American Chemistry Council Comments on the 2024 Draft Risk Evaluation for Formaldehyde Prepared Under the Toxic Substances Control Act Docket ID Number EPA-HQ-OPPT-2023-0613

Submitted by:

The American Chemistry Council's
Formaldehyde Panel

Washington, DC
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Executive Summary

The American Chemistry Council (ACC) Formaldehyde Panel appreciates the opportunity to provide comments to the EPA Science Advisory Committee on Chemicals (SACC), the EPA Office of Pollution Prevention and Toxics, and the EPA Office of Pesticides Programs on the 2024 Draft Risk Evaluation for Formaldehyde prepared under the Toxic Substances Control Act (TSCA). Formaldehyde is a naturally occurring substance that is an ever-present part of our world produced by every living organism – including humans. It is a well-studied compound and, thanks to decades of innovation, has become a critical component used safely in everyday goods including housing, automobiles and electric vehicles, wood products, medical devices, vaccines, fertilizers, and antimicrobials. Products that are based on formaldehyde technologies have broad roles in the economy and are critical to the integrity of supply chains, supporting 987,000 jobs and $552.7 billion in sales in 2022 in the United States.

The importance of ensuring that the TSCA Formaldehyde Risk Evaluation complies with the statute, as amended by the 2016 Frank R. Lautenberg Chemical Safety for the 21st Century Act (informally referred to as the Lautenberg Act), including its scientific standards, has been one of the drivers of the Formaldehyde Panel's active engagement with all of the EPA Program Offices assessing formaldehyde and with the National Academies (NAS). The Formaldehyde Panel has provided comments to EPA and the NAS to try to ensure that EPA is aware of and relying on information consistent with the TSCA scientific standards, including standards for best available science. These comments have not yet been addressed by EPA nor have they been incorporated in the Draft IRIS Assessment. In addition to providing scientific comments, we have also documented significant procedural shortcomings in the NAS review of the Draft Formaldehyde IRIS Assessment, which provides critical scientific underpinnings for the Draft TSCA Risk Evaluation.

The Draft Formaldehyde IRIS Assessment is not fit for purpose, and the Office of Pollution Prevention and Toxics' reliance on it has compromised the Draft TSCA Risk Evaluation. The draft IRIS document has not undergone a substantive and Federal Advisory Committee Act-compliant peer review and is still in draft form, in a state of transition, subject to change, and inconsistent with the TSCA standards requiring that risk evaluations be consistent with the best available science.

Formaldehyde's unique chemistry, including the fact that it does not follow Haber's Law, meaning that the incidence and severity of a toxic effect does not depend on both the exposure and duration, must be appropriately weighed and considered when looking at the best available science to inform the human health assessment. The Draft IRIS Assessment looked only at chronic hazard, and OPPT conducted a separate evaluation for acute hazard. This parsing has led to two disparate assessments. Instead, EPA should have conducted a robust single review that also considers what we know about health effects at background levels, and OPPT should have used a weight of the scientific evidence approach to develop defensible hazard and Occupational Exposure Values (OEVs) that represent the best available science. Robust scientific studies, representing the gold standard for human exposures, have been used by other authoritative bodies to evaluate formaldehyde, yet EPA has not appropriately considered them.

Instead, EPA has developed a draft OEV for formaldehyde of 11 ppb. Use of this value incorrectly suggests that typical indoor air levels, including in more than 50 percent of residential environments, present an unreasonable risk. EPA's preliminary "unreasonable risk" determinations for virtually all evaluated uses of formaldehyde, from manufacturing to distribution in commerce to consumer uses, could result in potentially onerous risk management approaches that are likely to have a significant impact on the domestic supply chain and the broader economy. It is important that EPA correct the science in this risk evaluation, rather than relying on remedying a flawed risk assessment with potentially unachievable, and unnecessary, risk management measures.

These are preposterous conclusions from a more than 1000-page scientific assessment. EPA has conducted a "tier 1" screening level assessment, but, where risks were identified, EPA has failed to conduct a more refined assessment that uses inputs that are representative of real-world exposures that are consistent with the best available science. And, while EPA acknowledges the natural and biogenic occurrence of formaldehyde, it has failed to develop a clear, consistent, transparent, and science-based framework that allows for an evaluation of formaldehyde that considers these natural exposures in a consistent and understandable manner. The agency must revise the OEV such that it represents an actual unreasonable risk level, and EPA must consider all relevant aspects of risk, as required by the statute, including what we know about the natural occurrence of formaldehyde.

The comments provided herein describe why the information EPA is relying upon is not consistent with the best available science and how EPA can assess and integrate the available information on hazards and exposures, including what is known from centuries of real-world exposure to ambient formaldehyde, to make a reasonable determination of the appropriate risk level. Other authoritative bodies have been able to successfully set safe levels for formaldehyde without having to contort their hazard evaluations, and EPA should be able to use the robust available scientific information to achieve the same result.

We look forward to continuing to provide input to the SACC as it conducts its review, and we look forward to working with EPA as it addresses concerns from the SACC and the public. For nearly all uses of formaldehyde, including uses that are essential to the national economy, national security, and critical infrastructure, there are no technically and economically feasible alternatives or cost-effective substitutes. EPA has an obligation to ensure its final risk evaluation upholds the intentional and rigorous standards of TSCA while not impeding or unduly creating unnecessary economic barriers.

I. Introduction

The American Chemistry Council (ACC) Formaldehyde Panel (the Formaldehyde Panel) appreciates the opportunity to provide comments to the EPA Science Advisory Committee on Chemicals (SACC), the EPA Office of Pollution Prevention and Toxics (OPPT), and the EPA Office of Pesticides Programs (OPP) on the 2024 Draft Risk Evaluation for Formaldehyde (Draft Formaldehyde Risk Evaluation) prepared under the Toxic Substances Control Act (TSCA).[1] When final, the risk evaluation will be used by EPA to inform potential future regulations under TSCA. OPP and OPPT have worked jointly on three formaldehyde assessments that support the draft risk evaluation, including the Environmental Hazard Assessment, the Chemistry, Fate, and Transport Assessment, and the Human Health Hazard Assessment. Although the SACC is not reviewing the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Registration Review Draft Risk Assessment for Formaldehyde and Paraformaldehyde (Draft FIFRA Assessment), OPP will use feedback received from public comments and the SACC to inform the final FIFRA assessment.[2]

Formaldehyde is a naturally occurring substance, made of carbon, hydrogen, and oxygen. It is an ever-present part of our world, produced by every living organism – including humans, who make and process about 1.5 ounces of formaldehyde per person every day. It is a well-studied compound and, thanks to decades of innovation, has become a critical component used safely in everyday goods including automobiles and electric vehicles, wood products, medical devices, vaccines, fertilizers, and antimicrobials. Formaldehyde is an essential building block, and its versatile chemical properties make it a common and beneficial part of modern life. Products that are based on formaldehyde technologies have broad roles in the economy and are critical to the integrity of supply chains, supporting 987,000 jobs and $552.7 billion in sales in 2022 in the United States.[3] Industries and sectors which rely on formaldehyde include housing; building and construction; food and agriculture; aerospace; science and preservation; semiconductors; automotive; national security; and medicine and medical technologies.[4] Attachment A provides summary information describing the important role formaldehyde plays in each of these sectors.

EPA's preliminary "unreasonable risk" determinations for virtually all evaluated uses of formaldehyde, from manufacturing to distribution in commerce to consumer uses, could result in potentially onerous risk management approaches that could include bans or unachievable workplace standards. It is also important to note that, for nearly all uses of formaldehyde, there is no "technically and economically feasible alternatives that benefit health or the environment," "safer alternatives," or cost-effective substitutes, as required by sections 6(c)(2) and 6(g) of

[1] The Draft Risk Evaluation is available at: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/risk-evaluation-formaldehyde, and supporting information is also available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613/document.

[2] EPA, *Registration Review Draft Risk Assessment for Formaldehyde and Paraformaldehyde*, Apr. 10, 2024, at page 6, available at: https://www.regulations.gov/document/EPA-HQ-OPP-2015-0739-0011. We are concerned by the absence of statutorily relevant peer review for this assessment, as discussed in the Formaldehyde Panel March 8 comments, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0007 (pg. 13-15).

[3] ACC, Formaldehyde Producers Boost U.S. Economy, available at: https://www.americanchemistry.com/industry-groups/formaldehyde/benefits-applications.

[4] Summary descriptions of formaldehyde's essential role in each of these sectors are available at: https://www.americanchemistry.com/industry-groups/formaldehyde/benefits-applications.

TSCA, and that these uses are essential to the national economy, national security, and critical infrastructure while providing "substantial benefit to health, the environment, or public safety."[5]

The Formaldehyde Panel's members include producers, suppliers, and users of formaldehyde and formaldehyde products, as well as trade associations representing important formaldehyde applications. The Formaldehyde Panel's primary activities include scientific research, education, and regulatory and legislative outreach. The Formaldehyde Panel is committed to informing and educating regulators, policymakers, the value chain, and the media on the best available science and weight of the scientific evidence supporting a safe threshold for formaldehyde exposure. Formaldehyde Panel members are also committed to the health and safety of our employees, the communities in which we operate, and the environment as a whole. This commitment includes compliance with existing occupational safety standards, rules, and regulations issued under OSHA and other government agencies. Additionally, Formaldehyde Panel companies that are members of ACC participate in Responsible Care®, the chemical industry's world-class environmental, health, safety, and security performance initiative. Companies that participate in Responsible Care report their progress annually on a variety of process safety and worker safety performance measures, and the reports are publicly available on ACC's website.

Members of the Formaldehyde Panel are actively engaged in research to understand potential human health effects that may be caused by formaldehyde exposure. This work has been ongoing since 2010 when EPA released its Integrated Risk Information System (IRIS) Toxicological Review of Formaldehyde-Inhalation (2010 IRIS Assessment). The National Research Council of the National Academies of Science (NAS) reviewed the draft 2010 IRIS Assessment and concluded that EPA had not sufficiently documented methods to identify or evaluate relevant scientific studies and had not adequately integrated the lines of evidence from the available animal, human, and mechanistic data. The NAS report also called the draft 2010 IRIS Assessment subjective and potentially problematic given the inconsistencies in the available scientific data. Since 2010, independent experts have developed peer-reviewed publications that ACC and its Formaldehyde Panel members fully expected to be incorporated into the 2022 Draft IRIS Formaldehyde Assessment, which provides the scientific support and rationale for the hazard and dose-response assessment for chronic inhalation exposure in the Draft Formaldehyde Risk Evaluation.[6] These independent, robust, data-driven studies, which are all available in the published literature, should have been considered in the proper application of a weight of the scientific evidence approach to evaluating formaldehyde's potential health effects.

ACC and the Formaldehyde Panel supported the 2016 Frank R. Lautenberg Chemical Safety for the 21st Century Act (informally referred to as the Lautenberg Act or TSCA Amendments), which created, among other things, "a separate risk evaluation process for determining whether a chemical substance presents or will present an unreasonable risk of injury" and added various provisions establishing mandatory standards for making science-based decisions under TSCA.

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[5] *See* TSCA sections 6(c)2 and 6(g).

[6] *See* NAS public access file materials available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0113; https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0114; https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0115; https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0116; and https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0117.

Passed with bipartisan support, the Lautenberg Act added new sections to ensure that TSCA is a risk-based statute requiring high quality scientific information. In particular, new section 26(h) requires that all science-based decisions under the Act rely on information that is consistent with the best available science.[7] New section 26(i) requires that EPA rely on the weight of the scientific evidence,[8] and sections 26(j) 26(k) and 6(b)(4)(F) require that EPA consider, assess, and integrate all available information on hazards, exposure, and conditions of use (COUs).[9]

In 2017, as required by the Lautenberg Act, EPA promulgated a rule establishing the procedures it would use to collect, assess, and integrate the available scientific information on the hazards and exposures of chemical substances entitled Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (referred to as the Risk Evaluation Framework Rule). Consistent with EPA's commitment, the procedures used in completing the risk evaluation for formaldehyde should be fully consistent with the requirements of this important Framework regulation.[10] The Formaldehyde Panel has relied upon EPA's representation that it will follow the 2017 Risk Evaluation Framework Rule, including a fulsome peer review process for all steps of the risk evaluation, as it has prepared for the risk review, including in deciding what comments to file and in connection with peer review nominations.[11]

The importance of ensuring that the TSCA Formaldehyde Risk Evaluation complies with the statute, as amended by the Lautenberg Act, has been one of the drivers of the Formaldehyde Panel's active engagement with all the EPA Program Offices assessing formaldehyde and with NAS. The Formaldehyde Panel has provided constructive and actionable written and oral comments to EPA and the NAS to ensure that EPA is aware of and relying on information consistent with the best available science and based on the weight of the scientific evidence.[12] The comments herein refer to many of these previous submissions; therefore, we explicitly incorporate by reference all the comment documents referred to in the footnotes in this comment letter. EPA's attention to these comments is critical for ensuring that the TSCA scientific standards are met. This is particularly important because the 2023 NAS Review of the Draft Formaldehyde IRIS Assessment was constrained by a narrow charge.[13] As stated in the 2023 NAS Report (emphasis added): "**[t]he committee also was not charged with commenting on other interpretations of scientific information relevant to the hazards and risks of**

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[7] 15 U.S.C. § 2625(h), available at: https://www.law.cornell.edu/uscode/text/15/2625.
[8] 15 U.S.C. § 2625(i), available at: https://www.law.cornell.edu/uscode/text/15/2625.
[9] 15 U.S.C. § 2625(k), 2625(j), 2605(b)(3)(F), available at: https://www.law.cornell.edu/uscode/text/15/2625, and https://www.law.cornell.edu/uscode/text/15/2605.
[10] Chemical Watch, "TSCA Risk Evaluation for Formaldehyde Will Follow Existing Procedural Rule," Nov. 17, 2023, https://chemicalwatch.com/894510/tsca-risk-evaluation-for-formaldehyde-will-follow-existing-procedural-rule. EPA "confirmed it will conduct its TSCA risk evaluation of formaldehyde following procedures in its existing risk evaluation 'framework' rule, rather than those set out in a recent regulatory proposal."
[11] *See* ACC Comments on Scientific and Legal Issues with EPA's Forthcoming Peer Review of Draft Evaluation of Formaldehyde under the Toxic Substances Control Act (TSCA) and Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Mar. 8, 2024, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0007.
[12] *See* NAS public access file materials available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0113; https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0114; https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0115; https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0116; and https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0117.
[13] *See* https://www.americanchemistry.com/chemistry-in-america/news-trends/blog-post/2023/national-academies-buries-the-lede-in-review-of-epa-formaldehyde-assessment.

formaldehyde, nor did its statement of task call for a review of alternative opinions on EPA's formaldehyde assessment."[14]

The comments below describe the Formaldehyde Panel's concerns with the Draft Formaldehyde Risk Evaluation, including a discussion of:

- The scientifically unsound hazard endpoints and points of departure used in the assessment and the inadequate approaches used to develop these values;
- OPPT's reliance on a draft IRIS Assessment that has not been through the required peer-review process, has not addressed significant public concern, and is not consistent with TSCA scientific standards;
- The development of an Occupational Exposure Value that is scientifically unsound;
- OPPT's unrealistic exposure assessment for occupational and consumer conditions of use;
- OPPT's evaluations of indoor air, ambient air, and general population exposures;
- OPPT's evaluation of environmental risks; and
- EPA's flawed application of the whole chemical approach.

II. A Standard IRIS Value/Reference Concentration (RfC) Approach Is Inappropriate for a Formaldehyde TSCA Risk Evaluation

Formaldehyde is a unique chemistry that is one of the most studied chemicals in use today. More than 40 years of advanced science and practical experience have informed numerous evaluations from authoritative bodies throughout the world that have assessed its safe use. This section describes why a typical IRIS approach, which separates acute and chronic exposures and seeks to use a RfC, is inappropriate for informing a TSCA risk evaluation.

A. Formaldehyde has unique properties

While formaldehyde is considered to be a volatile organic carbon (VOC), it is not typical. Formaldehyde is naturally produced as a metabolic byproduct by all living organisms. At room temperature, formaldehyde is a colorless, flammable gas that has a distinct, pungent smell which is typically detectable above 1 ppm. Dermal contact to formaldehyde solutions at sufficient concentration can cause severe injury to the skin accompanied by drying, cracking, and scaling. Inhalation exposures have been extensively characterized in controlled studies with human volunteers, including asthmatics and other sensitive individuals, which provide a robust database from which a point of departure can be determined.

[14] NAS, Review of EPA's 2022 Draft Formaldehyde Assessment (2023), at page 1, available at: https://nap.nationalacademies.org/catalog/27153/review-of-epas-2022-draft-formaldehyde-assessment.

The kinetics of formaldehyde inside the body have also been well studied.[15] Formaldehyde is a normal product of intermediary metabolism in mammals, formed endogenously from serine, methionine, choline, and glycine by demethylation of N-, O-, and S-methyl compounds. It is present at concentrations near 0.1-0.2mM in blood and tissues.[16] Due to its high reactivity with water (it forms a reversible hydrate), formaldehyde is taken up readily into epithelial tissues as it passes through the nose and has a significant anterior to posterior concentration gradient along the nasal epithelium.[17] The nasal tissues already have a level of endogenous formaldehyde, and low concentration exposures are not expected to cause any appreciable increase above background. Additional dosimetry modeling has also explored whether exogenous formaldehyde can increase endogenous levels, and at doses up to 1.9 ppm the models showed that any increase in endogenous formaldehyde would be far below existing endogenous levels.[18] This important finding informs the biological plausibility of systemic effects.

Importantly, consistent with the findings of the EPA Human Studies Review Board (HSRB), which was asked to review some formaldehyde literature for OCSPP,[19] formaldehyde does not follow Haber's Law, and there is no meaningful difference in formaldehyde-induced sensory irritation regardless of whether the exposure is acute or chronic.[20] This important distinction is discussed in further detail later in these comments, but the important point is that EPA has inappropriately tried to treat acute and chronic sensory irritant effects as different, when they should be treated similarly. Furthermore, protecting for sensory irritation protects for all other adverse effects of formaldehyde (including nasal tumors) when a threshold-based mode of action (MOA) for nasal tumors is applied. EPA is ignoring the core principles of MOA and evidence integration, which are key elements of EPA's Framework for Human Health Risk Assessment for Decision-Making.[21] The purpose of considering evidence in an MOA context is the recognition that chemicals initiate a series of biological responses in a dose-dependent and temporally related way. The (upstream) effects observed at low doses and early time points are plausibly linked to the (downstream) effects observed at high doses and later time points. This is well understood for formaldehyde, including for the MOA for nasal tumors. As noted above, an

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[15] Golden, R., *Identifying an indoor air exposure limit for formaldehyde considering both irritation and cancer hazards*, Crit. Rev. in Toxic, 2011: 41(8): 672-721; available at: *https://www.tandfonline.com/doi/full/10.3109/10408444.2011.573467?role=tab&tab=permissions&aria-labelledby=reprints-perm&scroll=top*.

[16] Heck, et al., *Determination of formaldehyde in biological tissues by gas chromatography/mass spectrometry, Biomed Mass Spectrom*.1982 Aug;9(8):347-53; Heck, et al., *Formaldehyde (CH2O) concentrations in the blood of humans and Fischer-344 rats exposed to CH2O under controlled conditions*, Am Ind Hyg Assoc J. 1985, Jan;46(1): 1-3.

[17] Kimbell et al., *Application of computational fluid dynamics to regional dosimetry of inhaled chemicals in the upper respiratory tract of the rat*, Toxicol Appl Pharmacol. 1993 Aug;121(2):253-63.

[18] Lu et al., *A Review of Stable Isotope Labeling and Mass Spectrometry Methods to Distinguish Exogenous from Endogenous DNA Adducts and Improve Dose-Response Assessments*, 2022, Chem Res Toxicol. Available at: https://pubmed.ncbi.nlm.nih.gov/34910474/.

[19] 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.

[20] Golden, R., *Identifying an indoor air exposure limit for formaldehyde considering both irritation and cancer hazards*, Crit. Rev. in Toxic, 2011: 41(8): 672-721; available at: https://www.tandfonline.com/doi/full/10.3109/10408444.2011.573467?role=tab&tab=permissions&aria-labelledby=reprints-perm&scroll=top.

[21] EPA, *Framework for Human Health Risk Assessment to Inform Decision Making* (2014), https://www.epa.gov/sites/default/files/2014-12/documents/hhra-framework-final-2014.pdf.

interesting aspect of the MOA for sensory irritation for formaldehyde is that it does not follow Haber's Law. Considering acute effects separately from chronic effects for sensory irritation ignores this available evidence on formaldehyde's MOA.

The concern here is compounded by the fact that the Draft IRIS Assessment looked only at chronic hazard, and thus OPPT did a separate evaluation for acute hazard. This parsing has led to two disparate assessments, which have made it more difficult to integrate dose-response and MOA information. Had EPA conducted a holistic evaluation, this may have been easier. The agency must still integrate MOA and dose-response assessment across assessments. When this is done, it is clear that there is no difference between protective levels for acute and chronic sensory irritant effects and that protecting for sensory irritation protects for all effects at higher concentrations, to include nasal tumors.

B. TSCA requires that EPA protect against unreasonable risk, but not "no appreciable" risk

"Unreasonable risk" does not mean no risk; it means that EPA must determine, on a case-by-case basis, whether the risks posed by a specific chemical substance are unreasonable in the circumstances of exposure and use. TSCA section 6(a) requires that EPA manage "unreasonable" risks of injury to health or the environment to the extent necessary so that the chemical substance or mixture no longer presents such risks.[22] In the IRIS program, evaluations are conducted to develop RfC values that are likely to be without an appreciable risk of deleterious effects during a lifetime.[23] By relying on an IRIS assessment, EPA is using values that are developed to protect against not just unreasonable risks, but essentially all risks. RfC values are commonly referred to as values below which there is "no appreciable risk,"[24] and when EPA has converted these values to existing chemical exposure levels (ECELs) for other chemicals, it has described these values as being a level below which an adult human would be unlikely to suffer adverse effects if exposed for a single 8-hour workday.[25] The ECEL, at least when based on RfC values, is essentially a zero risk level.

As is shown in Figure 1 below, there is a continuum of risk that exists between unreasonable risk and zero risk. Within that continuum, there is "reasonable risk," and there is "no appreciable risk." TSCA requires the mitigation of unreasonable risk, while the IRIS program develops RfC values and points of departure that seek to mitigate to a level of "no appreciable risk." By relying on hazard information developed for the IRIS program, the TSCA risk evaluation is now relying on endpoints that define and mitigate risk well beyond the level required by statute. This is particularly important for formaldehyde, where sensory irritation is a reversible effect that is not considered to be an adverse effect.[26] And, importantly, if a person is protected from sensory

[22] 15 U.S.C. § 2605(a).
[23] See: https://www.epa.gov/iris/basic-information-about-integrated-risk-information-system.
[24] EPA, *IRIS Glossary*, where EPA defines an RfC as "An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime." Available at: https://www.epa.gov/iris/iris-glossary#r.
[25] 88 Fed. Reg. at 74721.
[26] *See*, for example, Comments from James Sherman to the HSRB, which state: "Odor detection and sensory irritation are normal physiological responses to environmental stimuli, including formaldehyde at ≤1 ppm, and do not reduce functioning or ability to respond to additional environmental challenge;" available at:

irritation, that person is also protected from developing other potentially adverse effects (e.g., cancer) which occur at exposure levels higher than levels where sensory irritation is seen.

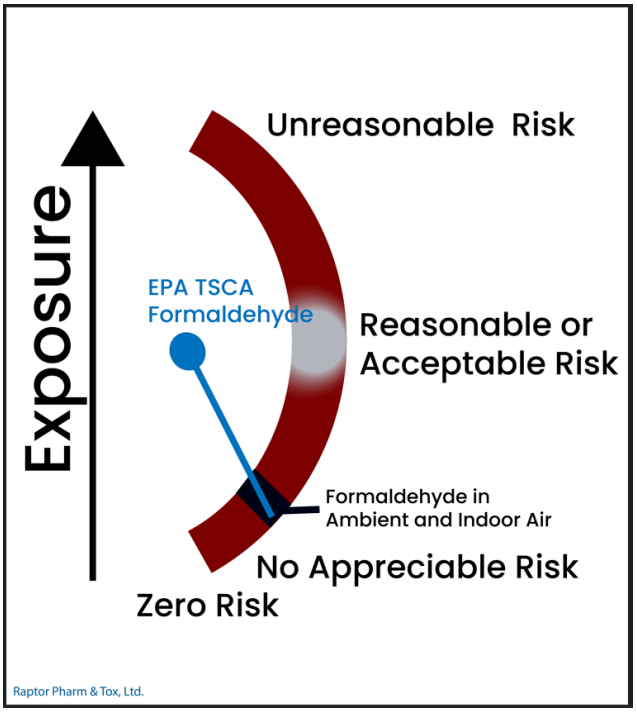

Figure 1. Understanding the Risk Continuum[27]

C. Ubiquitous background levels of formaldehyde must be considered as part of the risk characterization

Formaldehyde exposures from ambient air, biogenic sources, and endogenous production must be considered when evaluating risks. As EPA acknowledges in the Draft TSCA Risk Evaluation, formaldehyde is found nearly everywhere. Plants, animals, and people produce and release formaldehyde, and when biomass breaks down in the environment or burns, such as in forest fires, formaldehyde is released.[28] EPA states that the natural occurrence of formaldehyde must be considered as part of a "pragmatic and holistic evaluation of hazard and exposure to formaldehyde."[29] However, a holistic (and scientifically valid) evaluation of hazard and exposure to formaldehyde would require that EPA quantify hazard and exposure from biogenic, TSCA-regulated, and non-TSCA-regulated sources of formaldehyde and transparently report the percentage contribution of the total risk from each. This is necessary to ensure that any future risk management actions are likely to have a measurable and meaningful impact on public health. Yet EPA did not provide a holistic evaluation. Instead, EPA considered biogenic sources

https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0106/attachment_7.pdf; and additional discussion of "adverse effects" in section III.A.3 of these comments.

[27] *See* comments submitted to the SACC from Dr. Lyle Burgoon, Raptor Pharm & Tox, Ltd., May 2024, available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

[28] EPA, *Executive Summary of the Draft Risk Evaluation for Formaldehyde*, Mar. 2024, at page 2, available at: Executive Summary of the Draft Risk Evaluation for Formaldehyde (epa.gov).

[29] *Id.*

of formaldehyde as "background," which obscures the large contribution of these sources to the overall risk while also artificially amplifying the comparatively smaller risk of TSCA-regulated uses that EPA considers in scope. This is inadequate and misleading for informing risk management decisions for human health protection.

Detailed information is available to EPA to quantify the relative contributions of various sources to overall formaldehyde exposure. Yet EPA did not quantify or integrate this information into its determinations of unreasonable risk. EPA merely notes that this complicates relying on risk benchmarks.[30] EPA should have used this information to inform what appropriate risk benchmarks should be. Furthermore, we have decades of reasonably available information to inform the extent of sensory irritation seen at typical background levels in both indoor and outdoor environments, and consideration of this is pragmatic as well as scientific. Nevertheless, instead of integrating this information into its assessment of hazard, EPA simply ignored it. EPA sought to use the standard approach it used to evaluate other TSCA chemicals that do not have biogenic exposures (such as asbestos, trichloroethylene, methylene chloride, etc.) without thinking about a more appropriate paradigm to evaluate health risks due to formaldehyde exposures. EPA must correct this error and must conduct the pragmatic and holistic evaluation that the agency recognizes is necessary.

D. Current workplace levels of formaldehyde do not present unreasonable risk

As noted in the section above, at typical indoor and outdoor exposure levels associated with TSCA uses of formaldehyde, sensory irritation does not occur. Even if it were to occur, when assessing unreasonable risks, EPA must consider that this effect is reversible and does not meet EPA's definition of an "adverse effect."[31] And, based on years of research on the mode of action of formaldehyde that considers dose-response, it is well accepted that if there is protection against sensory irritation, then there is protection against all other potential adverse effects, including asthma, pulmonary effects, and nasopharyngeal carcinomas (NPC), because these other effects occur at higher doses.

Authoritative European Union (EU) scientific bodies have evaluated formaldehyde in the past 15 years, including the European Chemicals Agency (ECHA), the Scientific Committee on Occupational Exposure Limits (SCOEL), and the Committee on Risk Assessment (RAC).[32] Each of these authorities used a weight of the scientific evidence approach and considered all the available information, including information regarding endogenous and biogenic exposures. All these authorities agree that there is a threshold below which adverse effects, including NPC cancer, do not occur. And all these authorities agree that this level is well above typical indoor

[30] *Id*.
[31] EPA, IRIS Glossary, where adverse effect is defined as "A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge." https://www.epa.gov/iris/iris-glossary.
[32] *See* Comments of Celanese Corporation on the Relevance of European Governmental Evaluations of Formaldehyde, Including Carcinogenicity Evaluations, to EPA's Formaldehyde Risk Evaluation, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2018-0438-0128; and EU, SCOEL/REC/125 Formaldehyde, Recommendation from the Scientific Committee on Occupational Exposure Limits, 2016, available at: https://op.europa.eu/en/publication-detail/-/publication/7a7ae0c9-c03d-11e6-a6db-01aa75ed71a1.

and outdoor exposure levels. In 2019, the European Parliament and the Council of the European Union adopted an occupational exposure value of an 8-hour TWA of 300 ppb.

As a result of this process, the EU has adopted protective occupational limits of 300 ppb without having to contort its hazard evaluation. The EU weight of the scientific evidence approach considered all the available information when evaluating hazard, and EPA should do the same. Setting an Existing Chemical Exposure Level (ECEL) or Occupational Exposure Value (OEV) at a level which is below background, as the Draft TSCA Risk Evaluation proposes to do, is not consistent with best available science, is not consistent with the weight of the scientific evidence, and does not appropriately consider and integrate available information.

III. The Draft Risk Evaluation Relies on Scientifically Unsound Hazard Endpoints and Points of Departure

A. The 2022 Draft IRIS Formaldehyde Assessment is not best available science and presents a flawed interpretation of non-cancer inhalation hazards

EPA's selection of studies for the point of departure for non-cancer inhalation effects is fundamentally flawed. Below we describe why the Draft IRIS Formaldehyde Assessment inappropriately relies on flawed epidemiological studies instead of existing controlled human exposure studies, which are the "gold standard" for toxicological evaluations of human risks. Formaldehyde's unique chemistry, including the fact that it does not follow Haber's Law, must be appropriately weighed and considered when looking at the best available science to inform the human health assessment. Below we describe why the IRIS Assessment and TSCA Risk Evaluation are not consistent with the best available science, given the available information regarding formaldehyde, including what we know about health effects at background levels, and we use a weight of the scientific evidence approach to develop defensible hazard and OEVs that represent the best available science.

1. Observational studies are not best available science

Observational epidemiological studies, also known as ecological studies, seek to evaluate the association between the occurrence of a disease and an exposure. Conflicting results from observational epidemiological studies that look at the risks to daily life, such as coffee, alcohol, chocolate, hormones, or carbohydrates have provided a constant source of stress and angst for the general public. We often find that, when further evaluated in randomized control trials, the results are contradicted. This is because confounding due to the presence of other factors in the exposure environment is hard to control for, and the poor design of many observational studies does not allow for a full accounting of these external influences. It is well accepted that a randomized control study will always be preferred, and, although often difficult and expensive, controlled human exposure studies (also known as chamber studies) are the most reliable "gold standard" for evaluating cause and effect.

In a controlled human exposure study, subjects are known, exposures are known, and confounders are known and controlled. Because of the challenges, and potential ethical concerns associated with controlled human exposure studies, we often do not have data from them, and

thus lesser quality epidemiological studies are used. In the case of formaldehyde, multiple high quality controlled human exposure studies exist and should be used.

2. Observational studies relied upon by IRIS for chronic non-cancer hazards should be replaced by controlled human exposure studies (charge questions 1.2, 3.3, 4.4, 5.6, and 6.5)

a. Understanding formaldehyde, sensory irritation, sensitive populations, and Haber's Law

Numerous studies evaluating formaldehyde have shown that the threshold for odor detection is generally lower than the ocular or nasal irritation threshold (also known as chemesthesis).[33] To date, no chemical has been identified as having an irritation threshold that is lower than its odor threshold, and formaldehyde is no exception.[34] Formaldehyde can be sensed at 100-500 ppb, and existing studies do not show sensory irritation occurring until 500-1000 ppb.[35] EPA's draft IRIS Assessment reliance solely on the data from the Hanrahan study has resulted in the identification of an irritation threshold that is orders of magnitude below the acknowledged odor threshold. The number of well conducted controlled exposure trials with no evidence of ocular irritation at 300-500 ppb provide ample evidence that maintaining exposures at or below these concentrations will provide sufficient protection from sensory irritation, including eye irritation. While we are pleased to see that EPA, in the Draft TSCA Risk Evaluation, has pivoted away from using the Hanrahan study, as is described below, the other observational studies are similarly flawed and should not be relied upon. Sensory irritation provides the appropriate lower bound on potential risk from adverse effects because any tissue irritation and other adverse effects will occur at concentrations higher than those where sensory irritation is observed.[36] The HSRB, which questioned whether sensory irritation meets the EPA IRIS definition of adverse, not only agreed that using this endpoint as a lower bound is appropriate, but also recommended that no uncertainty factor need be applied when sensory irritation is used as the point of departure.[37] 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."[38]

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[33] Doty, R. L., J. E. Cometto-Muñiz, A. A. Jalowayski, P. Dalton, M. KendalReed and M. Hodgson (2004). *Assessment of upper respiratory tract and ocular irritative effects of volatile chemicals in humans*, Critical Review in Toxicology 34(1): 85-142.

[34] Dalton, P., comments to NAS 2022, PAF-20, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0114 and also comments at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0086 and https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613/comments.

[35] *Id*.

[36] See Celanese comments to EPA, Oct. 13, 2023, in particular the summary discussion of the SCOEL opinion regarding the mechanistic support for threshold effects, at page 8, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2018-0438-0128.

[37] 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.

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

It is also important to recognize that the well-established declines in olfactory and trigeminal (chemesthetic) sensitivity with age and age-related diseases means a younger, healthier population (which is typically the demographic of participants in controlled exposure studies) will be most sensitive to the odor and irritancy of formaldehyde.[39] Other authoritative bodies have this same conclusion. The NAS found that, at exposure concentrations at or below 3 ppm, asthmatic individuals do not appear to be at greater risk of suffering airway dysfunction than non-asthmatic individuals.[40] WHO, in its 2010 evaluation, concluded that there is no evidence indicating an increased sensitivity to sensory irritation to formaldehyde among people often regarded as susceptible.[41] In addition, chemosensory expert Dr. Pamela Dalton has reviewed numerous studies, controlled and observational, that included asthmatics and other sensitive individuals, and these studies do not show that asthma and other health conditions predispose individuals to be more sensitive to formaldehyde.[42] Thus, when it comes to formaldehyde, consistent with the findings of the HSRB,[43] it is important to remember that a younger and generally healthier population will be the most sensitive. Thus, there is no disproportional effect on populations that are typically considered to be potentially exposed or susceptible subpopulations.

Finally, and perhaps most important, the observation that neither formaldehyde sensory nor tissue irritation adhere to Haber's Law has been noted in several publications in the peer-reviewed literature, including in evaluations conducted by NAS.[44] 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.[45] Tissue irritation only occurs at concentrations higher than those that elicit sensory irritation. Recognizing the sequence of effects at increasing air concentrations, NAS also stated that at air concentrations that did not produce chronic tissue irritation, risk of cancer and other health effects (including asthma) appeared negligible.[46]

On May 18, 2023, in response to the HSRB questions asking why EPA disregarded information about the inapplicability of Haber's Law, EPA responded with two arguments. The first argument cited limited low concentration data from the Andersen and Mølhave (1983) study

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[39] See Dalton, P., comments to NAS 2022, PAF-20, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2018-0438-0107.

[40] NAS, *Emergency and Continuous Exposure Guidance Levels for Selected Submarine Contaminants Volume 1*, 2007, at page 108, available at: https://nap.nationalacademies.org/download/11170#.

[41] World Health Organization (WHO) (2010): Regional Office for Europe. *WHO Guidelines for Indoor Air Quality: Selected Pollutants*. Copenhagen, Denmark: World Health Organization.

[42] Dalton, P, Comments to EPA on the Draft IRIS Formaldehyde Assessment, June 13, 2023, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0086 and https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613/comments.

[43] 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.

[44] 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#.

[46] *Id*.

which indicated symptoms may increase over time at low concentration and higher concentration data that indicated symptoms may decrease over time. However, the HSRB review of the Andersen and Mølhave (1983) study, among other concerns, raised questions about the reliability of the study due to the lack of details presented and expressed concerns with the small sample size, highly variable responses, lack of dose response, and inclusion of potential confounders in the data. Based on these concerns, the HSRB final report recommends that EPA only use this study qualitatively.[47] The study was determined to not provide reliable evidence to inform the inapplicability of Haber's Law. And the final HSRB report supports the finding that formaldehyde effects do not adhere to Haber's Law.[48] As seen with formaldehyde exposures, accommodation to low concentrations that cause short-term irritation has been reported, and in such cases irritation subsides with exposure duration. This was also an important consideration of the NAS during its review of emergency exposure levels.[49] Because Haber's Law does not apply, short term exposure studies can indeed be used to inform chronic exposures, and there is no basis for the application of adjustment or uncertainty factors. After reviewing all the evidence, the HSRB disagreed "with EPA's assumption of Haber's Law for formaldehyde and recommends that EPA not make duration adjustments to develop the PODs."[50]

In summary, with formaldehyde, when evaluating the best available science and conducting a weight of the evidence evaluation, the SACC and EPA must be mindful that sensory irritation is the most sensitive endpoint which protects against other health effects, and that 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. The observational studies used for chronic non-cancer hazards are highly flawed and unreliable for identifying a point of departure

For the derivation of non-cancer inhalation effects, EPA relies predominantly on Krzyzanowski et al. (1990), with support from Annesi-Maesano et al. (2012), Matsunaga et al. (2008), and Venn et al. (2003).[51] 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 the best available science. Detailed comments by independent experts have been provided to EPA and the SACC on the weaknesses of these studies.[52] A short summary is provided below. It is important to note that OPPT has not independently reviewed these studies but is relying on the Draft Formaldehyde IRIS Assessment for its evaluation of these studies.

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[47] 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.
[48] *Id*.
[49] 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#.
[50] *Id*.
[51] EPA, *Human Health Risk Assessment for Formaldehyde*, Mar. 2024, available at: formaldehyde-draft-re-human-health-risk-assessment-public-release-hero-march-2024.pdf (epa.gov).
[52] *See* Comments submitted to the SACC, May 2024, from Dr. Dennis Paustenbach (P&A), Linda Dell (Ramboll), Dr. Stewart Holm (AF&PA) and Renee Kalmes and Dr. Pamela Dopart (E[x]ponent), available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

The 1990 study by Krzyzanowski et al. was inexplicably assigned high confidence by the IRIS program for its findings of decreased pulmonary function in children. In support of this confidence rating, EPA describes the study as addressing confounders "including asthma status, smoking status, socioeconomic status, NO_2 levels, episodes of acute respiratory illness, and the time of day." However, there are significant transparency concerns with this study, which were also noted by the NAS in both its 2011 and 2023 reviews of the Draft Formaldehyde IRIS Assessments. Study characteristics are not fully reported, there is no information provided on NO_2 levels (even though the study says measurements were taken), readers cannot discern how the authors picked the preferred best model, the study design is unclear, and, although information on symptoms was collected, no information on the relationship between these symptoms and pulmonary function are presented. This was a cross-sectional study conducted over two weeks, where only two measurements of formaldehyde levels were taken for each participant, and four pulmonary function measurements were taken each day. However, the observations presented in the data tables represent, on average, only two measurements per day per person, not four measurements per day. Day-to-day and morning-to-night fluctuations in formaldehyde levels in indoor air were not accounted for. And, although EPA reports that confounding was addressed, in the final model used there was no adjustment for smoking status, NO_2, or episodes of acute respiratory illness. Finally, while the study also evaluated respiratory effects in adults, no effects in adults were associated with formaldehyde exposures.

Putting aside the weaknesses above, and other weaknesses that are not mentioned here, Krzyzanowski et al. is simply not reliable for conducting dose-response analysis to identify a point of departure. The study's ability to determine causality specific to formaldehyde is weak at best. Dr. Paustenbach in his review refers to the point of departure derived from the study as "scientifically unsound" due to the plethora of confounders that were not addressed, and Linda Dell in her review considers the study to be simply "uninformative."

The Draft Formaldehyde IRIS Assessment also relies on other observational epidemiological studies and endpoints to support the point of departure determined from the Krzyzanowski study. Annesi-Maesano et al. was assigned high confidence for its finding of increased prevalence of rhinoconjunctivitis (as a marker of allergy-related conditions) in children and medium confidence for the outcome of current asthma in children. Matsunaga et al. was assigned high confidence for its finding of allergic rhinitis and atopic eczema in pregnant women and Venn et al. was assigned medium confidence for its finding of reduced symptom control among children with asthma. Matsunaga et al. notes that its results cannot be generalized to an adult population, and the other two studies were in populations of children, which are not relevant for an occupational hazard value. Independent reviews of each of these studies do not support EPA's confidence ratings and do not support confidence in the conclusions of these studies.[53]

For instance, in Annesi-Maesano et al., a temporal relationship between formaldehyde exposure and prevalence of rhinoconjunctivitis was not established. Complicating the study is the admission from the authors that, while formaldehyde was measured in school classrooms, the five-day measurements may not be representative of the students' usual school exposure. Prevalence of rhinoconjunctivitis and asthma symptoms in this study was based on a parental

[53] *See*, in particular, Comments from Linda Dell (Ramboll) submitted to the SACC, May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

report for the previous 12 months, but concentrations of formaldehyde were only measured over a five-day period. There was no statistically significant exposure-response trend, and there was an unexplained inconsistency between results for rhinoconjunctivitis and allergic asthma. There was also no statistically significant exposure-response trend for current asthma; therefore, there is simply no basis for setting a toxicity value to protect against an adverse effect that is not identified in the study.

The Matsunaga et al. study is also not reliable for dose-response characterization. The study investigators reported that there was no increased prevalence of allergic rhinitis related to formaldehyde exposure. Although formaldehyde and nitrogen dioxide were measured, study investigators did not report concentrations of nitrogen dioxide or otherwise evaluate nitrogen dioxide as a potential confounder. Additionally, the study explained that rhinitis symptoms during pregnancy may be due to hormonal changes during pregnancy and cannot be distinguished from allergic rhinitis, and the association between formaldehyde exposure and atopic eczema was only seen in pregnant women with a negative family history of allergies and not in pregnant women with a positive family history of allergies.

Finally, the Venn et al. study is also not reliable for dose-response characterization. In this cross-sectional study, Venn et al. found no significant effect of formaldehyde on asthma risk but did report that formaldehyde exposure increased "disease severity" among cases (i.e., those with asthma). Disease severity was measured by "peak flow variability, frequent symptomatic days, and frequent symptomatic nights (symptoms were recorded in a diary on 10% or more of days/nights)." 10% of days (or nights) is approximately 3 days (or 3 nights) over a 4-week period; however, EPA mistakenly reports these data as symptoms reported on ≥10 consecutive days. There is significant uncertainty about the window of exposure relative to the effect findings in this study, and, while the study reports that control for potential confounding had little impact on the results seen, these results are simply not presented. Interestingly, this study also evaluated pulmonary function, similar to Krzyzanowski et al., and, while EPA does not report on this endpoint in the Venn et al. evaluation, the findings are not consistent with Krzyzanowski et al.

With regard to the reported associations between formaldehyde exposures and childhood or adult asthma risk, there remain a number of unanswered questions. In exploring possible mechanisms for formaldehyde-induced bronchoconstriction, Thompson and Grafstrom (2008) noted that "The potential for formaldehyde to provoke asthma, hypersensitivity, and airway constriction in adults and children has received extensive attention over the years, yet data regarding these effects remain equivocal."[54] Although the hypothetical mechanism proposed by those authors may or may not lead to a better understanding of whether formaldehyde plays a causative role in asthma-related bronchoconstriction, at present the evidence suggests that asthma is neither caused nor exacerbated by low-level exposure (i.e., less than 1-2 ppm).[55]

[54] Thompson, C. M. and R. C. Grafstrom (2008). *Mechanistic Considerations for Formaldehyde-Induced Bronchoconstriction Involving S-Nitroglutathione Reductase*. Journal of Toxicology and Environmental Health Part A [US CPSC] US Consumer Product Safety Commission 1982. Release # 82-005. Available from: 71: 244-248, available at: https://doi.org/10.1016/j.taap.2008.09.011.

[55] Noisel N, le Bouchard M, Carrier G. *Evaluation of the health impact of lowering the formaldehyde occupational exposure limit for Quebec workers*. Regul Toxicol Pharmacol. 2007;48:118–127.

Additional mechanistic support, as reported in multiple publications, explaining why asthmatics are not more sensitive to formaldehyde at environmentally relevant levels is the well documented effective scrubbing of low levels of formaldehyde in the upper airways below 3 ppm.[56] As a result, little formaldehyde at these concentrations reaches the mid- to lower airways where an asthmatic reaction may be triggered. The lack of sensitivity of asthmatics at these lower air levels in controlled human studies is consistent with expected patterns of absorption in the upper airways. While formaldehyde is clearly a sensory irritant at sufficient concentrations, its potential to cause or exacerbate asthma is far less certain, particularly at low exposure levels (<1-2 ppm). OSHA regulations state that "[c]oncentrations of above 5 ppm readily cause lower airway irritation characterized by cough, chest tightness, and wheezing."[57] It is also worth noting that there are no studies in which exposure to formaldehyde alone has been shown to cause or exacerbate asthma. Instead, studies that have reported this effect are all observational studies which have been confounded, to an unknown extent, by simultaneous co-exposures to other chemicals, many of which have been associated with exacerbating asthmatic symptoms.[58]

c. Understanding the strengths of the controlled human exposure studies

EPA asked the HSRB to evaluate the controlled human exposure studies to inform acute exposures. The HSRB 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), and the HSRB also noted that the controlled chamber studies have "a preferred study design and greater scientific rigor than the observational studies."[59] As noted above, controlled human exposure studies provide great advantages over observational studies, and in each of the studies evaluated by the HSRB, the subjects, exposures, and confounders are known and controlled.

In particular, the HSRB recommended relying on Mueller et al. and Lang et al., and particularly Lang et al.. for deriving a point of departure consistent with the best available science and based on a weight of the evidence approach. The OPP Data Evaluation Records (DERs) for Mueller and Lang also concluded that both of these studies provide data for quantitative use for deriving a point of departure.[60] While OPP was focused on points of departure for acute inhalation, based

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[56] *See* for example, Schlosser PM, Lilly PD, Conolly RB, Janszen DB, Kimbell JS. *Benchmark dose risk assessment for formaldehyde using airflow modeling and a single-compartment DNA-protein cross-link dosimetry model to estimate human equivalent doses*. Risk Anal. 2003;23:473–487; Kimbell JS, Gross EA, Joyner DR, Godo MN, Morgan KT. *Application of computational fluid dynamics to regional dosimetry of inhaled chemicals in the upper respiratory tract of the rat*. Toxicol Appl Pharmacol. 1993;121:253–263; Kimbell JS, Overton JH, Subramaniam RP, Schlosser PM, Morgan KT, Conolly RB, Miller FJ. *Dosimetry modeling of inhaled formaldehyde: Binning nasal flux predictions for quantitative risk assessment*. Toxicol Sci. 2001;64:111–121; Overton JH, Kimbell JS, Miller FJ. *Dosimetry modeling of inhaled formaldehyde: The human respiratory tract.* Toxicol Sci. 2001;64:122–134; and, Garcia GJ, Schroeter JD, Segal RA, Stanek J, Foureman GL, Kimbell JS. *Dosimetry of nasal uptake of water-soluble and reactive gases: A first study of interhuman variability*. Inhal Toxicol. 2009;21:607–618.

[57] 29 C.F.R. § 1910.1048. Formaldehyde Appendix C.

[58] *See* comments submitted to the SACC from AF&PA, May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

[59] 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.

[60] *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-

on what we know regarding formaldehyde's properties as an exception to Haber's Law, these findings should apply equally to chronic durations. Commenting on the applicability of these findings for the weight of evidence for the chronic point of departure was not part of the charge to the HSRB because EPA only sought its input on acute findings.

d. Findings from other authoritative bodies

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.[61] In 2017, ACGIH relied upon Lang et al., and in 2016, 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 exposures 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.

3. EPA's application of uncertainty factors to the acute point of departure is not best available science (charge question 1.1)

EPA chose the appropriate studies for the acute inhalation point of departure by relying on Kulle, Lang et al. and Mueller et al. However, EPA is overly conservative when applying an uncertainty factor for human variability. EPA states that the application of a 10x uncertainty factor "is also consistent with high variability across individuals reported in all controlled exposure studies."[62] However, EPA never explains what variability they are referring to. Furthermore, as sensory irritation is a transient and reversible effect that does not affect the form or function of the tissue or organism, it does not meet EPA's definition of an adverse effect.[63] In the past, when EPA has relied on a non-adverse effect as a point of departure, uncertainty factors have not been applied.[64]

As described above, and in detail in Goyak and Holm, many factors support the fact that an additional uncertainty factor is not needed, including the recommendations from the HSRB

0613-0106/attachment_3.pdf and https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0106/attachment_2.pdf.

[61] *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: 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.

[62] EPA, *Draft Human Health Hazard Assessment for Formaldehyde*, Mar. 2024, at page 18, available at: https://www.epa.gov/system/files/documents/2024-03/formaldehyde-draft-re-human-health-hazard-assessment-for-formaldehyde-public-release-hero-march2024.pdf.

[63] EPA, IRIS Glossary, where adverse effect is defined as "A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge." https://www.epa.gov/iris/iris-glossary.

[64] *See* for example EPA's IRIS assessment for perchlorate and also the EPA OPP assessment of chloropicrin.

regarding the understanding that young adults are most sensitive to sensory effects. The EU SCOEL also recognized that an uncertainty factor was not necessary when deriving its occupational exposure value. In fact, available evidence does not support a large distinction in sensitivity among population groups.[65]

EPA must also recognize that available information puts EPA's acute value in the range of typical rural air background exposures.[66] To set an acute value at this level would not make sense, and EPA must consider what we know about typical exposures when setting an acute hazard level.

Additionally, the studies by Kulle et al., Lang et al., and Mueller et al. reported the standard deviations in the measurements of formaldehyde concentrations, with all three studies reporting standard deviations up to 50 ppb to 60 ppb for at least one concentration for real-time and/or HPLC measurements. Lang et al. reported a standard deviation of 50 ppb at a nominal concentration of 0 ppb when measured in real time, indicating that EPA's OEVs could not be differentiated from zero in this study. The OEVs must arguably be appreciably greater than the maximum standard deviations in the studies used to support the acute inhalation endpoint.

The weight of the scientific evidence, including this information, coupled with the lack of adversity of sensory irritation effects, is inconsistent with EPA's application of an uncertainty factor to the chosen point of departure.

4. The best available scientific approach for inhalation hazards

Based on the totality of information, including information on the science of formaldehyde and our understanding of the prevalence of formaldehyde in indoor and outdoor environments, EPA should not artificially evaluate acute and chronic hazards separately. By relying on the Draft IRIS Assessment for chronic exposures and separately developing an acute exposure value, and by having very different assessments reviewed, using divergent scopes of review by the NAS and the HSRB, EPA has unnecessarily overcomplicated this evaluation.

Reliable high quality controlled human exposure studies should be used for both exposure durations. In fact, both the Lang et al., and Mueller et al. studies had 4-hour exposure durations. Lang et al. was over a 10-day period, and Mueller et al. was over a 5-day period. Both studies are very reasonable approximations for an occupational environment, since it is not typical for a worker to do a single task continuously for the entire workday. As concentration, not duration, is the driver for formaldehyde effects, as Haber's Law does not apply, no adjustments for duration are necessary for the determination of the hazard value nor the derivation of an OEV.

Additionally, sensory irritation is the most appropriate health effect endpoint. It is protective of all other non-cancer and cancer effects and in itself is not adverse. Since sensitive young adults were the exposed study population, no adjustments or uncertainty factors are necessary. EPA and the SACC should be aware of forthcoming human exposure studies being conducted by the

[65] 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: https://doi.org/10.1016/j.yrtph.2024.105587.

[66] As EPA reports, the AHHS II study finds typical indoor air levels to be 0.3 ug/m^3 to 124.2 ug/m^3.

Monell Chemical Senses Center and the Leibniz Research Centre which are currently evaluating the effects of formaldehyde to inform setting standards for formaldehyde.[67]

Finally, considering all reasonably available information, including what we know about biogenic formaldehyde exposures and typical indoor and outdoor formaldehyde levels, the approach taken by the EU SCOEL committee, which set an occupational exposure limit at 300 ppb, is consistent with the best available science based on the weight of the scientific evidence.

B. The 2022 Draft IRIS Formaldehyde Assessment is not best available science and does not incorporate available information to inform cancer hazards (charge questions 3.4, 4.5, 5.7, and 6.6)[68]

As described above, EPA must rely on the best available science and incorporate available information. The Inhalation Unit Risk (IUR) derived in the 2022 Draft IRIS Formaldehyde Assessment is not consistent with either of these important TSCA science standards and overestimates the increased cancer risks from inhalation exposures.

1. The IUR for NPCs in the 2022 Draft IRIS Formaldehyde Assessment is flawed and overestimates risk

The IUR analysis for NPC that EPA relies on from the 2022 Draft IRIS Formaldehyde Assessment has been criticized for over a decade, and EPA has still not addressed these concerns. In 2011, after reviewing EPA's 2010 Draft IRIS Formaldehyde Assessment, NAS recommended that EPA conduct an independent analysis of the National Cancer Institute (NCI) cohort that EPA relied upon and also recommended that EPA consider alternative models, consistent with EPA's 2005 Cancer Guidelines.[69] Despite these recommendations, EPA did not conduct an independent analysis, and instead based the IUR on undocumented personal communications with Dr. Beane-Freeman, who is a lead author on the NCI cohort publications. Furthermore, EPA has given no consideration to the application of alternative models. For instance, while NAS 2011 recommended a Cox proportional hazards model, EPA continued to rely on external publications as well as communications with Dr. Hauptmann and Dr. Beane Freeman (as described by EPA on pages 2-49 and D-37 of the 2022 Draft IRIS Formaldehyde Assessment), rather than conduct an independent analysis.

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[67] *See*, for example a research plan for studies at the Monell Chemical Senses Center available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2018-0438-0117, and comments submitted to the SACC, May 2024, from Christoph van Thriel (IfADo - Leibniz Research Centre for Working Environment and Human Factors, Dortmund, Germany), available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

[68] This section informs responses to charge questions 3.4, 4.5, 5.7, and 6.6. EPA inappropriately limits the SACC to commenting on the use of the IUR for the characterization of risk. As this section discusses, the flaws in the IUR developed in the 2022 Draft Formaldehyde IRIS Assessment make it inappropriate for the characterization of formaldehyde risks for all exposure scenarios. In addition, EPA has not responded to public comments and has not conducted a robust peer review of the science in the 2022 Draft Formaldehyde IRIS Assessment. As such, it would be inappropriate to rely upon any finalized IRIS Assessment until robust and fit-for-purpose peer review is conducted, and EPA has responded to all public comments.

[69] 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.

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. A former director of the IRIS program (Dr. James Cogliano) is one of four authors of the first peer-reviewed publication detailing the cytotoxicity with regenerative hyperplasia MOA for nasal tumors (McGregor et al. 2006), which was recently updated and published by Thompson et al. (2020).[70] McGregor et al. (2006) was cited incorrectly in one paragraph of the 2022 Draft IRIS Formaldehyde Assessment as evidence against the cytotoxic MOA. The exclusion of the Thompson et al. (2020) study of cytotoxicity with regenerative hyperplasia (following the IPCS MOA framework) from the 2022 Draft IRIS Formaldehyde Assessment is noteworthy. This MOA, as described by Thompson et al., for nasal tumors was recently adopted by the European Chemicals Agency (ECHA) and approved by the 32 countries in the European Union. While the 2022 Draft IRIS Formaldehyde Assessment says that nasal tumors/NPC is presumed to have a mutagenic MOA, there is no formal determination as described in and required by in the EPA Cancer Guidelines. Nor was an assessment performed according to a data-driven, recognized framework (i.e., cytotoxicity with regenerative hyperplasia assessed according to the IPCS MOA framework), as is also described and required by the EPA (2005) Cancer Risk Assessment Guidelines.[71]

A detailed discussion of how EPA's 2022 Draft IRIS Formaldehyde Assessment fails to consider MOA, misinterprets critical scientific information from peer-reviewed publications that inform the mode of action, and is inconsistent with EPA's Cancer Guidelines was provided to NAS in 2023 to inform its review.[72] In addition, the ACC Formaldehyde Panel provided significant technical comments to EPA, which were also shared with NAS.[73] Nonetheless, consistent with its charge, NAS did not consider alternative information. As such, public comments, which presented voluminous amounts of scientific analyses, were not considered in the limited peer-review that was conducted.[74] The concerns with the NAS process are discussed in more detail in section III.D. of these comments.

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

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[70] Thompson et al. (2020). An updated mode of action and human relevance framework evaluation for formaldehyde related nasal tumors. Critical Reviews in Toxicology. 50(10): 919-952.

[71] The EPA Cancer Guidelines, when discussing procedures for cancer modeling, state that, if the information "is consistent with one or more biologically based models as well as with the default option, the alternative models and the default option are both carried through the assessment and characterized for the risk manager." at page 1-9, available at: https://www.epa.gov/sites/default/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf.

[72] 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.

[73] ACC, Formaldehyde Panel Comments on the 2022 Draft IRIS Assessment for Formaldehyde, these comments provide additional information about scientific studies which EPA misinterpreted when evaluating the epidemiological data and mode of action information relating to NPC, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0127/attachment_7.pdf.

[74] While the NAS thanked public commenters for their input, there is no indication in the NAS report that NAS considered any public comments in their review.

Formaldehyde Assessment.[75] This new analysis shows how EPA's treatment of formaldehyde is inconsistent with the approach taken in the TSCA risk evaluation for 1,4-dioxane, where EPA acknowledged that there are nonlinearities in response to exposure to genotoxic agents.

As described above, robust scientific information that has been provided to EPA, but not considered in the 2022 Draft IRIS Formaldehyde Assessment, supports a non-genotoxic mode of action where protecting against sensory irritation would also be protective of cancer.[76] In addition, the CIIT Formaldehyde Biologically Based Dose Response (BBDR) model has been updated to address uncertainties associated with modeling DNA adducts and nasal tumors due to formaldehyde exposure. This model predicts that the probability of tumors from chronic exposure of rats to 1 ppm formaldehyde would be indistinguishable from controls.[77] Despite recommendations from NAS, EPA has not relied upon this model.

An analysis which sought to ground-truth EPA's NPC IUR projects that, using the draft IUR, background exposures of formaldehyde at levels of 5 and 20 ppb will cause 20 or 51 percent of the annual incidence of NPC in the U.S. population.[78] These values do not match the available literature, which shows that minimal, if any, NPC are due to background levels of formaldehyde. And this finding is also inconsistent with molecular dosimetry data that indicates that little to no exogenous formaldehyde is entering human cells at average indoor air concentrations.[79] EPA's approach, which uses linear modeling for NPC, has led to an unrealistic and overestimated IUR.

In addition to longstanding concerns with EPA's analysis, and the implausibility of the draft IUR as noted above, significant scientific information available in the peer-reviewed literature was not considered in the 2022 Draft IRIS Formaldehyde Assessment. This information meets the TSCA "reasonably available" standard and was shared with EPA in a timely manner, such that EPA knew it was available and could have incorporated it.[80] Yet EPA did not consider this information in its weight of the scientific evidence analysis in the 2022 Draft IRIS Formaldehyde

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[75] 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.

[76] MacGregor 2006, and Panel 2010 comments at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0029, document 5 etc.

[77] Conolly RB, Schroeter J, Kimbell JS, Clewell H, Andersen ME, Gentry PR. 2023. *Updating the biologically based dose-response model for the nasal carcinogenicity of inhaled formaldehyde in the F344 rat*. Toxicol Sci. 193(1):1-17. https://doi.org/10.1093/toxsci/kfad028. PMID: 36912747; PMCID: PMC10176246.

[78] ACC Formaldehyde TSCA Risk Evaluation Consortium comments on the 2022 Draft Formaldehyde IRIS Assessment, pages 46-54, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0127/attachment_8.pdf.

[79] *Id*.

[80] See multiple data submissions on the missing studies submitted to the IRIS docket from study authors, including Dr. Robinan Gentry, June 9, 2022, available at https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0074, Dr. Chad Thompson, June 13, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0087, and Dr. Rory Conolly, June 9, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0075, and the ACC Formaldehyde Panel comments on the 2022 Draft Formaldehyde Assessment, June 13, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0103, and the ACC Formaldehyde TSCA Risk Evaluation Consortium comments on the 2022 Draft Formaldehyde Assessment, June 13, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0100, ACC comments submitted to NAS, March 31, 2023, *Summary of Insufficient U.S. Environmental Protection Agency (EPA) Responses to the Recommendations From the National Academy of Sciences (NAS) 2011 Review*, available at: PAF-76, https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_7.pdf. These comments are also available in this docket: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

Assessment. In the 2022 Draft IRIS Formaldehyde Assessment, EPA used systematic review criteria which allowed the agency to ignore important studies (such as Thompson et al.) because they were not considered to be primary literature. EPA sought to include only studies that provided new data sets, not re-analysis of existing information. EPA's refusal to consider studies that provide a reanalysis means that no matter how flawed the initial study may be, EPA is precluding analyses that point out fundamental flaws in the study.

However, under the TSCA scientific standards, EPA must consider all available information. Therefore, even though EPA discounted some studies as not relevant to the Draft IRIS Assessment, in order to meet the TSCA scientific standards for reasonably available information and best available science, EPA must consider how this additional information would change the Draft IRIS Assessment upon which the TSCA program relies. EPA must correct its approach and consider how the additional literature, which the TSCA program disregarded, would lead to significant scientific changes in the IUR for NPC. Relying solely on an IRIS Assessment, which is not fit for purpose and was not developed using an approach that is consistent with the TSCA scientific standards, has led to the use of an IUR for NPC that is not consistent with the best available science and does not meet the scientific standards of TSCA.

2. Associations between formaldehyde and myeloid leukemia are not supported by the weight of the scientific evidence

Despite a 2011 NAS recommendation that EPA provide a clear causality framework for determinations regarding LHP cancers, the Draft Formaldehyde IRIS Assessment simply lacks such a framework.[81] NAS 2011 noted inconsistencies in the epidemiologic data, weak animal data, and the lack of mechanistic data leading to a conclusion that "there is a noticeable lack of evidence of a causal relationship of formaldehyde exposure and Hodgkin lymphoma or leukemia."[82] In response to these comments, the 2022 Draft Formaldehyde IRIS Assessment did two important things:

1) EPA acknowledged that "the lack of systemic distribution of formaldehyde is sufficiently supported" (at page D-6) and admits that "no MOA has been established to explain how formaldehyde inhalation can cause myeloid leukemia without systemic distribution" (at pages liv, 2-43); and,

2) EPA put in place a causality framework that allows it to ignore the strong mechanistic evidence against the systematic effects they acknowledge above and relies upon the inconsistent epidemiological data, questionable biomarker data to characterize mutagenic or genotoxic potential, evidence against lymphohematopoietic malignancies of any kind in animal models (e.g., "Increased LHP cancers have not been observed in well-reported chronic rodent bioassays…. Further, positive associations with leukemia have not been reported in rodent studies" (page 1-435)), and an assumption about hypothetical key

[81] ACC, *Summary of Insufficient U.S. Environmental Protection Agency (EPA) Responses to the Recommendations From the National Academy of Sciences (NAS) 2011 Review* at page 15 for a detailed discussion, available at: PAF-76, https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_7.pdf.

[82] NAS, *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde*, 2011, at page 135, available at: https://nap.nationalacademies.org/catalog/13142/review-of-the-environmental-protection-agencys-draft-iris-assessment-of-formaldehyde.

events with a lack of defined mode of mechanisms of action to find that the "evidence demonstrates" that formaldehyde inhalation causes myeloid leukemia.

This cannot be what NAS 2011 intended when recommending that EPA develop a clear, non-subjective framework that uses the weight of the evidence to assess causality. Yet EPA has developed a flawed causality framework that allows it to ignore robust mechanistic information (e.g., molecular dosimetry documenting no systemic distribution of inhaled formaldehyde) and no evidence of leukemia in multiple cancer bioassays in multiple species, while continuing to evaluate epidemiological information in an inconsistent manner (despite NAS 2011 recommendations for clear criteria) outside of any recognized framework for data integration. Each of these points is addressed, in detail, in a comment letter the Formaldehyde Panel provided to NAS on March 31, 2023.[83] The Formaldehyde Panel and external scientific experts have also provided significant comments to EPA discussing the lack of scientific rigor in EPA's analyses related to myeloid leukemia.[84]

EPA simply did not consider existing MOA information in an integrative framework. Using the well-established international, consensus-based World Health Organization (WHO)/ International Programme on Chemical Safety (IPCS) MOA framework, Gentry et al., 2020, evaluated postulated MOAs for leukemia following formaldehyde inhalation.[85] 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 leukemia 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.

More recently, Vincent et al., 2024, conducted a systematic review focusing on the relationship between formaldehyde and LHP cancers, including myeloid leukemia.[86] This systematic review found "no credible explanation linking inhaled formaldehyde to LHP cancers, and no evidence of

[83] ACC, *Summary of Insufficient U.S. Environmental Protection Agency (EPA) Responses to the Recommendations From the National Academy of Sciences (NAS) 2011 Review* at page 15 for a detailed discussion, available at: PAF-76, https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_7.pdf.

[84] *See*, for example references in ACC Formaldehyde Panel comments on Draft 2022 Formaldehyde Assessment to Gentry/Checkoway/Mundt/Rhomberg papers, June 13, 2022, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0127/attachment_7.pdf, and comments submitted to the SACC from Dr. Harvey Checkoway, May 1, 2024, where he states "Based on my review of the draft EPA report, I do not find that its conclusions are grounded in the best available science and also fails to fully incorporate key recommendations from previous peer reviews, " available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0140.

[85] Gentry, R., Thompson, C.M., Franzen, A., Salley, J., Albertini, R., Lu, K. and Greene, T., 2020. *Using mechanistic information to support evidence integration and synthesis: a case study with inhaled formaldehyde and leukemia*. Critical reviews in toxicology, 50(10), pp. 885-918.

[86] 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.

formaldehyde entering the bone marrow or blood when inhaled" and determined that causation is unlikely.[87]

As summarized above, because the Draft Formaldehyde IRIS Assessment does not properly weigh the available information, it does not represent the best available science. Nor does the Draft Formaldehyde IRIS Assessment integrate available information into a weight of the scientific evidence framework. The TSCA risk evaluation must properly integrate new publicly available information, as well as existing information that the Formaldehyde Panel has already provided, including the Gentry et al., 2020 publication and other information that informs MOA,[88] in lieu of relying on the Draft Formaldehyde IRIS Assessment.

3. The IUR for NPC should not be framed as an underestimate of cancer risks

As described above, the NPC IUR discounts important information about the MOA of formaldehyde and overpredicts NPC cancer risks by using linear modeling. In the Draft Formaldehyde Risk Evaluation, while EPA recognizes that that the myeloid leukemia findings are not sufficient to develop quantitative estimates of cancer risk, it also suggests that the cancer risks presented in the risk evaluation are an underestimate and that, if myeloid leukemia were considered, the IUR could increase by as much as four-fold.[89] It is inconsistent and scientifically unsound for EPA to suggest that the risks cannot be quantified and at the same time provide an estimate for those uncertain risks. As described above and discussed in previous comments,[90] due to the biological implausibility of formaldehyde causing myeloid leukemia, as well as the weaknesses in the epidemiological literature upon which EPA relies, there is no sound scientific reason for EPA to suggest that using the NPC IUR underestimates cancer risks due to a hypothetical potential for myeloid leukemia. Publicly available publications which considered all

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[87] 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/.

[88] *See*, Examples of Excluded Science, including Key Studies, Recent Publications, and Authoritative Reviews, available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613 and Attachment B, at pages 23-33 of ACC Formaldehyde Panel Comments for May 3, 2024 SACC Meeting - American Chemistry Council.

[89] EPA, *Draft Human Health Risk Assessment for Formaldehyde*, Mar. 2024, at pages 9, 77, 104,and 107, available at https://www.epa.gov/system/files/documents/2024-03/formaldehyde-draft-re-human-health-hazard-assessment-for-formaldehyde-public-release-hero-march2024.pdf.

[90] See multiple data submissions on the missing studies submitted to the IRIS docket from study authors, including Dr. Robinan Gentry, June 9, 2022, available at https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0074, Dr. Chad Thompson, June 13, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0087, and Dr. Rory Conolly, June 9, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0075, and the ACC Formaldehyde Panel comments on the 2022 Draft Formaldehyde Assessment, June 13, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0103, and the ACC Formaldehyde TSCA Risk Evaluation Consortium comments on the 2022 Draft Formaldehyde Assessment, June 13, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0100, ACC comments submitted to NAS, March 31, 2023, *Summary of Insufficient U.S. Environmental Protection Agency (EPA) Responses to the Recommendations From the National Academy of Sciences (NAS) 2011 Review*, available at: PAF-76, https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_7.pdf, and 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. These comments are also available in this docket: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

available information, including MOA and mechanistic data, in robust integrative frameworks found that causality is improbable and not supported by the evidence. It is false and misleading for EPA to suggest that there is an underestimate of cancer risk, especially when EPA's linear modeling of NPC cancers leads to an overestimate of cancer risk.

C. EPA's dermal hazard value and POD are not best available science (charge question 1.3)

Formaldehyde is known to cause allergic contact dermatitis. As EPA recognizes, OSHA requires that skin contact with 1% or more of formaldehyde be prevented by chemical protective clothing and equipment (standard 1910.1048). As described by EPA, and consistent with the literature, formaldehyde's allergic response is localized to sites of dermal exposure and does not lead to systemic effects. Formaldehyde's effects are minimally adverse, unlike some respiratory sensitizers where severe health effects could be observed in individuals not previously identified as sensitized. In sensitized individuals, contact dermatitis clears in days to weeks after dermal exposure to formaldehyde. This minimizes the chance for any repeat or severe health effects, and potential future exposures can be minimized or eliminated.

In June 2023, the Formaldehyde Panel submitted a robust dataset of occupational exposure information to OPPT. These data included a robust discussion regarding conclusions on dermal risks due to formaldehyde exposure from EPA, the European Chemicals Agency (ECHA), and the National Institute for Occupational Safety and Health (NIOSH).[91] As was noted in the cover letter to those comments, dermal contact with formaldehyde in the vapor phase was not included in the conceptual model of worker exposure in EPA's Scoping Document for the formaldehyde risk evaluation, due to its volatility. At that time, EPA correctly recognized that, "[d]ue to formaldehyde's high volatility, EPA expects the inhalation pathway to be the most likely source of exposure to workers and ONUs." Although dermal exposure to formaldehyde-containing liquids is theoretically possible for some applications, routine skin contact is not plausible in manufacturing for two reasons. First, the irritating and absorptive properties of formaldehyde preclude ongoing skin contact and systemic effects. ECHA has noted that "Dermal exposure to formaldehyde solutions is expected to occur only acutely or accidentally, but duration is expected to be short due to the irritating property," and "Absorption appears to be limited to cell layers immediately adjacent to the point of contact and formaldehyde is rapidly metabolised at the initial site of contact. Due to rapid metabolism, distribution of formaldehyde molecules to other more distant organs is not likely, except from exposure to high concentrations." Second, the nature of the operations and tasks in the manufacturing and processing COUs (often closed systems) for the Formaldehyde Panel users preclude significant dermal contact with formaldehyde. Further, NIOSH states that "data on in vivo toxicokinetics in animals suggest that formaldehyde has limited potential to be absorbed through the skin (i.e., percent absorption of less than 10%."[92]

In the Draft Formaldehyde Risk Evaluation, EPA discusses dermal sensitization generally, including the two phases of induction and elicitation. EPA relies on two studies for the dermal

[91] See ACC Formaldehyde TSCA Risk Evaluation Consortium comments, submitted to EPA May 11, 2023, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2018-0438-0118.
[92] See ACC Formaldehyde TSCA Risk Evaluation Consortium comments, cover letter, submitted to EPA May 11, 2023, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2018-0438-0118.

point of departure, and, while the HSRB commented on these studies, it did not review EPA's overall weight of the scientific evidence determination. EPA is using an acute endpoint of induction and elicitation of dermal sensitization at a dose of 1 ug/m^3 based on a combination of points of departure (which applied uncertainty factors) from animal (induction) and human (elicitation) studies for risk assessment via the dermal route of exposure. Although sensitization is an appropriate candidate critical effect given the potential sensitizing effects of formaldehyde, the methods used by EPA to evaluate sensitization do not align with standard and accepted approaches for risk assessment of sensitizers, and the final derived benchmark does not reflect the concentrations of formaldehyde likely associated with an increased risk of sensitization. As such, it is important that the SACC review EPA's findings.[93]

For workplace exposures, individuals that may be sensitized (which is a rare event) would immediately be removed from the workplace. And, as described in detail in comments submitted by Integral, dermal sensitization by formaldehyde is rare, and sensitization responses are highly variable; so, in the occupational sector, the emphasis is placed upon prevention of induction.[94] Thus, the elicitation endpoint is much less relevant, and induction is the more relevant endpoint. Due to the corrosive and irritating effects of formaldehyde, it is not reasonable, based on available information, for EPA to expect that sensitized individuals would have continued exposure.

Relying on the Flyvholm et al. 1997 study is problematic because effects were seen only in occluded patch tests where the patch was left on the skin for two days. Under non-occluded test conditions, Flyvholm et al. (1997) reported there was no response seen in sensitive individuals at similar exposure concentrations that are more reflective of real-world exposure conditions. It is unreasonable to assume workers or consumers are dermally exposed to formaldehyde under occluded conditions continuously for multiple days, making these results unrepresentative of typical workplace exposures. In addition, EPA did not follow its typical benchmark dose modeling criteria and instead simply chose the lowest benchmark dose lower limit value.[95] This resulted in a benchmark dose lower limit value that is below what should have been used if EPA had followed its benchmark dose guidance.[96] Instead, EPA relied on a policy decision, inappropriately in the risk evaluation, to develop a conservative benchmark dose value. Finally, EPA is far too conservative in suggesting that an additional 10x uncertainty factor is necessary for sensitive individuals. The sensitization that was reported was seen in sensitive individuals and under unrealistic exposure circumstances. Adding an additional uncertainty factor is compounding conservatisms, moving EPA further from providing an assessment reflective of the best available science. In addition, as described in independent comments provided by Integral

[93] We note that charge question 1.3 seeks comment on EPA's overall weight of the scientific evidence, but in the *Draft Human Health Hazard Assessment*, no WOSE narrative is presented for the dermal hazard values.
[94] *See* Comments submitted to the SACC from Heather Lynch and Andrew Maier of Integral, May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.
[95] EPA, *Draft Human Health Hazard Assessment*, Mar. 2024, at page 52 where EPA states "Based on the criteria of lowest AIC alone, multistage degree and quantal could be considered viable model choices, and yield BMDL values in the range of 12 to 15 µg/cm^2. The log-probit model was also considered as it yielded the lowest BMDL at 10.5 µg/cm^2… representing a more conservative BMDL selection, the log-probit model was selected for the BMDL." Available at https://www.epa.gov/system/files/documents/2024-03/formaldehyde-draft-re-human-health-hazard-assessment-for-formaldehyde-public-release-hero-march2024.pdf.
[96] EPA, *Benchmark Dose Technical Guidance*, 2012, available at: https://www.epa.gov/sites/default/files/2015-01/documents/benchmark_dose_guidance.pdf.

and by Dr. Elaine Freeman of E[x]ponent, sensitization benchmarks, often referred to as No Expected Sensitization Induction Levels (NESILs), typically do not apply uncertainty factors. There is no scientific justification for applying an uncertainty factor because NESILs, due to the way they are developed, yield a margin of safety, not a margin of exposure.[97]

As further described by Dr. Elaine Freeman, EPA states in the draft human health risk assessment, that skin sensitization is the result of exposure at the site of contact and therefore there are no pharmacokinetic differences to account for with the margin of safety. This would reduce the human variability uncertainty factor to 3X. Additionally, the hazard data for skin sensitization is based on controlled human exposures in adult volunteers, which are already sensitized to formaldehyde and is corroborated by animal and *in vitro* evidence. As the human pharmacodynamic data are already based on sensitive, formaldehyde-sensitized individuals, there is no need for a 3X pharmacodynamic uncertainty factor to account for sensitivity differences between humans, thus reducing the human variability uncertainty factor to 1x. The point of departure is taken from a sensitive population and there is no evidence to support that pre-existing diseases or susceptibility to formaldehyde would be more sensitive to elicitation of a skin sensitization response to formaldehyde beyond humans already sensitized to formaldehyde.[98]

The Fischer et al. 1995 study is also not reliable for use by EPA. EPA has updated the Data Evaluation Report (DER) for the Fischer et al. study to incorporate the recommendations of the HSRB.[99] This updated DER includes a table (Table 4) with a footnote stating that "[t]otal number of positive results based on assumption those reacting at lowest concentration also react to higher test concentrations." Without making this assumption, EPA could not have derived a dose response curve for this study. However, we note that EPA's updated DER for Flyvholm et al. reports individual #6 reacting at 250 ppm and 500 ppb, does not report this individual at 1000 ppm, and reports this individual reacting at higher doses.[100] This indicates that individuals who react at lower doses do not always react at higher doses. Also, Flyvholm et al. indicates that some individual reactions do not always increase in severity with increasing dose. These observations are consistent with the large variability in elicitation of the sensitization responses that are described in comments provided by Integral and also undermine EPA's assumptions made regarding the Fischer et al., dataset. Dr. Joel Cohen has also provided comments to EPA describing how the lack of guideline studies for the elicitation response, and the variability in elicitation responses in humans, makes relying on these studies impractical for setting a point of departure.[101]

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[97] *See* Comments submitted to the SACC from Heather Lynch and Andrew Maier of Integral, May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613, and comments from Dr. Elaine Freeman of E[x]ponent, *Occupational and Consumer Exposures Related to Wood Products*, May 2024, available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613

[98] *See* Comments from Dr. Elaine Freeman of E[x]ponent, *Occupational and Consumer Exposures Related to Wood Products*, May 2024, available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

[99] *See* 45. DER Fischer 1995 Draft Risk Evaluation for Formaldehyde.

[100] *See* 44. DER Flyvholm 1997 Draft Risk Evaluation for Formaldehyde.

[101] *See* Comments submitted to the SACC from Dr. Joel Cohen of Gradient, May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

ACC is also concerned that EPA can be seen as modifying the dose-response curve by including an assumption that was never reported in the underlying study that purportedly supports the result, contrary to TSCA and FIFRA standards. These concerns are not alleviated by the transparency with which EPA noted this assumption was being made. We therefore strongly encourage EPA to abandon the analysis or derivation of a point of departure, and subsequent interpretations for risk evaluation, that rest on the assumption that individuals positive for sensitization at lower doses were also positive for sensitization at higher doses in the Fischer et al. study. This study is not fit for use in the TSCA risk evaluation.

The induction threshold is typically used for dermal sensitization safety thresholds. EPA identified a benchmark for sensitization of 100 µg/m^2 based on a local lymph node assay (LLNA) assay in animals (Basketter et al., 2008). The study selected produced an appropriate effective concentration inducing a stimulation index of three (EC3) value. EPA also considered *in vitro* data where an EC3 value was predicted based on a battery of *in vitro* sensitization assays reporting EC3s ranging from 85 to 130 µg/cm^2. Basketter (2008) and the *in vitro* evidence indicate the dermal sensitization induction threshold may be in the 85 to 130 µg/m^2 range, if not higher. EPA then applies uncertainty factors of 10 for animal to human extrapolation and 10 for human variability. These uncertainty factors are unnecessary.

When using LLNA data, it is well accepted that uncertainty factors for interspecies extrapolation are unnecessary.[102] For example, Basketter and Safford, 2016, state "the LLNA EC3 value, has been correlated directly with human experimental induction threshold data, which therefore has any interspecies variation implicitly built into it."[103] We also refer you to the Integral analysis which looked at other studies that could be used to derive a NESIL based on EC3 nonclinical data which found that the Basketter et al. study yields one of the lowest benchmarks.

As further described by Dr. Elaine Freeman when looking at human variability, as EPA recognizes that formaldehyde skin sensitization is the result of exposure at the site of contact, there are no pharmacokinetic differences to account for with the margin of safety. For induction studies, this would reduce the human variability uncertainty factor from 10x to 3x.[104]

In summary, EPA's dermal hazard values are overly conservative and not consistent with the best available science and methodologies for considering skin sensitization. It is important that the SACC provide critical and constructive comments to EPA to assist them in improving their methodology so that it is predictive and fit for purpose.

D. OPPT's reliance on the Draft IRIS Assessment is a fatal flaw

Since early 2022, the Formaldehyde Panel has catalogued the numerous legal and scientific issues with EPA's (or other regulatory bodies') use of a draft IRIS assessment as the basis for

[102] *Id.*
[103] Basketter D, Safford B, *Skin sensitization quantitative risk assessment: A review of underlying assumptions*, Regul Toxicol Pharmacol. 2016 Feb:74:105-16.
[104] *See* Comments from Dr. Elaine Freeman of E^{x}ponent, *Occupational and Consumer Exposures Related to Wood Products*, May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

any future action.[105] This action also clearly violates EPA's updated draft Scientific Integrity Policy, released in January 2024, which states that it is "policy of EPA to … [e]nsure that draft documents … are not relied upon for decision making."[106] Finalizing the Draft IRIS Assessment before the final Formaldehyde Risk Evaluation is finalized does not remedy this concern because the significant substantive public and peer review comments signal that significant changes to the Draft IRIS Assessment are warranted. By relying on an assessment that is still in draft form and needs to undergo substantive modification before it becomes final, EPA is creating significant confusion for stakeholders and the public, which undermines the legitimacy of the entire public notice and comment process in violation of the Administrative Procedure Act. This concern, and other concerns with the Draft IRIS Assessment, are discussed in the sections below.

1. Reliance on a *draft* IRIS assessment violates TSCA's best available science requirement

EPA's reliance on a draft IRIS assessment, regardless of the content of the assessment, violates the TSCA statutory requirements for best available science. Under TSCA, when undertaking rulemaking and risk evaluations of substances, the administrator is required to "use scientific information, technical procedures, measures, methods, protocols, methodologies, or models, employed in a manner consistent with the best available science." The administrator must consider, among other factors, "the extent to which the variability and uncertainty … are evaluated and characterized" and "the extent of independent verification or peer review of the information or of the procedures, measures, methods, protocols, methodologies, or models."[107]

EPA's reliance on a draft assessment, which has not completed a robust external peer review, is not consistent with a best available science standard. In fact, the only review which EPA has conducted on the Draft Formaldehyde IRIS Assessment violated the Federal Advisory Committee Act.[108] By relying on a draft assessment which is in a state of transition and will likely be modified and changed, OPPT is creating significant confusion for stakeholders. The IRIS program has not responded to public comments nor incorporated feedback from peer reviewers, and thus the underlying values that OPPT is relying upon in the TSCA risk evaluation would need to change. Significant changes are warranted because the IRIS Program received considerable scientific comments from the public, including from the Formaldehyde Panel, on the Draft IRIS Assessment.[109]

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[105] *See* April 8, 2022 letter from ACC regarding Preventing Inappropriate Use of U.S. EPA's Draft Formaldehyde Assessment, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0127/attachment_1.pdf

[106] EPA, Draft Scientific Integrity Policy, Jan. 2024, available at: https://www.regulations.gov/document/EPA-HQ-ORD-2023-0240-0002.

[107] 15 U.S.C. § 2625(h).

[108] ACC, Letter Regarding FACA Violations, May 10, 2024, available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

[109] See the 84 comments from the public submitted to the IRIS docket, available at: https://www.regulations.gov/docket/EPA-HQ-ORD-2010-0396/comments, in particular the ACC Formaldehyde Panel comments, June 13, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0103, and the ACC Formaldehyde TSCA Risk Evaluation comments, June 13, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0100. These comments are also available at this docket: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

Moreover, the fact that EPA is not relying on a final IRIS assessment makes it impossible for the public and the SACC to provide comments to EPA. EPA's approach further compromises the credibility of the SACC peer review because the SACC does not have full awareness of what modifications EPA is considering for the final IRIS assessment. While EPA may finalize the IRIS assessment before the TSCA risk evaluation is finalized, the entire peer review will still have been compromised by EPA's reliance on a draft document that needs substantial revision. This is not best available science, and the TSCA program has an obligation to meet this standard.

2. The NAS review of the Draft IRIS Assessment was flawed

The charge that EPA provided to NAS for its review of the 2022 Draft IRIS Formaldehyde Assessment was significantly flawed and not fit for purpose.[110] EPA unduly narrowed the charge, and this prevented the NAS from conducting a robust review of the scientific analyses in the assessment. Instead of conducting an independent assessment of the formaldehyde science, the committee only evaluated whether the 2022 Draft IRIS Formaldehyde Assessment "adequately and transparently" evaluated the scientific literature provided by EPA and used appropriate methods to synthesize the state of the science.[111] The NAS committee was not charged with commenting on the full body of literature relevant to the hazards and risks of formaldehyde, nor was it charged with reviewing alternative scientific opinions.[112] The NAS committee repeatedly referred to evaluating whether EPA's approach was consistent with "its state of practice" methods. While this term was not defined, the NAS committee focused on whether EPA's approaches were consistent with EPA guidance documents. And, because the NAS report states that the committee "was not charged with … reviewing alternative opinions of EPA's assessment," it is doubtful that public comments were considered relevant to the NAS committee. The narrow charge provided to NAS for its review is not consistent with EPA's Peer Review Handbook and the requirements for highly influential scientific assessments.[113]

The NAS review was also flawed and not fit for purpose because it did not ask that the reviewers consider the important TSCA scientific standards, including best available science, weight of the scientific evidence, and reasonably available information. Because the peer reviewers were not asked to evaluate EPA's analyses and literature choices, including feedback on over 100 peer-

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[110] For additional details on this topic, see the ACC letter submitted to EPA and NASEM on Apr. 13, 2022, which details the requirements for peer review as described in EPA's Peer Review Handbook, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0127/attachment_3.pdf and the ACC blog https://www.americanchemistry.com/chemistry-in-america/news-trends/blog-post/2023/epa-human-studies-review-board-peer-review-shows-that-not-all-peer-reviews-are-equal-a-tale-of-two-peer-reviews-on-formaldehyde.

[111] NAS, Review of EPA's 2022 Draft Formaldehyde Assessment (2023), available at: https://nap.nationalacademies.org/catalog/27153/review-of-epas-2022-draft-formaldehyde-assessment.

[112] ACC has provided information to NASEM and EPA noting that over 100 peer-reviewed scientific studies were excluded from the Draft IRIS Assessment. Because NASEM was not asked to comment on excluded information and was not asked to comment on alternative scientific information, none of this information was considered by NASEM during its peer review. Those letters are available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2018-0438-0067 and https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0103 (see Appendix A). The list of excluded studies was also provided to the SACC and EPA on May 3, 2024, available at pages 23-33: ACC Formaldehyde Panel Comments for May 3, 2024 SACC Meeting - American Chemistry Council.

[113] ACC Letter to EPA and NASEM Regarding Comment on the Charge Questions and Committee Task for Peer Review of Draft Formaldehyde Assessment, Apr. 13. 2022, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0127/attachment_3.pdf.

reviewed scientific studies that EPA excluded from the Draft IRIS Assessment,[114] EPA did not receive feedback that would inform whether the IRIS assessment is appropriate for use under TSCA, which requires that EPA integrate and assess available information. The superficial review that was conducted was predominantly to determine if EPA had followed its own IRIS guidelines. This type of review is insufficient for information that will underlie a TSCA risk evaluation and which must consider reasonably available information.

The NAS review also did not resolve many important scientific issues that are relevant to formaldehyde. For example:

- NAS did not evaluate if EPA's assessment meets requirements for the use of the "best available science." Instead, the NAS committee indicates that many EPA methods were "consistent with EPA's state-of-practice approach," a distinction which is irrelevant to the statutory scientific standards in TSCA.

- NAS did not address validity of the toxicity values in EPA's 2022 draft IRIS assessment, stating "the committee did not conduct an independent hazard evaluation or dose-response assessment, and therefore does not recommend alternative hazard identification conclusions or toxicity values."

The NAS review was additionally compromised due to procedural shortcomings and FACA violations including and a lack of fair balance on the committee.[115] ACC raised serious concerns related to fair balance including the overall process by which the provisional committee was established, the Study Director assigned to oversee and manage the committee, the overall composition and balance of the committee, and several of the provisional appointees who should have been disqualified because of appearance of a lack of impartiality or independence.[116] Yet NAS did not address the concerns with the committee in violation of NAS's policies and guidelines and in conflict with OMB and EPA Guidelines for Peer Review.

3. EPA has not responded to NAS or public comments

As noted above, because EPA has not completed peer review of the Draft IRIS Assessment, it has not provided responses to NAS or to public commenters.[117] The confusion and lack of clarity created by EPA's reliance on a draft assessment that needs to change before the TSCA risk

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[114] The Formaldehyde Panel repeatedly provided documentation to NAS and EPA regarding important studies that were not considered, integrated and assessed. Those letters are available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2018-0438-0067 and https://www.regulations.gov/comment/EPA-HQ-ORD-2010-0396-0103 (see Appendix A). The list of excluded studies was also provided to the SACC and EPA on May 3, 2024, available at pages 23-33 at ACC Formaldehyde Panel Comments for May 3, 2024 SACC Meeting - American Chemistry Council.

[115] *See* for example, ACC Comments to NASEM on Committee Composition, Aug. 25, 2022; ACC Letter to NASEM on Information Requests, Sept. 9, 2022; and NASEM Response to ACC on Information Gathering Session Request Mar. 6, 2023, all available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0126.

[116] ACC, Comments to NASEM on Committee Composition, Aug. 25, 2022, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0126.

[117] See *OMB Information Quality Bulletin for Peer Review*, Jan. 14, 2005, at page 2670, which states "A peer review is considered completed once the agency considers and addresses the reviewers' comments. All reviewer comments should be given consideration and be incorporated where relevant and valid" 70 Fed. Reg. 2670, available at: https://www.govinfo.gov/content/pkg/FR-2005-01-14/pdf/05-769.pdf.

evaluation is finalized compromises the entire SACC review process. The underpinnings for the inhalation hazard values and cancer IUR are essentially a moving target, and there is no clarity regarding what the final IRIS assessment will look like. In the Draft TSCA Risk Evaluation, there is only one section that notes a change due to the feedback received by NAS.[118] In this case, the Draft TSCA Risk Evaluation notes that OPP and OPPT are deviating from the Draft IRIS Evaluation. However, considering the extensive public comments that EPA received and that have not been addressed at all, stakeholders and the SACC have no clarity on other changes that EPA might be considering for the IRIS assessment, and thus there is no understanding of how these potential changes will impact the TSCA risk evaluation. As EPA states, "[i]n the future, any relevant revisions being made to the IRIS assessment for NAS comments will be incorporated into the OPP and OPPT evaluations as appropriate."[119]

Further discussion of these concerns is available in comments that the Formaldehyde Panel has previously provided to EPA and the NAS.[120] To ensure the TSCA Risk Evaluation is consistent with best available science, EPA should not rely on a Draft IRIS Assessment that is still being revised. Even if EPA finalizes the IRIS Assessment before the TSCA risk evaluation is complete, this will not correct the fact that the SACC and public commenters did not have full awareness of the changes that are being considered for the underlying IRIS assessment.

E. The Draft Formaldehyde IRIS Assessment is not best available science, does not incorporate available information, and is not fit for informing the TSCA Risk Evaluation

In addition to the clear scientific inadequacies described above, the Draft Formaldehyde IRIS Assessment is not fit for purpose and should not be relied upon for informing TSCA or FIFRA. ACC has provided comments to the EPA IRIS program describing many of the concerns, and they are summarized in the sections below.[121]

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[118] *See* EPA, *Draft Human Health Hazard Assessment for Formaldehyde*, Mar. 2024, at page 19 where EPA notes that HSRB and NASEM comments lead OPPT and OPP to have lower confidence in the Hanrahan et al., study, available at: https://www.epa.gov/system/files/documents/2024-03/formaldehyde-draft-re-human-health-hazard-assessment-for-formaldehyde-public-release-hero-march2024.pdf.

[119] *Id*. at pages 19-20.

[120] *See* ACC Comments on Scientific and Legal Issues with EPA's Forthcoming Peer Review of Draft Evaluation of Formaldehyde under the Toxic Substances Control Act (TSCA) and Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Mar. 8, 2024, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0007, and Nov 7, 2023 ACC comments on Consideration of Public Comments and Peer Review of Formaldehyde Science, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2018-0438-0130.

[121] *See* ACC Comments on Scientific and Legal Issues with EPA's Forthcoming Peer Review of Draft Evaluation of Formaldehyde under the Toxic Substances Control Act (TSCA) and Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Mar. 8, 2024, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0007; and Mar 31, 2023 ACC letter to Jonathan Samet regarding Summary of Insufficient EPA Responses to the Recommendations From the NAS 2011 Review of EPA's 2010 Draft IRIS Assessment of Formaldehyde, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_7.pdf; and March 31, 2023 ACC letter to Jonathon Samet regarding Inconsistencies Between EPA's 2022, Draft Formaldehyde Assessment and EPA's December 22, 2022, Final IRIS Handbook, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_6.pdf; and Apr 8, 2022 ACC Letter Regarding Preventing Inappropriate Use of U.S. EPA's Draft Formaldehyde Assessment; available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0127/attachment_1.pdf; and Mar 10, 2022 ACC Letter Regarding Concerns About NASEM's Review of

1. The Draft Formaldehyde IRIS Assessment is not consistent with the IRIS Handbook

After years of work, the IRIS program finalized and released in 2022 the *ORD Handbook for Developing IRIS Assessments* (IRIS Handbook).[122] The IRIS Handbook implements some of the recommendations and input from the NAS, EPA agency reviewers, other federal agencies, EPA's Science Advisory Board (SAB), and experts in systematic review and provides the operating procedures to the scientists in the IRIS program. While still needing significant improvement, these procedures are necessary steps to help ensure a consistent and transparent science-based approach to the development of hazard assessments. The IRIS Handbook articulates the importance of a structured seven-step process. Unfortunately, the Draft Formaldehyde IRIS Assessment is not consistent with this process.[123]

EPA's failure to be consistent with the IRIS Handbook starts with step one of the process, where EPA simply failed to implement step one and never released an IRIS assessment plan, which would have included scoping and problem formulation materials. Inexplicably, formaldehyde is the only one of the 17 chemicals under review by the IRIS Program for which EPA has not developed an IRIS Assessment Plan or Systematic Review Protocol. These work products – the IRIS assessment plan, the systematic review protocol, and the identification of key science issues – are not trivial or inconsequential. For instance, the systematic review protocol is a central component of the systematic review which should guide the entire IRIS assessment. EPA has used post hoc rationalizations to describe why its failure to meet these requirements is not problematic, but these arguments are not convincing and do not correct EPA's failure to provide a clear systematic review framework for public comment and input before the assessment was developed.[124]

The IRIS Handbook also requires that study evaluation be conducted independently by at least two reviewers.[125] However, when explaining its approach to the NAS, EPA described a process whereby the secondary reviewer was not blinded to the primary reviewer's analysis.[126] This failure to have independent review of individual studies jeopardizes the integrity of the entire systematic review underpinning the Draft IRIS Assessment. And, notably, as is discussed further

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EPA's 2022 Draft Formaldehyde Assessment, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0127/attachment_2.pdf.

[122] EPA, *ORD Handbook for Developing IRIS Assessments* (IRIS Handbook), Dec. 22, 2022, available at: https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=356370.

[123] *See* detailed ACC comments provided to EPA and NAS on this topic including: Letter to Kathryn Guyton regarding Procedural Deficiencies in Developing the 2022 Draft IRIS Formaldehyde Assessment, Oct. 25, 2022 available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0114/attachment_9.pdf, and Letter to Jonathan Samet regarding Summary of Insufficient EPA Responses to the Recommendations From the NAS 2011 Review of EPA's 2010 Draft IRIS Assessment of Formaldehyde, Mar. 31, 2023, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_7.pdf.

[124] *See* ACC Letter to Jonathan Samet regarding Summary of Insufficient EPA Responses to the Recommendations From the NAS 2011 Review of EPA's 2010 Draft IRIS Assessment of Formaldehyde, Mar. 31, 2023, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_7.pdf.

[125] EPA, *IRIS Handbook*, at page 4-4.

[126] *See* EPA responses to NAS, Jan. 17. 2023, at page 16, available at: https://www.nationalacademies.org/documents/embed/link/LF2255DA3DD1C41C0A42D3BEF0989ACAECE3053A6A9B/file/D68387109D2AC09286D94B621C4C6E83410005858BE3?noSaveAs=1.

below, EPA's process for the inclusion and exclusion of studies deviated from the IRIS Handbook requirements; therefore, the Draft IRIS Assessment failed to consider key studies.[127]

Finally, the Draft IRIS Assessment is also inconsistent with the IRIS Handbook's requirement that EPA integrate separate evidence streams to identify health hazards that are plausibly associated with the chemical.[128] When it came to evaluating formaldehyde and leukemia, EPA relied on only epidemiological studies and did not consider the biological plausibility based on MOA information. EPA acknowledged the lack of plausibility but did not incorporate this information into its hazard determination.

2. The Draft Formaldehyde IRIS Assessment was not developed to meet the TSCA Scientific Standards

Passed with bipartisan support, the Lautenberg Act added new sections to TSCA which focus on ensuring that TSCA is a risk-based statute driven by high quality scientific evaluations. In particular, new section 26(h) requires that all decisions related to the evaluation and regulation of new and existing chemicals be based on scientific methods and procedures that are consistent with the best available science.[129] This new provision of TSCA explicitly requires EPA to consider, as applicable:

> (1) the extent to which the scientific information, technical procedures, measures, methods, protocols, methodologies, or models employed to generate the information are reasonable for and consistent with the intended use of the information;
>
> (2) the extent to which the information is relevant for the Administrator's use in making a decision about a chemical substance or mixture;
>
> (3) the degree of clarity and completeness with which the data, assumptions, methods, quality assurance, and analyses employed to generate the information are documented;
>
> (4) the extent to which the variability and uncertainty in the information, or in the procedures, measures, methods, protocols, methodologies, or models, are evaluated and characterized; and
>
> (5) the extent of independent verification or peer review of the information or of the procedures, measures, methods, protocols, methodologies, or models.[130]

Additionally, and equally important, the new provisions of TSCA also include section 26(i), which requires that EPA rely on the weight of the scientific evidence,[131] and sections 26(k), and

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[127] *See* ACC Letter to Jonathan Samet regarding Summary of Insufficient EPA Responses to the Recommendations From the NAS 2011 Review of EPA's 2010 Draft IRIS Assessment of Formaldehyde, Mar. 31, 2023, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_7.pdf.
[128] EPA, *IRIS Handbook*, at page xvi.
[129] 15 U.S.C. § 2625(h), available at: https://www.law.cornell.edu/uscode/text/15/2625.
[130] *Id*.
[131] 15 U.S.C. § 2625(i), available at: https://www.law.cornell.edu/uscode/text/15/2625.

6(b)(4)(F), which require that EPA consider, assess, and integrate all available information on hazards, exposure, and conditions of use.[132]And, as described earlier in these comments, when finalized, the Formaldehyde Risk Evaluation should be fully consistent with the requirements of the 2017 Risk Evaluation Framework regulation.[133]

EPA's Draft Formaldehyde IRIS Assessment is not based on the weight of scientific evidence as required by TSCA. EPA[134] and Congress[135] have endorsed a definition of "weight of scientific evidence" that means "a systematic review method … that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently, identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance." As ACC has catalogued on numerous occasions since 2022, the Draft Formaldehyde IRIS Assessment is the only IRIS assessment undergoing development for which no pre-established systematic review protocol was released, including for public comment.[136] As EPA's February 2024 IRIS Program Outlook makes clear, formaldehyde is the only assessment out of 17 under development for which the agency deviated from this practice. NAS was highly critical of the absence of a pre-published systematic review protocol in 2023, noting "EPA did not develop a set of specific protocols for the 2022 Draft Assessment in a fashion that would be consistent with the general state of practice that evolved during the prolonged period when the assessment was being developed…. The committee concluded that prepublished protocols are essential for future IRIS assessments to ensure transparency for systematic reviews in risk assessment."[137]

The Draft Formaldehyde IRIS Assessment, like other IRIS assessments, was developed to serve as a source of toxicity information used by EPA, state and local health agencies, other federal agencies, and international health organizations.[138] While the IRIS Handbook and other guidance documents provide procedures for conducting IRIS assessments, neither the IRIS Handbook nor other guidance documents incorporate the TSCA scientific requirements added in 2016. When the Draft IRIS Assessment was developed, its authors did not seek to ensure that the best available science was used consistent with the weight of the scientific evidence. Nor did the IRIS program seek to ensure the consideration and integration of available information. When EPA

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[132] 15 U.S.C. § 2625(k), 2625(j), 2605(b)(3)(F), available at: https://www.law.cornell.edu/uscode/text/15/2625, and https://www.law.cornell.edu/uscode/text/15/2605.
[133] EPA, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act*, Jul. 20, 2017, available at: https://www.regulations.gov/document/EPA-HQ-OPPT-2016-0654-0108.
[134] 40 CFR § 702.33.
[135] https://www.congress.gov/114/crpt/hrpt176/CRPT-114hrpt176.pdf (p. 33).
[136] *See* Mar. 31, 2023 ACC letter to Jonathon Samet regarding Inconsistencies Between EPA's 2022, Draft Formaldehyde Assessment and EPA's December 22, 2022, Final IRIS Handbook, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_6.pdf; Apr. 13, 2022 ACC Comments on the Charge Questions and Committee Task for Peer Review of Draft Formaldehyde Assessment, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0127/attachment_3.pdf; June 13, 2022 ACC Formaldehyde Panel Comments on the Draft 2022 Formaldehyde Assessment, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0127/attachment_7.pdf; Oct. 25, 2022 ACC Letter to NASEM on Procedural Deficiencies in Developing the 2022 Draft IRIS Formaldehyde Assessment, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0114/attachment_9.pdf; Appendix A, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0114/attachment_10.pdf
[137] https://nap.nationalacademies.org/login.php?record_id=27153 (p. 5).
[138] *See* IRIS program description at: https://www.epa.gov/iris/basic-information-about-integrated-risk-information-system.

sought a narrow review from the NAS, the NAS was not charged with considering whether the Draft IRIS Assessment was consistent with the TSCA standards. In fact, the narrow charge that was provided to the NAS makes no mention of "best available science" and did not allow for an independent review of key elements of the hazard, dose-response, or exposure assessments, which is not consistent with what EPA had publicly committed to in the final scoping document for the formaldehyde risk assessment.[139] As such, it is inappropriate for EPA to rely so heavily on an IRIS Assessment that is simply not consistent with the TSCA scientific standards. The March 8, 2024, letter which the Formaldehyde Panel provided to EPA further describes many of these concerns.

3. The Draft Formaldehyde IRIS Assessment does not consider available information

As mentioned above, the Draft Formaldehyde IRIS Assessment did not consistently apply inclusion and exclusion criteria during the systematic review step. And, as also noted above, instead of seeking to include all available information in the Draft Formaldehyde IRIS Assessment, EPA chose to rely on only what it considered to be "primary" studies. EPA also overlooked some studies that it would consider to be "primary." Thus, the assessment did not consider peer-reviewed re-analyses of data or critically important mode of action information. The Formaldehyde Panel has identified over 100 publications relating to important scientific issues including sensory irritation, formaldehyde modeling, weight of evidence, dermal exposure, and systematic review methods that have all been excluded from the Draft IRIS Assessment that are therefore also excluded from the Draft Formaldehyde Risk Evaluation. A list of these key studies was provided to the SACC as part of our comments to inform the May 7 preparatory review meeting.[140] Due to its reliance on the Draft IRIS Assessment, the Draft Formaldehyde Risk Evaluation also does not integrate conclusions and methods from other authoritative bodies like the EU, World Health Organization, or other offices at EPA.

Because TSCA requires that EPA make decisions based on the "best available science" and the "weight of scientific evidence," and directs EPA risk evaluations to "integrate and assess" available information on hazards and exposures for the conditions of use of the chemical substance…," relying on an inadequate IRIS assessment that does not include available information makes it impossible for the TSCA risk evaluation to meet the required scientific standards.

4. The Draft Formaldehyde IRIS Assessment does not address previous NAS recommendations

The Draft Formaldehyde IRIS Assessment was informed by a 2011 NAS review of an earlier 2010 Draft Formaldehyde IRIS Assessment. In the 2022 Draft IRIS Formaldehyde Assessment,

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[139] *See* ACC Comments on Scientific and Legal Issues with EPA's Forthcoming Peer Review of Draft Evaluation of Formaldehyde under the Toxic Substances Control Act (TSCA) and Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Mar. 8, 2024, at page 6, available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0007.

[140] See List of Excluded Science, available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613 and at pages 23-33 at ACC Formaldehyde Panel Comments for May 3, 2024 SACC Meeting - American Chemistry Council.

EPA provides a cursory summary of responses to the NAS 2011 recommendations in Appendix D. However, as we described in the March 31, 2023 comments to the NAS, there are many important scientific areas where EPA has not addressed important comments from 2011.[141] These important areas include: responding to NAS comments related to understanding the MOA of formaldehyde; recognizing that formaldehyde is present in exhaled breath; following recommendations related to evaluating NPC; appropriately characterizing portal-of-entry effects, including the appropriate application of uncertainty factors and quantification of effects; and ensuring that LHP cancers were appropriately grouped.

The TSCA standard for best available science includes consideration of "the extent of independent verification or peer review of the information." It is important that the TSCA risk evaluation relies on information that has not only undergone peer review, but also has completed the peer review process, including providing responses to peer review comments received. The 2022 Draft Formaldehyde IRIS Assessment has not satisfied this requirement.

IV. EPA's Occupational Exposure Value is Illogical and Must be Revised and/or Removed (charge questions 3.3 - 3.4)

EPA has developed a draft Occupational Exposure Value (OEV) for formaldehyde of 11 ppb or 14 ug/m^3. The American Healthy Homes Survey II (AHHS II) study reliably shows that typical indoor air levels are 0.3 to 124.2 ug/m^3, with the 50th percentile value in average homes at 19.77 ug/m^3 and most homes below 40 ug/m^3.[142] EPA does not dispute these values.

It is simply nonsensical for EPA to suggest that an unreasonable risk exists in more than 50 percent of U.S. households due to formaldehyde exposures. EPA must revise this value such that it represents an actual unreasonable risk level and considers all relevant aspects of risk, including the extent of adversity of the effect, as required by the statute.[143] EPA has not incorporated important information regarding the key contributions to typical exposures, including natural/biogenic, secondary formation, combustion, fire-related, mobile, residential, and behavioral (i.e. candle burning) sources. This includes key information from EPA's National Emissions Inventory, National Air Toxics Assessments, and other recent studies. Typical background exposures of formaldehyde, due to predominantly biogenic sources, are not causing unreasonable risks.

At the heart of this flawed OEV is EPA's reliance on the point of departure and uncertainty factors suggested by the Draft IRIS Formaldehyde Assessment. The IRIS Assessment recommends relying on the Krzyzanowski et al., study, which as described above is an unreliable study and should not be used for dose-response assessment. It is not a high-quality study, and it does not represent the best available science. In addition, the endpoint EPA relies upon from this poorly designed observational epidemiological study is reported associations between formaldehyde exposure and pulmonary function decrements in children 6-15 years old with

[141] *See* ACC Letter to Jonathan Samet regarding Summary of Insufficient EPA Responses to the Recommendations From the NAS 2011 Review of EPA's 2010 Draft IRIS Assessment of Formaldehyde, Mar 31, 2023, available at: https://downloads.regulations.gov/EPA-HQ-OPPT-2023-0613-0117/attachment_7.pdf.
[142] EPA, Draft Indoor Air Exposure Assessment for Formaldehyde, Mar. 2023, at chapter 3, available at Formaldehyde Draft RE Indoor Air Exposure Assessment March 2024 (pdf).
[143] *See* 15 U.S.C. § 2605(b).

asthma. Selecting a point of departure based on effects in children is not appropriate for application to an OEV, given that children younger than fifteen years old would not be working in the chemical industry. Moreover, children have different lung physiology than adults and undergo rapid changes during growth and development, which typically make them more sensitive to asthma triggers than adults and make extrapolations of pulmonary function testing results across ages difficult. And importantly, Krzyzanowski et al. did look at pulmonary outcomes in adults, and no effects due to formaldehyde exposure were seen.

The Draft Formaldehyde IRIS Assessment, while relying on the Krzyzanowski et al. study, also notes that three additional studies also support using a similar point of departure. These other three studies (Annesi-Maesano et al. (2012), Matsunaga et al. (2008), and Venn et al. (2003)) are also flawed epidemiological studies. Concerns with these studies have been described above and are also discussed in further detail in comments submitted by Ramboll.[144]

As described in detail above, EPA instead should use an approach consistent with the approach taken by the competent EU authorities. EPA should be using data from the high-quality controlled chamber studies which support a value of 300 ppb or higher. The chamber studies should be used to inform both acute and chronic exposures. As described in sections above, it is well accepted, as confirmed by the EPA HSRB, that formaldehyde-induced observed symptoms of sensory irritation are dependent on concentration and not on the length of time (i.e., duration) of exposure. No adjustment factor is necessary for accounting for different durations of exposure.[145]

We also note that EPA's OEV calculation includes a breathing rate adjustment factor, although EPA provides no discussion as to why this is necessary. Breathing rate adjustments are not generally used to evaluate inhalation exposure in risk evaluations (ATSDR 2021).[146] If a specific activity is evaluated in which breathing rates are higher than normal (e.g., intense physical exertion at exercise facilities), a factor can be incorporated for the relevant time period that the increased exertion occurs. However, there is no basis that workers evaluated in the COUs engage in activities with increased breathing rates over the entire 8-hour shift that would justify use of a generic scaling factor. Furthermore, considering the basis of the non-cancer point of departure and that the threshold effect was only reported in children and not municipal employee adults, there is no justifiable rationale for incorporating a worker scaling factor. We note that the breathing rate adjustment factor does not appear to be incorporated into other Risk Evaluations, including those for TCE (Appendix M), PCE, methylene chloride and 1-brompropane, nor is it recommended in EPA Guidance.[147]

An OEV value of 300 ppb or higher is supported by not only high-quality scientific studies which inform the point of departure, but also MOA and mechanistic information which informs sensitive subpopulations and would be protective for both workers and the general population. It

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[144] *See*, Comments from Linda Dell (Ramboll) submitted to the SACC, May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613

[145] 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.

[146] ATSDR, *Guidance for Inhalation Exposures*. Sept. 8, 2021.

[147]EPA, *Risk Assessment Guidance for Superfund Volume 1: Human Health Evaluation Manual, Part F*, Supplemental Guidance for Inhalation Risk Assessment January 2009.

also allows EPA to consider and integrate available scientific information, including what we know about the lack of sensory irritation and pulmonary effects at typical indoor levels.

Relying on the sensory irritation endpoint, which is reversible and protective of all other adverse effects, is a conservative approach. Reversible sensory effects are not considered adverse effects, and they surely are not "unreasonable risks." And, by protecting against sensory irritation, EPA would be protective of other adverse effects which may be considered unreasonable risks. Consistent with the recommendation of the HSRB, EPA need not apply a 10x uncertainty factor.[148] The HSRB recognized that the key chamber studies included hypersensitive individuals and/or younger individuals, and, given that younger people appear to be more sensitive to sensory irritation than older ones, they did not recommend a 10x uncertainty factor. Instead, they recommended the approach that EPA's OPP had previously used for chloropicrin, which is also a sensory irritant and acts similarly to formaldehyde.

V. EPA Must Develop a Transparent Framework for Unreasonable Risk Determinations

A. EPA does not provide a transparent framework for unreasonable risk determinations

TSCA section 6 requires that EPA determine whether a chemical substance, under its conditions of use, presents an unreasonable risk of injury to health or the environment. In conducting a risk evaluation, EPA must meet all TSCA section 26 requirements, including requirements related to best available science, weight of the scientific evidence, and reasonably available information; however, the unreasonable risk determination may not consider costs or other non-risk factors. While neither TSCA nor the 2017 Risk Evaluation Framework Rule define what constitutes an "unreasonable risk," the Risk Evaluation Framework rule discusses factors that EPA must consider in making an unreasonable risk determination. EPA states:

> The Administrator will consider relevant factors including, but not limited to: The effects of the chemical substance on health and human exposure to such substance under the conditions of use (including cancer and non-cancer risks); the effects of the chemical substance on the environment and environmental exposure under the conditions of use; the population exposed (including any susceptible populations), the severity of hazard (the nature of the hazard, the irreversibility of hazard), and uncertainties.[149]

In the *Draft Unreasonable Risk Determination of the Draft Formaldehyde Risk Evaluation*, EPA provides determinations regarding which uses "contribute to" unreasonable risk, but there is no clear framework describing how these determinations were reached. EPA recognizes the challenges posed by the ubiquity of formaldehyde in the natural environment and also claims that the agency "has high level of certainty of the contribution to the unreasonable risk of formaldehyde from a COU when the risk from such COU is much greater than the risk expected from the formaldehyde based on monitored concentrations in the indoor air, and EPA is less certain of the contribution by the COU when the risk from the COU is within the expected risk

[148] *Id*.
[149] 82 Fed. Reg. 33735 (Jul. 20, 2017).

based on monitored concentrations in the indoor air."[150] However, this discussion regarding the certainty of the contribution does not provide any framework for making a risk determination. And, while EPA discusses which COUs "contribute to" unreasonable risk, it has not described a single COU that presents an unreasonable risk. This concern is further discussed in section XI of these comments.

In the *Draft Human Health Risk Assessment*, when discussing risk characterization, EPA notes that it is unable to rely on the risk values developed.[151] This is appropriate, particularly since the development of the risk values is not consistent with best available science, as has been described above. Relying on a non-cancer benchmark value, which is below typical indoor air exposures and is at a level at which adverse effects are not seen in a general or occupational population, would be illogical. The flaws in EPA's development of these values do not allow them to be used. Instead, when referring to specific exposure scenarios, EPA states that "the decision of whether those risks are unreasonable is both case-by-case and context driven. In the case of formaldehyde, EPA is taking the risk estimates of this draft human health risk assessment (HHRA) in combination with a thoughtful consideration of other sources of formaldehyde, to interpret the risk estimates in the context of an unreasonable risk determination."[152]

Appropriately, EPA is not setting unreasonable risk at the 95th percentile indoor air level as described in the AHHS II survey; however, the Draft Formaldehyde Risk Evaluation does not provide any other exposure level that could be used to inform determining whether a condition of use presents an unreasonable risk.[153] In fact, EPA does not provide any discussion of the factors which are presented in the 2017 Risk Evaluation Framework rule. For example, it is not clear how, if at all, EPA has considered the population exposed, the level of severity of the point of departure, or the irreversibility of the effect. While EPA tells us that there was "thoughtful consideration" when making unreasonable risk determinations, no framework is provided, and, for each individual condition of use, stakeholders are left to guess at the considerations that EPA used to reach its conclusions for each COU.

EPA must provide stakeholders with a clear, consistent, transparent, and science-based framework. In describing the basis for its unreasonable risk determination, EPA states that it is considering "other risk-related factors" apart from the calculated risk estimates in the risk characterization. EPA identifies only two considerations in the context of its unreasonable risk determination, a confidence rating in the information used to inform the hazard and exposure values and "other sources" of formaldehyde. But EPA does not explain why those considerations are appropriate in this context, how they were applied, or any rational connection between those considerations and the unreasonable risk determination. EPA should develop a transparent framework, apply it to formaldehyde, and consider re-proposing the Draft Formaldehyde Risk Evaluation.

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[150] EPA, *Unreasonable Risk Determination of the Draft Risk Evaluation for Formaldehyde*, Mar. 2024, at page 5, available at: https://www.regulations.gov/document/EPA-HQ-OPPT-2023-0613-0046.
[151] EPA, *Human Health Risk Assessment for Formaldehyde*, Mar. 2024, at page 79; available at: https://www.regulations.gov/document/EPA-HQ-OPPT-2023-0613-0022.
[152] *Id*.
[153] Per conversations with Jeff Morris and the ACC Formaldehyde Panel on Apr. 11, 2024, and as presented by Jeff Morris at the Small Business Administration Office of Advocacy Roundtable on Apr. 22, 2024.

B. Using best available science would allow EPA to develop a clear and reproducible framework for unreasonable risk determinations

If EPA had followed the best available science and considered the unique properties of formaldehyde, consistent with other authoritative bodies, it would not be setting health risk values at levels that are below background levels and at levels at which no unreasonable adverse effects are seen in general or occupational populations. Following the science would make it much easier for EPA to have a transparent framework for unreasonable risk determinations. If EPA were to rely on a value that represents the best available science and the weight of the scientific evidence, such as 300 ppb as a starting point, then it would be much easier to articulate how it considered the necessary factors before reaching risk determinations for each COU.

C. EPA's overly conservative approach, which seeks to eliminate all risk, complicates its ability to develop a clear and reproducible framework for unreasonable risk determinations

Despite lacking a decision framework, EPA has piled multiple conservative measures on top of each other to reach its unreasonable risk determination. EPA's approach appears to be driven by a policy decision to be irrationally protective, rather than implementing an approach that would be predictive of actual risks. For instance, for occupational risks, EPA is relying on a hazard endpoint for which no effects in adults were noted. EPA is also applying uncertainty factors, even though there is a large amount of data available, and the effect EPA is proposing to rely on was seen in a sensitive population. And, as we describe below, the inputs to EPA's exposure assessments for the different COUs are worst case scenarios, not predictive of the most common uses.

In addition to the compounding conservatisms described above, EPA is seeking to eliminate all risks, not simply unreasonable risks. This approach is not consistent with TSCA, which directs EPA to evaluate unreasonable risks. Instead of recognizing that acceptable risks exist, EPA is conflating acceptable risk with unreasonable risk. EPA has developed hazard values in a manner consistent with the IRIS program, which uses points of departure combined with uncertainty factors to set health benchmarks at a level below which there are not likely to be any appreciable adverse effects. In fact, EPA has referred to these health benchmarks as levels below which no adverse effects are expected.[154] By using this approach in the Draft Formaldehyde Risk Evaluation, EPA is setting the stage for risk management rules that will be seeking to reduce risks beyond the extent necessary. EPA must instead set health benchmarks at levels that are commensurate with protection against unreasonable risk, not all effects. In setting these health benchmarks, EPA should take into account factors such as the level of adversity of the effects, the reversibility of effects, and the susceptibilities of the populations exposed.

[154] *See* ECEL derivations for trichloroethylene, available at: https://www.regulations.gov/document/EPA-HQ-OPPT-2020-0642-0128, perchloroethylene, available at https://www.regulations.gov/document/EPA-HQ-OPPT-2020-0720-0043, and methylene chloride, available at: https://www.regulations.gov/document/EPA-HQ-OPPT-2020-0465-0092.

VI. EPA's Occupational Exposure Assessment Is Overly Conservative (charge questions 3.1 - 3.4)

The occupational exposure assessment conducted by EPA is inappropriately conservative, is not reflective of the best available science and does not apply a consistent and transparent framework for judging the quality of exposure information.

We could not understand how EPA came to its findings for unreasonable risk, particularly when the confidence in the exposure assessment was slight or slight to moderate. EPA's findings appeared to be inconsistent. For instance, for leather tanning, EPA rated the exposure weight of the scientific evidence as slight for 8 hours and slight to moderate for the 15-minute exposure window. However, EPA states that it has a high level of certainty for the contributions to acute unreasonable risk and less certainty for the chronic contribution to unreasonable risk. For industrial use of automotive products, industrial use of lubricants, and commercial use of fertilizers, all the exposure data was modeled and not based on monitoring data, yet EPA has moderate confidence. It is not clear why EPA did not consider the confidence to be low since no monitoring data were available. For some of the COU evaluated, EPA has high confidence in modeled risks, whereas when actual monitoring data was used, the confidence was lower. EPA's findings appear counterintuitive: EPA should have less confidence in the data when modeled data are used. EPA may want to consider revisiting the data quality metrics for exposure data that are embedded in the systematic review protocol that was used.

EPA must also better clarify how the confidence in the data supports the "certainty of contribution" to the unreasonable risk. We note that for 13 of the COUs, EPA states that the weight of the scientific evidence is slight to moderate confidence for the exposure data, and EPA finds that the data provide "plausible estimates of exposure." EPA uses this terminology for some COUs where all the samples are below the level of detection. EPA never describes the standard for "plausible." "Plausible" is not a standard in TSCA. We recommend that EPA instead benchmark findings to the TSCA best available science standard. It appears that EPA is likely using this term to represent overestimates of exposure and risk. In cases where all samples are below the level of detection, EPA should have high confidence that the values are an overestimate of exposure and risk.

For exposure data, EPA obtained air sampling data from the OSHA Chemical Exposure Health Database (CEHD). This database is based on targeted, not random, OSHA inspections which often seek to catch worst-case chemical exposures which are only a snapshot in time. While EPA often does not use the CEHD database exclusively, for some scenarios (e.g., wood product manufacturing), the large majority of samples are from CEHD, and, although EPA's systematic review protocol says the CEHD database has low to medium quality, depending on the quality domain evaluated,[155] EPA rates the exposure data for composite wood product manufacturing as "medium to high" and the overall weight of the evidence as "moderate to robust." EPA does not transparently present what the exposure values would be with and without the CEHD data, thus prohibiting determinations of representativeness of the CEHD data.

[155] EPA, *Systematic Review Supplemental File: Data Quality Evaluation and Data Extraction Information for Environmental Release and Occupational Exposure*, Mar. 2024, available at: https://www.regulations.gov/document/EPA-HQ-OPPT-2023-0613-0039.

Renee Kalmes, CIH, provided a high-level review of the CEHD data provided in the *Draft Inhalation Occupational Monitoring Data and Exposure Summary* and found that over 2,200 PBZ (personal breathing zone) samples (across all Occupational Exposure Scenarios (OESs)) reported sample durations between 200 and 330 minutes.[156] For some OESs, samples in this range represented a significant proportion of all available exposure data. For example, samples with a sampling duration between 200 and 330 minutes represented 42% of all PBZ samples (n=509) in the Foundries OES and 35% of all PBZ samples (n=193) in the Furniture Manufacturing OES. In order to determine whether 330 minutes is an appropriate cut-point value for the evaluation of 8-hour time-weighted average (TWA) exposures, EPA should conduct sensitivity analyses to assess the impact of selecting other sampling duration cut-points (e.g., 200 minutes or 240 minutes) on the 8-hour TWAs for those COUs that indicate a large proportion of sample durations below 330 minutes. EPA should also consider whether it is appropriate to use the same sampling duration cut-point value for all OESs or whether this value should be OES-specific and based on 1) the general understanding of the OES-specific process information and worker activities and 2) the availability of sampling data for which sample duration is provided.

There also appears to be significant conservatism in EPA's dermal and inhalation modeling approach. As is described in detail below, EPA appears to use the highest level of percent weight of formaldehyde for the exposure scenarios, regardless of whether or not this value is representative.[157] In justifying the use of concentrations of 30 to 60 percent, EPA stated "EPA does not have higher confidence in the reported values because the Agency did not have monitored formaldehyde dermal exposure data to ground truth these exposure estimates."[158] For some categories, it appears EPA has relied on a single safety data sheet (SDS), rather than the required weight of the evidence approach that considers all the available data. If there is variability in products, EPA must account for this because, while one product might contribute to an unreasonable risk, another product that has a different percent formaldehyde may not contribute to unreasonable risk. EPA has an obligation in the risk evaluation to be transparent regarding which products would be acceptable and which would lead to an unreasonable risk.

A specific example of conservatisms in EPA's dermal assessment is presented in comments provided by Dow.[159] In this example, EPA used the default dermal loading of 2.1 mg/cm^2, which grossly overestimates exposure for the COU ("Processing as a reactant. Manufacturing of basic chemicals"). The EPA document "Occupational Dermal Exposure Assessment. A review of Methodologies and Field Data" (1996) indicates that the level of dermal exposure for "intermittent contact with a liquid" should be in the range of 0.00054 - 0.009 mg/cm^2 instead of the 2.1 mg/cm^2 value used in the draft risk assessment, which is based upon a default value from

[156] *See* Comments submitted to the SACC from Renee Kalmes and Dr. Pamela Dopart (E^{x}ponent), May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.
[157] For example, EPA states "For non-spray applications [incorporation into an article], EPA assumes that routine dermal exposure may occur. EPA assessed at a concentration of 60 percent, based on a maximum concentration range of 30 to 60 percent reporting from solvent-based paints category in the 2020 CDR (U.S. EPA, 2020a). This relatively high concentration is conservatively assessed in cases that sites received concentrated raw materials that they may dilute or mix prior to application."
[158] EPA, *Draft Human Health Hazard Assessment for Formaldehyde*, Mar. 2024, at page 10, available at: https://www.epa.gov/system/files/documents/2024-03/formaldehyde-draft-re-human-health-hazard-assessment-for-formaldehyde-public-release-hero-march2024.pdf.
[159] *See* Comments submitted to the SACC from Dow, May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

ChemSteer. It appears the 2.1 mg/cm^2 value was generated from a patch test measurement during mixing, spreading, and pressing tasks in the manufacture of rubber-coated fabrics. This value appears to be derived based on tasks in which wetted materials are directly handled by workers, which is nothing like the exposure scenario for the Dow COU, where exposure to the hands would be the exception based upon the information supplied to EPA in July 2023 comments. For the Dow COU, the formaldehyde solution is contained in closed vessels and transfer lines, and workers wear gloves as an extra protective measure to prevent contact with the skin, not because they expect to come into contact with the liquid. Thus, the range of 0.00054 - 0.009 mg/cm^2 should be used as the default for this COU. Additionally, EPA used the default concentration of 60% formalin solution even though they cite the typical solution concentration range of 37 to 40%, which more accurately matches the COU. It is not clear why EPA did not use the available information that was provided to the agency to inform this risk evaluation. Additionally, PPE is required to be used in this industrial setting because formaldehyde at this use level is corrosive. The PPE is only used as a precaution since exposure to the hands is not expected to occur based upon the operational controls. In the unlikely event that exposure to the hands does occur, gloves that are worn (widely available from many vendors) demonstrate 0% breakthrough of formaldehyde after 8-hour of exposure. Therefore, actual dermal exposure would be zero even in the case of exposure to gloves. Lastly, as an added precaution, if exposure does occur, employees are required to enter a safety shower immediately. All this information was available to EPA and should have been considered in the draft risk evaluation.

EPA's conservative approach may be appropriate for a Tier 1 screening level assessment. However, in cases where EPA uses overly conservative assumptions and finds potential risks, such as in the example above, EPA makes no effort to refine its inputs and results. This is inconsistent with EPA guidance and best practices. For example, for "Processing as a reactant. Manufacturing of basic chemicals," EPA uses this one COU to represent a number of tasks such as collecting samples, changing filters, and connecting/disconnecting railcars for both dermal and inhalation exposures. EPA grouped all the monitoring data for these diverse tasks into one set of exposure concentrations.[160] The tasks mentioned above represent different activity times, exposure conditions, frequency, etc., and grouping all the monitoring data to represent all these tasks provides a gross overestimation of exposure. While this would be fine if the risk evaluation passed with acceptable MOEs, in this case it did not. Therefore, EPA should refine the risk evaluation to break out the tasks and determine where there is a potential risk. This additional analysis is necessary to have a full understanding of the risks and for industry to properly inform EPA's assessment of operations.

An additional independent evaluation of EPA's dermal exposure assessment was also provided by Insight Exposure & Risk Sciences Group.[161] This evaluation found that it was difficult to clearly identify EPA's decision-making as to which OES exposure assessment results were used in the ultimate risk characterization and risk determination for certain mapped COUs and also

[160] EPA, *Draft Occupational Exposure Assessment for Formaldehyde*, Mar. 2024, See Table 4-8, page 50, available at: https://www.regulations.gov/document/EPA-HQ-OPPT-2023-0613-0023.
[161] See Comments submitted to the SACC, May 2024, from Paul DeLeo (ACC) regarding *Review and Analysis of Dermal Exposure Assessment Approaches Used in the EPA TSCA Risk Evaluation for Formaldehyde*, Insight Exposure & Risk Sciences Group, May 8, 2024, available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.

recommended that EPA use a flux-based approach for dermal exposure assessment.[162] Importantly, Insight Exposure & Risk Sciences Group recommended that EPA follow its guidance on applying a tiered approach to exposure and risk assessment and use an approach which is more refined and goes beyond the "screening-level, generic approaches" used in the assessment.[163] Additional comments on the dermal exposure assessment, including recommendations for improving the default values for dermal loading, for providing a distributional analysis for weight fractions, and for conducting an uncertainty analysis are also in the comments from Insight Exposure & Risk Sciences Group.[164]

Finally, as discussed earlier in these comments, we have significant concerns with EPA relying on the Krzyzanowski et al. 1990 study for the occupational value. Please see additional comments from Renee Kalmes, CIH, who describes in further detail why the study is methodologically deficient for evaluating occupational health risks and why the application of a breathing rate adjustment is unnecessary and inconsistent with EPA standard practice.[165]

VII. The Consumer Exposure Assessment in the Draft Risk Evaluation Is Overly Conservative (charge questions 4.1 - 4.3)

For consumer exposures, EPA used the Consumer Exposure Model (CEM). As described in comments from Dr. Salthammer, EPA's model is suitable for a worst-case analysis which estimates theoretically achievable maximum concentrations.[166] EPA used many simplifying assumptions, including using a reference room which does not take into account sink effects or the aging of materials; thus the modeled values will be much higher than actual measured concentrations. Instead, in order to provide a more accurate prediction of exposures, EPA should use a full mass balance equation, as was done in Salthammer 2019.[167]

It is unclear how EPA can find that there is a high level of certainty for the contributions of many consumer COUs to an unreasonable risk finding. This is due to the conservatism in the CEM model, as described above, as well as other conservatism in EPA's approach. For the dermal and inhalation exposures, EPA used the maximum percent rate of formaldehyde in products and has not provided any discussion or justification for this choice. For instance, for the toys, playground, and sporting equipment category, as well as other categories, EPA assumed that there is 30% formaldehyde in these solid objects.[168] EPA has not explained how this is reasonable or realistic. For example, EPA's assumption that some solid rubber and plastic products contain 30% free formaldehyde should have been a red flag that highlighted that mistaken inputs were being used. The 30% assumption appears to be based on outdated Chemical Data Reporting (CDR) entries. Further, the CDR dropdown entry for this category is 1

[162] *Id*.
[163] *Id*.
[164] *Id*.
[165] *See* Comments submitted to the SACC, May 2024, from Renee Kalmes and Dr. Pamela Dopart (E[x]ponent), available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.
[166] See comments submitted to the SACC, May 2024, from Dr. Tunga Salthammer (Fraunhofer WKI), available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.
[167] Salthammer, T., *Formaldehyde sources, formaldehyde concentrations and air ex-change rates in European housings*, 2019, Building and Environment 150, 219-232.
[168] EPA, *19. Consumer Modelling Supplement A*, Mar. 2024, at "% weight" tab, available at: 19. Formaldehyde Draft RE Consumer Modeling Supplement A Public Release March 2024.

– 30%, which is an example that the CDR is not an appropriate best science information source for this evaluation. Even if CDR was an appropriate place to derive these modeling parameters, EPA should use updated information from 2020 or 2024.

In many cases, EPA does not fully describe how these percent weight formaldehyde values were obtained.[169] For some categories, it appears EPA has relied on a single SDS, or decade-old CDR from single sites, rather than the required weight of the evidence approach that considers all the available data. If there is variability in products, or types of products within a COU, EPA must account for this because, while one product might contribute to an unreasonable risk, another product, that has a different percent formaldehyde, may not contribute to unreasonable risk. EPA has an obligation in the risk evaluation to be transparent regarding which products would be acceptable and which would not be. Instead, EPA uses a worst-case scenario and deems this scenario representative of entire product categories. EPA also relies on an outdated database to retrieve product SDS's, instead of relying on Smart Label, which provides more recent product data.[170] EPA's approach is not consistent with best available science or reasonably available information for many of the consumer products evaluated.

EPA's thin-film model for consumer dermal exposures uses a Qu value of 10.3 mg/cm^3. This is derived from a mineral oil immersion test retention study that does not consider drying/wiping of hands. And, of all the vehicles tested, EPA chose to use mineral oil, not because it was representative, but because it yielded the highest level of liquid retained on the surface of the hands after immersion. This Qu thus likely overestimates dermal loading for many COUs because it was calculated assuming the "worst case" oil-based formulation, while most formaldehyde products are likely water-based and would also be far more volatile than the substances studied by EPA in the 1992 report which is relied upon. As many consumer products are water based, it is not appropriate to assume that all consumer products are mineral oil-based, leading to higher exposures than would be expected. In addition, while the CEM model assumes there is product on the palms of both hands, the thin-film model used for consumer exposures appears to assume the product is in contact with the entire surface area of two hands. This assumption is not realistic.

Significantly, both the CEM model and the thin-film model ignore the fact that formaldehyde emissions in products decrease over time. For wood products, this concept of "decay" is well accepted. Due to decay, many products emit decreasing amounts of formaldehyde over time, and, because the models used simply ignore this parameter, they will significantly overestimate exposures. A detailed discussion of decay in wood products is provided in comments provided to the SACC by the Composite Panel Association.[171] EPA at a minimum must provide a sensitivity analysis to evaluate the impact of decay on the modeling results.

For all consumer exposure scenarios, EPA selected the "stay-at-home" activity pattern for CEMs inhalation model. This extremely conservative option does not represent a real-world scenario,

[169] For additional comments on uncertainties for other categories of products, see comments submitted to the SACC from Integral Consulting, May 2024, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.
[170] EPA appears to be using the EPA CPDat/ChemExpo database which houses SDSs. However, this database does not extract SDS's from Smart Label, which is the current industry standard.
[171] See comments submitted to the SACC, May 2024, from the Composite Panel Association, available at https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613

particularly for the chronic exposure assessment. It assumes that the user and bystander are in the home for 20-21 hours per day (depending on product use location at the start time of 9 a.m.), every day, throughout the entire use day for acute exposures and the entire 60 days of modeling for chronic exposures. This leads to a significant overestimate of exposure for most product applications. Even a part-time activity pattern would provide a more realistic, yet still highly conservative, estimate of exposure.

EPA also does not present any findings for the average or most typically used weight percentage of formaldehyde in each product. Without additional detail it is impossible to determine if EPA's conclusions would be different if it had used typical, not worst-case, values. It is also unclear why EPA chose to use scenarios that yielded the highest exposures as "representative scenarios."[172] EPA used a similar approach for inhalation risks, again using the highest exposure scenarios as "representative scenarios."[173] This approach of presenting only the worst-case scenario is not consistent with EPA's presentation of the exposure analysis for other chemicals which have been evaluated under TSCA.[174] Additionally, EPA assumes that all the formaldehyde is present in the product as free unreacted formaldehyde. As formaldehyde is often used in products as a reactant, this assumption leads to large overestimates in the amount of available formaldehyde. The Draft Formaldehyde Risk Evaluation provides no substantive discussion of the assumption to treat all formaldehyde as unreacted and available.

Importantly, a notable omission from EPA's modeling is the effect that physical barriers in products have on reducing emissions of formaldehyde, impacting both dermal and inhalation exposures. For instance, wood panels are rarely used without some form of finish, laminate, painting, or coating. These finishes and coatings impact formaldehyde releases because laminates and surface coatings physically impede diffusion, with effectiveness dependent on the porosity or permeability of the coverings. For example, it has been found that some coatings reduce emissions more that 80-95%.[175] Yet EPA's exposure models have no consideration of the impact of physical barriers. EPA should have integrated available information from other parts of EPA which provides important information that informs product composition and formaldehyde content.[176] EPA has also failed to incorporate insights from other federal programs that have

[172] EPA, *20. Consumer Acute Dermal Risk Calculator*, Mar. 2024, at "read me" tab, available at: 20. Formaldehyde Draft RE Consumer Acute Dermal Risk Calculator Supplement B Public Release March 2024.
[173] EPA, *21. Consumer Indoor Acute and Chronic Inhalation Risk Calculator*, Mar. 2024, at "read me" tab, available at: 21. Formaldehyde Draft RE Consumer Indoor Air Acute and Chronic Inhalation Risk Calculator Supplement B Public Release March 2024.
[174] See for instance, EPA's Risk Evaluation for Perchloroethylene (2020), where EPA's main report presented multiple scenarios for each consumer use.
[175] Composite Panel Association, *VOC Emission Barrier Effects of Laminates, Overlays and Coatings for Particleboard, Medium Density Fiberboard (MDF) and Hardboard*, 2023. (Reprint of 2003 edition), available at: https://www.compositepanel.org/wp-content/uploads/23-CPA-0072_Print_Technical-Bulletin_4_VOC-Emission-Barrier_FINAL-2.pdf.
[176] *See* for example, EPA's 2023 rulemaking (National Emissions Standards for Hazardous Air Pollutants for the Plywood and Composite Wood Products Sector), where EPA determined that nearly all amino-phenolic resin, which constitutes at least half of all formaldehyde used in the U.S., contain less than 0.1% percent formaldehyde, available at: https://www.regulations.gov/document/EPA-HQ-OAR-2016-0243-0420 and additional information provided to EPA in 2023, available at: https://www.regulations.gov/document/EPA-HQ-OAR-2016-0243-0409.

established *de minimis* levels for product formaldehyde standards due to the dearth of products containing higher levels.[177]

The largest uncertainties in EPA's consumer modeling hazard assessment comes from EPA's choice of the hazard points of departure as discussed earlier in these comments. However, as described in this section, there are also important uncertainties due to EPA's choice of using the highest exposure scenarios as "representative scenarios" and other conservatisms in the consumer exposure assessment, including for instance the lack of consideration of physical barriers and decay. EPA should redo the analysis and instead, as required by EPA's Risk Characterization Handbook[178] and consistent with the TSCA standards, provide a robust analysis that is representative of actual exposures. EPA's analysis is a worst-case analysis, not an analysis representative of best available science.

VIII. EPA's Evaluation of Indoor and Ambient Air Is Overly Conservative

A. Indoor air general population evaluation (charge questions 5.1 - 5.4)

Although the Draft Formaldehyde Risk Evaluation considered indoor air levels as a comparator when determining whether a COU presented a "high level of certainty" or "less certainty" in the COU's contribution to unreasonable risk, to understand general population risks EPA also assessed whether indoor air and ambient air contribute to unreasonable risk for the general population.

EPA's indoor air evaluation modeled four specific COUs:

- Construction and building materials covering large surface areas, including wood articles; construction and building materials covering large surface areas, including paper articles; metal articles; stone, plaster, cement, glass, and ceramic articles
- Fabric, textile, and leather products not covered elsewhere
- Floor coverings; foam seating and bedding products; cleaning and furniture care products; furniture and furnishings including stone, plaster, cement, glass, and ceramic articles; metal articles; or rubber articles
- Paper products; plastic and rubber products; toys, playground, and sporting equipment

For each of the COUs assessed, EPA states the confidence in the modeling is "medium," and that confidence is decreased because of the inability to account for half-life in the modeled exposure estimates. EPA notes that applicability of the model results to assess indoor air exposures to formaldehyde is also medium confidence.[179] Even in the charge questions provided, EPA

[177] *See* EPA reporting requirements of section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA) (aka Toxics Release Inventory) (0.1 percent); OSHA Hazard Communication Standard (0.1 percent); CPSC sensitizer substance requirements under Federal Hazardous Substance Act (1.0 percent).
[178] EPA, *Risk Characterization Handbook*, 2001, at page 37, available at: https://www.epa.gov/risk/risk-characterization-handbook.
[179] EPA, *Human Health Risk Assessment of the Draft Risk Evaluation of Formaldehyde*, Mar. 2024, at page 96, available at: https://www.regulations.gov/document/EPA-HQ-OPPT-2023-0613-0022.

acknowledges that "relatively high emission rate and persistence (rather than temporary transient emissions)" were used to model the COUs.[180] EPA appropriately finds that none of these COUs contribute to unreasonable risk to the general population as shown in table 2.2 of the *Unreasonable Risk Determination* chapter of the Draft Assessment.

Charge questions 5.1 - 5.3 seek comment on the exposure assessment and the modeling EPA conducted for the indoor air scenario. As noted above, EPA recognizes the conservative nature of the modeling approach. This conservative approach has been confirmed by Dr. Salthammer, an international expert on indoor air emissions and the chairman of the Indoor Air Hygiene Commission of the German Federal Environment Agency.[181] EPA's inputs are overly conservative and at best representative of worst-case scenarios. We agree that it was not appropriate for EPA to quantify chronic cancer risks associated with these exposures due to the high uncertainty in the exposure estimates. Based on the exposure modeling conducted, as well as the inappropriate and overly conservative human health point of departure used, EPA should have high confidence that the four COUs evaluated do not contribute to unreasonable risk due to formaldehyde exposure.

EPA relied on the AHHS II as the most representative data set for indoor air formaldehyde levels. We agree with Dr. Salthammer that this is a well planned and well conducted study for evaluating typical residential and aggregate indoor air levels.[182] However, we are concerned that EPA is inconsistently using this data set. In the Draft Human Health Risk Assessment chapter, at page 82, EPA refers to the 95th percentile as being approximately 40 ug/m^3, while Table 3-4 in the Draft Indoor Air Assessment chapter shows the 90th percentile at 41.8 ug/m^3. Thus, the 95th percentile is likely above 42 ug/m^3. Considering the low levels at which EPA proposes to set an occupational exposure value, we recommend that EPA be more precise and consistent when using the AHHSII data.

B. Ambient outdoor air general population evaluation (charge questions 6.1 - 6.4).

1. EPA's ambient air approach excludes available information, resulting in an inaccurate assessment of non-industrial drivers of outdoor formaldehyde exposure (charge questions 6.1 – 6.4)

EPA relied on the Ambient Monitoring Technology Information Center (AMTIC) database, which includes over 30,000 samples, to characterize ambient outdoor air exposures, although these samples are limited to just over 100 sites and may be limited by geographic heterogeneity as well as inconsistent sampling timing for any long-term, national conclusions. We agree that this is a useful ambient monitoring dataset available to inform EPA's analysis. We do not agree that the monitored data allow EPA to identify the influence of specific facilities on regional air levels. Without a much more granular review of individual monitors and local sources and emission and meteorological characteristics that may influence the sample concentrations, these

[180] EPA, Charge to the Toxic Substances Control Act (TSCA) Science Advisory Committee on Chemicals (SACC): Peer Review of the 2024 Draft Risk Evaluation for Formaldehyde, Mar 2024, at charge questions 5-1.
[181] See comments submitted to the SACC from Dr. Tunga Salthammer (Fraunhofer WKI), May 2024, available at: https://www.regulations.gov/docket/EPA-HQ-OPPT-2023-0613.
[182] *Id*.

data should not be used to evaluate specific facilities. We also do not support using AMTIC to characterize indoor air concentrations and note that recent peer-reviewed literature focuses on a so-called "formaldehyde dilemma." This section outlines how secondary formaldehyde contributions, including non-industrial sources in the ambient and urban air, could negate the effects of a sole focus on primary indoor sources, especially when utilizing an unrealistically low reference value.[183]

ACC's November 2023 comments on EPA's proposed Air Emissions Reporting Requirements rule outline how EPA's National Emissions Inventory, AirToxScreen, and past determinations, as well as state environmental comments, support the overwhelming influence of biogenic, fire, and secondary sources (and the insignificance of industrial sources or "TSCA uses") for ambient formaldehyde concentrations. While generally lower than some indoor levels, these outdoor levels drive "non-TSCA" sources and may be at or above levels of "unreasonable risk" given EPA's draft OEV of 11 ppb. These comments also note studies that find disagreement between ambient formaldehyde concentrations through ground-based observations, satellite measurements, and modeled results.[184]

Charge question 6.1 asks reviewers to comment "on the extent to which the WOSE narrative is supported by current outdoor ambient air monitoring information for formaldehyde." EPA states that it has high confidence in the overall characterization of ambient air exposures, and it also acknowledges that its "conservative assumptions and default model inputs may be viewed as a limitation and uncertainty."[185] EPA also determines that the findings "are not overly conservative and generally represent a more health protective, yet still realistic exposure."[186] Consistent with EPA's Risk Characterization Handbook, EPA should strive to present a best or central estimate, while acknowledging the primary drivers of these ambient air formaldehyde concentrations.[187]

EPA also asks if there are ways to adjust the AMTIC data to better align it with the exposures and timeframes used for the human health points of departures. We do not support adjusting

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[183] Salthammer, Tunga. "The formaldehyde dilemma." *International journal of hygiene and environmental health* 218, no. 4 (2015): 433-436; Salthammer, Tunga. "Formaldehyde in the ambient atmosphere: from an indoor pollutant to an outdoor pollutant?" *Angewandte chemie international edition* 52, no. 12 (2013): 3320-3327; Liu, Cong, Xinyao Miao, and Jingguang Li. "Outdoor formaldehyde matters and substantially impacts indoor formaldehyde concentrations." Building and Environment158 (2019): 145-150; Qiu, Shuolin, Zirui He, Guangdong Liu, Zhen Ding, Zhongming Bu, Jianping Cao, Wenjing Ji et al. "Ambient formaldehyde concentrations in summer in 30 Chinese cities and impacts on air cleaning of built environment." *Energy and Built Environment* 5, no. 4 (2024): 493-499; Qu, Meihua, Jing Lu, and Rongqiao He. "Formaldehyde from environment." *Formaldehyde and cognition* 1 (2017): 1-19; Salthammer, Tunga. "Emerging indoor pollutants." *International Journal of Hygiene and Environmental Health* 224 (2020): 113423; Zhang, Hemiao, Zihao Zheng, Tao Yu, Cong Liu, Hua Qian, and Jingguang Li. "Seasonal and diurnal patterns of outdoor formaldehyde and impacts on indoor environments and health." *Environmental research* 205 (2022): 112550; Lin, Yaolin, Tao Huang, Wei Yang, Xiancun Hu, and Chunqing Li. "A Review on the Impact of Outdoor Environment on Indoor Thermal Environment." *Buildings* 13, no. 10 (2023): 2600.

[184] See ACC comments on EPA's proposed technical amendments to its "Revisions to the Air Emissions Reporting Requirements" (AERR) rulemaking, Nov. 17, 2023, at pages 24-25, available at: https://www.regulations.gov/comment/EPA-HQ-OAR-2004-0489-0263.

[185] EPA, *Ambient Air Exposure Assessment*, Mar. 2024, at page 32-33, available at: Formaldehyde Draft RE Ambient Air Exposure Assessment March 2024 (pdf).

[186] *Id*.

[187] EPA, *Risk Characterization Handbook*, 2001, at page 37, available at: https://www.epa.gov/risk/risk-characterization-handbook.

these data to fit them to the health effects benchmarks. Instead, as discussed in many of the comments above, EPA should take a more holistic approach and develop human health benchmarks that are representative of the fact that we are all exposed to formaldehyde 24/7, not only when using specific products or when completing specific occupational tasks. If EPA took a more integrative approach which considered available information to develop points of departure, and considered the lack of sensory irritation and other health effects at typical background exposure levels, it would not be struggling with how to contort unrealistic unreasonable risk measures (e.g., an OEV of 11 ppb) to account for background exposures.

2. HEM modeling provides a conservative assessment of community exposures (charge question 6.3)

EPA has used Human Exposure Model (HEM) to evaluate source contributions to ambient outdoor air. This model would be appropriate if EPA were using appropriate source and emissions data. However, for the modelling conducted in the Draft Risk Evaluation, EPA used unrealistic and generic source data for representing point releases, stacks, fugitive releases, and unplanned releases. This conservatism leads to an inaccurate estimate of community exposures.

3. AirToxScreen overestimates source contributions to ambient air (charge question 6.4)

In the Draft Formaldehyde Risk Evaluation, EPA used AirToxScreen data to estimate a 95th percentile of census tract concentrations from all biogenic sources to establish a baseline concentration for ambient formaldehyde concentrations not caused by humans. This was done for the purpose of comparing the biogenic contribution to total ambient formaldehyde to model-predicted concentrations of formaldehyde from anthropogenic sources. The results presented do not consider the variations in the biogenic portion of ambient formaldehyde that might be present in smaller amounts in industrialized areas or larger amounts in more rural areas. As described in comments provided by All4, the AirToxScreen impacts from point sources are likely overestimated.

The National Exposure Inventory (NEI) provides important information about the sources of formaldehyde. Fires (primarily wildfires) and natural/biogenic emissions (vegetation and soil) dominate emissions of formaldehyde in the U.S., representing 90 percent of emissions. These natural/biogenic emissions contribute nearly 2500 times more formaldehyde than industrial processes associated with chemical manufacturing. Absent from the list of top 10 sectoral sources of formaldehyde emissions are any sectors involving formaldehyde manufacturing or processing.

EPA's use of AMTIC and AirToxScreen and the development of the HEM model would also be greatly improved through direct engagement with state environmental agencies and the agency's Office of Air Quality Planning and Standards, who could provide critical understanding of underlying emissions inventories, atmospheric chemistry around biogenic/secondary formation, and risk communication. There are also a number of important limitations to the use of the 2019

AirToxScreen, including the lack of a technical support document, failure to model biogenic sources, and the absence of secondary formation from biogenic sources.[188]

IX. EPA's Evaluation of Environmental Risks Is Reasonable (charge questions 2.1 - 2.2)

EPA acknowledges that formaldehyde, either in a solution as formalin (formaldehyde, methanol, and water) or in solid as paraformaldehyde dissolves rapidly in water and reacts with most other chemicals encountered in the environment. As formaldehyde is not persistent in water and soil due to its reactivity, we agree with the finding that negligible exposure to aquatic organisms, terrestrial organisms, or humans via water and land pathways is expected. Formaldehyde is also readily degraded by wastewater treatment, and we agree that there is no concern of risks from the applications of wastewater treatment and biosolids management with regards to TSCA condition of uses.

EPA states that there is high confidence in the overall fate and transport profile of formaldehyde and paraformaldehyde. It is less confident in the overall fate and transport of the transformation products methylene glycol and poly(oxy)methylene glycol. When limited fate and transport data was available, EPA conservatively relied on physical and chemical properties to describe the expected fate and transport of the respective chemicals. While EPA recognizes that there is potential uncertainty in the precision of specific parameter values, it states that it has confidence in the overall fate and transport profile of formaldehyde. We find that, to ensure that uncertainties are addressed and considered, the agency is overly conservative with regard to formaldehyde in the environment and likely overestimates the presence of formaldehyde from TSCA conditions of use.

EPA has also concluded that there is no risk to terrestrial organisms through soil exposures is anticipated due to formaldehyde because it does not persist in or on land and exposure is also not anticipated. Similarly, EPA concluded that there is no risk to terrestrial mammals, and other terrestrial taxa, through inhalation as air concentrations are at least an order of magnitude lower than the most sensitive toxicity values. We agree with EPA's analyses and conclusions and support the finding that there is also no risk to environmental or human receptors through exposure these pathways.

X. EPA's Qualitative Approach to Aggregate Exposures Is Reasonable (charge questions 7.1 - 7.2)

To evaluate combined exposures, EPA considered numerous data sources including AMTIC monitoring data, AirToxScreen modeling, HEM risk modeling, and the Integrated Indoor/Outdoor Air Calculator Model (IIOAC). EPA concluded that there is too much uncertainty in the individual analyses underlying exposure and risks from individual pathways to support a quantitative aggregate analysis.[189] We also agree that there is significant uncertainty in

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[188] https://www.epa.gov/AirToxScreen/airtoxscreen-technical-support-document; https://www.epa.gov/system/files/documents/2023-02/AirToxScreen_2018%20TSD.pdf (p. 25, a-2); https://www.epa.gov/system/files/documents/2023-02/AirToxScreen_2018%20TSD.pdf (p. a-2); https://www.epa.gov/AirToxScreen/airtoxscreen-assessment-methods.

[189] EPA, *Draft Human Health Risk Assessment for Formaldehyde*, Mar. 2024, at page 112, available at: Formaldehyde Draft RE Human Health Risk Assessment March 2024 (pdf).

combining indoor and outdoor exposures, but, as noted above, EPA has failed to assess and integrate the latest science regarding the potential limitations of indoor/occupationally focused risk management particularly with unachievably low exposure values.

XI. Formaldehyde Is a Perfect Example of Why EPA's "Whole Chemical" Approach Is Flawed and a Disservice to Public Health

The 2017 Risk Evaluation Framework Rule, the procedural regulation under which the Draft Formaldehyde Risk Evaluation was developed, requires that as part of the risk evaluation EPA determine whether the chemical substance presents an unreasonable risk of injury to health or the environment under each condition of use.[190] This approach provides all stakeholders, including chemical users and state and local regulators, with clarity regarding which specific uses of a chemical are of concern and which are not. Instead, in the Draft Formaldehyde Risk Evaluation, EPA uses an approach referred to as the "whole chemical approach," where EPA makes a single risk determination for the chemical disregarding whether any individual use may or may not present an unreasonable risk. EPA explicitly said that it would apply procedures from the 2017 Framework Rule to the formaldehyde risk evaluation. Based on EPA's representation, the Formaldehyde Panel relied on EPA's 2017 interpretation of the statute during its participation and engagement with SACC and EPA. In addition to EPA's single unreasonable risk determination approach upending the reasonably settled expectations of the Formaldehyde Panel, the single determination approach is not fit for purpose for the formaldehyde evaluation and is inconsistent with the statute because it reads out of the statute "under" the conditions of use and replaces it with "based" on the conditions of use. The single determination approach is also incompatible with Congressional intent that EPA focus its analytical efforts on conditions of use that raise the greatest potential for risk within TSCA's strict deadlines.

In addition to not being consistent with the statute, EPA's approach lacks clarity and utility. EPA states that "formaldehyde presents an unreasonable risk of injury to human health under the COUs."[191] But EPA does not clarify which COUs actually present an unreasonable risk. Instead EPA describes which of those COUs "contributes to unreasonable risk."[192] EPA describes COUs where the agency has a "high level of certainty" and "less certainty" regarding the "contribution to" unreasonable risk, but there is no clarity regarding whether or not a single COU that contributes to unreasonable risk, regardless of the level of certainty, is actually causing an unreasonable risk.

As EPA states on its website, consistent with the 2017 Framework Rule,[193] there are only two outcomes for a condition of use that is undergoing risk evaluation. EPA must determine whether there is "unreasonable risk" or "no unreasonable risk." Instead, for each COU in the Draft Formaldehyde Risk Evaluation, the public only knows which COUs "contribute to" unreasonable risk. EPA provides no explanation of what it means to "contribute to" unreasonable risk, and there is no clarity regarding which individual COUs actually lead to an unreasonable risk.

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[190] 40 C.F.R. § 702.47.
[191] EPA, *Unreasonable Risk Determination of the Draft Risk Evaluation for Formaldehyde*, Mar. 2024, at page 4, available at: https://www.regulations.gov/document/EPA-HQ-OPPT-2023-0613-0046.
[192] *Id*.
[193] 82 Fed. Reg. 33752 and EPA website at: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/risk-evaluations-existing-chemicals-under-tsca.

Furthermore, as noted in comments above (see section V), while EPA describes the risk-related factors that it considers when making an unreasonable risk determination, it provides no framework for understanding how it reached its conclusions regarding its unreasonable risk determination for the chemical or its individual determinations of contributions to unreasonable risk for the COUs.

Without transparency regarding COUs, there is no way for stakeholders to understand which COUs are actually leading to health concerns or unreasonable risks. Regardless of whether or not there is forthcoming regulation, the public is unable to make informed decisions to mitigate potential risks, and this is a disservice to public health. It surely is not what Congress intended when the Lautenberg Act was enacted in 2016. EPA has an obligation to clarify for the public which conditions of use cause unreasonable risks. EPA has not met this obligation in the Draft Formaldehyde Risk Evaluation.

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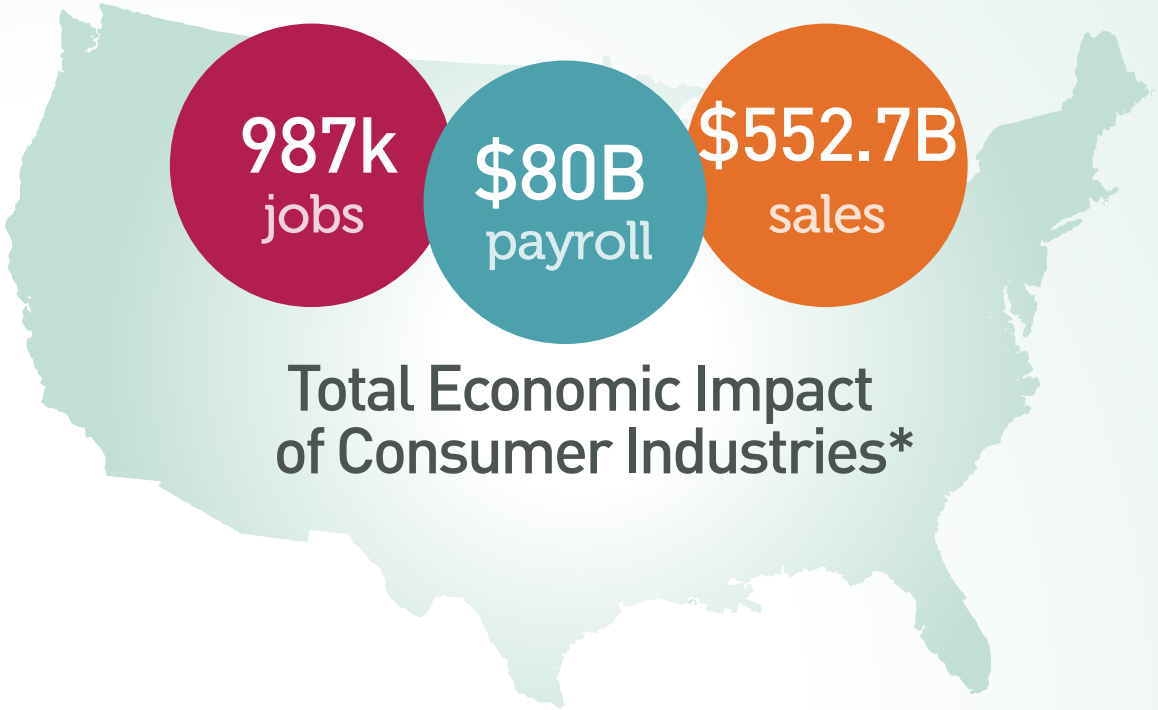
Thank you for considering our comments. Should you have any questions, please reach out to Sahar Osman-Sypher, Senior Director, Formaldehyde Panel, at sahar_osman-sypher@americanchemistry.com or 202-249-6721.

Attachment A: Summary Information on Formaldehyde Benefits and Applications

Formaldehyde Producers Boost U.S. Economy

Impact Spans Key Consumer Industries

Formaldehyde's unique and versatile chemical properties make it a common and beneficial part of modern life. From the construction industry to the automotive, aerospace and health care industries – products that are based on formaldehyde technologies have broad roles in the economy, are critical to the integrity of the supply chains, supporting 987,000 jobs and $552.7 billion in sales in 2022 in the United States.



Total Economic Impact of Consumer Industries*

Total Economic Impact

(Includes Direct Production** and Supplier Industries***)

	Construction Materials	Furniture	Light Vehicles	Other Transportation	Appliances	Industrial/ Electrical/ Machinery	Other Products
	72.9k jobs	104k jobs	225k jobs	282k jobs	197k jobs	14k jobs	142k jobs	25k jobs
	$5.7B payroll	$7.3B payroll	$12.5B payroll	$22.8B payroll	$22.1B payroll	$0.9B payroll	$11.5B payroll	$2.9B payroll
	$36.2B sales	$59.1B sales	$53.1B sales	$280.1B sales	$81.9B sales	$6.5B sales	$49.9B sales	$22.1B sales

* The use of formaldehyde and its derivatives supports economic activity throughout multiple sectors. These estimates are based on economic activity generated by businesses that use formaldehyde.

** Direct Impact: Jobs, wages, and output generated from the manufacturing of formaldehyde and derivative chemistries.

*** Indirect Impact (Supply Chain): Jobs, wages, and output created by the businesses in the supply chain that sell goods and services.

2022 data estimates from the U.S. Bureau of Labor Statistics and the U.S. Census Bureau.

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AEROSPACE APPLICATIONS

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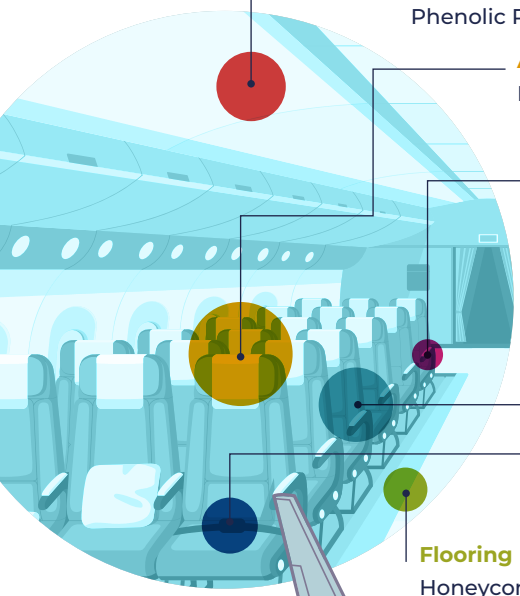


Interior Panel Structures
Phenolic Resins/ Epoxy Molding Compounds

Airplane Seats
Polyurethanes

Plastic Molding (decorative closeouts, trim strips, food trays, and arm rests):
Acrylonitrile-butadiene-styrene

Resin System:
Phenolic Resins/
Epoxy Molding Compounds

Plastic component of seatbelts
Polyurethanes

Flooring
Honeycomb material reinforced with phenolic resins

Metal Castings
Urethane/Phenolic Resins

Door Lock Systems
Polyurethanes

Door and Window Insulation
Phenolic Resins

Cargo Liner in the Luggage Area
Phenolic Resins

Fuel Additives
Alkyl Phenols, Formaldehyde Derivatives

Airplane wings
Phenolic Honeycomb

Lubricant Additives
Alkyl Phenols

Airplane Turbine Lubricant
Pentaerythritol/Neopolyol Esters

Mirrors
Polyurethanes

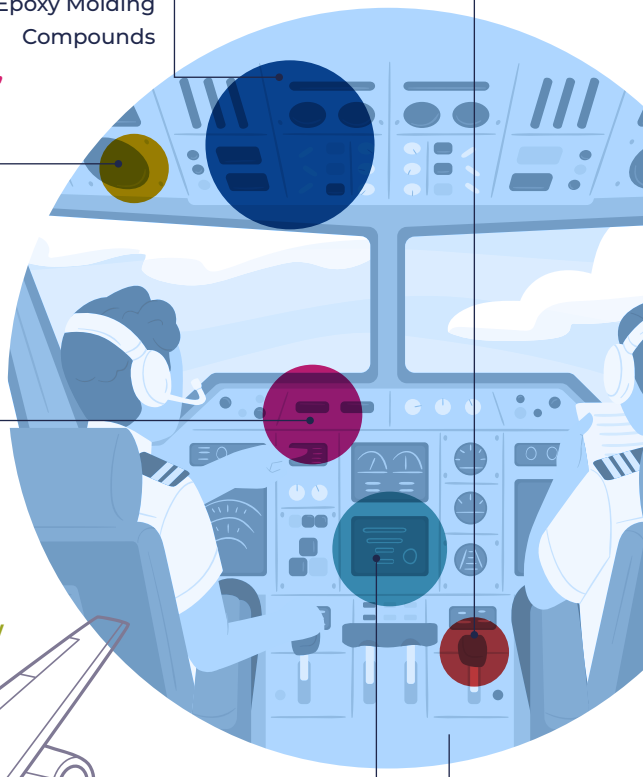
Vulcanised Rubber
Hexamine

Brake Pads
Phenolic Resins

Landing Gear Components
Phenolic Resins

Airplane Brakes
Phenol Formaldehyde Polymer

Underhood Components
Phenolic Resins/Epoxy Molding Compounds



Speaker Grills
Polyurethanes

Safety Systems:
Polyurethanes

Door Module
Polyurethanes

Auto Electrical Systems
Polyurethanes

Chemicals and polymers derived from formaldehyde are used in aerospace because of their flame resistance, thermal protection, and impact resistance. Polyurethanes are used to make polyurethane foams that provide support and comfort in airplane seats. The cabin flooring and cargo liner are made from honeycomb material reinforced with phenolic resins which provide high impact resistance. We also see a phenolic honeycomb in the wings which needs to have a higher heat resistance material because of its proximity to the engines.

Formaldehyde is essential to safety and economic stability in food, agriculture sectors

Formaldehyde is a naturally occurring substance found within human bodies and all living things, including fruits, vegetables, and meats. Across the agricultural industry, formaldehyde helps American families access safe meat, poultry, and aquaculture products.

Formaldehyde helps protect livestock against diseases capable of causing catastrophic economic losses for farming operations across the United States.

Federal agencies, including the U.S. Environmental Protection Agency, oversee formaldehyde's agricultural applications, improving safe use practices. While these conditions of use involve limited application of formaldehyde and formaldehyde-based products, these products provide critical applications for crop production, veterinary medicine, animal agriculture, and aquaculture.

American agriculture relies on formaldehyde

Egg producers rely on formaldehyde during incubation to help protect hatching eggs against bacteria like Salmonella, which can cause poor chick quality, growth, and performance and cost farmers millions of dollars. Farmers follow specific guidance on formaldehyde's concentration so it is high enough to effectively kill bacteria, yet safe enough for chick embryos.

Pork farmers use formaldehyde to reduce virus infectivity in pigs and as a barn disinfectant to protect against Salmonella. Ongoing research suggests that formaldehyde could be used in the future as an effective risk mitigation tool against the spread of African Swine Fever (ASF), one of the most dangerous diseases to pigs. This would help keep the U.S. pork industry protected against a catastrophic outbreak.

Poultry producers rely on effective disinfection methoids to ensure bird health and food safety. The safe application of formaldehyde continues to be an important disinfection tool to protect against viruses and bacteria, including Salmonella, E. coli, and staph, among others, that can present significant disease challenges greatly impacting the health and well-being of poultry.

Animal feed can become contaminated with bacteria that are capable of causing diseases. To mitigate risks, animal agriculture producers use formaldehyde-based feed additives that fight bacteria, improving healthy end-products for consumers and safe operations for animals and farm hands.

Formaldehyde-based products increase crop yields, can help optimize agricultural production worldwide while reducing runoff. Fertilizer and crop protection manufacturers rely on formaldehyde solutions, urea formaldehyde concentrate, and liquid and solid slow release nitrogen.

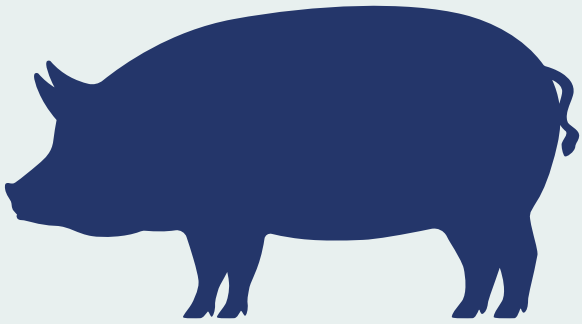
The aquaculture industry relies on formaldehyde to control fungi in finfish egg hatcheries and to treat external infections that can be incredibly deadly, like Columnaris disease, a common bacterial disease that impacts almost all finfish, including catfish, rainbow trout, tilapia, and more. As a water additive, formaldehyde helps kill parasites that impact finfish and shrimp.

Learn more: AmericanChemistry.com/formaldehyde

Scientifically unjustified regulation of formaldehyde would cost the U.S. food system billions

Formaldehyde regulations that do not consider the full body of scientific evidence could result in scientifically unjustified regulation, jeopardize the safety of critical food products, and send ripple effects across the U.S. economy.

Research suggests formaldehyde could be a risk mitigation tool against African swine fever in U.S. pork



In recent years, ASF outbreaks in China, the world's largest pork producer, have had far-reaching economic consequences, including a 20 percent drop in the country's pork output that significantly impacted global pork prices.

Estimates indicate a similar outbreak in the U.S. could decimate the U.S. pork industry, reducing live hog prices by 40 to 50 percent and resulting in nearly $50 billion in economic losses to America's farmers. Shortages caused by such an outbreak would strain the U.S. food system and dramatically raise prices for consumers.

Beyond ASF, formaldehyde helps protect against substantial, disease-induced economic losses across U.S. animal agriculture:

Poultry Production

$3.7 billion

lost to Salmonella each year.

Aquaculture

$40 to $50 million

lost to Columnaris disease each year.

Pork Production

$1.9 billion

lost to Salmonella each year.

Without formaldehyde's critical applications in these industries, losses could dramatically exceed these figures and catastrophically damage not only U.S. farmers' livelihoods but also the broader domestic economy.

For additional information, see comments from the American Veterinary Medical Association, American Feed Industry Association, National Chicken Council, National Pork Producers Council, National Turkey Federation, and U.S. Poultry & Egg Association, and Rep. Sanford Bishop (GA-02), Chairman of the House Appropriations Subcommittee on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies.

Learn more: AmericanChemistry.com/formaldehyde

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AUTOMOTIVE APPLICATIONS

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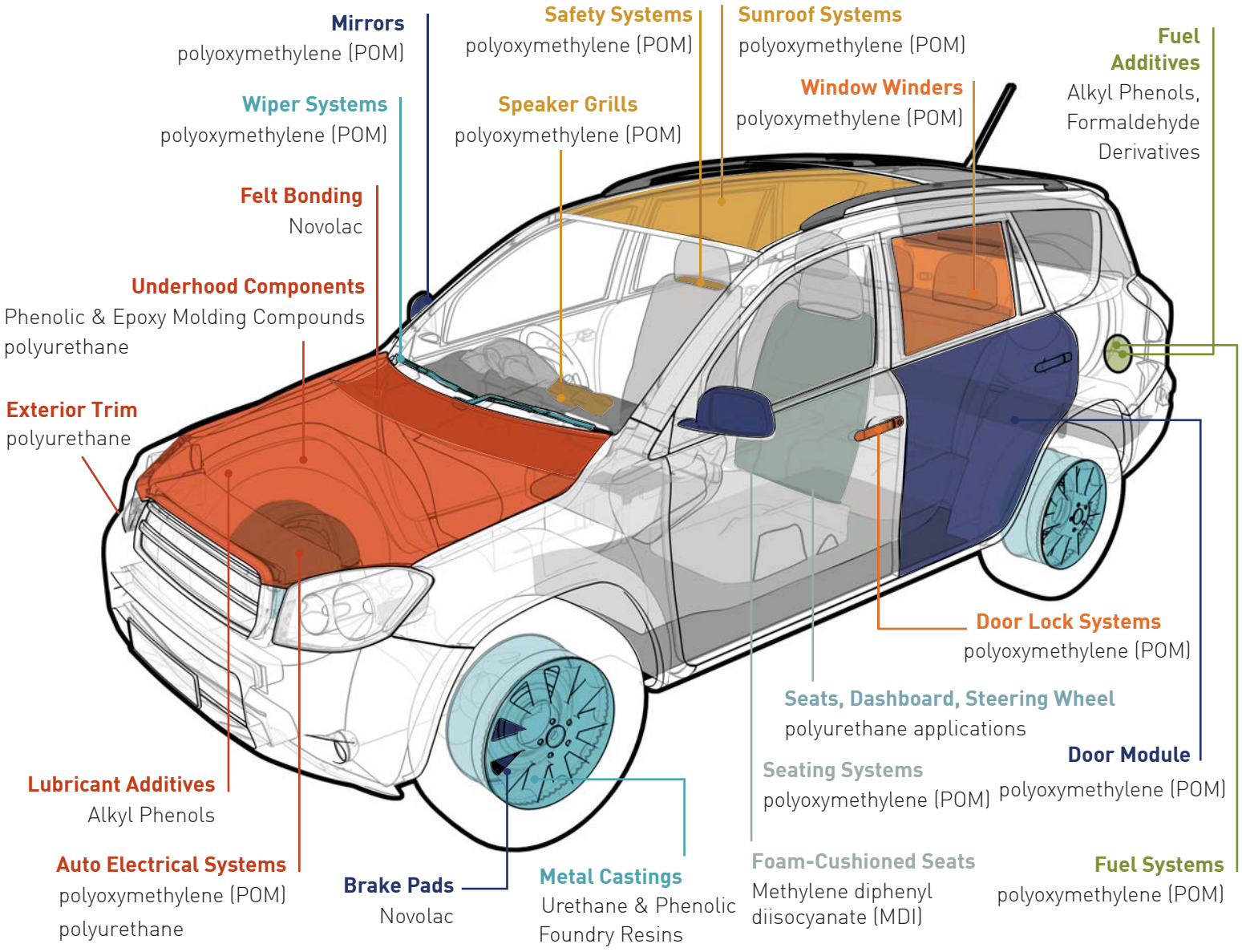

Formaldehyde Technologies Contribute to Lighter Vehicles and Higher Fuel Efficiency

In the automotive industry, formaldehyde-based technologies are used to make interior molded and under-the-hood components that allow for higher fuel efficiency by reducing vehicle weight. It is also used in the production of highly durable exterior primers, clear coat paints, tire-cord adhesives, brake pads and fuel system components.

Few compounds can replace formaldehyde as a raw material without compromising quality and performance or making the final products more expensive. While formaldehyde is an essential building block in a diverse range of products, its end use is primarily in a converted form. That means virtually all the formaldehyde is consumed in making the final product.

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FORMALDEHYDE
HOUSING APPLICATIONS

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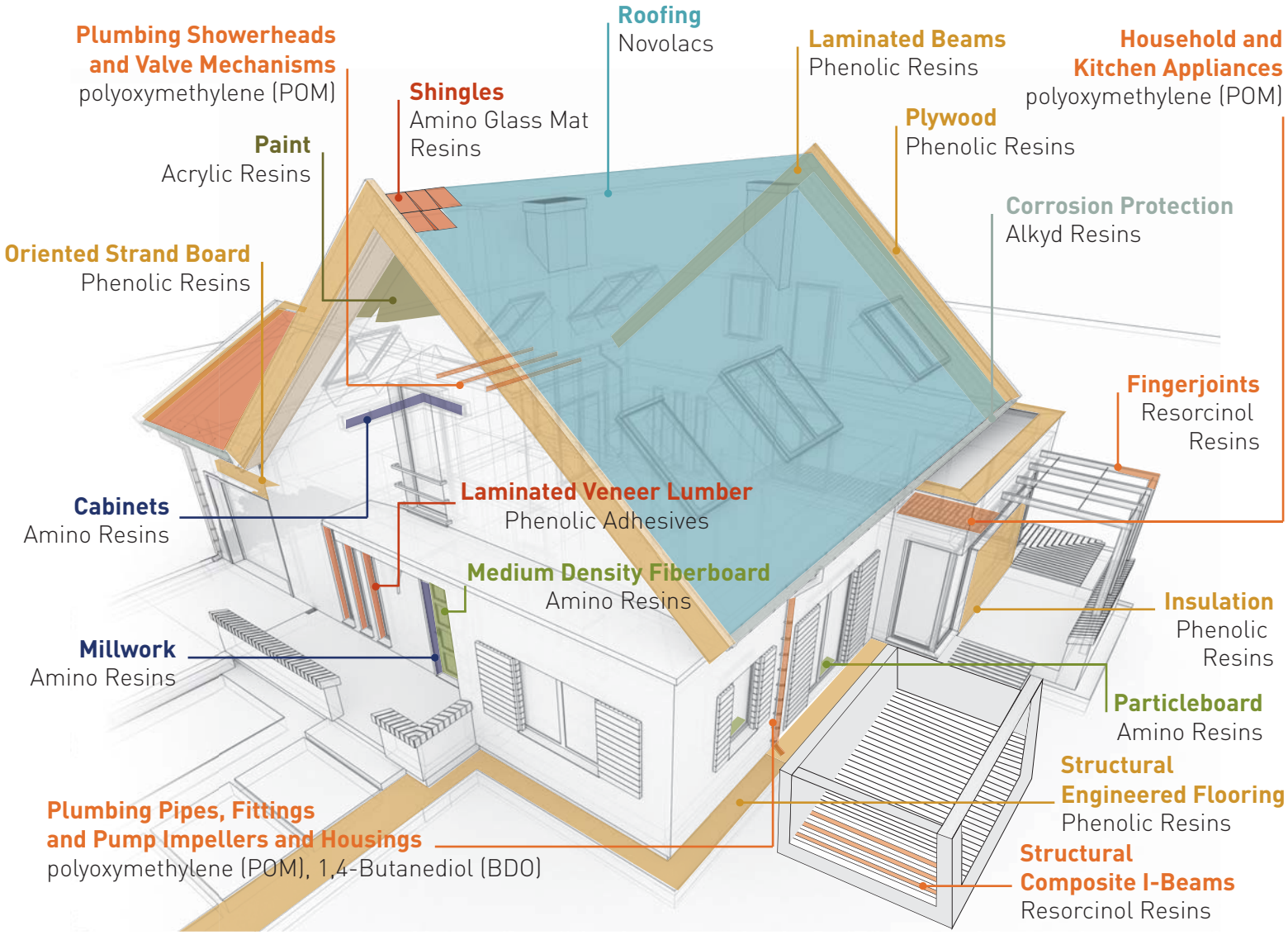


Formaldehyde Technologies Contribute to Sustainable Building Materials

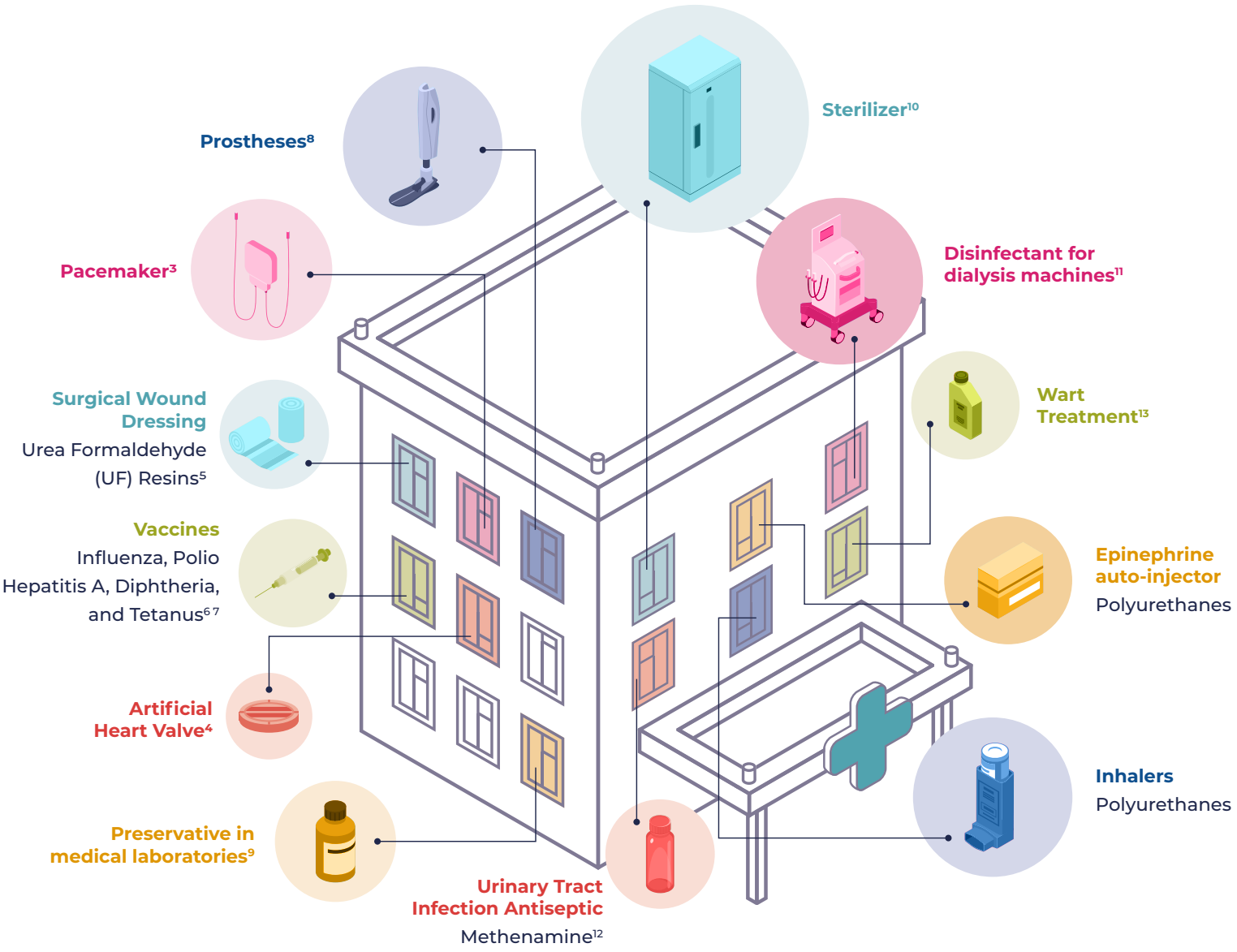
The wood-based panel industry relies heavily on the dependable performance of formaldehyde-based resins for wood products such as plywood, particleboard and fiberboard, which are used in laminated countertops, cabinets, moulding and other applications.

Formaldehyde-based resins are also used in the housing industry to make sheathing and cladding, asphalt shingles, furniture and paneling, insulation and flooring systems, as well as paints and varnishes. In addition, formaldehyde-based resins are used to make household and kitchen appliances, such as washers and dryers – and for plumbing applications, such as: plumbing pipes, fittings and pump impellers and housings; as well as showerheads, valve mechanisms for blending hot and cold water and in faucets' on/off operations.

Few compounds can replace formaldehyde as a raw material without compromising quality and performance or making the final products more expensive. While formaldehyde is an essential building block in a diverse range of products, its end use is primarily in a converted form. That means virtually all the formaldehyde is consumed in making the final product.

FORMALDEHYDE
MEDICINE & MEDICAL APPLICATIONS

American Chemistry Council



Formaldehyde and its derivatives are used early in the upstream supply chain to make compounds used in the creation of life-saving medical devices (for example: pacemakers, artificial heart valves, and prostheses). Formaldehyde is well known as a preservative in medical laboratories and its use as a sterilizer. Formaldehyde is an active ingredient in anti-infective drugs and is used in gel capsules to promote maximum absorption.[1] It is also used in the manufacture of certain viral and bacterial vaccines. For example, influenza, polio, cholera, hepatitis A, diphtheria, tetanus vaccines use formaldehyde to inactivate viruses and detoxify bacterial toxins. There are also medical research applications for formaldehyde including pharmaceutical research in proteomics and genomics.[2]

[1] Formacare

[2] Formacare

[3] ACC Formaldehyde Benefits & Applications

[4] ACC Formaldehyde Benefits & Applications

[5] S&P Global's Amino Resins Chemical Economics Handbook (30 Sep 2020)

[6] ACC Formaldehyde Benefits & Applications

[7] Formacare

[8] ACC Formaldehyde Benefits & Applications

[9] ACC Formaldehyde Benefits & Applications

[10] ACC Formaldehyde Benefits & Applications

[11] Centers for Disease Control and Prevention

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FORMALDEHYDE
NATIONAL SECURITY APPLICATIONS

American® Chemistry Council

Formaldehyde is a critical building block and an essential ingredient in producing resilient, advanced, and high-reliability products used across the United States' national security enterprise. It has a long history of safe use in the national security sector. According to Rep. Jack Bergman (MI), Chair of the House Armed Services Intelligence and Special Operations Subcommittee, "EPA... risk evaluation activities for formaldehyde.... would not only have enormous economic impacts across dozens of industries and impact the competitiveness of American manufacturers, but also threaten national security."[1]

Here are some common uses of formaldehyde in national security:

1 

Munitions/Ballistics: Formaldehyde is needed to make munitions and ballistics as well as used in the production of tires and other materials. Without the ability to produce formaldehyde domestically, the US would be forced to source it from other countries.

2 

Military Equipment: Formaldehyde-based resins are used to produce lightweight, durable equipment that can reduce carry weights by as much as 20 pounds. This reduced weight helps increase user agility and safety in accordance with the U.S. Department of Defense War Fighting Science and Technology Plan.[2]

3 

Military Uniforms: Military uniforms and gear are made with formaldehyde-based resins to enhance their durability and resistance to wear and tear, improve crease resistance, and increase the flame retardancy of military-issue textiles. Military textiles treated with formaldehyde also show improved infrared camouflage capabilities.[3]

4 

Anti-Corrosive: In military storage facilities, formaldehyde may be used as an anti-corrosive treatment to maintain equipment and vehicle readiness.

5 

Theater Military Bases: Many theater military bases utilize sustainable wood products created with formaldehyde, like plywood, particleboard, and fiberboard, to build barracks, offices, and other structures. Shipping containers used to transport these materials and build temporary base structures are also treated with formaldehyde-derived polymers.[4]

6 

Military Vehicles: In the automotive industry, formaldehyde-based technologies are used to make interior molded and under-the-hood components that allow for higher fuel efficiency by reducing vehicle weight. It is also used in the production of highly durable exterior primers, clear coat paints, tire-cord adhesives, brake pads and fuel system components.[1]

7 

Decontamination: Formalin, a solution of formaldehyde in water, is used by the military as a decontaminant to neutralize biological threats, including bacterial spores.[5]

8 

Food Supply: Outside of the U.S. Defense Department, formaldehyde also helps protect our country's food supply, which is key to our national security. It is used in the agricultural industry for various purposes including crop protection and crop nutrition products, like slow-release fertilizers, herbicides, and pesticides. Formaldehyde can also treat animal feed and help prevent salmonella and African Swine Fever.[6]

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FORMALDEHYDE
APPLICATIONS IN SCIENCE AND PRESERVATION

American Chemistry Council

Formaldehyde is a versatile chemical compound that has various applications in science and preservation across different fields. Some common uses of formaldehyde and formalin (a solution of formaldehyde in water) include:

1 Biological Research

Formaldehyde is utilized in various molecular biology techniques, including DNA and RNA cross-linking. This is crucial for studying protein-DNA interactions, chromatin structure, and gene expression. It is also used in the preparation of specimens for microscopy. It aids in preserving cell structures, allowing researchers to study cellular morphology and other characteristics.

2 Histological Exams/Microscopy

Formaldehyde is widely used to preserve biological tissues for histological examination. It works by cross-linking proteins, preventing their degradation, and maintaining the structural integrity of tissues.[1] It is considered a widely used fixation method[2] that results in low levels of shrinkage and good preservation of cellular structure for a wide range of cells and tissues and does not appear to result in significant structural changes to proteins.

3 Vaccine Production

Formaldehyde is used in the production of certain vaccines. It can inactivate toxins or viruses, rendering them non-infectious while still maintaining their ability to stimulate an immune response. This includes the flu shot, used to inoculate against seasonal flu variants which according to the CDC,[3] sickened as many as 54 million Americans in 2022-23.

4 Disinfection and Sterilization

Formaldehyde has disinfectant properties and can sterilize equipment and laboratory surfaces. According to the CDC,[4] formaldehyde is used as a disinfectant and sterilant in both its liquid and gaseous states. The aqueous solution is a bactericide, tuberculocide, fungicide, virucide, and sporicide. It helps in preventing the spread of contaminants and ensuring aseptic conditions.

5 Taxidermy

Taxidermy preserves elements of an animal for study or display after the animal has died.[5] Formaldehyde or formalin is preferred for injecting and fixing specimens whenever possible. It effectively preserves the tissues, preventing decomposition and maintaining the lifelike appearance of the taxidermy specimen over time. Its properties make it an ideal fixative for taxidermists aiming to create long-lasting and high quality displays.[6]

6 Preservation of Zoology Specimens in Museums

In museum collections, it is common for zoology specimens to be preserved in a formaldehyde and water solution known as formalin. For example, at the Florida Museum of Natural History's Division of Ichthyology, fish specimens are fixed by immersion in a solution of 10% formalin.[7]

FORMALDEHYDE
APPLICATIONS IN SCIENCE AND PRESERVATION

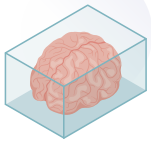
American® Chemistry Council

7

Preservation of Botanical Specimens

Most plants will deteriorate after two or three days if they are not dried or preserved in some fashion. If they are refrigerated, they can be kept a day or two longer. According to the Missouri Botanical Garden,[8] a 30% formaldehyde solution is used to help preserve specimens before drying. Preserved plant specimens provide us with important information about plant diversity and distribution.[9]

8



Anatomical and Forensic Studies

Formaldehyde is used for embalming and preserving cadavers such as bodies donated for science. During an autopsy,[10] formaldehyde solution is used to determine if the person was breathing at the time of death. This process helps in studying anatomy, conducting medical research, and forensic investigations.[11]

9

Funeral Services

Formaldehyde is still the primary preservative in the majority of embalming fluids today and is preferred by funeral service professionals due to its ability to accomplish the three primary purposes of embalming: preservation, sanitation, and presentation of human remains to families. Formaldehyde use is essential for veterans where the current wait time for the burial at Arlington National Cemetery or national cemeteries can be up to and over six months. There are no other known preservatives that would work appropriately for this length of time. Also, some northern states like Maine are unable to do ground burials during the winter months so some deceased must be embalmed. This allows mourners to pay their last respects and say their goodbyes while the body is still preserved.

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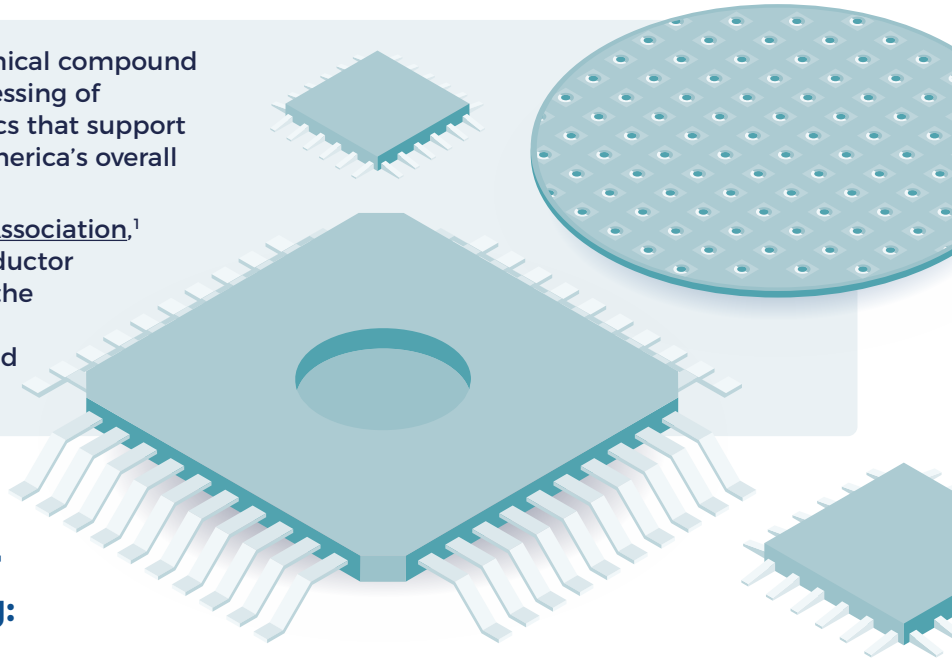
FORMALDEHYDE
SEMICONDUCTORS

American® Chemistry Council

Formaldehyde is a naturally occurring chemical compound that is vital to the manufacturing and processing of semiconductors found in modern electronics that support virtually all aspects of our daily lives and America's overall economy.

According to the Semiconductor Industry Association,[1] the U.S. is the global leader in the semiconductor sector. Our continued leadership is vital to the success of industries including IT, telecommunications, healthcare, energy, and national defense.



Key formaldehyde applications in semiconductor manufacturing and processing:

1. **Surface Coatings:** Formaldehyde is used in the surface coating of metal-semiconductor products.[2]
2. **Photoresist Stripping:** Formaldehyde is used to strip photoresist, a light-sensitive material used to create semiconductor wafer patterns, from final products.
3. **Mold/Surface Cleaning:** Formaldehyde helps remove organic and inorganic contaminants from the wafer's surface, ensuring that the semiconductor's performance is not compromised.
4. **Anti-Corrosion:** Formaldehyde can be used to protect semiconductor devices from environmental factors and prevent corrosion.[3]
5. **Energy Conversion:** Formaldehyde-based resins can act as efficient, metal-free semiconductor photocatalysts for solar-to-hydrogen peroxide energy conversion.[4]
6. **Adhesives and Thermal Management:** Formaldehyde-based adhesives help bond semiconductor chips to their packages and provide thermal management.[5]
7. **Wafer Metallization:** Formaldehyde may be contained in electroless copper plating used to connect a finished chip to a substrate, circuit board, or another semiconductor chip.

The use of formaldehyde in semiconductor plating and lithography resins is considered an industry standard, and it is widely used by manufacturers around the globe. It is important to note that formaldehyde does not remain in finished semiconductor products in the U.S.

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