December 17, 2024

Submitted Electronically via Department of Ecology Public Comment Form

CBC Comments on Draft Identification of Priority Products Report to the Legislature: Safer Products for Washington Cycle 2

The American Chemistry Council Center for Biocide Chemistries (CBC)[1] and the American Cleaning Institute (ACI) appreciate the opportunity to provide comments on the Draft Identification of Priority Products Report to the Legislature: Safer Products for Washington Cycle 2 (Draft Report). CBC and ACI reviewed the Draft Report from the perspective of registrants and formulators of antimicrobial pesticides. In this context, CBC and ACI strongly oppose the inclusion of formaldehyde releasers used in cleaning and household care products as a priority products category. We also express our support for the comments submitted by the American Chemistry Council and the Formaldehyde Panel.

Cleaning and household care products, including surface cleaners, disinfectants, and other household products, are essential for maintaining public health and hygiene. Preservatives, including formaldehyde-releasing antimicrobial chemistries, play crucial roles in ensuring the safety and sustainability of water-based products. CBC and ACI's comments outline the existing regulatory findings supporting the use of formaldehyde releasers in cleaning and household products, identify issues with the scope and underlying scientific rationale in the Draft Report, and underscore the importance of preservatives and formaldehyde-releasing agents, and provide rationale as to why the use of formaldehyde-releasing chemistries should not be restricted.

I. Regulation as Pesticides

Formaldehyde-releasing chemistries are registered as pesticides by the U.S. Environmental Protection Agency (EPA) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and by the Washington Department of Agriculture. The use of formaldehyde-releasing chemistries as preservatives in cleaning products is a regulated antimicrobial pesticidal use. This means that EPA considers a significant amount of data, including exposure and use data specific to the use pattern of preserving cleaning and household products, in its review of registered formaldehyde releasing chemistries and as part of each chemistry's Registration Review case.

EPA is in the process of developing draft risk assessments for antimicrobial chemistries considered by EPA to be formaldehyde releasers. These draft risk assessments are expected to be released for public comment in Fiscal Year (FY) 2025. As part of this risk assessment process,

[1] ACC's Center for Biocide Chemistries represents 47 manufacturers and formulators of antimicrobial pesticides.

EPA will review data on which chemistries are registered for and actually used to preserve cleaning and household care products. EPA will consider exposure to human health and the environment because of this use pattern and identify any risks that should be mitigated and identify those risks in a draft risk assessment (DRA).

After EPA releases the DRA for public comment and reviews the comments received, EPA will address any risks identified with proposed mitigations in its Proposed Interim Decision (PID). EPA will also consider the benefits of these chemistries for each use, including information on available alternatives for each use and weigh risks with the benefits of these chemistries in each use.

CBC and ACI maintain that the use of formaldehyde releasers in cleaning and household care products should not be regulated under the Safer Products Program. Should Ecology move forward with this regulatory action, CBC and ACI urge Ecology to pause action until EPA completes its Registration Review decisions for each formaldehyde releasing chemistry case. This will give Ecology the best available risk and benefit information on the uses of these chemistries in the applications of concern to Ecology.

II. Scope of Listing and Scientific Rationale

The Draft Report refers to the category of "formaldehyde releasers" in cleaning and household care products. The specific chemistries included within this category of formaldehyde releasers are not named. Ecology should be specific in naming which chemistries are included in this category. For example, bronopol is often categorized as a formaldehyde releaser, but the bronopol does not directly release formaldehyde as part of its function as a preservative. Bronopol works by disrupting the cellular processes of microorganisms, rendering them unable to reproduce and grow.

CBC recently submitted comments[2] on EPA's draft risk assessment for formaldehyde and paraformaldehyde. In those comments, CBC argues that the DRA for formaldehyde should not be used in the evaluation of formaldehyde releasing chemistries. There are key differences in each chemistry's profile and uses, and each chemistry should be evaluated separately. We encourage Ecology to refer to CBC's comments, including the argument that it is not appropriate for EPA to utilize the draft IRIS assessment of formaldehyde as the basis for key elements of its risk assessment for formaldehyde and paraformaldehyde and that the draft IRIS assessment does not utilize the best available science. CBC notes concerns with the sensory irritation endpoint, use of observational studies for evaluation of chronic non-cancer hazards, failure to incorporate reasonably available information to inform cancer hazards, and identification of skin sensitization risks.

While EPA's Registration Review case for formaldehyde releasers is not completed, these chemistries have been assessed by EPA previously and found to pose no unreasonable risk to

[2] CBC Comments on Pesticide Registration Review; Draft Risk Assessment for Formaldehyde and Paraformaldehyde (Docket ID: EPA-HQ-OPP-2015-0739). See Attachment 1.

human health or the environment from their use in cleaning and household products. Additionally, the European Chemicals Agency (ECHA) recently (July 2023) completed its review of formaldehyde and formaldehyde releasers and released its final restriction proposal. As part of the restriction process, ECHA reviewed all sources of exposure to formaldehyde from formaldehyde and formaldehyde releasers and did not find that the use in cleaning and household products posed a risk needed further restriction. Specifically, ECHA noted in the restriction, "Based on available literature and the outcome of the exposure estimation, the Dossier Submitter concluded that **human health risks from formaldehyde release from mixtures for consumer use are adequately controlled**."[3]

Further, in the Annex XV restriction report, ECHA notes, "The cleaning and detergents industry has confirmed that formaldehyde may be present in the mixture in concentrations not exceeding 200 ppm (0.02%). Furthermore, a voluntary industry agreement was signed with the intention to not exceed the WHO guideline value of formaldehyde in indoor environments (0.1 mg/m3) from the use of cleaning products."[4]

Given the strong data supporting that exposure to formaldehyde from the use of formaldehyde releasers as preservatives in cleaning and household products is minimal, it is unclear why Ecology has selected these chemistries and use patterns as a priority product in the Draft Report. We encourage Ecology to defer to the U.S. EPA, ECHA, and other regulatory agencies that are assessing a significant volume of data specific to these chemistries' uses and use patterns to determine whether there is a risk to public health or the environment.

III. Importance of Preservatives in Cleaning and Household Products

Preservatives are an essential component in cleaning product formulations. They serve to protect consumers and ensure the safety, effectiveness, and longevity of the product throughout its lifecycle. Cleaning products, especially those in liquid or aqueous form, are susceptible to microbial contamination.

Formaldehyde-releasing preservatives generally work by slowly releasing small amounts of formaldehyde over time, which acts as a powerful antimicrobial agent. Formaldehyde-releasing preservatives are highly effective at low concentrations, making them an ideal choice for cleaning product manufacturers who need reliable and economical solutions for microbial control. These preservatives offer broad-spectrum antimicrobial activity, addressing a wide range of bacteria, fungi, and other pathogens that could otherwise compromise product integrity.

Not all preservatives can be used in every type of cleaning and household products. Each preservative must be approved by EPA for use in a particular type of cleaning product and household product. When EPA reviews cleaning and household products that make pesticidal claims, preservatives are considered as inert ingredients and approved as part of EPA's review of data on the final formulated product. Substituting preservatives can be an extremely difficult

[3] COMMISSION REGULATION (EU) 2023/1464 of 14 July 2023 amending Annex XVII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council as regards formaldehyde and formaldehyde releasers

[4] https://echa.europa.eu/documents/10162/ee418b46-92cc-8db2-de97-5c7599df763c

process. Product formulators must consider how the preservative works with the overall product, such as impacts on pH, physical state of the product, etc.

It's also extremely important for product formulators to have a wide range of preservative choices. Utilizing various types of preservatives helps to limit microbial tolerance to various preservatives. It is also important for supply chains to have a range of acceptable preservatives and choices.

Due to regulatory restrictions and hurdles to innovation of new preservatives, the range of available preservatives for use in household and cleaning products is shrinking. Formaldehyde releasers are an important class of preservatives, and should they be further restricted by Ecology, it would likely have a tremendous impact on the overall availability of products to control microbial growth. Should Ecology move forward with further action on this identified Priority Product category, the benefits and availability of alternative chemistries must be strongly considered before regulatory action is taken.

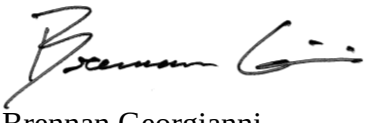
IV. Conclusion

Preservatives, including formaldehyde-releasing agents, are vital to ensuring the safety, efficacy, and stability of cleaning products. They play an essential role in preventing microbial contamination and extending shelf life, thereby protecting consumers from potential health risks associated with product degradation or contamination. We strongly urge regulators to consider the established safety of formaldehyde-releasing chemistries and to avoid unnecessary restrictions that could undermine the quality, safety, and availability of cleaning products. Any regulation or policy that restricts the use of formaldehyde-releasing preservatives should be based on sound scientific evidence and consider the overall benefits these agents provide in maintaining product safety and consumer health.

We appreciate your consideration of these comments and look forward to continued dialogue on this important issue.

Sincerely,

Anastasia Swearingen
Executive Director
American Chemistry Council's Center for Biocide Chemistries



Brennan Georgianni
Senior Director, State Government Affairs
American Cleaning Institute

Attachment 1

June 18, 2024

Submitted Electronically

Kendall Ziner
Antimicrobials Division
Office of Pesticide Programs
Environmental Protection Agency
Ziner.Kendall@epa.gov

RE: Comments on Pesticide Registration Review; Draft Risk Assessment for Formaldehyde and Paraformaldehyde (Docket ID: EPA-HQ-OPP-2015-0739)

Dear Ms. Ziner:

The American Chemistry Council (ACC) Center for Biocides Chemistries' (CBC) appreciates the opportunity to provide comments on the U.S. Environmental Protection Agency's (EPA or Agency) Pesticide Registration Review; Draft Risk Assessment for Formaldehyde and Paraformaldehyde (DRA).[5]

CBC notes that its members are not registrants of formaldehyde as an active pesticidal ingredient. However, CBC's Formaldehyde Releasers Task Force represents registrants of pesticides considered to be formaldehyde releasers or donors. In the DRA, EPA refers to potential cumulative exposure to formaldehyde from the use of specific formaldehyde releasers in several use patterns. CBC is concerned that EPA's evaluation of the risks posed by formaldehyde in these use patterns could be used as the basis for EPA's draft risk assessments of formaldehyde donor chemistries. While the requested GDCI data was not submitted for formaldehyde, this is not the case for the formaldehyde donor chemistries. **CBC strongly opposes the use of the formaldehyde DRA in the evaluation of the formaldehyde donor chemistries, noting the key differences in these chemistries and the importance of evaluating the data on each chemistry individually.**

The following comments identify key issues in the underlying data and approaches used to evaluate the potential human health risks identified in the formaldehyde DRA. CBC urges EPA to reconsider these approaches as it develops risk assessments for the remaining chemistries under the Registration Review process, particularly formaldehyde donor chemistries.

I. Use of the Draft Formaldehyde IRIS Assessment

The Draft Risk Assessment for Formaldehyde and Paraformaldehyde utilizes the draft Integrated Risk Information System (IRIS) assessment on formaldehyde inhalation to evaluate the cancer and non-cancer hazards associated with the chronic inhalation exposures for the pesticidal uses

[5] EPA-HQ-OPP-2015-0739.

of formaldehyde. The Draft IRIS Assessment has not undergone a substantive and Federal Advisory Committee Act-compliant peer review and is still in draft form, subject to change, and does not meet the Federal Insecticide, Fungicide, and Rodenticide Act requirements that risk evaluations utilize the best available scientific data. It is not appropriate for OPP to utilize a draft IRIS assessment as the basis for key elements of its risk assessment for formaldehyde and paraformaldehyde because the draft IRIS assessment does not utilize the best available science.

A. Sensory Irritation Endpoint

The DRA notes that for acute inhalation exposures, EPA identified sensory irritation as the most sensitive endpoint and included four controlled human exposure studies as part of the weight of evidence (WOE) for Point of Departure (POD) determination. The Human Studies Review Board (HSRB), questioned whether sensory irritation meets the EPA IRIS definition of adverse. It also agreed that using this endpoint as a lower bound for potential adverse effects is appropriate, and also recommended that no uncertainty factor need be applied when sensory irritation is used as the point of departure.[6] Other inhalation experts have also questioned the adversity of the sensory irritation endpoint, noting that the "chemesthesis response to formaldehyde is a normal physiological response and does not reflect adverse health effects unless the sensory organs are overwhelmed to the point of being functionally impaired or objectively incapacitating."[7]

Further, several publications in the peer reviewed literature, including those conducted by the National Academies of Science (NAS) note that neither formaldehyde sensory nor tissue irritation adhere to Haber's Law.[8] NAS, which considered sensory irritation the primary health effect of concern, agreed with the literature that found that exposure to concentrations that do not produce short-term sensory irritation also do not result in sensory irritation after repeated exposure. After reviewing all the evidence, the HSRB final report is clear that "[t]he HSRB disagrees with EPA's assumption of Haber's Law for formaldehyde and recommends that EPA not make duration adjustments to develop the PODs."[9] OPP should consider that sensory irritation is the most sensitive endpoint which protects against other health effects, a younger population will be more sensitive than an older or asthmatic population, and that concentration, not duration, is the driver of whether effects will be seen.

B. Use of Observational Studies for Evaluation of Chronic Non-Cancer Hazards

---

[6] HSRB Final Report, Oct. 5, 2023, available at july-2023-hsrb-report-woe-formaldehyde_0.pdf (epa.gov)

[7] Kaden, D comments to NAS 2022, PAF-43, available at https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0115/attachment_10.pdf

[8] See comments submitted to the HSRB, May 16, 2023, by Dr. Holm on behalf of the American Forest & Paper Association and the American Wood Council, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0106/attachment_8.pdf. See also NAS 2007, Emergency and Continuous Exposure Guidance Levels for Selected Submarine Contaminants Volume 1, 2007, available at: https://nap.nationalacademies.org/download/11170#. 45 NAS, Emergency and Continuous Exposure Guidance Levels for Selected Submarine Contaminants Volume 1, 2007, at page 105, available at: https://nap.nationalacademies.org/download/11170#.

[9] HSRB Final Report, Oct. 5, 2023, available at july-2023-hsrb-report-woe-formaldehyde_0.pdf (epa.gov)

The draft IRIS assessment's use of observational epidemiological studies, rather than available high quality controlled human exposure studies, to evaluate the chronic non-cancer hazards of formaldehyde is problematic. Observational studies present challenges such as confounding factors that cannot be controlled for and often have poor study design. Controlled human exposure studies where the subjects, exposures, and confounders are known and controlled, are a higher quality source of data. In the case of formaldehyde, multiple high quality controlled human exposure studies exist and should be used.

For the derivation of non-cancer inhalation effects, EPA relies predominantly on the observational study Krzyzanowski et. al. (1990), with support from Annesi-Maesano et. al. (2012), Matsunaga et. al. (2008), and Venn et al. (2003).[10] EPA proposes to use a point of departure of 0.017 ppm and recommends an uncertainty factor of 3 for human variability. EPA's reliance on these methodologically deficient studies is misplaced and is not consistent with an approach that requires consideration and use of the best available science. Detailed comments by independent experts, have been provided to the SACC on the weaknesses of these studies[11] and ACC's Formaldehyde Panel's comments on the TSCA risk evaluation of formaldehyde.[12]

The HSRB evaluated the controlled human exposure studies to inform acute exposures and did not find any ethical issues with the key studies identified by EPA (Mueller et. al. 2013, Lang et.al 2008, Kulle et. al. 1987, and Andersen and Mølhave, 1983). The HSRB also noted that the controlled chamber studies have "a preferred study design and greater scientific rigor than the observational studies."[13] The OPP Data Evaluation Records (DERs) for Mueller and Lang also concluded that both these studies provide data for quantitative use for deriving a point of departure.[14] While OPP was focused on points of departure for acute inhalation, based on what we know regarding how formaldehyde does not follow Haber's law, these findings should apply equally to chronic studies.

When evaluating formaldehyde for the determination of occupational limits, other authoritative bodies have chosen to rely on controlled human exposure studies over observational epidemiological studies and in doing so relied upon sensory irritation effects as protective of all other non-cancer and cancer effects.[15] In 2017, ACGIH relied upon Lang et.al. and in 2016,

---

[10] EPA, *Draft Human Health Hazard Assessment for Formaldehyde*, Mar. 2024, available at EPA-HQ-OPP-2015-0739-0013.

[11] See comments submitted to the SACC from Dr. Dennis Paustenbach, Linda Dell (Ramboll), Dr. Stewart Holmes (AF&PA) and Renee Kalmes and Dr. Pamela Dopart (Exponent).

[12] See comments by ACC Formaldehyde Panel available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0235.

[13] HSRB Final Report, Oct 5, 2023, available at: https://www.epa.gov/system/files/documents/2023-10/july-2023-hsrb-report-woe-formaldehyde_0.pdf.

[14] See DERs for Lang et al. 2008 and Mueller et al. 2013, available at 42. DER Lang 2008 Draft Risk Evaluation for Formaldehyde and 43. DER Mueller 2013 Draft Risk Evaluation for Formaldehyde, and Debra Kaden presentation to the HSRB on Lang et al. and Mueller et al., available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-

[15] See Goyak and Holm (2024). Sensory irritation and use of the best available science in setting exposure limits: Issues raised by a scientific panel review of formaldehyde human research studies. Reg Tox Pharm., available at:

SCOEL relied on Mueller et. al. and Lang et.al. In 2010, for general population exposures, WHO also relied on controlled human exposure studies (Lang et. al.), and in 2007, the NAS also recommended controlled human exposure studies when evaluating formaldehyde in submarines.

These organizations evaluated the weight of the evidence and determined that the best science came from relying on studies where the populations, exposures and confounders were controlled. EPA should similarly use the controlled human exposure studies for points of departure for evaluating the occupational, consumer, indoor air, and ambient air scenarios.

CBC encourages OPP to consider high quality controlled human exposure studies as higher quality data than observational studies in the development of its risk assessments.

C. Failure to Incorporate Reasonably Available Information to Inform Cancer Hazards

CBC notes that one of the biggest criticisms of the draft IRIS assessment has been the lack of consideration of all available evidence to inform the cancer hazards of formaldehyde. For over a decade, the Inhalation Unit Risk (IUR) analysis for nasopharyngeal carcinomas (NPC) that EPA relies on in the draft IRIS assessment has been criticized by experts and EPA has not addressed these concerns. In 2011, the NAS reviewed EPA's 2010 Draft IRIS Formaldehyde Assessment, recommended that EPA conduct an independent analysis of the National Cancer Institute cohort that EPA relied upon, and recommended that EPA consider alternative models, consistent with EPA's 2005 Cancer Guidelines.[16] EPA neither conducted the independent analysis nor considered the application of alternative models. Consideration of alternative models, including non-linear models, is necessary because, over the past 30 years, a mode of action (MOA) of cytotoxicity with regenerative hyperplasia for NPC has become globally accepted.

Further information on how EPA's draft IRIS assessment fails to consider MOA information, among other flaws, was provided to NAS in 2023.[17] A more recent analysis, provided to the SACC by Drs. Thompson and Gentry, also describes the detailed scientific flaws in EPA's IUR analysis for NPC and describes some of the scientific publications that EPA must also consider before relying on the IUR in the 2022 Draft IRIS Formaldehyde Assessment.[18]

The draft IRIS assessment failed to consider significant scientific information that would have informed its evaluation of cancer hazards, such as:

---

https://doi.org/10.1016/j.yrtph.2024.105587; and Celanese comments, to EPA, Oct. 13, 2023, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2018-0438-0128.

[16] NAS, *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde*,2011, at page 134, available at: https://nap.nationalacademies.org/catalog/13142/review-of-the-environmental-protection-agencys-draft-iris-assessment-of-formaldehyde.

[17] ACC, Summary of Insufficient U.S. Environmental Protection Agency (EPA) Responses to the Recommendations From the National Academy of Sciences (NAS) 2011 Review of EPA's 2010 Draft IRIS Assessment of Formaldehyde, Mar. 31, 2023, at pages 4-7, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_7.pdf.

[18] See Comments submitted to the SACC, May 2024, from Dr. Chad Thompson and Dr. Robinan Gentry, available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613

- Gentry et. al, 2020, postulated MOAs for leukemia following formaldehyde inhalation. Using the IPCS framework, the authors showed that a significant amount of research supports the null hypothesis that there is no causal association between formaldehyde inhalation exposure and leukemia. The analysis showed a lack of confidence in any of the postulated MOAs currently in the published literature and a lack of dose-response or concordance with many of the key events postulated in the EPA 2022 Draft Assessment, most of which require systemic delivery. This increases confidence in the conclusion that there is a lack of biological plausibility for a causal association between formaldehyde inhalation exposure and leukemia. Not only did EPA not use a similar framework, but EPA also did not consider the findings of this publication.
- Vincent et.al, 2024, conducted a systematic review focusing on the relationship between formaldehyde and LHP cancers, including myeloid leukemia.[19] This systematic review found "no credible explanation linking inhaled formaldehyde to LHP cancers, and no evidence of formaldehyde entering the bone marrow or blood when inhaled" and determined that causation is unlikely.[20]

Therefore, in relying on the draft IRIS assessment for a classification of formaldehyde's cancer risk in the DRA, OPP is not relying upon the best available science. CBC strongly emphasizes the need for EPA to review all available scientific data in the development of its FIFRA risk assessments.

II. Identification of Skin Sensitization Risks

The DRA establishes dermal endpoints based on skin sensitization for both induction and elicitation. Utilizing these endpoints, EPA identified dermal exposure risks from several formaldehyde use patterns. CBC refers to the comments submitted by Integral that emphasize the lack of guideline studies for elicitation response and the variability in elicitation responses in humans, making setting a point of departure for elicitation unreliable.[21]

CBC also reiterates comments submitted by its Isothiazolinones Task Force on the DRAs in the Isothiazolinones Registration Review Cases, which emphasize the need for EPA to consider how exposure to an active ingredient is impacted by its use in a matrix. These comments also underscore the need for scientifically valid approaches to evaluating skin sensitization endpoints.

CBC notes that the data and approach used to identify the dermal endpoints in the formaldehyde DRA is problematic. For example, in the Flyvholm et al. 1997 study, which EPA used to select the elicitation threshold, effects were seen only in occluded patch tests where the patch was left

---

[19] M J Vincent, S Fitch, L Bylsma, C Thompson, S Rogers, J Britt, D Wikoff, *Assessment of associations between inhaled formaldehyde and lymphohematopoietic cancer through integration of epidemiological and toxicological evidence with biological plausibility*, Toxicological Sciences, 2024;, kfae039, https://doi.org/10.1093/toxsci/kfae039.

[20] Truth in Science, *Why Robust Methods in Systematic Review Matter: The Case of Formaldehyde and Myeloid Leukemia*, available at: https://truthinscience.org/why-robust-methods-in-systematic-review-matter-the-case-of-formaldehyde-and-myeloid-leukemia%ef%bf%bc/.

[21] see comments submitted to the SACC from Integral Consulting, May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613

on the skin for two days. Under non-occluded test conditions, the study reported no response seen in sensitive individuals at similar exposure concentrations that are more reflective of real-world exposure conditions. These results are not representative of typical workplace scenarios as it is unreasonable to assume workers or consumers are dermally exposed to formaldehyde under occluded conditions continuously for multiple days. CBC refers to comments submitted by Integral and the ACC Formaldehyde Panel for further information on dermal sensitization risks for formaldehyde.

III. Conclusion

CBC underscores the importance of evaluating formaldehyde releasing chemistries distinctly from EPA's evaluation of formaldehyde. The draft IRIS assessment should not be utilized in the risk assessment of formaldehyde releasing chemistries, for the reasons stated in section I above. We also note the importance of scientifically rigorous evaluations of dermal sensitization risks, based on the induction threshold, for future risk assessments under Registration Review.

Should you have any questions, please do not hesitate to contact me at Anastasia_Swearingen@americanchemistry.com or (202) 265-6505.

Sincerely,

Anastasia Swearingen
Executive Director
ACC Center for Biocide Chemistries