and shall contain not more than 3 weight percent of total polymer units derived from*N*-methylolacrylamide, and shall contain not more than 2 weight percent of polymer units derived from acrylamide.	
Styrene-maleic anhydride copolymer, amidated, ammonium sodium salt; having, in a 25 percent by weight aqueous solution at pH 8.8, a minimum viscosity of 600 centipoises at 25 deg. C as determined by Brookfield model LVT viscometer using a No. 3 spindle at 60 r.p.m. (or equivalent method)	For use only as a surface size at a level not to exceed 1 percent by weight of paper or paperboard substrate.
Styrene-maleic anhydride copolymer, sodium salt (minimum molecular weight 30,000)	For use only:1. As a coating thickening agent at a level not to exceed 1% by weight of coating solids.2.

	As surface size at a level not to exceed 1% by weight of paper or paperboard substrate.
Styrene-methacrylic acid copolymer, potassium salt (minimum molecular weight 30,000)	For use only as a coating thickening agent at a level not to exceed 1% by weight of coating solids.
Synthetic wax polymer prepared by the catalytic polymerization of alpha olefins such that the polymer has a maximum iodine number of 18 and a minimum number average molecular weight of 2,400	For use only as a component of petroleum wax and/or synthetic petroleum wax complying with 178.3710 or 178.3720 of this chapter at levels not to exceed 5 percent by weight of the wax:1. Under conditions of use F and G described in table 2 of paragraph (c) of this section for all foods.2. Under conditions of use E described in table 2 of paragraph (c) of this section for food Types I, II, IV-B, VI, VII-B and VIII as described in table 1 of paragraph (c) of this section.
Tallow	
Tallow alcohol	
Tallow alcohol, hydrogenated	
Tallow fatty acid, hydrogenated	
Tallow hydrogenated	
Tallow sulfated, ammonium, potassium, or sodium salt	
Tetraethylenepentamine	For use only as a modifier for amino resins.
1,4,4a,9a-Tetrahydro-9, 10-anthracenedione (CAS Reg. No. 56136-14-2)	For use only as a catalyst in the alkaline pulping of lignocellulosic materials at levels not to exceed 0.1 percent by weight of the raw lignocellulosic materials.
N,*N*,*N*',*N*'-Tetramethylethylenediamine polymer with bis-(2-chloroethyl) ether, first reacted with not more than 5 percent by weight 1-chloro-2,3-epoxypropane and then reacted with not more than 5 percent by weight poly (acrylic acid) such that a 50 percent by weight aqueous solution of the product has a nitrogen content of 4.7-4.9 percent and viscosity of 350-700 centipoises at 25 deg. C as determined by LV series Brookfield viscometer using a No. 2 spindle at 60 r.p.m. (or by other equivalent method)	For use only as a flocculent, drainage aid or retention aid employed prior to the sheet forming operation in the manufacture of paper and paperboard and limited to use at a level not to exceed 0.2 percent by weight of the finished dry paper and paperboard fibers.
Tetrasodium*N*- (1,2-dicarboxyethyl) -*N*- octadecylsulfo-succinamate	For use only as an emulsifier in aqueous dispersions of rosin sizes complying with 178.3870(a)(4) of this chapter and limited to use prior to the sheet-forming operation in the manufacture of paper and paperboard at a level not to exceed 0.02 pct by weight of finished paper and paperboard.

Triethanolamine	For use only to adjust pH during the manufacture of amino resins permitted for use as components of paper and paperboard.
Triethylene glycol adipic acid monoester produced by reacting equimolar quantities of triethylene glycol and adipic acid	For use only as a curl-control agent at a level not to exceed 2% by weight of coated or uncoated paper and paperboard.
Triethylenetetramine	For use only as a modifier for amino resins.
1,3,5-Triethylhexahydro-1,3,5-triazine (CAS Registry No. 7779-27-3)	For use only as an antimicrobial agent for coating, binder, pigment, filler, sizing, and similar formulations added prior to the heat drying step in the manufacture of paper and paperboard and limited to use at a level between 0.05 and 0.15 percent by weight of the formulation.
Undecafluorocyclohexanemethanol ester mixture of dihydrogen phosphate, compound with 2,2' iminodiethanol (1:1); hydrogen phosphate, compound with 2,2'-iminodiethanol (1:1); and P,P'-dihydrogen pyrophosphate, compound with 2,2'-iminodiethanol (1:2); where the ester mixture has a fluorine content of 48.3 pct to 53.1 pct as determined on a solids basis	For use only as an oil repellent at a level not to exceed 0.087 lb (0.046 lb of fluorine) per 1,000 ft^2 of treated paper or paperboard, as determined by analysis for total fluorine in the treated paper or paperboard without correction for any fluorine which might be present in the untreated paper or paperboard, when such paper or paperboard is used in contact with food only of the types identified in paragraph (c) of this section, table 1, under Types IVA, V, VIIA, VIII, and IX, and under the conditions of use B through G described in table 2 of paragraph (c) of this section.
Viscose rayon fibers	
Wax, petroleum	Complying with 178.3710 of this chapter.
Xanthan gum, conforming to the identity and specifications prescribed in 172.695 of this chapter, except that the residual isopropyl alcohol shall not exceed 6,000 parts per million	For use only at a maximum level of 0.125 percent by weight of finished paper as a suspension aid or stabilizer for aqueous pigment slurries employed in the manufacture of paper and paperboard.
Xylene sulfonic acid-formaldehyde condensate, sodium salt	For use only as an adjuvant to control pulp absorbency and pitch content in the manufacture of paper and paperboard prior to the sheet-forming operation.
Zeolite Na-A (CAS Reg. No. 68989-22-0)	For use as a pigment extender at levels not to exceed

	5.4 percent by weight of the finished paper and paperboard.
Zinc formaldehyde sulfoxylate	For use only as polymerization catalyst.
Zinc octoate	
Zirconium oxide	For use only as a component of waterproof coatings where the zirconium oxide is present at a level not to exceed 1 percent by weight of the dry paper or paperboard fiber and where the zirconium oxide is produced by hydrolysis of zirconium acetate.

(b) Substances identified in paragraphs (b) (1) and (2) of this section may be used as components of the food-contact surface of paper and paperboard, provided that the food-contact surface of the paper or paperboard complies with the extractives limitations prescribed in paragraph (c) of this section.
(1) Substances identified in 175.300(b)(3) of this chapter with the exception of those identified in paragraphs (b)(3) (v), (xv), (xx), (xxvi), (xxxi), and (xxxii) of that section and paragraph (a) of this section.
(2) Substances identified in this paragraph (b)(2) follow:

List of substances	**Limitations**
Acrylamide copolymerized with ethyl acrylate and/or stryene and/or methacrylic acid, subsequently reacted with formaldehyde and butyl alcohol	
Acrylamide copolymerized with ethylene and vinyl chloride in such a manner that the finished copolymers have a minimum weight average molecular weight of 30,000 and contain not more than 3.5 weight percent of total polymer units derived from acrylamide, and in such a manner that the acrylamide portion may or may not be subsequently partially hydrolyzed	For use only as coatings or components of coatings.
2-Acrylamido-2-methyl-propanesulfonic acid, homopolymer, sodium salt (CAS Reg. No. 35641-59-9)	For use only in coatings at a level not to exceed 0.01 mg/in^2
Acrylic and modified acrylic polymers	Complying with 177.1010 of this chapter.
Acrylic copolymers produced by copolymerizing 2 or more of the acrylate monomers butyl acrylate, ethyl acrylate, ethyl methacrylate, methyl acrylate, methyl methacrylate, and*n*-propyl methacrylate, or produced by copolymerizing one or more of such acrylate monomers together with one or more of the monomers acrylic acid, acrylonitrile, butadiene, 2-ethyl-hexyl acrylate, fumaric acid, glycidyl methacrylate,*n*-hexyl-methacrylate, itaconic acid, methacrylic acid, styrene, vinyl acetate, vinyl chloride, and vinylidene chloride. The finished copolymers shall contain at least 50 weight percent of polymer units derived from one or more of the monomers butyl acrylate, ethyl acrylate, ethyl methacrylate, methyl acrylate, methyl methacrylate, and*n*-propyl methacrylate; and shall contain not more than 5 weight percent of total polymer units derived from acrylic acid, fumaric acid, glycidyl methacrylate,*n*-hexyl methacrylate, itaconic acid, and methacrylic acid. The provision limiting the finished acrylic copolymers to not more	

than 5 units derived from acrylic acid, fumaric acid, glycidyl methacrylate,*n*-hexyl methacrylate, itaconic acid, and methacrylic acid is not applicable to finished acrylic copolymers used as coating adjuvants at a level not exceeding 2 weight percent of total coating solids	
Alkyl mono- and disulfonic acids, sodium salts (produced from*n*-alkanes in the range of C_{10}-$C_{18}$with not less than 50 percent C_{14}-C_{16}).	For use only:1. As emulsifiers for vinylidene chloride copolymer coatings and limited to use at levels not to exceed 2 percent by weight of the coating solids.2. As emulsifiers for vinylidene chloride copolymer or homopolymer coatings at levels not to exceed a total of 2.6 percent by weight of coating solids. The finished polymer contacts food only of types identified in paragraph (c) of this section, table 1, under Types I, II, III, IV, V, VIA, VIB, VII, VIII, and IX and under conditions of use E, F, and G described in table 2 of paragraph (c) of this section.
2-Bromo-4'-hydroxyacetophenone	For use only as a preservative for coating formulations, binders, pigment slurries, and sizing solutions at a level not to exceed 0.006 percent by weight of the coating, solution, slurry or emulsion.
Butanedioic acid, sulfo-1,4-di-(C_9-C_{11}alkyl) ester, ammonium salt (also known as butanedioic acid, sulfo-1,4-diisodecyl ester, ammonium salt [CAS Reg. No. 144093-88-9]).	For use as a surface active agent in package coating inks at levels not to exceed 3 percent by weight of the coating ink.
Butylbenzyl phthalate	Complying with 178.3740 of this chapter.
Butyl oleate, sulfated, ammonium, potassium, or sodium salt	
Butyraldehyde	
Captan (*N*-trichloromethylmercapto-4-cyclohexene-1, 2-dicarboximide)	For use only as a mold- and mildew-proofing agent in coatings intended for use in contact with food only of the types identified in paragraph (c) of this section, table 1, under Type I, II, VI-B, and VIII.
Castor Oil, polyoxyethylated (42 moles ethylene oxide)	For use only as an emulsifier in nitrocellulose coatings for paper and paperboard intended for use in contact with food only of the types identified in paragraph (c) of this section, table 1, under Types IV A, V, VII A, VIII, and IX; and limited to use at a level not to exceed 8 percent by weight of the coating solids.
1-(3-Chloroallyl)-3,5,7-triaza-1- azoniaadamantane chloride (CAS Reg. No. 4080-31-3)	For use only:1. As a preservative at a level of 0.3

	weight percent in latexes used as pigment binders in paper and paperboard intended for use in contact with nonacidic, nonalcoholic food and under the conditions of use described in paragraph (c) of this section, table 2, conditions of use E, F, and G.2. As a preservative at a level not to exceed 0.07 weight percent in latexes and 0.05 weight percent in pigment slurries used as components of coatings for paper and paperboard intended for use in contact with food.
5-Chloro-2-methyl-4-isothiazolin-3-one (CAS Reg. No. 26172-55-4) and 2-methyl-4-isothiazolin-3-one (CAS Reg. No. 2682-20-4) mixture at a ratio of 3 parts to 1 part, manufactured from methyl-3-mercaptopropionate (CAS Reg. No. 2935-90-2). The mixture may contain magnesium nitrate (CAS Reg. No. 10377-60-3) at a concentration equivalent to the isothiazolone active ingredients (weight/weight)	For use only:1. As an antimicrobial agent for polymer latex emulsions in paper coatings at a level not to exceed 50 parts per million (based on isothiazolone active ingredients) in the coating formulation.2. As an antimicrobial agent for finished coating formulations and for additives used in the manufacture of paper and paperboard including fillers, binders, pigment slurries, and sizing solutions at a level not to exceed 25 parts per million (based on isothiazolone active ingredients) in the coating formulations and additives.
Copper 8-quinolinolate	For use only as preservative for coating formulations.
Cyclized rubber produced when natural pale crepe rubber dissolved in phenol is catalytically cyclized so that the finished cyclized rubber has a melting point of 145 deg. C to 155 deg. C as determined by ASTM method E28-67 (Reapproved 1982), "Standard Test Method for Softening Point by Ring-and-Ball Apparatus," which is incorporated by reference (Copies may be obtained from the American Society for Testing Materials, 100 Barr Harbor Dr., West Conshohocken, Philadelphia, PA 19428-2959, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*), and contains no more than 4000 ppm of residual-free phenol as determined by a gas liquid chromatographic procedure titled "Determination of Free Phenol in Cyclized Rubber Resin," which is incorporated by reference. Copies are available from the Center for Food Safety and Applied Nutrition (HFS-200), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740, or available for inspection at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*	For use only in coatings for paper and paperboard intended for use in contact with food only of the types identified in paragraph (c) of this section, table 1, under Types VIII and IX.

1,2-Dibromo-2,4-dicyanobutane (CAS Reg. No. 35691-65-7)	For use only as a preservative at levels not more than 0.05 weight percent and not less than 0.01 weight percent: in latexes used as pigment binders in coatings; in pigment slurries used in coatings; and/or in coatings themselves. The total level of the preservative in the finished coating shall not exceed 0.04 weight percent of the finished coating solids.
Dibutyl phthalate	
Dibutyl sebacate	
Di(C_7,C_9-alkyl) adipate	Complying with 178.3740 of this chapter.
Dicyclohexyl phthalate	
Diethylene glycol dibenzoate (CAS Reg. No. 120-55-8)	For use only as a plasticizer for polyvinyl acetate coatings at a level not to exceed 5 percent by weight of the coating solids under conditions described in paragraph (c) of this section, table 2, conditions of use E, F, and G.
Diethylene glycol ester of the adduct of terpene and maleic anhydride	
Dihydroxy dichlorodiphenyl methane	For use only as preservative for coating formulations.
Dimethylpolysiloxane, 100 centistokes viscosity	
Dimethylpolysiloxane-beta-phenylethyl methyl polysiloxane copolymer (2:1), 200 to 400 centistokes viscosity	
N,*N'*-Diphenyl-*p*-phenylenediamine	For use only as polymerization inhibitor in 2-sulfoethyl methacrylate, sodium salt.
Dipropylene glycol dibenzoate (CAS Reg. No. 27138-31-4)	1. For use only as a plasticizer for polyvinyl acetate coatings at a level not to exceed 5 percent by weight of the coating solids under conditions described in paragraph (c) of this section, table 2, condition of use E.2. For use only as a plasticizer for polyvinyl acetate coatings at a level not to exceed 10 percent by weight of the coating solids under conditions described in paragraph (c) of this section, table 2, conditions of use F and G.
Disodium*N*-octadecylsulfosuccinamate	For use only as an emulsifier in resin latex coatings and limited to use at a level not to exceed 0.05% by

	weight of the coating solids.
EDTA (ethylenediaminetetraacetic acid) and its sodium and/or calcium salts	
Ethanedial, polymer with tetrahydro-4-hydroxy-5-methyl-2(1H)pyrimidinone, propoxylated (CAS Reg. No. 118299-90-4)	For use only as an insolubilizer for starch-based coatings and limited to use at a level not to exceed 5.0 percent by weight of the coating.
Ethylene-acrylic acid copolymers produced by the copolymerization of ethylene and acrylic acid and/or their partial ammonium salts. The finished copolymer shall contain no more than 25 weight percent of polymer units derived from acrylic acid and no more than 0.35 weight percent of residual monomeric acrylic acid, and have a melt index not to exceed 350 as determined by ASTM method D1238-82, "Standard Test Method for Flow Rates of Thermoplastics by Extrusion Plastometer," which is incorporated by reference. Copies may be obtained from the American Society for Testing Materials, 100 Barr Harbor Dr., West Conshohocken, Philadelphia, PA 19428-2959, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*	
Formaldehyde	For use only as preservative for coating formulations.
Glyoxal	For use only as an insolubilizing agent in starch- and protein-based coatings that contact nonalcoholic foods, and limited to use at a level not to exceed 6 percent by weight of the starch or protein fraction of the coating solids.
Glyceryl monobutyl ricinoleate	
Hydroxymethyl derivatives (mixture of mono and poly) of [N-(1, 1-dimethyl-3-oxobutyl) acrylamide] produced by reacting 1 mole of the [N-(1,1-dimethyl-3-oxobutyl) acrylamide] with 3 moles of formaldehyde such that the finished product has a maximum nitrogen content of 6.2 percent and a maximum hydroxyl content of 15 percent by weight on a dry basis	For use only as a comonomer in polyvinyl acetate latex coatings and limited to use at a level not to exceed 1 percent by weight of dry polymer solids.
Isobutyl oleate, sulfated, ammonium, potassium, or sodium salt	
Maleic anhydride adduct of butadiene-styrene copolymer	
[alpha]-Methylstyrene-vinyltoluene copolymer resins (molar ratio 1[alpha]-methylstyrene to 3 vinyltoluene)	
Modified kaolin clay (CAS Reg. No. 1344-00-9) is produced by the reaction of sodium silicate (CAS Reg. No. 1344-09-8) and kaolinite clay (CAS Reg. No. 1332-58-7) under hydrothermal conditions. The reaction product has a molecular weight between 246 and 365 and consists of 46 to 55 percent silicon dioxide ($Si0_2$), 28 to 42 percent aluminum oxide ($A1_20_3$), and 2 to 7 percent	For use only as a component of coatings in paper and paperboard products at a level not to exceed 9 percent by weight of the coating intended for use in contact with food of Types I through IX described in table 1 of

of sodium oxide (Na_20). The reaction product will not consist of more than 70 percent modified kaolin clay	paragraph (c) of this section under conditions of use C through H described in table 2 of paragraph (c) of this section.
Naphthalene sulfonic acid-formaldehyde condensate, sodium salt	
Oleyl alcohol	
Oxazolidinylethylmethacrylate (CAS Registry No. 46236-15-1) copolymer with ethyl acrylate and methyl methacrylate, and containing not more than 6 percent by weight of oxazolidinylethylmethacrylate. Maximum nitrogen content shall be 0.5 percent and number average molecular weight of that portion of the copolymer soluble in tetrahydrofuran shall be not less than 50,000	For use only as a binder for pigment coatings as a binder level not to exceed 4.0 percent by weight of dry paper or paperboard.
Pentaerythritol tetrastearate	
Petroleum alicyclic hydrocarbon resins, or the hydrogenated product thereof, meeting the following specifications: Softening point 97 deg. C minimum, as determined by ASTM method E28-67 (Reapproved 1982), "Standard Test Method for Softening Point by Ring and Ball Apparatus;" aniline point 120 deg. C minimum, as determined by ASTM method D611-82, "Standard Test Methods for Aniline Point and Mixed Aniline Point of Petroleum Products and Hydrocarbon Solvents," which are incorporated by reference (Copies may be obtained from the American Society for Testing Materials, 100 Barr Harbor Dr., West Conshohocken, Philadelphia, PA 19428-2959, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*). Specific gravity 0.96-0.99 (20 deg. C/20 deg. C). Such petroleum hydrocarbon resins are produced by the catalytic polymerization of dienes and olefins from low-boiling distillates of cracked petroleum stocks that contain no material boiling over 200 deg. C and that meet the ultraviolet absorbance limits prescribed in 172.880(b) of this chapter when subjected to the analytical procedure described in 172.886(b) of this chapter, modified as follows: Treat the product as in the first paragraph under "Procedure" in 172.250(b)(3) of this chapter. Then proceed with 172.886(b) of this chapter, starting with the paragraph commencing with "Promptly complete transfer of the sample * * *"	For use only as modifiers in waxpolymer blend coatings for corrugated paperboard intended for use in bulk packaging or raw fruits, raw vegetables, iced meat, iced fish, and iced poultry; and limited to use at a level not to exceed 30 weight-percent of the coating solids.
Polyester resin formed by the reaction of the methyl ester of rosin, phthalic anhydride, maleic anhydride and ethylene glycol, such that the polyester resin has an acid number of 4 to 11, a drop-softening point of 70 deg. C-92 deg. C., and a color of K or paler	
Polyester resin produced by reacting the acid groups in montan wax with ethylene glycol	
Polyethylene, oxidized	Complying with 177.1620 of this chapter.
Polyethylene reacted with maleic anhydride such that the modified polyethylene has a	

saponification number not in excess of 6 after Soxhlet extraction for 24 hours with anhydrous ethyl alcohol	
Polyoxyethylated (40 moles) tallow alcohol sulfate, sodium salt	Not to exceed 300 p.p.m. in finished coated paper or paperboard.
Polyoxypropylene-polyoxyethylene block polymers (minimum molecular weight 6,800)	
Polyvinyl acetate	
Polyvinyl alcohol (minimum viscosity of 4% aqueous solution at 20 deg. C. of 4 centipoises)	
Polyvinyl butyral	
Polyvinyl formal	
Polyvinylidene chloride	
Polyvinyl pyrrolidone	
Polyvinyl stearate	
Propylene glycol mono- and diesters of fats and fatty acids	
Siloxanes and silicones; platinum-catalyzed reaction product of vinyl-containing dimethyl polysiloxane (CAS Reg. Nos. 68083-19-2 and 68083-18-1) with methyl hydrogen polysiloxane (CAS Reg. No. 63148-57-2) or dimethyl (methyl hydrogen) polysiloxane (CAS Reg. No. 68037-59-2). Diallyl maleate (CAS Reg No. 999-21-3), dimethyl maleate (CAS Reg. No. 624-48-6), 1-ethynyl-1-cyclohexanol (CAS Reg. No. 78-27-3) and vinyl acetate (CAS Reg. No. 108-05-4) may be used as optional polymerization inhibitors	For use only as a surface coating. Platinum content not to exceed 200 parts per million.1. In coatings for paper and paperboard provided the coating contacts food only of the types identified in paragraph (c) of this section, table 1, under Types I, II, VI, and VII-B when used under conditions of use E, F, and G described in table 2 of paragraph (c) of this section.2. In coatings for paper and paperboard provided the coating contacts food only of the types identified in paragraph (c) of this section, table 1, under Types III, IV, V, VII-A, VIII, and IX when used under conditions of use A through H described in table 2 of paragraph (c) of this section.
Siloxanes and silicones; platinum-catalyzed reaction product of vinyl-containing dimethylpolysiloxane (CAS Reg. Nos. 68083-19-2 and 68083-18-1), with methyl hydrogen polysiloxane (CAS Reg. No. 63148-57-2). Dimethyl maleate (CAS Reg. No. 624-48-6), vinyl acetate (CAS Reg. No. 108-05-4), dibutyl maleate (CAS Reg. No. 105-76-0) and diallyl maleate (CAS Reg. No. 999-21-3) may be used as optional polymerization inhibitors. The polymer may also contain C_{16}-C_{18}olefins (CAS Reg. No. 68855-60-7) as a control release agent	Platinum content not to exceed 100 parts per million. For use only as a release coating for pressure sensitive adhesives.
Sodium decylbenzenesulfonate	

Sodium dihexyl sulfosuccinate	
Sodium*n*-dodecylpolyethoxy (50 moles) sulfate-sodium isododecylphenoxypolyethoxy (40 moles) sulfate mixtures	For use only as an emulsifier in coatings that contact food only of the types identified in paragraph (c) of this section, table 1, under Types IV-A, V, VII, VIII, and IX; and limited to use at levels not to exceed 0.75 percent by weight of the coating solids.
Sodium 2-ethylhexyl sulfate	
Sodium oleoyl isopropanolamide sulfosuccinate	
Sodium pentachlorophenate	For use only as preservative for coating formulations.
Sodium*o*-phenylphenate	Do.
Sodium vinyl sulfonate polymerized	
Sodium xylenesulfonate (CAS Reg. No. 1300-72-7)	For use only in paper and paperboard coatings at levels not to exceed 0.01 percent by weight of the finished paper and paperboard.
Styrene copolymers produced by copolymerizing styrene with maleic anhydride and its methyl and butyl (*sec*- or*iso*-) esters. Such copolymers may contain [beta]-nitrostyrene as a polymerization chain terminator	For use only as a coating or component of coatings and limited to use at a level not to exceed 1% by weight of paper or paperboard substrate.
Styrene polymers made by the polymerization of any combination of styrene or alpha methyl styrene with acrylic acid, methacrylic acid, 2-ethyl hexyl acrylate, methyl methacrylate, and butyl acrylate. The styrene and alpha methyl styrene, individually, may constitute from 0 to 80 weight percent of the polymer. The other monomers, individually, may be from 0 to 40 weight percent of the polymer. The polymer number average molecular weight (M_n) shall be at least 2,000 (as determined by gel permeation chromatography). The acid number of the polymer shall be less than 250. The monomer content shall be less than 0.5 percent	For use only in contact with foods of Types IV-A, V, and VII in table 1 of paragraph (c) of this section, under use conditions E through G in table 2 of paragraph (c), and with foods of Types VIII and IX without use temperature restriction.
Styrene-acrylic copolymers (CAS Reg. No. 25950-40-7 produced by polymerizing 77 to 83 parts by weight of styrene with 13 to 17 parts of methyl methacrylate, 3 to 4 parts of butyl methacrylate, 0.5 to 2.5 parts of methacrylic acid, and 0.1 to 0.3 part of butyl acrylate such that the finished copolymers have a minimum number average molecular weight greater than 100,000 and a level of residual styrene monomer in the polymer not to exceed 0.1 percent by weight	For use only as a component of coatings and limited to use at a level not to exceed 20 percent by weight of the coating solids.
Styrene-butadiene copolymers produced by copolymerizing styrene-butadiene with one or more of the monomer: acrylamide, acrylic acid, fumaric acid, 2-hydroxyethyl acrylate, itaconic acid, and methacrylic acid. The finished copolymers shall contain not more than 10 weight percent of total polymer units derived from acrylic acid, fumaric acid, 2-hydroxyethyl acrylate, itaconic acid and methacrylic acid, and shall contain not more than 2 weight percent of polymer units derived	

from acrylamide	
Styrene-butadiene copolymers with 2-hydroxyethyl acrylate and acrylic acid containing not more than 15 weight percent acrylic acid and no more than 20 weight percent of a combination of 2-hydroxyethyl acrylate and acrylic acid	
Styrene-butadiene-vinylidene chloride copolymers containing not more than 40 weight percent of vinylidene chloride in the finished copolymers. The finished copolymers may contain not more than 10 weight percent of total polymer units derived from acrylic acid, fumaric acid, 2-hydroxyethyl acrylate, itaconic acid, and/or methacrylic acid	For use only as coatings or components of coatings.
Styrene-dimethylstyrene-[alpha]-methylstyrene copolymers produced by polymerizing equimolar ratios of the three comonomers such that the finished copolymers have a minimum average molecular weight of 835 as determined by ASTM method D2503-82, "Standard Test Method for Molecular Weight (Relative Molecular Mass) of Hydrocarbons by Thermoelectric Measurement of Vapor Pressure," which is incorporated by reference. Copies may be obtained from the American Society for Testing Materials, 100 Barr Harbor Dr., West Conshohocken, Philadelphia, PA 19428-2959, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*	For use only in coatings for paper and paperboard intended for use in contact with nonfatty food and limited to use at a level not to exceed 50% by weight of the coating solids.
Styrene-isobutylene copolymers (weight average molecular weight not less than 6,300)	For use only in coatings for paper and paperboard intended for use in contact under conditions of use D G described in table 2 of paragraph (c) of this section, with food of Types I, II, IV-B, VI-B, VII-B, and VIII described in table 1 of paragraph (c) of this section; and limited to use at a level not to exceed 40 percent by weight of the coating solids.
Styrene-maleic anhydride copolymers	For use only as a coating or component of coatings and limited for use at a level not to exceed 2 percent by weight of paper or paperboard substrate.
Styrene-methacrylic acid copolymers containing no more than 5 weight percent of polymer units derived from methacrylic acid	
Styrene-vinylidene chloride copolymers containing not more than 40 weight percent of vinylidene chloride in the finished copolymers. The finished copolymers may contain not more than 5 weight percent of total polymer units derived from acrylic acid, fumaric acid, itaconic acid, and/or methacrylic acid	For use only as coatings or components of coatings.
2-Sulfoethyl methacrylate, sodium salt [Chemical Abstracts Service No. 1804-87-1]	For use only in copolymer coatings under conditions of use E, F, and G described in paragraph (c) of this section,

	table 2, and limited to use at a level not to exceed 2.0 percent by weight of the dry copolymer coating.
[alpha]<[em>p-(1,1,3,3-Tetramethylbutyl) phenyl]-*omega*-hydroxypoly (oxyethylene) hydrogen sulfate, sodium salt mixture with [alpha]-<[em>p-(1,1,3,3-tetramethylbutyl)-phenyl]-*omega*-hydroxypoly (oxyethylene) with both substances having a poly(oxyethylene) content averaging 3 moles	For use only as a surface-active agent at levels not to exceed 3 percent by weight of vinyl acetate polymer with ethylene and*N*-(hydroxymethyl) acrylamide intended for use in coatings for paper and paperboard intended for use in contact with foods:1. Of the types identified in paragraph (c) of this section, table 1, under Types I, II, III, IV, VI-B, and VII, and under the conditions of use described in paragraph (c) of this section, table 2, conditions of use E, F, and G.2. Of the types identified in paragraph (c) of this section, table 1, under Types V, VIII and IX and under the conditions of use described in paragraph (c) of this section, table 2, conditions of use C, D, E, F, and G.
Tetrasodium*N*-(1,2-dicarboxyethyl)-*N*-octadecylsulfo-succinamate	For use only as an emulsifier in resin latex coatings, and limited to use at a level not to exceed 0.05% by weight of the coating solids.
Toluenesulfonamide-formaldehyde resins	
Vinyl acetate copolymers produced by copolymerizing vinyl acetate with one or more of the monomers acrylamide, acrylic acid, acrylonitrile, bicyclo-[2.2.1]*hept*-2-ene-6-methylacrylate, butyl acrylate, crotonic acid, decyl acrylate, diallyl fumarate, diallyl maleate, diallyl phthalate, dibutyl fumarate, dibutyl itaconate, dibutylmaleate, di(2-ethylhexyl) maleate, divinyl benzene, ethyl acrylate, 2-ethyl-hexyl acrylate, fumaric acid, itaconic acid, maleic acid, methacrylic acid, methyl acrylate, methyl methacrylate, mono(2-ethylhexyl) maleate, monoethyl maleate, styrene, vinyl butyrate, vinyl crotonate, vinyl hexoate, vinylidene chloride, vinyl pelargonate, vinyl propionate, vinyl pyrrolidone, vinyl stearate, and vinyl sulfonic acid. The finished copolymers shall contain at least 50 weight percent of polymer units derived from vinyl acetate and shall contain no more than 5 weight percent of total polymer units derived from acrylamide, acrylic acid, crotonic acid, decyl acrylate, dibutyl itaconate, di(2-ethylhexyl) maleate, fumaric acid, itaconic acid, maleic acid, methacrylic acid, mono(2-ethylhexyl) maleate, monoethyl maleate, vinyl butyrate, vinyl hexoate, vinyl pelargonate, vinyl propionate, vinyl stearate, and vinyl sulfonic acid	
Vinyl acetate polymer with ethylene and*N*-(hydroxymethyl) acrylamide containing not more than 6 weight percent of total polymer units derived from*N*-(hydroxymethyl) acrylamide	For use only in coatings for paper and paperboard intended for use in contact with foods:1. Of the types identified in paragraph (c) of this section,

	table 1, under Types I, II, III, IV, VI B, and VII and under the conditions of use described in paragraph (c) of this section, table 2, conditions of use E, F, and G.2. Of the types identified in paragraph (c) of this section, table 1, under Types V, VIII, and IX and under the conditions of use described in paragraph (c) of this section, table 2, conditions of use C, D, E, F, and G.
Vinyl chloride copolymers produced by copolymerizing vinyl chloride with one or more of the monomers acrylonitrile; fumaric acid and its methyl, ethyl, propyl, butyl, amyl, hexyl, heptyl, or octyl esters; maleic acid and its methyl, ethyl, propyl, butyl, amyl, hexyl, heptyl, or octyl esters; maleic anhydride; 5-norbornene-2, 3-dicarboxylic acid, mono-*n*-butyl ester; vinyl acetate-and vinylidene chloride. The finished copolymers shall contain at least 50 weight percent of polymer units derived from vinyl chloride: shall contain no more than 5 weight percent of total polymer units derived from fumaric and/or maleic acid and/or their methyl, ethyl, propyl, butyl, amyl, heptyl, or octyl monoesters or from maleic anhydride or from mono-*n*-butyl ester of 5-norbornene-2, 3-dicarboxylic acid (however, in any case the finished copolymers shall contain no more than 4 weight percent of total polymer units derived from mono-*n*-butyl ester of 5-norbornene-2,3-dicarboxylic acid)	
Vinyl chloride-vinyl acetate hydroxyl-modified copolymers	
Vinyl chloride-vinyl acetate hydroxyl-modified copolymers reacted with trimellitic anhydride	
Vinylidene chloride copolymers produced by copolymerizing vinylidene chloride with one or more of the monomers acrylamide acrylic acid, acrylonitrile, butyl acrylate, butyl methacrylate ethyl acrylate, ethyl methacrylate, fumaric acid, itaconic acid, methacrylic acid, methyl acrylate, methyl methacrylate, octadecyl methacrylate, propyl acrylate, propyl methacrylate, vinyl chloride and vinyl sulfonic acid. The finished copolymers shall contain at least 50 weight percent of polymer units derived from vinylidene chloride; and shall contain no more than 5 weight percent of total polymer units derived from acrylamide, acrylic acid, fumaric acid, itaconic acid, methacrylic acid, octadecyl methacrylate, and vinyl sulfonic acid	
Colorants:	
Aluminum	For use as a colorant only.
Aluminum hydrate	Do.
Aluminum and potassium silicate (mica)	Do.
Aluminum mono-, di-, and tristearate	Do.

Aluminum silicate (China clay)	Do.
Barium sulfate	Do.
Bentonite	Do.
Bentonite, modified with dimethyldioctadecylammonium ion	Do.
Burnt umber	Do.
Calcium carbonate	Do.
Calcium silicate	Do.
Calcium sulfate	Do.
Carbon black (channel process)	Do.
Cobalt aluminate	Do.
Diatomaceous earth	Do.
Iron oxides	Do.
Magnesium oxide	Do.
Magnesium silicate (talc)	Do.
Phthalocyanine blue (C.I. pigment blue 15, 15:1, 15:2, 15:3, and 15:4; C.I. No. 74160; CAS Reg. No. 147-14-8)	Do.
Raw sienna	Do.
Silica	Do.
Tartrazine lake (certified FD+C Yellow No. 5 only)	Do.
Titanium dioxide	Do.
Titanium dioxide-barium sulfate	Do.
Titanium dioxide-magnesium	Do.
silicate	
Zinc carbonate	Do.
Zinc oxide	Do.

(c) The food-contact surface of the paper and paperboard in the finished form in which it is to contact food, when extracted with the solvent or solvents characterizing the type of food, and under conditions of time and temperature characterizing the conditions of its intended use as determined from tables 1 and 2 of this paragraph, shall yield net chloroform-soluble extractives (corrected for wax, petrolatum, mineral oil and zinc extractives as zinc oleate) not to exceed 0.5 milligram per square inch of food-contact surface as determined by the methods described in paragraph (d) of this section.

Table 1--Types of Raw and Processed Foods

I. Nonacid, aqueous products; may contain salt or sugar or both (pH above 5.0).
II. Acid, aqueous products; may contain salt or sugar or both, and including oil-in-water emulsions of low- or high-fat content.
III. Aqueous, acid or nonacid products containing free oil or fat; may contain salt, and including water-in-oil emulsions of low- or high-fat content.
IV. Dairy products and modifications:
    A. Water-in-oil emulsions, high- or low-fat.
    B. Oil-in-water emulsions, high- or low-fat.
    V. Low-moisture fats and oil.
VI. Beverages:
    A. Containing up to 8 percent of alcohol.
    B. Nonalcoholic.
    C. Containing more than 8 percent alcohol.
VII. Bakery products other than those included under Types VIII or IX of this table:
    A. Moist bakery products with surface containing free fat or oil.
    B. Moist bakery products with surface containing no free fat or oil.
VIII. Dry solids with the surface containing no free fat or oil (no end test required).
IX. Dry solids with the surface containing free fat or oil.

Table 2--Test Procedures with Time Temperature Conditions for Determining Amount of Extractives From the Food-Contact Surface of Uncoated or Coated Paper and Paperboard, Using Solvents Simulating Types of Foods and Beverages

Condition of use	Types of food (see table 1)	Food-simulating solvents			
		Water	Heptane[1]	8 percent alcohol	50 percent alcohol
		Time and temperature	Time and temperature	Time and temperature	Time and temperature
A. High temperature heat-sterilized (e.g., over 212 deg. F)	I, IV-B, VII-B	250 deg. F, 2 hr			
	III, IV-A, VII-A	.....do	150 deg. F, 2 hr		
B. Boiling water sterilized	II, VII-B	212 deg. F, 30 min			
	III, VII-A	.....do	120 deg. F, 30 min		
C. Hot filled or pasteurized above 150 deg. F	II, IV-B, VII-B	Fill boiling, cool to 100 deg. F			
	III, IV-A, VII-A	.....do	120 deg. F, 15 min		
	V, IX		.....do		

D. Hot filled or pasteurized below 150 deg. F	II, IV-B, VI-B,				
	VII-B	150 deg. F, 2 hr			
	III, IV-A, VII-A	.....do	100 deg. F, 30 min		
	V, IX		.....do		
	VI-A			150 deg. F, 2 hr	
	VI-C				150 deg. F, 2 hr.
E. Room temperature filled and stored (no thermal treatment in the container)	I, II, IV-B, VI-B, VII-B	120 deg. F, 24 hr			
	III, IV-A, VII-A	.....do	70 deg. F, 30 min		
	V, IX		.....do		
	VI-A			120 deg. F, 24 hr	
	VI-C				120 deg. F, 24 hr.
F. Refrigerated storage (no thermal treatment in the container)	III, IV-A, VII-A	70 deg. F, 48 hr	70 deg. F, 30 min		
	I, II, IV-B, VI-B, VII-B	.....do			
	VI-A			70 deg. F, 48 hr	
	VI-C				70 deg. F, 48 hr.
G. Frozen storage (no thermal treatment in the container)	I, II, IV-B, VII-B	70 deg. F, 24 hr			
	III, VII-A	.....do	70 deg. F, 30 min		
H. Frozen or refrigerated storage: Ready-prepared foods intended to be reheated in container at time of use:					
1. Aqueous or oil-in-water emulsion of high- or low-fat	I, II, IV-B, VII-B	212 deg. F, 30 min			
2. Aqueous, high- or low-free oil or fat	III, IV-A, VII-A, IX	.....do	120 deg. F, 30 min		

[1]Heptane extractability results must be divided by a factor of five in arriving at the extractability for a food product having water-in-oil emulsion or free oil or fat. Heptane food-simulating solvent is not required in the case of wax-polymer blend coatings for corrugated paperboard containers intended for use in bulk packaging of iced meat, iced fish, and iced poultry.

(d)*Analytical methods* --

(1)*Selection of extractability conditions.* First ascertain the type of food product (table 1, paragraph (c) of this section) that is being packed commercially in the paper or paperboard and the normal conditions of thermal treatment used in packaging the type of food involved. Using table 2, paragraph (c) of this section, select the food-simulating solvent or solvents and the time-temperature exaggerations of the paper or paperboard use conditions. Having selected the appropriate food-simulating solvent or solvents and the time-temperature exaggeration over normal use, follow the applicable extraction procedure.

(2)*Reagents* --(i)*Water.* All water used in extraction procedures should be freshly demineralized (deionized) distilled water.

(ii)*n-Heptane.* Reagent grade, freshly redistilled before use, using only material boiling at 208 deg. F.

(iii)*Alcohol.* 8 or 50 percent (by volume), prepared from undenatured 95 percent ethyl alcohol diluted with demineralized (deionized) distilled water.

(iv)*Chloroform.* Reagent grade, freshly redistilled before use, or a grade having an established consistently low blank.

(3)*Selection of test method.* Paper or paperboard ready for use in packaging shall be tested by use of the extraction cell described in "Official Methods of Analysis of the Association of Official Analytical Chemists," 13th Ed. (1980), sections 21.010-21.015, under "Exposing Flexible Barrier Materials for Extraction," which is incorporated by reference (Copies may be obtained from the AOAC INTERNATIONAL, 481 North Frederick Ave., suite 500, Gaithersburg, MD 20877, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*); also described in ASTM method F34-76 (Reapproved 1980), "Standard Test Method for Liquid Extraction of Flexible Barrier Materials," which is incorporated by reference (copies may be obtained from the American Society for Testing Materials, 100 Barr Harbor Dr., West Conshohocken, Philadelphia, PA 19428-2959, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*), except that formed paper and paperboard products may be tested in the container by adapting the in-container methods described in 175.300(e) of this chapter. Formed paper and paperboard products such as containers and lids, that cannot be tested satisfactorily by any of the above methods may be tested in specially designed extraction equipment, usually consisting of clamping devices that fit the closure or container so that the food-contact surface can be tested, or, if flat samples can be cut from the formed paper or paperboard products without destroying the integrity of the food-contact surface, they may be tested by adapting the following "sandwich" method:

(i)*Apparatus.* (*a*) Thermostated (+/-1.0 deg. F) water bath, variable between 70 deg. F and 120 deg. F water bath cover capable of holding at least one 800-milliliter beaker partially submersed in bath.

(*b*) Analytical balance sensitive to 0.1 milligram with an approximate capacity of 100 grams.

(*c*) Tongs.

(*d*) Hood and hot-plate facilities.

(*e*) Forced draft oven.

For each extraction, the following additional apparatus is necessary:

(*f*) One No. 2 paper clip.

(*g*) One 800-milliliter beaker with watch-glass cover.

(*h*) One 250-milliliter beaker.

(*i*) Five 21/2-inch-square aluminum screens (standard aluminum window screening is acceptable).

(*j*) One wire capable of supporting sample stack.

(ii)*Procedure.* (*a*) For each extraction, accurately cut eight 21/2-inch-square samples from the formed paper or paperboard product to be tested.
(*b*) Carefully stack the eight 21/2-inch-square samples and the five 21/2-inch-square aluminum screens in sandwich form such that the food-contact side of each sample is always next to an aluminum screen, as follows: Screen, sample, sample, screen, sample, sample, screen, etc. Clip the sandwich together carefully with a No. 2 paper clip, leaving just enough space at the top to slip a wire through.
(*c*) Place an 800-milliliter beaker containing 100-milliliters of the appropriate food-simulating solvent into the constant temperature bath, cover with a watch glass and condition at the desired temperature.
(*d*) After conditioning, carefully lower the sample sandwich with tongs into the beaker.
(*e*) At the end of the extraction period, using the tongs, carefully lift out the sample sandwich and hang it over the beaker with the wire.
(*f*) After draining, pour the food-simulating solvent solution into a tared 250-milliliter beaker. Rinse the 800-milliliter beaker three times, using a total of not more than 50 milliliters of the required solvent.
(*g*) Determine total nonvolatile extractives in accordance with paragraph (d)(5) of this section.
(4)*Selection of samples.* Quadruplicate samples should be tested, using for each replicate sample the number of cups, containers, or preformed or converted products nearest to an area of 100 square inches.
(5)*Determination of amount of extractives* --(i)*Total residues.* At the end of the exposure period, remove the test container or test cell from the oven and combine the solvent for each replicate in a clean Pyrex (or equivalent) flask or beaker being sure to rinse the test container or cell with a small quantity of clean solvent. Evaporate the food-simulating solvents to about 100 milliliters in the flask or beaker, and transfer to a clean, tared evaporating dish (platinum or Pyrex), washing the flask three times with small portions of solvent used in the extraction procedure, and evaporate to a few milliliters on a nonsparking, low-temperature hotplate. The last few milliliters should be evaporated in an oven maintained at a temperature of approximately 221 deg. F. Cool the evaporating dish in a desiccator for 30 minutes and weigh the residue to the nearest 0.1 milligram, (*e*). Calculate the extractives in milligrams per square inch of the container or sheeted paper or paperboard surface.
(*a*)*Water and 8- and 50-percent alcohol.* Milligrams extractives per square inch=(*e*)/(*s*).
(*b*)*Heptane.* Milligrams extractives per square inch=*(e)/(s)(F)*
where:
e =Milligrams extractives per sample tested.
s =Surface area tested, in square inches.
F =Five, the ratio of the amount of extractives removed by heptane under exaggerated time-temperature test conditions compared to the amount extracted by a fat or oil under exaggerated conditions of thermal sterilization and use.
e '=Chloroform-soluble extractives residue.
ee '=Corrected chloroform-soluble extractives residue.
e' or*ee'* is substituted for*e* in the above equations when necessary.
If when calculated by the equations in paragraph (d)(5)(i) (*a*) and (*b*) of this section, the extractives in milligrams per square inch exceeds the limitations prescribed in paragraph (c) of this section, proceed to paragraph (d)(5)(ii) of this section (method for determining the amount of chloroform-soluble extractives residues).
(ii)*Chloroform-soluble extractives residue.* Add 50 milliliters of chloroform (freshly distilled reagent grade or a grade having an established consistently low blank) to the dried and weighed residue, (*e*), in the evaporating dish obtained in paragraph (d)(5)(i) of this section. Warm carefully, and filter through Whatman No. 41 filter paper (or equivalent) in a Pyrex (or equivalent) funnel, collecting the filtrate in a clean, tared evaporating dish (platinum or Pyrex). Repeat the chloroform extraction, washing the filter paper with this second portion of chloroform. Add this filtrate to the original filtrate and evaporate the total down to a few milliliters on a low-temperature hotplate. The last few milliliters should be evaporated in an oven maintained at approximately 221 deg.

F. Cool the evaporating dish in a desiccator for 30 minutes and weigh to the nearest 0.1 milligram to get the chloroform-soluble extractives residue (′). This′ is substituted for *e* in the equations in paragraph (d)(5)(i) (*a*) and (*b*) of this section. If the chloroform-soluble extractives in milligrams per square inch still exceeds the limitation prescribed in paragraph (c) of this section, proceed to paragraph (d)(5)(iii) of this section (method for determining corrected chloroform-soluble extractives residue).

(iii)*Corrected chloroform-soluble extractives residue* --(*a*)*Correction for zinc extractives.* Ash the residue in the evaporating dish by heating gently over a Meker-type burner to destroy organic matter and hold at red heat for about 1 minute. Cool in the air for 3 minutes, and place the evaporating dish in the desiccator for 30 minutes and weigh to the nearest 0.1 milligram. Analyze this ash for zinc by standard Association of Official Agricultural Chemists methods or equivalent. Calculate the zinc in the ash as zinc oleate, and subtract from the weight of chloroform-soluble extractives residue (′) to obtain the zinc-corrected chloroform-soluble extractives residue (*e′*). This*e′* is substituted for *e* in the equations in paragraph (d)(5)(i) (*a*) and (*b*) of this section.

(*b*)*Correction for wax, petrolatum, and mineral oil* --(*1*)*Apparatus.* Standard 10 millimeter inside diameter * 60 centimeter chromatographic column (or standard 50-milliliter buret with an inside diameter of 10-11 millimeters) with a stopcock of glass, perfluorocarbon resin, or equivalent material. The column (or buret) may be optionally equipped with an integral coarse, fritted glass disc and the top of the column (or buret) may be optionally fitted with a 100-millimeter solvent reservoir.

(*2*)*Preparation of column.* Place a snug pledget of fine glass wool in the bottom of the column (or buret) if the column (or buret) is not equipped with integral coarse, fritted glass disc. Overlay the glass wool pledget (or fritted glass disc) with a 15-20 millimeter deep layer of fine sand. Measure in a graduated cylinder 15 milliliters of chromatographic grade aluminum oxide (80-200 mesh) that has been tightly settled by tapping the cylinder. Transfer the aluminum oxide to the chromatographic tube, tapping the tube during and after the transfer so as to tightly settle the aluminum oxide. Overlay the layer of aluminum oxide with a 1.0-1.5 centimeter deep layer of anhydrous sodium sulfate and on top of this place an 8-10 millimeter thick plug of fine glass wool. Next carefully add about 25 milliliters of heptane to the column with stopcock open, and allow the heptane to pass through the column until the top level of the liquid just passes into the top glass wool plug in the column, and close stopcock.

(*3*)*Chromatographing of sample extract* --(*i*)*For chloroform residues weighing 0.5 gram or less.* To the dried and weighed chloroform-soluble extract residue in the evaporating dish, obtained in paragraph (d)(5)(ii) of this section, add 20 milliliters of heptane and stir. If necessary, heat carefully to dissolve the residue. Additional heptane not to exceed a total volume of 50 milliliters may be used if necessary to complete dissolving. Cool to room temperature. (If solution becomes cloudy, use the procedure in paragraph (d)(5)(iii)(*b*)(*3*)(*ii*) of this section to obtain an aliquot of heptane solution calculated to contain 0.1-0.5 gram of chloroform-soluble extract residue.) Transfer the clear liquid solution to the column (or buret). Rinse the dish with 10 millimeters of additional heptane and add to column. Allow the liquid to pass through the column into a clean, tared evaporating dish (platinum or Pyrex) at a dropwise rate of about 2 milliliters per minute until the liquid surface reaches the top glass wool plug; then close the stopcock temporarily. Rinse the Pyrex flask which contained the filtrate with an additional 10-15 milliliters of heptane and add to the column. Wash (elute) the column with more heptane collecting about 100 milliliters of total eluate including that already collected in the evaporating dish. Evaporate the combined eluate in the evaporating dish to dryness on a steam bath. Dry the residue for 15 minutes in an oven maintained at a temperature of approximately 221 deg. F. Cool the evaporating dish in a desiccator for 30 minutes and weigh the residue to the nearest 0.1 milligram. Subtract the weight of the residue from the weight of chloroform-soluble extractives residue (′) to obtain the wax-, petrolatum-, and mineral oil-corrected chloroform-soluble extractives residue (*e′*). This*e′* is substituted for *e* in the equations in paragraph (d)(5)(i) (*a*) and (*b*) of this section.

(*ii*) For chloroform residues weighing more than 0.5 gram. Redissolve the dried and weighed chloroform-soluble extract residue as described in paragraph (d)(5)(iii)(*b*)(*3*)(*i*) of this section using proportionately larger quantities of heptane. Transfer the heptane solution to an appropriate-sized volumetric flask (i.e., a 250-milliliter flask for about 2.5 grams of residue) and adjust to volume with additional heptane. Pipette out an aliquot (about 50 milliliters) calculated to contain 0.1-0.5 gram of the chloroform-soluble extract residue and analyze chromatographically as described in paragraph (d)(5)(iii)(*b*)(*3*)(*i*) of this section. In this case the weight of the dried residue from the heptane eluate must be multiplied by the dilution factor to obtain the weight of wax,

petrolatum, and mineral oil residue to be subtracted from the weight of chloroform-soluble extractives residue (′) to obtain the wax-, petrolatum-, and mineral oil-corrected chloroform-soluble extractives residue (*e′*). This*e′* is substituted for*e* in the equations in paragraph (d)(5)(i) (*a*) and (*b*) of this section. (Note: In the case of chloroform-soluble extracts which contain high melting waxes (melting point greater than 170 deg. F), it may be necessary to dilute the heptane solution further so that a 50-milliliter aliquot will contain only 0.1-0.2 gram of the chloroform-soluble extract residue.)
(e) Acrylonitrile copolymers identified in this section shall comply with the provisions of 180.22 of this chapter, except where the copolymers are restricted to use in contact with food only of the type identified in paragraph (c), table 1 under Category VIII.
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