February 2, 2026

**Comments from Scientists, Academics, and Clinicians on the Updated Draft Risk Calculation Memorandum for Formaldehyde Under TSCA**

***Submitted online via Regulations.gov to docket EPA-HQ-OPPT- 2018-0438-0240***

These comments are submitted on behalf of the undersigned scientists, academics, and clinicians. We declare that we have no direct or indirect financial or fiduciary interests in the subjects of these comments. The co-signers' institutional affiliations are included for identification purposes only and do not imply institutional endorsement or support.

We appreciate the opportunity to provide written comments on EPA's proposed revisions to the Formaldehyde Risk Evaluation, including the Formaldehyde Updated Draft Risk Calculation Memorandum, the Revised Draft Human Health Hazard Assessment for Formaldehyde, and the Revised Draft Unreasonable Risk Determination of the Risk Evaluation for Formaldehyde (collectively, the "Proposed Revisions") conducted under the Toxic Substances Control Act (TSCA). TSCA requires EPA to evaluate chemical risks using the "best available science"[1] and "to determine whether a chemical presents an unreasonable risk of injury to health or the environment, without consideration of costs."[2]

Formaldehyde is a well-established human carcinogen,[3] and more than one billion pounds of formaldehyde[4] are manufactured in the US for use in composite wood products, plastics, paints, adhesives, and sealants. Formaldehyde is also formed in the atmosphere through the degradation of precursor chemicals originating from petrochemical production, fossil fuels combustion, and biogenic sources. As a result, people are routinely exposed to formaldehyde in their workplaces, homes, and through ambient air from releases associated with its manufacture, processing and use.

In a 2024 Toxicological Review, EPA's Integrated Risk Information System (IRIS) Program identified multiple non-cancer health effects associated with formaldehyde exposure, including sensory irritation, respiratory tract pathology, decreased lung function, asthma and allergic conditions, as well as reproductive and developmental effects.[5] These findings reflect a robust and systematic evaluation of the scientific literature, and formed part of the basis for hazard and risk determinations in EPA's December 2024 Final Risk Evaluation for Formaldehyde ("Final Formaldehyde Risk Evaluation").[6]

However, the Proposed Revisions represent a profound departure from the scientific findings and risk conclusions in the Final Formaldehyde Risk Evaluation. Instead, the Proposed Revisions dismantle core components of EPA's risk assessment framework and propose approaches to

[1] 15 USC §2625(h).
[2] 15 U.S.C. § 2605(b)(4)(A)
[3] International Agency for Research on Cancer (June 2004). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 88 (2006): Formaldehyde, 2-Butoxyethanol and 1-tert-Butoxypropan-2-ol.
[4] U.S. EPA (2024). Final Scope of the Risk Evaluation for Formaldehyde, p. 34.
[5] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation).
[6] U.S. EPA (2024). Human Health Risk Assessment for Formaldehyde.

hazard and risk assessment that would severely underestimate human health risk. For the first time under the amended TSCA, EPA proposes to disregard well-established best available scientific evidence demonstrating that formaldehyde causes cancer and instead adopts a threshold-based approach that assumes zero cancer risk below a certain exposure level. This approach directly conflicts with longstanding, evidence-based conclusions by authoritative scientific bodies, including EPA's IRIS Program and the National Academies of Sciences. Engineering, and Medicine (NASEM), especially for chemicals like formaldehyde for which a mutagenic mode of action has been established.

EPA further proposes to dismiss quantitative cancer risk assessment of formaldehyde altogether, asserting that a single measure of acute sensory irritation is protective of all other health effects, including cancer. This assertion is inconsistent with the well-established scientific record. Formaldehyde's carcinogenicity has been evaluated and affirmed by multiple authoritative bodies, including IRIS, NASEM, the National Toxicology Program (NTP), and the International Agency for Research on Cancer (IARC), all of which have established a causal relationship between formaldehyde exposure and certain cancers. Disregarding this evidence and eliminating cancer risk characterization for formaldehyde is inconsistent with the best available science and undermines TSCA's core public-health protections.

In addition, EPA proposes to narrow the entire human health risk assessment—across acute and chronic exposures and across all populations evaluated (including workers, consumers, the general population, and potentially exposed or susceptible subpopulations)--to reliance on a single study. EPA asserts that a single point of departure derived from one study of acute inhalation sensory irritation is sufficient to characterize risk for all exposure durations and all populations. EPA also proposes to eliminate the intraspecies uncertainty factor intended to account for variability in response to formaldehyde exposure across the human population. Together, these changes would significantly weaken health protections and represent an unprecedented departure from established EPA risk assessment practice.

EPA has not provided an evidence-based justification for these sweeping changes. Instead, EPA selectively relies on opinions expressed by certain members of its *ad hoc* Science Advisory Committee on Chemicals (SACC) for formaldehyde, a committee with representatives that had clear financial conflicts of interest, including members with direct ties to the American Chemistry Council. Our review indicates that the specific SACC positions EPA relies upon closely mirror arguments advanced by the chemical industry and trade associations representing formaldehyde producers and users, rather than the broader scientific literature or input from academic experts, public health professionals, or affected communities.

If finalized, the Proposed Revisions would substantially underestimate the risks posed by formaldehyde and would set a dangerous precedent for future TSCA risk evaluations by allowing EPA to disregard well-established carcinogenic hazards, collapse a complex spectrum of human health hazards into a single acute endpoint, and eliminate long-standing protections for variability and susceptibility in the human population. Such an outcome would be fundamentally inconsistent with TSCA's statutory mandate to protect public health using the best available science.

Our detailed comments address the following issues:

a. **EPA's proposed adoption of a threshold approach to characterizing carcinogenic risks is not scientifically justified and is inconsistent with the requirements of TSCA to use reasonably available information and the best available science.**
    a. **EPA ignored strong evidence that formaldehyde causes cancer by a mutagenic mode of action (MOA).**
        i. **Formaldehyde is genotoxic.**
        ii. **Formaldehyde induces upper respiratory tract (URT) tumors by a mutagenic mode of action (MOA).**
    b. **EPA disregards evidence undermining its position regarding a cytotoxicity mode of action (MOA) for carcinogenicity.**
    c. **EPA ignored findings of the National Academies regarding the IRIS mode of action analysis and inhalation unit risk for formaldehyde upper-respiratory tract tumors.**
    d. **EPA's Proposed Revisions rely on opinions expressed in a report by the Science Advisory Committee on Chemicals (SACC), but the SACC did not conduct a comprehensive review of the reasonably available information concerning formaldehyde's carcinogenic mode of action (MOA).**
    e. **EPA's Proposed Revisions ignore EPA's own Guidelines for Carcinogen Risk Assessment.**
    f. **EPA should continue to use the inhalation unit risk (IUR) derived by IRIS for nasopharyngeal cancers in the Final Formaldehyde Risk Evaluation to support development of the forthcoming TSCA risk management rule for formaldehyde.**
    g. **EPA should characterize the risks of leukemia from formaldehyde exposure and use the results to inform its forthcoming TSCA risk management rule.**

2. **EPA's reliance on an acute inhalation point of departure (POD) only for characterizing formaldehyde risk is not protective of other serious health effects or other exposure durations.**
    a. **EPA must ensure that chronic formaldehyde risks are quantified and incorporated into the unreasonable risk determination.**
    b. **EPA's application of the acute inhalation POD across all exposure durations and scenarios is scientifically unsupported.**

3. **EPA's Proposed Revisions do not adequately account for human susceptibility and variability and fail to protect potentially exposed or susceptible subpopulations (PESS), as required by TSCA.**
    a. **EPA's removal of uncertainty factors is not consistent with the best available science, as mandated by TSCA.**
    b. **EPA's identification of PESS has important gaps that risk underestimating harms to overburdened groups.**
    c. **EPA's Proposed Revisions preclude a health-protective fenceline assessment.**

4. **EPA's selective reliance on statements from a financially conflicted and inadequately balanced SACC panel undermines the scientific integrity of the risk evaluation.**
    a. **EPA must ensure that SACC membership is balanced and free from financial conflicts of interest.**
    b. **EPA's *ad hoc* formaldehyde SACC did not meet FACA requirements and included members with clear financial conflicts of interest.**
    c. **In the Proposed Revisions, EPA selectively cited statements from the SACC report that were also reflected in chemical industry comments to support conclusions that downplay health risks.**

We appreciate the opportunity to provide public input. Please do not hesitate to contact us with any questions regarding these comments.

Sincerely,

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Detailed Comments:

1. **EPA's proposed adoption of a threshold approach to characterizing carcinogenic risks is not scientifically justified and is inconsistent with the requirements of TSCA to use reasonably available information and the best available science.**

EPA's Proposed Revisions regarding carcinogenic risks fail to reflect the best available science, use all reasonably available relevant evidence, and comply with the Agency's Guidelines for Carcinogen Risk Assessment. TSCA requires EPA to make use of "reasonably available"[7] information and rely on the "best available science"[8] when conducting risk evaluations and regulating existing chemicals. EPA's Proposed Revisions disregard reasonably available information regarding formaldehyde's mutagenic mode of action (MOA) and instead propose that there is a safe threshold of formaldehyde exposure below which there is no risk of cancer. EPA makes this assertion based on a selective and biased reading of a small subset of the literature and citations from a Science Advisory Committee on Chemicals (SACC) report that presents only summary conclusions and opinions, but does not systematically identify, review and synthesize the relevant evidence. The Proposed Revisions also rely on citations to documents that are not thorough, comprehensive, unbiased, or up-to-date, and fail to provide an explanation of how evidence was selected or whether procedures to ensure transparency and avoidance of bias were implemented.

The reasonably available information and best available science demonstrate that formaldehyde's mutagenic MOA is well established. This includes a comprehensive scientific review conducted by EPA's Integrated Risk Information System (IRIS) program in a 2024 EPA document the *Toxicological Review of Formaldehyde* that has received extensive public scrutiny and peer review, including by the National Academies of Sciences, Engineering, and Medicine (NASEM). Instead of continuing to use this reasonably available information and best available science, as it did in the December 2024 final formaldehyde risk evaluation, EPA's Proposed Revisions discard the IRIS assessment altogether and instead rely on selected opinions that are not supported by a comprehensive review of the literature and set aside decades of extensive evidence demonstrating formaldehyde's mutagenic MOA.

The Proposed Revisions and the SACC report do not provide a substantive basis for rejecting the strong conclusions of the 2024 EPA IRIS assessment regarding formaldehyde's mode of action (MOA) and linear dose-response relationship. The Proposed Revisions were prepared in less than one year (the final Risk Evaluation of Formaldehyde was released on January 2, 2025 the Proposed Revisions were released on December 3, 2025), are remarkably brief (the text on cancer hazard from inhalation exposure to formaldehyde is slightly more than one page). The Proposed Revisions would thus replace the thorough and comprehensive IRIS analysis of the evidence with a hasty set of biased assertions based on a small cherry-picked selection of the relevant and reasonably available evidence that fails to match the transparency, clarity, comprehensiveness, extent of thorough and public peer review, and safeguards against bias provided by the IRIS assessment. EPA should continue to use the thorough Gold Standard MOA

[7] 15 U.S.C. 2625(k).
[8] 15 USC §2625(h).

analysis from the IRIS assessment and discontinue efforts to assert an absence of carcinogenic risk below a threshold exposure level.

**a. EPA ignored strong evidence that formaldehyde causes cancer by a mutagenic mode of action (MOA).**

EPA's Guidelines for Carcinogen Risk Assessment states that linear dose-response methods with no threshold should be applied to mutagenic chemicals:

> *Linear extrapolation* should be used when there are MOA data to indicate that the dose-response curve is expected to have a linear component below the POD. Agents that are generally considered to be linear in this region include:
>
> - agents that are DNA-reactive and have direct mutagenic activity.[9]

In the Final Formaldehyde Risk Evaluation, EPA appropriately applied the Cancer Guidelines and characterized the carcinogenic risk of formaldehyde using the inhalation unit risk (IUR) derived in EPA's IRIS assessment of formaldehyde, applying a linear extrapolation approach. Linear extrapolation was strongly supported because the IRIS assessment found that upper respiratory tract cancers result from direct mutagenic activity of formaldehyde and a mutagenic MOA.

> In accordance with the EPA cancer guidelines (U.S. EPA, 2005a, b), given the strong evidence for mutagenicity as a contributing MOA and the evidence-based understanding that mutagens can give rise to cancers with an apparently low-dose linear response, a linear low-dose extrapolation was performed.[10]

In the Proposed Revisions, EPA's Office of Chemical Safety and Pollution Prevention (OCSPP) proposes that a threshold acute formaldehyde exposure level of 0.3 ppm will result in no cancer risk:

> OCSPP is proposing that the best available science supports using an acute inhalation POD of 0.3 ppm as protective of all durations and inhalation hazards, including cancer.[11]

EPA does not present any review of the primary scientific evidence regarding formaldehyde's mode of action to support its position; rather, it selectively quotes a report by the SACC (see subsection d below). The SACC report itself does not present a comprehensive review of the primary scientific evidence regarding formaldehyde's MOA. It instead presents a set of assertions based on the opinions of a subset of SACC panel members with selective citations, without any systematic approach to identifying, evaluating and synthesizing evidence regarding formaldehyde's carcinogenic MOA.

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[9] U.S. EPA (2005). Guidelines for Carcinogen Risk Assessment, p. 3-21.
[10] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 5-82.
[11] U.S. EPA (2025). Revised Draft Human Health Hazard Assessment for Formaldehyde, p. 13.

In contrast, EPA's 2024 IRIS assessment of formaldehyde, which was used as the basis for Final Formaldehyde Risk Evaluation, presents a comprehensive review of the mechanistic evidence. The IRIS assessment concludes, consistent with EPA's Guidelines for Carcinogen Risk Assessment, that formaldehyde operates through a mutagenic MOA with no threshold in inducing upper respiratory tract (URT) tumors. EPA's IRIS assessment presents a detailed and comprehensive review of the evidence regarding formaldehyde's carcinogenic MOA. The IRIS assessment was prepared over multiple years, is carefully documented and supported by citations to numerous mechanistic studies, and was subject to Gold Standard peer review by the NASEM, the nation's premier scientific body. The IRIS assessment also includes extensive documentation of how relevant studies were identified, synthesized and integrated to develop its conclusions.

### i. Formaldehyde is genotoxic.

The EPA IRIS assessment conclusively demonstrates that formaldehyde is genotoxic in humans. Appendix C.3 of the assessment consists of more than 100 pages reviewing the evidence of genotoxicity, presenting extensive and consistent evidence of genotoxicity in animal test systems (*in vivo* and *in vitro*) and in humans. Demonstrated genotoxicity endpoints include gene mutations, chromosomal aberrations, micronuclei, aneuploidy, DNA adducts, DNA-DNA crosslinks (DDCs), DNA-protein crosslinks (DPXs), DNA strand breaks, sister chromatid exchange (SCE), and other genotoxic effects (cell transformation; DNA repair inhibition; unscheduled DNA synthesis; gene conversion, crossing over and translocation). The IRIS assessment summarizes the evidence as follows:

> Formaldehyde is a direct-acting chemical that has been shown to be genotoxic or mutagenic in a variety of in silico and in vitro test systems; experimental animals including mice, rats, and monkeys; as well as in humans. Formaldehyde exposure typically induces genotoxicity, mutagenicity, or related endpoints in a concentration- and duration-dependent manner, including deletions and point mutations; DNA-protein and DNA-DNA crosslinks (DPX and DDC, respectively) and DNA mono (hmDNA) adducts; clastogenic-related effects such as micronuclei (MN) and chromosomal aberration (CA) formation, as well as sister chromatid exchanges (SCEs), single-strand and double-strand breaks (SSBs, DSBs, respectively); and unscheduled DNA synthesis (UDS), DNA repair inhibition, and cellular transformation…Inhaled formaldehyde primarily encounters cellular macromolecules at POE [point-of-entry] tissues, including both nasal and buccal epithelial cells in humans, while preferentially affecting the nasal epithelium in rodents, which are obligate nose-breathers. In these barrier tissues, formaldehyde can interact directly with DNA, resulting in DPX and DDC, DNA mono (hmDNA) adducts, SSBs, MN, and CAs.[12]
>
> Across the available database, formaldehyde consistently induces various endpoints consistent with mutagenicity, such as base pair mutations, deletions, insertions and point mutations, SCEs, SSBs, UDS, and DNA repair inhibition in various cells in vitro, in experimental animal models in vivo, as well as in exposed humans.[13]

[12] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), pp. 3-299 to 3-300.
[13] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 3-301.

> Formaldehyde is genotoxic. This conclusion is supported by several streams of evidence including observations of CAs, MN, and SSBs in exposed humans across a range of studies, occupations, and exposure scenarios, with supporting, similar findings in exposed rodents and in vitro systems, and consistent observations of DPXs detected in multiple experimental systems, showing a pattern of concentration-dependent increases. Together, these multiple streams of evidence (from human, animal, in vitro and nonmammalian systems) converge to clearly indicate that formaldehyde is genotoxic in most systems tested, is mutagenic in systems specifically evaluating genetic or chromosomal mutations, and exhibits strong evidence for mutagenicity in the URT [upper respiratory tract] of rodents and humans following inhalation exposure.[14]

The U.S. National Toxicology Program (NTP) similarly found extensive and conclusive evidence of formaldehyde's genotoxicity:

> Formaldehyde is a direct-acting genotoxic compound and has given positive results for almost all genetic end points evaluated in bacteria, yeast, fungi, plants, insects, nematodes, and cultured mammalian cells. It caused base-pair gene mutations in *Salmonella typhimurium* and DNA adducts, DNA-protein crosslinks, DNA-DNA crosslinks, DNA single-strand breaks, unscheduled DNA synthesis, inhibition of DNA repair, gene mutations, cell transformation, and cytogenetic effects (sister chromatid exchange, chromosomal aberrations, and micronucleus formation) in cultured mammalian cells (NTP 2010). It was also genotoxic in experimental animals and humans exposed *in vivo.*[15]

> Formaldehyde causes genetic damage to the nasal tissues of both experimental animals and humans exposed by inhalation. DNA-protein crosslinks were detected in the nasal mucosa of rats exposed to formaldehyde (Casnaova *et al.* 1989, 1994, NTP 2010) and in the nasal turbinates (Heck *et al.* 1989, Casanova *et al.* 1991) and the respiratory tract (larynx, trachea, carina, and bronchi) (Casanova *et al.* 1991) of rhesus monkeys exposed to formaldehyde, which correspond to the observed tumor sites in humans (nasal and nasopharyngeal). In dose-response studies in rats, DNA crosslinks were correlated with tumor incidence (Liteplo and Meek 2003). DNA-protein crosslinks were also correlated with the severity and anatomical location of proliferative nasal lesions in rhesus monkeys (Casanova *et al.* 1991). *N*2-hydroxmethyl-deoxyguanosine (dG) DNA monoadducts and dG-dG crosslinks were found in rat nasal mucosa (Lu *et al.* 2010)...Numerous studies of industrial workers and professional groups exposed to formaldehyde found that formaldehyde exposure increased the frequency of micronuclei in the nasal epithelium and buccal epithelium (Ballarin *et al.* 1992, Suruda *et al.* 1993, Titenko-Holland *et al.* 1996, Kitaeva *et al.* 1996, Ying *et al*. 1997, Burgaz *et al.* 2001, 2002, Ye *et al*. 2005).[16]

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[14] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 3-301.
[15] National Toxicology Program (2021). Report on Carcinogens, Fifteenth Edition.
[16] National Toxicology Program (2021). Report on Carcinogens, Fifteenth Edition.

The unrefuted and extensive evidence of formaldehyde's genotoxicity represents the best available science and provides the foundation for a strong conclusion that formaldehyde operates by a mutagenic MOA.

### ii. Formaldehyde induces upper respiratory tract (URT) tumors by a mutagenic mode of action (MOA).

The EPA IRIS assessment further assembles the evidence of genotoxicity into a detailed explanation of the process by which formaldehyde's genotoxic effects lead to upper respiratory tract (URT) tumors. The Proposed Revisions claim that cytotoxicity is more important than genotoxicity in inducing the URT tumors, but the IRIS assessment convincingly explains that the cytotoxicity and cellular proliferation contribute to a MOA in which mutagenicity is predominant:

> The coherence of strong and consistent evidence for genotoxicity spans multiple evidence types from exposed humans to relevant model systems and species, in analogous POE and surrogate tissues, incorporating pertinent aspects of dose-response and temporality (i.e., preceding other mechanistic events), all of which strongly supports a role for direct DNA damage leading to mutagenicity in formaldehyde-induced URT carcinogenesis.[17]
>
> In F344 rats chronically exposed to formaldehyde, there is a clear temporal, dose-responsive, and biological relationship in the appearance of exposure-related genotoxicity, sustained epithelial damage, cellular proliferation, and eventual SCC or PA development, consistent with similar relationships evident in analogous URT tissues from both the nonhuman primate and human databases. Furthermore, the chronic formaldehyde exposure concentrations reported to elicit nasal cytotoxic pathology appear to be higher in the rats and nonhuman primates evaluated experimentally ($\geq$3 mg/m$^3$), compared with the results from human epidemiological cohorts ($\geq$0.3 mg/m$^3$; see Table 3-42), whereas formaldehyde-associated genotoxicity has been induced in analogous POE tissues from rats, nonhuman primates, and humans exposed to similar formaldehyde concentrations (see Table 3-42). **Together, genotoxicity, cellular proliferation, and cytotoxicity-induced tissue regenerative proliferation exhibit multiple layers of coherence as a function of species and anatomy, temporality, concentration, and duration of exposure. When integrated, this evidence forms a biologically relevant MOA for formaldehyde exposure-induced URT carcinogenesis** (U.S. EPA, 2005a).[18] (emphasis added)
>
> Strong and consistent evidence for formaldehyde-induced direct genotoxicity and mutagenicity comes from studies in mammalian cell lines, controlled inhalation studies in rodents and nonhuman primates, and occupationally exposed humans, wherein mutagenicity anatomically coincides with and temporally precedes URT tumorigenesis…Evidence supporting the URT cancer MOA depends not only on temporality, duration, and concentration of exposure, but also anatomical location within

[17] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 3-317.
[18] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), pp. 3-322 to 3-323.

the URT (i.e., incidence or severity of all primary mechanistic considerations decreases following an anterior-to-posterior gradient within the URT).[19]

**Mechanistic changes associated with the development of cancer in the nasal cavity were consistently observed in humans and experimental systems, including genotoxicity, epithelial damage and proliferation, and eventual cancer development in relevant URT tissues. The mechanistic changes and URT lesions exhibited a temporal and dose-response relationship coherent with carcinogenesis and supportive of a mutagenic MOA**…The observed formaldehyde exposure-induced nasal tumors and mechanistic changes in animals are considered directly relevant to changes in the human nasopharynx (the nasopharynx is part of the nasal cavity and a recognized target of inhaled nasal toxicants).[20] (emphasis added)

Multiple well-conducted studies demonstrate effects associated with mutagenicity (e.g., chromosomal changes) at exposure levels well below those causing cellular cytotoxicity, **which is incompatible with a theory of carcinogenesis based solely upon exceedance of a cytotoxicity-based threshold**. In accordance with the EPA cancer guidelines (U.S. EPA, 2005a, b), given the strong evidence for mutagenicity as a contributing MOA and the evidence-based understanding that mutagens can give rise to cancers with an apparently low-dose linear response, a linear low-dose extrapolation was performed.[21] (emphasis added)

EPA's IRIS assessment presents a biologically cogent integration of all of the reasonably available evidence regarding the MOA for formaldehyde URT carcinogenicity that incorporates both the extensive evidence of genotoxicity and the evidence of cytotoxicity and cellular proliferation. The IRIS assessment correctly applies the dose-response procedures from EPA's Guidelines for Carcinogen Risk Assessment to derive an inhalation unit risk for nasopharyngeal cancer. EPA's Proposed Revisions disregard this comprehensive peer-reviewed IRIS analysis of the evidence in favor of a selective reading of a subset of the relevant literature.

**b. EPA disregards evidence undermining its position regarding a cytotoxicity mode of action (MOA) for carcinogenicity.**

The Proposed Revisions state that formaldehyde URT tumors are induced by a cytotoxicity and cellular proliferation MOA rather than a mutagenic MOA. This claim, however, disregards evidence from multiple other cytotoxic chemicals that are not mutagenic and do <u>not</u> induce URT tumors. As summarized by the IRIS assessment:

Chemical URT irritants such as dimethylamine, glutaraldehyde, ethylacrylate, hydrogen chloride, and chlorine gas cause rhinitis, inflammation, and cytotoxicity leading to squamous metaplasia or hyperplasia, but do not induce rat nasal tumors following chronic exposure (Wolf et al., 1995b; Sellakumar et al., 1985; NRC, 2014b; Mcgregor et al.,

[19] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 3-329.
[20] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 3-334.
[21] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 5-82.

> 2006; Buckley et al., 1985; Albert et al., 1982). However, a number of genotoxic chemicals that also induce pathological changes in the rat nasal epithelium similar to formaldehyde (e.g., acetaldehyde, acrolein, 4-[N-methyl-N-nitrosamino]-1-[3-pyridyl]-1-butanone [NNK] and 1,2-epoxybutane) also induce nasal tumors including SCCs and PA-like lesions (Woutersen et al., 1986; U.S. EPA, 2003; NTP, 1988, 2011; Monticello et al., 1990b; Monticello et al., 1993). The comparison between formaldehyde and glutaraldehyde is particularly informative, as similar rat nasal cytotoxic pathology (e.g., squamous metaplasia, hyperplasia, inflammation) is elicited by exposure to both aldehydes (Hester et al., 2005), and yet glutaraldehyde exposure does not induce rat nasal tumors even after 24 months of exposure, while such tumors are induced following ≥12 months of formaldehyde exposure (Mcgregor et al., 2006)...The observation that a more effectively cytotoxic but less effectively mutagenic agent, glutaraldehyde, induces similar cytotoxicity-induced regenerative URT pathology to formaldehyde, yet appears unable to elicit rat URT tumors, suggests that **cytotoxicity-induced regenerative proliferation alone is insufficient to induce URT carcinogenesis resulting from formaldehyde exposure**.[22] (emphasis added)

Rather, the IRIS assessment provides compelling evidence that formaldehyde's cytotoxicity enhances the carcinogenic action initiated by formaldehyde's genotoxicity:

> Several lines of evidence converge to support the conclusion that while inflammation, squamous metaplasia, or hyperplasia alone are clearly not sufficient to induce nasal cancer in rats (Monticello et al., 1993), the amplified cellular proliferation occurring in regenerating tissues may be a mechanism by which genotoxicity-induced DNA mutation rates are augmented, facilitating neoplastic transformation.[23]

> Based on this detailed analysis conducted according to EPA's cancer MOA framework (U.S. EPA, 2005a), there is sufficient evidence to conclude that formaldehyde induces URT carcinogenicity via at least two primary mechanistic considerations: genotoxicity-associated mutagenicity and cytotoxicity-induced regenerative proliferation. By means of its fundamentally mutagenic activity, formaldehyde damages DNA and increases the mutational burden of the URT mucosa when this damage is not adequately repaired, while mucosal cytotoxicity creates a tissue microenvironment driving continuous proliferation, facilitating the accumulation of mutations arising from both direct and indirect genotoxicity, thereby increasing the rate at which initiated clones are formed as well as stimulating the expansion of existing neoplastic colonies (see Table 3-43). **The involvement of both mutagenicity and cytotoxicity-induced proliferation in the URT cancer MOA is strongly supported and internally consistent with the available formaldehyde evidence, and is also externally consistent with the described activities of other reported URT toxins and carcinogens.**[24] (emphasis added)

> **Strong and consistent evidence supports the contribution of both direct genotoxicity and mutagenicity as well as cytotoxicity-induced regenerative proliferation** as

[22] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 3-328.
[23] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), pp. 3-328 to 3-329.
[24] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), pp. 3-329 to 3-330.

primary mechanistic considerations relevant to the pathogenesis of formaldehyde-associated URT cancer in rodents.[25] (emphasis added)

EPA's assertion in Proposed Revisions (quoting the statement supported by some members of the SACC) that "the non-genotoxic mode of action predominates"[26] is not supported by the overall body of evidence presented in the IRIS assessment, including evidence for other chemicals.

### c. EPA ignored findings of the National Academies regarding the IRIS mode of action analysis and inhalation unit risk for formaldehyde upper-respiratory tract tumors.

A draft of EPA's IRIS assessment of formaldehyde was reviewed in a Consensus Study Report by the NASEM. The extensive procedures employed by the NASEM are detailed in general terms on the NASEM website.[27] NASEM Consensus Study Reports employ the most rigorous and transparent peer review process applied to scientific reports prepared by the EPA, which is why EPA and the U.S. Congress have frequently requested that the NASEM review EPA reports and scientific assessment processes for the most critical issues facing the IRIS program. NASEM reports have included a 2011 review of an earlier draft of the IRIS formaldehyde assessment, and subsequent guidance to EPA on IRIS assessment procedures in 2014 (Review of EPA's IRIS Process), 2018 (Progress Toward Transforming the IRIS Program), and 2022 (Review of US EPA's ORD Staff Handbook for Developing IRIS Assessments).

In its 2023 report, the NASEM endorsed the IRIS analysis of formaldehyde's MOA for URT cancers:

> Finding: With respect to evidence on MOA for upper respiratory tract cancers, EPA used its state-of-practice methods to synthesize the evidence.[28]
>
> While there is uncertainty in the degree to which nonmutagenic processes may also contribute to the carcinogenic activity of formaldehyde inhalation at the point-of-entry tissues, there is sufficient evidence to support the assumption that a mutagenic MOA is involved in the carcinogenesis of formaldehyde in the upper aerodigestive tract in humans.[29]

The NASEM also endorsed the IRIS assessment's derivation of a linear IUR based on human data:

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[25] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 3-344.
[26] U.S. EPA (2025). Revised Draft Human Health Hazard Assessment for Formaldehyde, p. 12.
[27] National Academies of Sciences, Engineering, and Medicine. https://www.nationalacademies.org/process
[28] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment, p. 101.
[29] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment, p. 121.

> EPA's selection of the inhalation unit risk based on human nasopharyngeal cancer is appropriate and acceptable.[30]

EPA's Proposed Revisions disregard NASEM's findings with respect to the IRIS assessment MOA analysis and IUR derivation, and instead override the IRIS assessment analyses by citing less-comprehensive analyses that have received much less scrutiny than the NASEM provided to the IRIS assessment.

The NASEM report on the EPA's 2022 formaldehyde assessment provided a rigorous scientific review by an *ad hoc* committee of experts, chaired by a member of the National Academy of Medicine. The process included multiple opportunities for oral and written public input, in line with requirements of the Federal Advisory Committee Act (FACA) Section 15.[31] The committee considered EPA's responsiveness to all relevant prior consensus recommendations from 2011 forward, and the committee's first open session included a presentation and question-and-answer session regarding the 2022 National Academies review of the IRIS handbook. Further, rigorous peer review of the NASEM's report by a group of independent experts anonymous to the committee ensured that the report was scientifically sound, clear, and objective before it was released it to the public. Specifics of how the review process was implemented are detailed in the consensus study report:

> The committee included expertise in public health risk assessment, systematic review methods, biostatistics, environmental epidemiology, toxicology, carcinogenesis (leukemogenesis), reproductive effects, developmental effects, neurotoxicology, respiratory effects (including asthma), biological modeling, exposure assessment, and dose-response analysis… the committee held nine meetings, including three open sessions with public comment periods.[32]

> In addition to the opportunities provided for oral remarks during the three public meetings, stakeholders were encouraged to submit written comments or other materials relevant to the committee's charge at any time during the course of the study.[33]

> The committee focused its review on whether the 2022 Draft Assessment adequately and transparently evaluated the available studies and data, and used appropriate methods in reaching hazard identification conclusions and dose-response analyses that are supported by the scientific evidence.[34]

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[30] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment, p. 117.
[31] National Academies of Sciences, Engineering, and Medicine. https://www.nationalacademies.org/index.php/project-comments-and-information
[32] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment, p. 16.
[33] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment, p. 17.
[34] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment, p. 19.

> This Consensus Study Report was reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise. The purpose of this independent review is to provide candid and critical comments that will assist the National Academies of Sciences, Engineering, and Medicine in making each published report as sound as possible and to ensure that it meets the institutional standards for quality, objectivity, evidence, and responsiveness to the study charge…all review comments were carefully considered.[35]

The extensive processes employed for NASEM Consensus Reports are why the NASEM is considered the Gold Standard of peer review bodies. Other bodies that have opined on EPA's formaldehyde assessments, including the EPA's SACC and Human Studies Review Board, cannot be considered the equal of the NASEM because their report development process is more abbreviated, less transparent, more biased, and less thorough.

**d. EPA's Proposed Revisions rely on opinions expressed in a report by the Science Advisory Committee on Chemicals (SACC), but the SACC did not conduct a comprehensive review of the reasonably available information concerning formaldehyde's carcinogenic mode of action (MOA).**

EPA had the SACC conduct a peer review of the draft Formaldehyde Risk Evaluation. The role of the SACC is to provide advice to EPA, not to conduct scientific assessments:

> The SACC provides independent scientific advice and recommendations to the EPA on the scientific and technical aspects of risk assessments, methodologies, and pollution prevention measures and approaches for chemicals regulated by TSCA.[36]

The charge to the SACC did not include preparing a review of formaldehyde's carcinogenic MOA, and the SACC did not prepare such a review. Some SACC members provided comments disagreeing with the IRIS MOA analysis, but these comments were not a consensus position – stated as the views of "Many Committee members"[37] while "Several Committee members disagreed."[38] The SACC comments disputing a mutagenic MOA and the IRIS IUR included many assertions without citations and generally presented only limited citations that do not represent the breadth of the literature integrated in the IRIS assessment.

EPA's Proposed Revisions inappropriately cite the SACC report as if it is an authoritative review of the literature regarding formaldehyde's carcinogenic MOA. The SACC report does not provide substantive evidence-based support for disregarding the IRIS assessment or for revising the Final Formaldehyde Risk Evaluation's characterization of URT cancer risk.

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[35] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment, p. vii.
[36] U.S. EPA. Science Advisory Committee on Chemicals Basic Information. https://www.epa.gov/tsca-peer-review/science-advisory-committee-chemicals-basic-information
[37] U.S. EPA (2024). Science Advisory Committee on Chemicals Meeting Minutes and Final Report No. 2024-01. Peer Review of the 2024 Draft Risk Evaluation for Formaldehyde, p. 83.
[38] U.S. EPA (2024). Science Advisory Committee on Chemicals Meeting Minutes and Final Report No. 2024-01. Peer Review of the 2024 Draft Risk Evaluation for Formaldehyde, p. 84.

### e. EPA's Proposed Revisions ignore EPA's own Guidelines for Carcinogen Risk Assessment.

EPA's 2024 Procedures for Chemical Risk Evaluation Under the Toxic Substances Control Act (TSCA) final rule (referred to as the risk evaluation framework rule) includes a set of "Evaluation requirements", which includes a statement that EPA will use its own guidance in preparing risk evaluations:

> EPA will use applicable EPA guidance when conducting risk evaluations, as appropriate and where it represents the best available science.[39]

EPA's 2005 Guidelines for Carcinogen Risk Assessment are applicable to the formaldehyde risk evaluation and represent the best available science. The 2005 Guidelines were developed by EPA expert toxicologists through a transparent public process over multiple years with multiple drafts made available for peer review and public comment. EPA has relied on the Guidelines for numerous assessments over the past 21 years. The Guidelines provide EPA risk assessors with procedures for assessing a substance's carcinogenic MOA and for conducting dose-response analysis. As discussed above, the Guidelines indicate that that linear dose-response methods with no threshold should be applied to mutagenic chemicals.

The NASEM found that EPA's IRIS assessment, including its derivation of a linear IUR was consistent with the Guidelines:

> Finding: The overall approach and conduct of the cancer dose-response analysis is consistent with EPA's state-of-practice methods for deriving inhalation unit risk estimates. The 2022 Draft Assessment adequately and transparently evaluates the scientific evidence, and generally documents the dose-response analysis overall in a well-organized and transparent manner. The analyses generally follow the process outlined in the 2022 IRIS Handbook and are consistent with the 2005 Guidelines for Carcinogen Risk Assessment.[40]
>
> Finding: EPA's calculation of the unit risk for mortality is appropriate and consistent with its Guidelines for Carcinogen Risk Assessment.[41]
>
> Finding: EPA's derivation of the unit risk estimate for formaldehyde-associated nasopharyngeal cancer incidence was appropriately done, and the preference for that estimate over the mortality-based unit risk estimate is appropriate and consistent with the 2022 IRIS Handbook (EPA, 2022, p. 8-4) and EPA's Guidelines for Carcinogen Risk Assessment (EPA, 2022, p. 3-12).[42]

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[39] 40 CFR 702.37(a)(1).
[40] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment, p. 105.
[41] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment, p. 108.
[42] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment, p. 109.

In contrast, the Proposed Revisions make no mention at all of the Guidelines for Carcinogen Risk Assessment. In place of the IRIS assessment, which used the Guidelines, and the IRIS IUR, EPA now proposes to adopt a threshold for cancer risk characterization, which is based only on the opinions of some SACC members and not on EPA's Guidelines. The opinions expressed in the SACC report itself supporting a threshold approach also do not mention or cite EPA's Guidelines. EPA's Proposed Revisions therefore do not use applicable EPA guidance and consequently violate the risk evaluation framework rule.

### f. EPA should continue to use the inhalation unit risk (IUR) derived by IRIS for nasopharyngeal cancers in the Final Formaldehyde Risk Evaluation to support development of the forthcoming TSCA risk management rule for formaldehyde.

In Final Formaldehyde Risk Evaluation, EPA used the IUR from the 2024 IRIS assessment to characterize nasopharyngeal cancer risks of formaldehyde exposure. The IRIS assessment conducted a thorough review of the literature, followed established EPA guidance, and was subject to rigorous peer review by the NASEM. EPA has not presented a substantive or scientifically defensible basis for discarding this cancer risk characterization or for adopting a threshold approach to characterizing the risk in the Proposed Revisions. EPA should retain the cancer risk assessment from the Final Formaldehyde Risk Evaluation and continue to use the IRIS IUR for characterizing nasopharyngeal cancer risks.

### g. EPA should characterize the risks of leukemia from formaldehyde exposure and use the results to inform its forthcoming TSCA risk management rule.

TSCA requires to use the best available science in conducting risk evaluations:

> the Administrator shall use scientific information, technical procedures, measures, methods, protocols, methodologies, or models, employed in a manner consistent with the best available science.[43]

EPA's decision not to quantify risks of leukemia from formaldehyde exposure in the Final Formaldehyde Risk Evaluation is not consistent with the best available science and should be reversed.

EPA's 2024 IRIS assessment concluded that there is convincing evidence that formaldehyde exposure causes leukemia in humans:

> The **evidence demonstrates** that formaldehyde inhalation causes myeloid leukemia in humans. This is based primarily on *robust* human evidence of an increased risk of the occurrence of myeloid leukemia in epidemiological studies among different populations exposed to occupational formaldehyde levels representing diverse exposure settings. The findings from the occupational cohorts are further supported by other studies of human

[43] 15 U.S.C. 2625(h).

> occupational exposure providing strong and coherent mechanistic evidence that formaldehyde exposure is associated with the detection of additional endpoints relevant to LHP cancers, including an increased prevalence of multiple markers of genotoxicity in peripheral blood and myeloid progenitors. Indirect support is also provided by evidence of other systemic health effects (e.g., reproductive or developmental toxicity) and mechanistic evidence indicating changes in immune cell populations and markers of inflammation (e.g., oxidative stress) in the peripheral blood of exposed humans and animals, although the exact pattern of immune-related changes across studies and species was difficult to interpret.[44]

The IRIS finding is consistent with the conclusions of the International Agency for Research on Cancer (IARC):

> The epidemiologic evidence shows that occupational exposure to formaldehyde causes leukaemia.[45]

> There is *sufficient evidence* in humans for the carcinogenicity of formaldehyde. Formaldehyde causes cancer of the nasopharynx and leukaemia.[46]

The IRIS finding is similarly consistent with the conclusions of the National Toxicology Program's (NTP) Report on Carcinogens:

> Epidemiological studies have demonstrated a causal relationship between exposure to formaldehyde and cancer in humans. Causality is indicated by consistent findings of increased risks of … lymphohematopoietic cancer, specifically myeloid leukemia among individuals with higher measures of exposure to formaldehyde (exposure level or duration), which cannot be explained by chance, bias, or confounding…although the mechanisms by which formaldehyde causes myeloid leukemia in humans are not known, a number of plausible mechanisms have been advanced.[47]

The NASEM agreed with NTP's finding:

> The committee found clear and convincing epidemiologic evidence of an association between formaldehyde exposure and myeloid leukemia…the committee concludes that there is a causal association between formaldehyde exposure and myeloid leukemia. Chance, bias, and confounding factors can be ruled out with reasonable confidence given the consistent pattern of association in the larger studies that had good exposure assessment.[48]

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[44] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), pp. 4-15 to 4-16.
[45] International Agency for Research on Cancer (2012). Chemical Agents and Related Occupations: A Review of Human Carcinogens. IARC monographs on the evaluation of carcinogenic risks to humans, Volume 100F, p. 409.
[46] International Agency for Research on Cancer (2012). Chemical Agents and Related Occupations: A Review of Human Carcinogens. IARC monographs on the evaluation of carcinogenic risks to humans, Volume 100F, p. 430.
[47] National Toxicology Program (2021). Report on Carcinogens, Fifteenth Edition.
[48] National Research Council (2014). Review of the Formaldehyde Assessment in the NTP 12th Report on Carcinogen, p. 16.

In the 2024 IRIS formaldehyde assessment, EPA derived an inhalation unit risk for leukemia of $3.4 \times 10^{-2}$ per mg/kg of exposure,[49] described as the "best available unit risk estimate for myeloid leukemia."[50] Although this estimate was not included in the overall final IRIS IUR for formaldehyde due to uncertainties in the data, TSCA's provision regarding use of the best available science requires EPA to quantify leukemia risk in the risk evaluation. If leukemia risks are not quantified, then the risk evaluation incorrectly assumes that there are no leukemia risks at all from formaldehyde exposure. Given that formaldehyde is known to cause leukemia – per the evaluations by IRIS, IARC, NTP and the NASEM quoted above – assuming zero leukemia cancers from formaldehyde exposures is inconsistent with the best available scientific evidence and ultimately understates health risk. In contrast, adoption of the IRIS leukemia IUR will produce a non-zero risk estimate that may either overestimate or underestimate leukemia risk, which better reflects the best available science than an estimate of zero risk that is clearly false. To satisfy TSCA's requirement to use the best available science, EPA must use the best available IUR for leukemia risk from formaldehyde, which is the estimate of $3.4 \times 10^{-2}$ per mg/kg provided in the IRIS assessment.

**2. EPA's reliance on an acute inhalation point of departure (POD) only for characterizing formaldehyde risk is not protective of other serious health effects or other exposure durations.**

**a. EPA must ensure that chronic formaldehyde risks are quantified and incorporated into the unreasonable risk determination.**

In the Proposed Revisions, EPA's proposal to treat the acute sensory irritation POD as "appropriate as the critical effect to protect for all other potential hazards, including cancer,"[51] and to "no longer [rely] on the EPA IRIS RfC or IUR,"[52] is inconsistent with the best available science, including EPA's own IRIS assessment conclusions. An acute sensory irritation endpoint is not protective of all other adverse health effects associated with formaldehyde exposure, including cancer and other chronic outcomes.

The biological processes underlying sensory irritation differ fundamentally from those driving carcinogenesis and chronic respiratory or systemic disease, as elaborated in the previous section. As a result, an acute POD, even if scientifically robust for short-term irritation, cannot be assumed to be protective of chronic outcomes without explicit analysis demonstrating such protectiveness. EPA has not provided such an analysis in the Proposed Revisions. Instead, EPA relies on a single acute POD as the benchmark for risk characterization across endpoints and time scales for which it was not derived and is not scientifically appropriate.

Formaldehyde is a well-established human carcinogen, and EPA itself has identified cancer and other chronic effects resulting from long-term inhalation exposure. EPA's own IRIS program identified an inhalation unit risk (IUR) estimate for nasopharyngeal cancer, including an ADAF-

[49] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), Table 5-45, p. 5-120.
[50] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 5-120.
[51] U.S. EPA (2025). Revised Draft Human Health Hazard Assessment for Formaldehyde, p. 6.
[52] U.S. EPA (2025). Revised Draft Human Health Hazard Assessment for Formaldehyde, p. 13.

adjusted unit risk estimate of $1.1 \times 10^{-5}$ per $\mu g/m^3$, and applied a "Carcinogenic to Humans" descriptor. IRIS also evaluated multiple noncancer outcomes (including pulmonary function, immune/allergic outcomes including asthma, respiratory tract pathology, nervous system effects, and reproductive/developmental toxicity) and identified adverse effects at much lower dose levels and across longer exposure durations than those captured by the proposed acute sensory irritation endpoint. For example, in the final IRIS Toxicological Review of Formaldehyde,[53] IRIS derived chronic exposure PODs of 0.082 $mg/m^3$ (0.066 ppm) for respiratory tract squamous metaplasia (high confidence),[54] and 0.021 $mg/m^3$ (0.017 ppm) for decreased pulmonary function in children (high confidence),[55] values 4 to 18 times lower, respectively, than the 0.3 ppm acute sensory irritation POD selected by EPA.[56] NASEM's review further underscores why EPA cannot shortcut cancer hazard/risk characterization in this way.[57] NASEM recommended that EPA provide clearer, systematic criteria for selecting studies and cancer endpoints for unit risk derivation, and emphasized the need for centralizing methods and organizing uncertainties. In other words, the National Academies called for more rigor and transparency in cancer dose-response analysis, not an abandonment of IRIS cancer values in favor of a single acute irritation POD.

EPA's memorandum acknowledges that "if human exposure occurs above 0.3 ppm for a sustained, long-term duration, there is potential for cancer to develop,"[58] yet still asserts that 0.3 ppm is "protective of effects for all durations, including cancer."[59] These statements are in direct conflict—if sustained exposures above 0.3 ppm increase cancer potential, EPA cannot reasonably conclude that evaluating only acute inhalation scenarios is sufficient to characterize and prevent unreasonable risk from all reasonably foreseeable exposures.

Under TSCA, EPA is required to use the best available science and to evaluate risks to potentially exposed or susceptible subpopulations. Treating an acute POD as a health-protective level for all outcomes systematically underestimates chronic risks, particularly for workers and communities experiencing repeated or long-term exposures. EPA should clearly acknowledge the limitations of the acute POD and ensure that its unreasonable risk determination reflects the full spectrum of formaldehyde-related health effects, including cancer. Accordingly, EPA must reject the Proposed Revisions and ensure that the Final Formaldehyde Risk Evaluation explicitly states that the acute inhalation POD is not protective of chronic health effects, including cancer, and ensure that all chronic risks are explicitly quantified and incorporated into the unreasonable risk determination. EPA should also retain conclusions from the Final Formaldehyde Risk Evaluation that formaldehyde leads to multiple adverse health outcomes beyond sensory irritation, and that a single endpoint cannot be presumed protective across all health endpoints, exposure patterns, and susceptible populations.

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[53] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. xix.
[54] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 5-62
[55] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 5-57.
[56] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. xix.
[57] National Academies of Sciences, Engineering, and Medicine (2023). Review of EPA's 2022 Draft Formaldehyde Assessment.
[58] U.S. EPA (2025). Revised Draft Human Health Hazard Assessment for Formaldehyde, p.13.
[59]U.S. EPA (2025). Revised Draft Human Health Hazard Assessment for Formaldehyde, p.13.

**b. EPA's application of the acute inhalation POD across all exposure durations and scenarios is scientifically unsupported.**

EPA's Proposed Revisions state that "the acute inhalation POD can be applied to all durations of exposure (including short- and long-term) and all populations, including occupational scenarios,"[60] citing that there is no meaningful relationship between exposure duration and toxicity for formaldehyde and that Haber's Law, or a scientific principle that the toxicity of a chemical is a function of its concentration and duration of exposure, does not apply to formaldehyde. EPA's rationale relies heavily on the premise that sensory irritation is driven by concentration rather than duration of exposure, [61] and that effects are not expected to be proportional to the duration of exposure, leading EPA to apply no duration adjustment and to treat the acute POD as comparable to all exposure durations. This approach is scientifically indefensible and inconsistent with TSCA's requirement to evaluate unreasonable risk under the conditions of use, including real-world, repeated, and chronic exposure circumstances experienced by workers and communities.

Haber's Law, in the context of risk assessment, is a tool that can be used for extrapolating effects across exposure durations, especially when direct duration-specific data are limited. For example, Haber's Law can be applied to inform extrapolation from subchronic-to-chronic exposure scenarios, typically in combination with a 10X uncertainty factor.[62] For chemical-specific endpoints or exposure durations where Haber's Law does not directly apply, the typical Haber's formulation ($c \times t = k$, where $c$ is concentration, $t$ is time, and $k$ is a mathematical constant) can be modified to a power function, such that $k = c^n \times t$, where $n$ is greater than 1.[63] If EPA chooses to reject the typical Haber's Law formulation, that does not justify ignoring exposure durations altogether. Rather, it means that this principle must be modified, not abandoned, to better predict extrapolation across exposure durations.

EPA's own cited evidence supports that a modified Haber's Law can be applied for formaldehyde. For example, the paper by Schusterman et al., which EPA relies on to argue that sensory irritation is primarily driven by concentration but not exposure duration, concludes that "in order to achieve progress in toxicologic modeling Haber's law as applied to descriptive and regulatory toxicology should be replaced with more generalized power function models."[64] The authors further noted that California EPA recommended "a power function….(described as a "modified Haber's law") for time extrapolation when using toxicity data to develop acute reference exposure levels."[65] EPA's IRIS assessment also concluded that a modified power

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[60] U.S. EPA (2025). Revised Draft Human Health Hazard Assessment for Formaldehyde, p.6.
[61] Dennis Shusterman, Elizabeth Matovinovic & Andrew Salmon (2006) Does Haber's Law Apply to Human Sensory Irritation?, Inhalation Toxicology, 18:7, 457-471, DOI: 10.1080/08958370600602322
[62] Gaylor DW. The use of Haber's law in standard setting and risk assessment. Toxicology. 2000 Aug 14;149(1):17-9. doi: 10.1016/s0300-483x(00)00228-6. PMID:10963857.
[63] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 3-170.
[64] Dennis Shusterman, Elizabeth Matovinovic & Andrew Salmon (2006) Does Haber's Law Apply to Human Sensory Irritation?, Inhalation Toxicology, 18:7, 457-471, DOI: 10.1080/08958370600602322
[65] Dennis Shusterman, Elizabeth Matovinovic & Andrew Salmon (2006) Does Haber's Law Apply to Human Sensory Irritation?, Inhalation Toxicology, 18:7, 457-471, DOI: 10.1080/08958370600602322

function for Haber's Law "may better represent formaldehyde…when interpreting short-term or subchronic exposure."[66]

Instead of modifying the approach to Haber's Law for extrapolating effects across exposure durations, EPA altogether disregarded health risks associated with repeated or chronic exposures. It is well established that formaldehyde increases the risk of adverse health outcomes from low-level, chronic exposures, as described above. [67] EPA's assertion that the Mueller et al. acute sensory irritation POD can serve as a surrogate for all exposure durations is therefore inconsistent with the best available science.

EPA's proposal to ignore long-term exposure durations is especially problematic when evaluating cancer risk for formaldehyde, which is genotoxic and mutagenic (as described above). As stated by David Gaylor in the journal *Toxicology*, Haber's Law always applies to genotoxic and mutagenic chemicals because cancer risk is driven by total lifetime dose rather than exposure timing alone:

> For a genotoxic carcinogen it is assumed that a molecule at the right time and place can interact with DNA resulting in instigating a stage of the carcinogenic process. If this is simply a stochastic event, the number of such occurrences is proportional to the total number of opportunities, i.e. proportional to the total number of molecules available. Very few molecules may interact with DNA and very few of these reactions may proceed through all stages to a tumor. But, the probability of a tumor is proportional to the total number of molecules available (total dose); hence, Haber's Law.[68]

EPA's approach to apply formaldehyde's lack of strict adherence to Haber's Law for acute sensory irritation is to write off all other health effects and exposure durations without scientific justification, which leaves workers, consumers, infants, children and the general population at increased risk of health harm. This approach also fails to meet TSCA's "best available science" requirement and results in a systematic and dangerous underestimation of unreasonable risk. For example, workers are routinely exposed to formaldehyde over extended periods, often across full work shifts, weeks, and years. Even if the marginal risk from each exposure event were assumed to decline over time, chronic exposure still occurs in aggregate, and the health consequences of that cumulative exposure must be assessed. EPA's revised approach effectively collapses time into a single acute metric, thereby obscuring real-world occupational exposure patterns and their associated risks, like various types of cancer. This approach is particularly concerning for workers in manufacturing, processing, and industrial or commercial uses, who may experience both peak exposures and sustained background exposures. By failing to explicitly model or characterize chronic worker risks using appropriate chronic endpoints and dose-response values, EPA risks underestimating unreasonable risks to a core potentially exposed subpopulation that TSCA was designed to protect.

EPA must abandon its unsupported claim in the Proposed Revisions that rejection of Haber's Law permits it to disregard exposure duration. Instead, EPA should apply a modified Haber's Law power function to inform exposure duration extrapolation, and explicitly characterize risks

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[66] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. 3-170.
[67] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. xx.
[68] Gaylor DW. The use of Haber's law in standard setting and risk assessment. Toxicology. 2000 Aug 14;149(1):17-9. doi: 10.1016/s0300-483x(00)00228-6. PMID:10963857.

across relevant exposure durations and health endpoints, including chronic occupational, general population, and consumer exposures in the Final Formaldehyde Risk Evaluation.

### 3. EPA's Proposed Revisions do not adequately account for human susceptibility and variability and fail to protect potentially exposed or susceptible subpopulations (PESS), as required by TSCA.

In the Proposed Revisions, EPA makes several substantive changes that systematically dismiss risks to fenceline communities, the general population, and workers, and fail to adequately protect PESS, as required by TSCA.[69] The changes represent a departure from the best available science, are inconsistent with EPA's statutory obligations under TSCA, and directly contradict comments made to EPA on the 2024 Draft Risk Evaluation of Formaldehyde regarding background exposure, cumulative risk, and increased susceptibility among communities already overburdened by toxic chemical exposure. EPA's revised approach relies on scientifically unsupported assumptions, the exclusion of important evidence, and the removal of key uncertainty factors, all of which have far-reaching implications.

#### a. EPA's removal of uncertainty factors is not consistent with the best available science, as mandated by TSCA.

EPA's proposal to eliminate the human variability ($UF_H$) uncertainty factor (reducing from 3x to 1x) represents a significant and troubling shift in its approach to risk assessment. EPA proposed this change despite clear evidence of inter-individual differences in response to formaldehyde, including IRIS's explicit conclusion that children and those with respiratory disease are most susceptible to formaldehyde's respiratory effects.[70] While EPA proposed to lower the acute inhalation POD (from 0.5 ppm to 0.3 ppm), claiming that this shift will result in stronger health protections, the simultaneous removal of $UF_H$ results in an overall reduction in health protectiveness – nearly doubling the amount of allowable acute formaldehyde exposure. The Agency's conclusion that several occupational conditions of use no longer present unreasonable risk rests heavily on the elimination of $UF_H$ .

EPA's decision to retain a $UF_H$ of 3x in the original draft risk evaluation was already underprotective given the variability in respiratory sensitivity, age-related susceptibility, pre-existing disease, and other factors within the human population.[71] Instead of increasing the use of science-based uncertainty factors to account for the wide range of vulnerability and variability in the human population that EPA itself has acknowledged, EPA removed them, resulting in an underestimation of risk, particularly for PESS. By eliminating all human variability factors, EPA

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[69] 15 U.S.C. §2605(b)(4)(A).
[70] U.S. EPA (2024). IRIS Toxicological Review of Formaldehyde (Inhalation), p. xix.
[71] Varshavsky, J. R., Rayasam, S. D. G., Sass, J. B., Axelrad, D. A., Cranor, C. F., Hattis, D., Hauser, R., Koman, P. D., Marquez, E. C., Morello-Frosch, R., Oksas, C., Patton, S., Robinson, J. F., Sathyanarayana, S., Shepard, P. M., & Woodruff, T. J. (2023). Current practice and recommendations for advancing how human variability and susceptibility are considered in chemical risk assessment. Environmental Health, 21(Suppl 1), 133. https://doi.org/10.1186/s12940-022-00940-1.

implicitly claims that the most sensitive individuals are no more vulnerable than the average healthy adult, contradicting decades of scientific research.[72]

Furthermore, the 10X default human variability ($UF_H$) uncertainty factor that EPA typically relies on to account for intra-species variability is based on a scientific recommendation made nearly 70 years ago. Since then, decades of scientific evidence suggest that this adjustment factor falls short of capturing the full range of human responses to chemical exposures, especially for susceptible subgroups.[73] Based on observed toxicokinetic differences in chemical metabolism between younger age groups and adults, California EPA's Office of Environmental Health Hazard Assessment (OEHHA) now relies on an intra-species adjustment factor that is three times higher than the one currently used by EPA.[74] The World Health Organization's (WHO) International Programme on Chemical Safety (IPCS) examined human variability in toxicokinetic and toxicodynamic responses to chemical exposures using a probabilistic method, and found that variability at the 99th percentile across the general population was up to more than four times higher than what is reflected in EPA's default intra-species adjustment factor.[75] Accordingly, the WHO recommends using larger uncertainty factors, up to 42X, just to account for normal variability in the human response to chemical exposures among healthy adults.[76,77]

**b. EPA's identification of PESS has important gaps that risk underestimating harms to overburdened groups.**

Our previous comments on the 2024 Draft Risk Evaluation for Formaldehyde highlight EPA's failure to identify, consider, and account for risk among PESS with a transparent methodology that utilizes the best available science.[78] The revised draft does not reflect any changes to better consider the risk to PESS, but instead, EPA removes the consideration and evaluation of several PESS. These revisions do not reflect the best available science and underestimate the risk to PESS due to inadequate identification and evaluation of PESS. The best available science

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[72] Varshavsky, J. R., Rayasam, S. D. G., Sass, J. B., Axelrad, D. A., Cranor, C. F., Hattis, D., Hauser, R., Koman, P. D., Marquez, E. C., Morello-Frosch, R., Oksas, C., Patton, S., Robinson, J. F., Sathyanarayana, S., Shepard, P. M., & Woodruff, T. J. (2023). Current practice and recommendations for advancing how human variability and susceptibility are considered in chemical risk assessment. Environmental Health, 21(Suppl 1), 133. https://doi.org/10.1186/s12940-022-00940-1.

[73] *Id.*

[74] California Environmental Protection Agency (2018), Technical Support Document for the Derivation of Noncancer Reference Exposure Levels. https://oehha.ca.gov/media/downloads/crnr/noncancertsdfinal.pdf.

[75] WHO. (2017). Guidance document on evaluating and expressing uncertainty in hazard characterization. Harmonization project document 11, 2nd edition. https://www.who.int/publications/i/item/9789241513548.

[76] WHO. (2017). Guidance document on evaluating and expressing uncertainty in hazard characterization. Harmonization project document 11, 2nd edition. https://www.who.int/publications/i/item/9789241513548.

[77] Varshavsky, J. R., Rayasam, S. D. G., Sass, J. B., Axelrad, D. A., Cranor, C. F., Hattis, D., Hauser, R., Koman, P. D., Marquez, E. C., Morello-Frosch, R., Oksas, C., Patton, S., Robinson, J. F., Sathyanarayana, S., Shepard, P. M., & Woodruff, T. J. (2023). Current practice and recommendations for advancing how human variability and susceptibility are considered in chemical risk assessment. Environmental Health, 21(Suppl 1), 133. https://doi.org/10.1186/s12940-022-00940-1.

[78] Comment submitted by University of California, San Francisco (UCSF) Program on Reproductive Health and the Environment (PRHE). Available at: https://www.regulations.gov/comment/EPA-HQ-OPPT-2023-0613-0077.

demonstrates that both intrinsic factors, which include biological traits like age, genetic makeup, and pre-existing health conditions, and extrinsic factors, which include psychosocial stress from experiencing income inequality, violence, racism, healthcare inequity, or food insecurity, can individually or collectively increase susceptibility to harm from chemical exposures.[79] Despite formaldehyde's well-established respiratory effects, EPA removed individuals with chronic respiratory disease from the list of identified PESS without scientific justification. Rather than evaluating whether the acute POD adequately protects these populations, EPA simply excludes them from consideration. Furthermore, the revised evaluation removes a prior statement acknowledging the qualitative consideration of race/ethnicity and sex/gender, as well as key information and citations related to sex-based differences in formaldehyde toxicity.[80] EPA provided no explanation for these deletions and thus effectively disregarded several important PESS. Studies have demonstrated that socio-demographic factors can influence a person's susceptibility to harm from toxic chemicals. These factors include income, housing status, access to healthy food, health care, access to green space, and other neighborhood factors that can impact a person's exposure to toxic chemicals[81] as well as their susceptibility to those exposures. For example, people experiencing poverty or racial discrimination may experience psychosocial stress that can enhance susceptibility to the adverse effects of toxic chemicals.[82] These groups must be identified as PESS, even if there is no direct chemical-specific evidence.

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[79] Woodruff, T. J., Rayasam, S. D. G., Axelrad, D. A., Koman, P. D., Chartres, N., Bennett, D. H., Birnbaum, L. S., Brown, P., Carignan, C. C., Cooper, C., Cranor, C. F., Diamond, M. L., Franjevic, S., Gartner, E. C., Hattis, D., Hauser, R., Heiger-Bernays, W., Joglekar, R., Lam, J., … Zeise, L. (2023). A science-based agenda for health-protective chemical assessments and decisions: Overview and consensus statement. Environmental Health,21(1), 132. https://doi.org/10.1186/s12940-022-00930-3; Rachel Morello-Frosch et al., *Understanding the Cumulative Impacts of Inequalities in Environmental Health: Implications for Policy*, 30 Health Affs. 879 (2011), https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.2011.0153; Cliona M. McHale et al., *Assessing Health Risks from Multiple Environmental Stressors: Moving from G×E to I×E*, 775 Mutational Rsch. 11 (2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5863617/; Devon C. Payne-Sturges et al*., Methods for Evaluating the Combined Effects of Chemical and Nonchemical Exposures for Cumulative Environmental Health Risk Assessment*, 15 Int'l. J. Env't Rsch. & Pub. Health 2797 (2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6313653/; Gilbert C. Gee et al., *Environmental Health Disparities: A Framework Integrating Psychosocial and Environmental Concepts*, 112 Env't Health Persps. 1645 (2004), https://doi.org/10.1289/ehp.7074; Gina M. Solomon et al., *Cumulative Environmental Impacts: Science and Policy to Protect Communities* 37 Ann. Rev. Pub. Health 83, 87–88 (2016), https://www.annualreviews.org/doi/pdf/10.1146/annurev-publhealth-032315-021807; Patricia D. Koman et al., *Population Susceptibility: A Vital Consideration in Chemical Risk Evaluation Under the Lautenberg Toxic Substances Control Act*, 17 PLoS Biology 1, 4 (2019), https://journals.plos.org/plosbiology/article?id=10.1371/

[80] U.S. EPA (2025). Revised Draft Human Health Risk Assessment, Table 4-3, Table_Apx B-2.

[81] Payne-Sturges, D. C., Taiwo, T. K., Ellickson, K., Mullen, H., Tchangalova, N., Anderko, L., Chen, A., & Swanson, M. (2023). Disparities in Toxic Chemical Exposures and Associated Neurodevelopmental Outcomes: A Scoping Review and Systematic Evidence Map of the Epidemiological Literature. *Environmental Health Perspectives*, *131*(9), 096001. https://doi.org/10.1289/EHP11750; Morello-Frosch, R., & Shenassa, E. D. (2006). The environmental "riskscape" and social inequality: Implications for explaining maternal and child health disparities. *Environmental Health Perspectives*, *114*(8), 1150–1153. https://doi.org/10.1289/ehp.8930; Pullen Fedinick, K., Yiliqi, I., Lam, Y., Lennett, D., Singla, V., Rotkin-Ellman, M., & Sass, J. (2021). A Cumulative Framework for Identifying Overburdened Populations under the Toxic Substances Control Act: Formaldehyde Case Study. *International Journal of Environmental Research and Public Health*, *18*(11), Article 11. https://doi.org/10.3390/ijerph18116002.

[82] Vesterinen, H. M., Morello-Frosch, R., Sen, S., Zeise, L., & Woodruff, T. J. (2017). Cumulative effects of prenatal-exposure to exogenous chemicals and psychosocial stress on fetal growth: Systematic-review of the human and animal evidence. *PLOS ONE*, *12*(7), e0176331. https://doi.org/10.1371/journal.pone.0176331; Varshavsky, J. R., Rayasam, S. D. G., Sass, J. B., Axelrad, D. A., Cranor, C. F., Hattis, D., Hauser, R., Koman, P. D., Marquez, E. C.,

To improve the identification and consideration of PESS, EPA should focus first on identifying susceptible subpopulations based on either chemical-specific evidence or the broader literature on intrinsic and extrinsic susceptibility factors, but this should not be contingent on chemical-specific data.[83] Then, as a separate step, EPA should consider how to adequately account for the elevated risks for each group, in some cases by using additional scientifically-supported uncertainty factors to those that are already being used to adequately account for human variability among healthy adults (e.g. 42X). The best available scientific evidence indicates that EPA should incorporate one or more additional uncertainty factors to account for multiple chemical and non-chemical stressors when assessing risk to potentially exposed or susceptible subpopulations, beyond the 42X to address intra-species variability.[84] This includes an assessment of risk to individuals with increased susceptibility due to factors such as race/ethnicity or poor nutrition. For example, people living in fenceline communities are more likely to be people of color and are more likely to experience increased exposures to multiple chemical and non-chemical stressors that make them more susceptible to harm, including a broad range of non-chemical stressors like pre-existing disease, racism, and poverty[85]—categories that EPA failed to fully evaluate in the Final Formaldehyde Risk Evaluation.

### c. EPA's Proposed Revisions preclude a health-protective fenceline assessment.

The Final Formaldehyde Risk Evaluation already presents a weak analysis of fenceline cancer risks and fails to account for real world formaldehyde exposures and heightened susceptibility in residents of fenceline communities.[86] The Proposed Revisions further weaken EPA's ability to accurately assess fenceline risks, effectively precluding a health-protective fenceline assessment. For example, EPA concludes in the Proposed Revisions that there is no unreasonable risk to the general population from ambient air exposure to formaldehyde, despite acknowledging potential risks for individuals living near facilities that release formaldehyde. This conclusion is based on the EPA's explicit limitation of its assessment of ambient air exposures to non-combustion sources:

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Morello-Frosch, R., Oksas, C., Patton, S., Robinson, J. F., Sathyanarayana, S., Shepard, P. M., & Woodruff, T. J. (2023). Current practice and recommendations for advancing how human variability and susceptibility are considered in chemical risk assessment. Environmental Health, 21, 1–20. https://doi.org/10.1186/s12940-022-00940-1; McHale, C. M., Osborne, G., Morello-Frosch, R., Salmon, A. G., Sandy, M. S., Solomon, G., Zhang, L., Smith, M. T., & Zeise, L. (2018). Assessing health risks from multiple environmental stressors: Moving from G×E to I×E. Mutation research. Reviews in mutation research, 775, 11–20. https://doi.org/10.1016/j.mrrev.2017.11.003; Payne-Sturges, D. C., Scammell, M. K., Levy, J. I., Cory-Slechta, D. A., Symanski, E., Carr Shmool, J. L., Laumbach, R., Linder, S., & Clougherty, J. E. (2018). Methods for Evaluating the Combined Effects of Chemical and Nonchemical Exposures for Cumulative Environmental Health Risk Assessment. International Journal of Environmental Research and Public Health, 15(12). https://doi.org/10.3390/ijerph15122797.

[83] Varshavsky et al. Current Practice and Recommendations for Advancing How Human Variability and Susceptibility Are Considered in Chemical Risk Assessment, 21(Suppl 1) Env't Health Article No. 133, at 3 (2023), https://doi.org/10.1186/s12940-022-00940-1.

[84] *Id.*

[85] Ronald White et al., Env't Just. Health All. For Chem. Pol'y Reform et al., Life at the Fence line: Understanding Cumulative Health Hazards in Environmental Justice Communities (2018), https://ej4all.org/assets/media/documents/Life%20at%20the%20Fenceline%20-%20English%20-%20Public.pdf.

[86]

> EPA targeted its review of environmental releases to point sources, and did not review the road, nonroad, other automotive exhaust information, or combustion information identified, as formaldehyde produced from combustion sources is not assessed as an independent COU subcategory in this risk evaluation.[87]

However, exposures via these pathways are highly relevant and reasonably foreseeable across the human population and cannot be excluded when evaluating the human health risks posed by formaldehyde. EPA is required under TSCA to account for all "reasonably foreseeable" pathways of exposure.[88] EPA must also conduct risk evaluations using "scientific information, technical procedures, measures, methods, protocols, methodologies, or models, employed in a manner consistent with the best available science."[89] By not estimating total exposure from all potential pathways, EPA is significantly underestimating the risks of harm of formaldehyde in the general population, especially in fenceline communities. Thus, all current exposures must be accounted for.

In addition, EPA's Final Formaldehyde Risk Evaluation fails to account for cumulative exposures to other chemicals and non-chemical stressors that exacerbate risk, or for background exposures to "non-TSCA" uses, including formaldehyde exposures due to secondary formation, tailpipe emissions and plastic food storage products, further undermining the validity of its conclusions for fenceline communities. Assessment of formaldehyde without considering other carcinogens for which co-exposures occur in the human population will underestimate risk because co-exposures to formaldehyde and multiple other carcinogens are prevalent in certain communities in the United States,[90] and co-exposures to these chemicals increases the likelihood of developing cancer.[91] Changes indicated in the Proposed Revisions, including EPA's decision to not consider human variability and susceptibility and its decision to ignore cancer and other chronic health endpoints altogether, further preclude its ability to conduct a robust and health-protective fenceline risk assessment.

4. **EPA's selective reliance on statements from a financially conflicted and inadequately balanced SACC panel undermines the scientific integrity of the risk evaluation.**

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[87] U.S. EPA (2025). Revised Draft Unreasonable Risk Determination of the Risk Evaluation for Formaldehyde.
[88] 15 U.S.C. § 2602 (4).
[89] 15 U.S.C. § 2625(h).
[90] Kristi Pullen Fedinick et al., A Cumulative Framework for Identifying Overburdened Populations under the Toxic Substances Control Act: Formaldehyde Case Study, 18 Int'l J. Env't Rsch. & Pub. Health 6002 (2021), https://doi.org/10.3390/ijerph18116002.
[91] NRC, *Phthalates and Cumulative Risk Assessment* at 5–6; Gina M. Solomon et al., *Cumulative Environmental Impacts: Science and Policy to Protect Communities* at 87– 88, 37 Annual Rev. Public Health (2016), https://www.annualreviews.org/doi/pdf/10.1146/annurev-publhealth-032315-021807; UCSF Program on Reproductive Health and the Environment, *Using the Best Available Science to Assess Hazards and Risks of Industrial Chemicals Will Ensure Better Public Health Decisions* at 3, https://prhe.ucsf.edu/sites/g/files/tkssra341/f/wysiwyg/UCSF%20PRHE%20EPA%20Chemical%20Policy%20v1.pdf ; Woodruff TJ, Caldwell J, Cogliano VJ, Axelrad DA. Estimating cancer risk from outdoor concentrations of hazardous air pollutants in 1990. Environ Res. 2000 Mar;82(3):194-206. doi: 10.1006/enrs.1999.4021. PMID: 10702327

### a. EPA must ensure that SACC membership is balanced and free from financial conflicts of interest.

EPA is required to nominate candidates for the SACC that represent relevant backgrounds and expertise. Pursuant to section 2625(o) of TSCA, the SACC is required to "provide independent advice and expert consultation, at the request of the Administrator, with respect to the scientific and technical aspects of issues relating to the implementation of this title" and will include "representatives of such science, government, labor, public health, public interest, animal protection, industry, and other groups as the Administrator determines to be advisable, including representatives that have specific scientific expertise in the relationship of chemical exposures to women, children, and other potentially exposed or susceptible subpopulations."[92]

Furthermore, when composing federal advisory committees like the SACC, EPA must ensure that members represent balanced interests and industry bias is publicly disclosed and avoided. The Federal Advisory Committee Act (FACA) imposes requirements on federal agencies when they establish or utilize any advisory committee, like the SACC.[93] For example, when an agency seeks to obtain such advice or recommendations, it must ensure the advisory committee: is "in the public interest;"[94] is "fairly balanced in terms of points of view represented and the function to be performed;"[95] and will not be "inappropriately influenced by . . . any special interest, but will instead be the result of the advisory committee's independent judgment."[96]

FACA prohibitions also call for special care with respect to the service on advisory committees of individuals whose employer or business would benefit financially from the committee's recommendations. Federal ethics regulations also require EPA to "[a]ssure that the interests and affiliations of advisory committee members are reviewed for conformance with applicable conflict of interest statutes."[97] Therefore, before finalizing the selection of individual SACC members, EPA must employ a vetting process for conflicts of interest that includes: publicly identifying and disclosing any conflicts that include financial ties with industry; determining whether a conflict of interest exists with the committee member; and finally implementing the necessary procedures to manage any conflicts of interest to ensure the composition of the SACC is free from financial conflicts of interest. This vetting process also ensures that the burden of vetting financial conflicts of interest does not inappropriately fall on the public.

While conflicts of interest information can be found in some published papers, not all funding arrangements can be tracked. Without disclosure of financial conflicts of interest, EPA cannot ensure that committee work products are free of biased scientific conclusions, as required by FACA. In addition, failing to prescreen candidates for ethics concerns places the burden of vetting candidates on the public, which could inappropriately allow candidates with potential conflicts of interest to be nominated to the SACC. EPA must evaluate potential conflicts of interest as the first step in determining whether an individual is eligible for nomination to the *ad hoc* SACC.

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[92] 15 U.S.C. § 2625(o).
[93] 5 U.S.C. App. II, § 3(2).
[94] Id. App. II, § 9(2).
[95] Id. § 5(b)(2).
[96] Id. § 5(b)(3).
[97] 41 C.F.R. § 102-3.105(h)

Additionally, research has shown that disclosing financial conflicts of interest alone is insufficient to prevent bias. Systematic reviews have confirmed that disclosed financial conflicts of interest in scientific studies are associated with research outcomes biased towards the financial sponsor and therefore demonstrate why disclosure is not a solution to reducing bias in guideline committees.[98] Even when controlling for methodological biases, studies sponsored by industry or that have an author with a financial conflict of interest are more likely to have results that favor the sponsor's products than studies with no industry sponsorship or author conflict of interest.[99,100,101,102] The influence of financial ties on research can be attributed to various types of biases, and this conflict of interest must be distinguished from non-financial interests in the research.[103]

Committee members who disclose conflicts of interest actually provide more biased advice due to the belief that they have adequately warned recipients of the information they have provided and/or to compensate for the fact that their advice will be disregarded.[104,105] Conflicts of interest among committee members are increasingly being recognized as significant contributors to bias in guideline recommendations.[106,107,108] For example, an association has been established between financial conflicts of interest among expert reviewers and clinical guideline recommendations that favor the interests of the industry providing support.[109,110] Several factors influence the extent to which committee members are likely to influence guidelines and recommendations, including the relevance of the topic to the committee members interest and

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[98] Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. Cochrane Database Syst Rev2017;2:MR000033.pmid:28207928

[99] Odierna DH, Forsyth SR, White J, et al. The cycle of bias in health research: a framework and toolbox for critical appraisal training. Account Res. 2013;20(2):127-41. 11

[100] Fabbri A, Lai A, Grundy Q, et al. The Influence of Industry Sponsorship on the Research Agenda: A Scoping Review. Am J Public Health. 2018;108(11):e9-e16. 12

[101] Psaty BM, Prentice RL. Minimizing bias in randomized trials: the importance of blinding. JAMA. 2010;304(7):793-4. 13

[102] Psaty BM, Kronmal RA. Reporting mortality findings in trials of rofecoxib for Alzheimer disease or cognitive impairment: a case study based on documents from rofecoxib litigation. JAMA. 2008;299(15):1813-7.

[103] Bero LA, Grundy Q. Why Having a (Nonfinancial) Interest Is Not a Conflict of Interest. PLoS Biol. 2016 Dec 21;14(12):e2001221. doi: 10.1371/journal.pbio.2001221. PMID: 28002462; PMCID: PMC5176169.

[104] Loewenstein G, Sah S, Cain DM. The unintended consequences of conflict of interest disclosure. JAMA2012;307:669-70. doi:10.1001/jama.2012.154. pmid:22337676

[105] Romain PL. Conflicts of interest in research: looking out for number one means keeping the primary interest front and center. Curr Rev Musculoskelet Med. 2015 Jun;8(2):122-7. doi: 10.1007/s12178-015-9270-2. PMID: 25851417; PMCID: PMC4596167.

[106] Blake P, Durão S, Naude CE, Bero L. An analysis of methods used to synthesize evidence and grade recommendations in food-based dietary guidelines.

[107] Tabatabavakili S, Khan R, Scaffidi MA, Gimpaya N, Lightfoot D, Grover SC. Financial conflicts of interest in clinical practice guidelines: a systematic review. Mayo Clin Proc Innov Qual Outcomes2021;5:466-75. Doi:10.1016/j.mayocpiqo.2020.09.016 pmid:33997642

[108] Brems JH, Davis AE, Clayton EW. Analysis of conflict of interest policies among organizations producing clinical practice guidelines. PLoS One2021;16:e0249267. doi:10.1371/journal.pone.0249267 pmid:33930893

[109] Nejstgaard CH, Bero L, Hróbjartsson A, et al. Association between conflicts of interest and favourable recommendations in clinical guidelines, advisory committee reports, opinion pieces, and narrative reviews: systematic review. BMJ2020;371:m4234.pmid:33298430

[110] Coyne DW. Influence of industry on renal guideline development. Clin J Am Soc Nephrol2007;2:3-7, discussion 13-4. doi:10.2215/CJN.02170606 pmid:17699377

type and magnitude of the relationship comprising the conflict.[111] Therefore, allowing SACC nominees with financial ties to any of the regulated chemical companies would risk biasing the recommendations they make towards industry interests. The "megaphone effect" that multiple SACC members with financial conflicts of interest could create by making aligned recommendations raises additional concerns and creates the potential for systemic bias.[112]

Therefore, individuals who have been nominated to the SACC who also have financial relationships with companies that can benefit from the recommendations of the committee should be excluded from consideration.[113,114,115,116,117] We further recommend that EPA use predetermined criteria in Table 1 below to evaluate and respond to the risk of bias from the interests of prospective SACC members, as outlined in Table 1 below. [118] For example, EPA should consider individuals as "High risk" if they have financial ties with a chemical company (a company employee, paid adviser or consultant, recipient of speaker fees, owner of financial holdings in the company (e.g., shares, patents, royalties), recipient of research grant money from company, recipient of monetary gift (e.g., to cover conference travel, accommodation, registration), managerial or advisory position, including unpaid) or position of control or decision making within such a chemical corporation.

**Table 1. Risk management model for financial conflicts of interest among *ad hoc* SACC nominees. Adapted from: Parker L, Bero L. Managing risk from conflicts of interest in guideline development committees BMJ 2022; 379 doi: https://doi.org/10.1136/bmj-2022-072252**

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[111] Parker L, Bero L. Managing risk from conflicts of interest in guideline development committees BMJ 2022; 379 :e072252 doi:10.1136/bmj-2022-072252

[112] Ralston R, Hil SE, da Silva Gomes F, Collin J. Towards preventing and managing conflict of interest in nutrition policy? an analysis of submissions to a consultation on a draft WHO tool. Int J Health Policy Manag2021;10:255-65.pmid:32610752

[113] Bero L, Anglemyer A, Vesterinen H, Krauth D. The relationship between study sponsorship, risks of bias, and research outcomes in atrazine exposure studies conducted in non-human animals: Systematic review and meta-analysis. Environment International. 2016;92-93:597-604.

[114] Yank V, Rennie D, Bero LA. Financial ties and concordance between results and conclusions in meta-analyses: Retrospective cohort study. British Medical Journal. 2007;335(7631):1202-5.

[115] Mandrioli D, Kearns CE, Bero LA. Relationship between Research Outcomes and Risk of Bias, Study Sponsorship, and Author Financial Conflicts of Interest in Reviews of the Effects of Artificially Sweetened Beverages on Weight Outcomes: A Systematic Review of Reviews. PLoS One. 2016;11(9):e0162198.

[116] Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. The Cochrane database of systematic reviews. 2017;2:MR000033-MR.

[117] Woodruff TJ, Rayasam SDG, Axelrad DA, Koman PD, Chartres N, Bennett DH, Birnbaum LS, Brown P, Carignan CC, Cooper C, Cranor CF, Diamond ML, Franjevic S, Gartner EC, Hattis D, Hauser R, Heiger-Bernays W, Joglekar R, Lam J, Levy JI, MacRoy PM, Maffini MV, Marquez EC, Morello-Frosch R, Nachman KE, Nielsen GH, Oksas C, Abrahamsson DP, Patisaul HB, Patton S, Robinson JF, Rodgers KM, Rossi MS, Rudel RA, Sass JB, Sathyanarayana S, Schettler T, Shaffer RM, Shamasunder B, Shepard PM, Shrader-Frechette K, Solomon GM, Subra WA, Vandenberg LN, Varshavsky JR, White RF, Zarker K, Zeise L. A science-based agenda for health-protective chemical assessments and decisions: overview and consensus statement. Environ Health. 2023 Jan 12;21(Suppl 1):132. doi: 10.1186/s12940-022-00930-3. PMID: 36635734; PMCID: PMC9835243.

[118] Parker L, Bero L. Managing risk from conflicts of interest in guideline development committees BMJ 2022; 379 :e072252 doi:10.1136/bmj-2022-072252

| Risk Level | Type of interest | Example | Examples of entity generating secondary interest | Suggested management |
|---|---|---|---|---|
| **High risk** | Financial link* with large national or multinational chemical corporation or position of control or decision making within such a corporation | Applicant, partner, or child is one of the following:<br>A company employee<br>Paid adviser or consultant<br>Recipient of speaker fees<br>Owner of financial holdings in the company (e.g., shares, patents, royalties)<br>Recipient of research grant money from company<br>Recipient of monetary gift (e.g., to cover conference travel, accommodation, registration)<br>Managerial or advisory position, including unpaid (e.g., director, trustee, member of advisory board) | Large international chemical product manufacturers (e.g., Unilever, Procter & Gamble, , 3M) Chemical companies providing raw material used in large scale manufacturing and processing (e.g., Monsanto, DuPont, BASF, Bayer, Dow Chemical, Syngenta)<br><br>Trade organizations and other groups that represent chemical company interests (e.g., American Chemistry Council, Treated Wood Council, Fertilizer Institute, Arsenic Science Task Force) | Reject committee membership until 3-5 years have passed since eliminating conflict(s) of interest (e.g., by divesting financial links, resigning from position, or rejecting speaker fees) |
| | Position of control or decision making over small industry company | Applicant, partner, or child is owner of small company | Local manufacturers such as boutique personal care product maker, small business,<br>Small scale manufacturing business | |
| Medium risk | Financial link* with chemical industry, with no decision making or control over corporation | Applicant, partner, or child is a small chemical company employee | Local manufacturers such as boutique personal care product maker, small business,<br>Small scale manufacturing business | Individual cannot chair and may have only restricted participation in guideline committee until 3-5 years have passed since eliminating conflict(s) of interest |
| | Financial link* with government-chemical industry partnership | Applicant, partner, or child receives grant funding for research from formal partnership between government department and multinational chemical company | Grant from government health department-multinational chemical company partnership to study health effects | |
| | Personal financial gain from chemical related work | Applicant, partner, or child is paid for self-employed work related to chemicals (e.g., book, consulting) | Not applicable | |

| Risk Level | Type of interest | Example | Examples of entity generating secondary interest | Suggested management |
|---|---|---|---|---|
| Low risk | Professional interests of prospective member | Author of empirical studies, systematic reviews (where the research and researchers are not funded by industry or other chemical sector business)<br>Recipient of research grant from non-industry sources (e.g., government)<br>Member of previous guidelines committee<br>Key opinion leader—e.g., author of opinion based articles, advocacy (not funded by industry or other chemical sector business)<br>Member of a professional society that is not industry funded<br>Working as a health professional in a public health/environmental health/medical related field (e.g., toxicologist, medical doctor) | Not applicable | Full participation |
| Minimal or no risk | Personal experiences, values, or lifestyle habits of prospective member | Political and economic views<br>Spiritual or religious affiliation<br>Cultural practices, upbringing, ethnicity<br>Professional and personal experiences<br>Lifestyle habits and preferences, including dietary patterns<br>Health problems, including dietary allergies and intolerances and those with recommended dietary restrictions<br>Social relationships, including professional interest group membership, friendly or | Not applicable | Full participation |

| Risk Level | Type of interest | Example | Examples of entity generating secondary interest | Suggested management |
|---|---|---|---|---|
| | | hostile connections with others | | |

### b. EPA's *ad hoc* formaldehyde SACC did not meet FACA requirements and included members with clear financial conflicts of interest.

The *ad hoc* formaldehyde SACC included several members with financial ties to chemical companies or the American Chemistry Council, listed below:

**Debra A. Kaden, PhD, ATS;** Senior Practitioner at Ramboll. Has received funding from Hexion and Formacare for her research on formaldehyde.[119,120] Formacare represents chemical and manufacturing companies that produce 95% of the formaldehyde in the European Union.[121]

**Sang-Tae Kim, PhD, DABT, ATS, ERT,** Senior Principal toxicologist at Ashland, a company that purchases and uses formaldehyde.[122] He is a member of committees at various Ashland supported industry associations, including the Society of Chemical Manufacturers and Affiliates (SOCMA),[123] which represents the interests of specialty batch chemical industries[124];

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[119] Albertini, R. J., & Kaden, D. A. (2017). Do chromosome changes in blood cells implicate formaldehyde as a leukemogen?. *Critical reviews in toxicology*, *47*(2). https://pubmed.ncbi.nlm.nih.gov/27685449/ ("This project was undertaken with funds provided to Ramboll Environ by Hexion Inc., a global manufacturer operating approximately 60 industrial facilities around the world with interest in FA and FA derivatives. Hexion participates in the American Chemistry Council Formaldehyde Panel")

[120] Lang, I., Bruckner, T., & Triebig, G. (2008). Formaldehyde and chemosensory irritation in humans: a controlled human exposure study. *Regulatory toxicology and pharmacology 50*(1), https://pubmed.ncbi.nlm.nih.gov/17942205/ ("The authors… thank the FormaCare sector group of CEFIC, Brussels, Belgium for the financial contribution to perform this study.").

[121] See Formacare, *About Fromacare,* https://www.formacare.eu/about-formacare/ (last visited Mar. 6, 2024), ("Formacare is the formaldehyde sector group of the European Chemical Industry Council (Cefic) representing key European producers of formaldehyde and derivatives ... Members of formacare represent approximately 95% of the formaldehyde produced in the EU 27, and Norway.")

[122] See Ashland, *Uses and Applications of Formaldehyde*, https://www.ashland.com/file_source/Ashland/Documents/Sustainability/rc%20formaldehyde.pdf, (last visited Mar. 6, 2024), ("Formaldehyde is used to produce chemical intermediates, formaldehyde containing resins and in the production of fertilizer, paper, and plywood. It is also used in the production of cosmetics and sugar, in well drilling fluids, as a preservative for grains and seed dressings, in the production of latex, in leather tanning, in embalming fluids, tissue preservation, in wood preservation, and in photographic film production. Ashland uses formaldehyde to produce phenol formaldehyde and urea formaldehyde resins and manufactures certain resins by reacting formaldehyde with polyacrylamide and guanidine-cyano blends").

[123] Nominee Bios at 15.

[124] See SOCMA, *About SOCMA,* https://www.socma.org/socma-unveils-key-findings-from-contract-manufacturing-outlook-survey-in-the-specialty-chemicals-industry/,(last visited Mar. 6, 2024), ("Solely dedicated to the specialty and fine chemical industry, SOCMA builds commercial connections, supports safe manufacturing and operations, and advocates for regulatory and legislative policies for the batch and specialty chemical sector."); *See also* current list of SOCMA members, which includes Ashland; https://www.socma.org/socma-membership/membership-list/, (last visited Mar. 6, 2024).

International Pharmaceutical Excipients Council-Americas (IPEC-Americas);[125] and for the ACC.[126] His research, conducted while employed at Ashland, found that the cancer risk from personal care and cosmetics products containing formaldehyde "is negligible".[127]

**Roget O. McClellan, DVM, MMS, DSc,** President Emeritus of the Chemical Industry Institute of Toxicology (CIIT)[128] and funded by the ACC.[129] Advocated for a formaldehyde cancer risk model developed by CIIT,[130] a study that was later used by industry to advocate for allowing

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[125] Nominee Bios at 15; *See also* current list of IPEC-Americas Member Companies, which includes Ashland; https://ipecamericas.org/join-us/member-companies, (last visited Mar. 6, 2024).
[126] Nominee Bios at 15; *See also;* ACC's 2020 Board of Directors, which includes Bill Wulfsohn, Chairman and CEO of Ashland; https://www.americanchemistry.com/chemistry-in-america/news-trends/press-release/2019/american-chemistry-council-elects-new-class-to-board-of-directors, (last visited Mar. 6, 2024).
[127] See Kim, S. T., Shao, K., Oleschkewitz, C., & Hamilton, R. (2023). Margin of exposure to free formaldehyde in personal care products containing formaldehyde-donor preservatives: Evidence for consumer safety. *Regulatory toxicology and pharmacology,* 145., https://www.sciencedirect.com/science/article/abs/pii/S0273230023001873.
[128] Based on Roger O. McClellan's Curriculum Vite, he served as the President Emeritus for the Chemical Industry Institute of Toxicology from 1999-2020, Accessed March 8, 2024, https://drive.google.com/file/d/1szZGEBDZ_W4B5EbU8PooJ5JRTmpM8vuE/view?usp=share_link, ("The institute which operated post-McClellan's tenure as the Hamner Institutes for Health Sciences closed in 2020 … The research was funded for many years primarily by 30 major chemical companies. This support base was expanded near the end of Dr. McClellan's term through a partnership with the American Chemical Council which represents 190 leading chemical companies.").
[129] *Hamner Inst. Closes its Doors*, C&EN 94, 2, 16–17 (Jan. 11, 2016) (explaining that "the Chemical Industry Institute of Toxicology," subsequently known as the Hamner Institutes for Health Sciences, "was founded by 11 chemical companies in 1974 to gauge the potential impact of chemicals on human health. In 2001, 90% of its $18 million budget came from the Long-Range Research Initiative of the American Chemistry Council."), https://pubs.acs.org/doi/full/10.1021/cen-09402-buscon008.
[130] https://downloads.regulations.gov/EPA-HQ-ORD-2010-0396-0097/attachment_1.pdf ("*In the interest of full disclosure as the President (1988–1999) of the Chemical Industry Institute of Toxicology I advocated for the study of formaldehyde as a prototypical chemical to advance the use of mechanistic toxicological evidence in understanding human health risks of chemicals. The Institute's expenditures on Formaldehyde research exceeded those on any other chemical. The Institute's research findings are at the core of the IRIS document.*"); *also see* Draft IRIS Toxicological Review of Formaldehyde (Inhalation); Formaldehyde Overview External Draft April 2022, Docket EPA-HQ-ORD-2010-0396 (April 26, 2022), https://downloads.regulations.gov/EPA-HQ-ORD-2010-0396-0040/content.pdf, ("A biologically based dose-response (BBDR) time-to-tumor model for the formaldehyde-induced rat nasal tumors was available (Conolly et al., 2003; CIIT, 1999). This model consisted of interfacing dosimetry models for formaldehyde and formaldehyde-induced DPX in the rat nasal passages (Kimbell et al., 2001a; Kimbell et al., 2001b; Conolly et al., 2000) with two-stage clonal expansion (TSCE) models for predicting the probability of occurrence of nasal SCC (Conolly et al., 2003)."); *see also research funded by ACC to update this model:* Conolly, R.B., Schroeter, J., Kimbell, J.S., Clewell, H., Andersen, E., & Gentry, P.R. (2023). Updating the Biologically Based Dose-Response Model for the Nasal Carcinogenicity of Inhaled Formaldehyde in the F344 Rat. *Toxicological Sciences* 193(1). https://academic.oup.com/toxsci/article/193/1/1/7076626 (Funding: "Foundation for Chemistry Research & Initiatives (FCRI), a 501(c)(3) tax-exempt organization established by the American Chemistry Council (ACC).").
[130] See, EPA "1999

plywood plants to continue emitting formaldehyde.[131,132,133] Conducted research in collaboration with authors from Dow opposing linear low dose methodology funded by ACC.[134]

**Judy A. Strickland, PhD, DABT**, Retired Principal Predictive Toxicologist with Inotiv, with undisclosed clients in the bio-pharmaceutical field. Member of the American Society for Cellular and Computational Toxicology whose sponsors include Corteva.[135]

**Lisa M. Sweeney, PHD, DABT, CHMM**, toxicologist with UES, Inc. with various customers in the aerospace and automobile industry.[136] Submitted commented on behalf of ACC on the use of Physiology Based Pharmacokinetic Models in Risk Assessment.[137]

**Douglas C. Wolf, PhD, DVM**, was a senior fellow at Syngenta Crop Protection, Greensboro, North Carolina, shortly before his tenure on the Formaldehyde ad-hoc SACC. Syngenta's commercial interests include chemicals subject to EPA review and risk assessment. Conducted research and authored several papers alongside industry-funded individuals.

The *ad hoc* SACC was asked to review and evaluate the validity of the methods used to estimate the health risks of formaldehyde. The final SACC report influenced EPA to revise its risk characterization methodologies that led to a significant underestimation of real-world formaldehyde risks, directly benefitting industries that advocate for retaining certain uses of the chemical. As such, it is questionable whether any employee of or consultant to a company that financially benefits from the production, use, or disposal of the chemical could serve on the *ad hoc* SACC without skirting FACA's safeguards.

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[131] See, EPA "1999 National-Scale Air Toxics Assessment; Formaldehyde" https://archive.epa.gov/airtoxics/nata1999/web/html/formald.html, (last updated Feb. 21, 2016), ("For the 1999 national-scale assessment, EPA is estimating risks from formaldehyde using a cancer unit risk (potency) estimate developed by the CIIT Centers for Health Research (formerly the Chemical Industry Institute of Technology), published in 1999. EPA has also used the CIIT cancer potency estimate for certain air toxics rules, such as the technology-based standard for the plywood industry.")

[132] https://www.latimes.com/archives/la-xpm-2004-may-21-na-plywood21-story.html

[133] Union of Concerned Scientists, "Plywood Rule Used Industry Funded Research, Ignored Independent Scientific Studies", Accessed March 8, 2024, https://www.ucsusa.org/resources/attacks-on-science/plywood-rule-used-industry-funded-research-ignored-independent, ("In 2004, the Environmental Protection Agency (EPA) adopted a new air pollution rule that would exempt many plywood manufacturers from restrictions on the emission of formaldehyde and other pollutants into the air").

[134] See: e.g., Rhomberg, L.R., Goodman, J.E., Haber, L.T., Dourson, M., Andersen, M.E., Klaunig, J.E., Meek, B., Price, P.S., McClellan, R.O., & Cohen, S.M. (2011). Linear Low-Dose Extrapolation for Noncancer Health Effects is the Exception, Not the Rule. *Crit. Rev. Toxicol*. 41(1). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3038594/ ("This paper was prepared with financial support provided by the American Chemistry Council to Gradco LLC d/b/a Gradient … This paper was prepared with financial support to Gradient, a private environmental consulting firm, and several other organizations from the American Chemistry Council.")

[135] American Society for Cellular and Computational Toxicology, *Current Organizational Sponsors,* https://www.ascctox.org/supporting-organizations (last accessed Mar. 12, 2024).

[136] UES, *Solving Scientific Challenges for 50 Years,* About | UES, Inc. (last accessed Mar. 12, 2024).

[137] *See, e.g.,* Comments of Michael L. Gargas, Lisa M. Sweeney, Christopher R. Kirman, and Robert G. Tardiff, Ph.D., ATS, all four of The Sapphire Group, Inc, on Approaches for the Application of Physiologically Based Pharmacokinetic (PBPK) Models and Supporting Data in Risk Assessment, Docket EPA-HQ-ORD-2005-0022 (Oct. 12, 2005), https://downloads.regulations.gov/EPA-HQ-ORD-2005-0022-0011/attachment_1.pdf, ("Acknowledgement: This work was sponsored by The Halogenated Solvents Industry Alliance, CropLife America and the American Chemistry Council.")

EPA's process of assembling the *ad hoc* SACC also raised several concerns. First, EPA failed to include transparent or effective financial conflict of interest disclosure statements. There are several candidates whose biographical profiles did not disclose publicly their financial relationships with industries, some of which have a particular interest in the topic of this committee. While this information can be found in some published papers, not all funding arrangements can be tracked. Disclosure and financial conflict of interest policies play an essential role in protecting EPA and committee work products from the possibility of biased scientific conclusions and must be strictly enforced and routinely addressed to ensure the quality of SACC reviews and other work products. Further, although disclosing conflicts of interest was previously seen as sufficient to manage committee members' interests, research has shown paradoxically that those members who disclose conflicts of interest provide more biased advice due to the belief that they have adequately warned recipients of the information they have provided and/or to compensate for the fact that their advice will be disregarded.[138,139] Systematic reviews have established that disclosed financial conflicts are associated with research outcomes biased towards the sponsor, demonstrating that disclosure alone is not a solution to reducing bias.[140] The most effective approach to avoiding bias is not to include those who have a financial conflict of interest.

Second, EPA failed to nominate candidates representing balanced viewpoints. For example, in violation of FACA, the *ad hoc* formaldehyde SACC members do not represent populations directly impacted, susceptible, vulnerable, and/or highly exposed to formaldehyde. There are many examples of successful implementation of approaches that have demonstrated that incorporating knowledge resources outside of traditional academic and science fields can greatly enrich the research and policy process.[141] Because the *ad hoc* SACC lacked this representation, it cannot be considered balanced under FACA and EPA must reconstitute the panel or convene a new advisory committee with appropriately balanced scientific perspectives and members without financial conflicts of interest before relying on the panel's conclusions in any final agency action.

### c. In the Proposed Revisions, EPA selectively cited statements from the SACC report and chemical industry comments to support conclusions that downplay health risks.

In the Proposed Revisions, EPA selectively cited and implemented statements from the SACC report and chemical industry comments that support conclusions minimizing risk, while disregarding comments from non-governmental organizations, academic scientists, and public health experts (see Table 2). Rather than engaging with the full scope of SACC critiques and

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[138] Romain PL. Conflicts of interest in research: looking out for number one means keeping the primary interest front and center. Curr Rev Musculoskelet Med. 2015 Jun;8(2):122-7. doi: 10.1007/s12178-015-9270-2. PMID: 25851417; PMCID: PMC459616.

[139] Loewenstein G, Sah S, Cain DM. The unintended consequences of conflict of interest disclosure. JAMA2012;307:669-70. doi:10.1001/jama.2012.154. pmid:22337676.

[140] Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. Cochrane Database Syst Rev2017;2:MR000033.pmid:28207928.

[141] Anderson, B.E., Naujokas, M.F. and Suk, W.A., 2015. Interweaving knowledge resources to address complex environmental health challenges. *Environmental health perspectives*, 123(11):1095-1099.

public comments, including concerns about underestimation of exposure, insufficient protection of PESS, and modeling limitations, EPA extracted isolated statements in the Proposed Revisions that endorsed reduced benchmarks and narrowed exposure pathways—points that were largely echoed in public comments submitted by the chemical industry or industries that financially benefit from the production of formaldehyde. This selective use of advisory input does not reflect a balanced or transparent evaluation of science, raises concerns about scientific integrity, and undermines the credibility of the risk evaluation conclusions. This approach is particularly concerning, given the presence of financial conflicts among some SACC members and commenters, as well as the significant disagreement on critical issues among panel members reflected in the SACC report (see for example Comment 1d above).

**Table 2: Analysis of Overlapping Recommendations from the SACC and Public Commenters on Formaldehyde**

| **SACC Recommendation Detail** *(Note: details listed in this column do not necessarily imply consensus agreement by the SACC)* | **SACC Recommendation Implemented in EPA's December 2025 Memo?** | **Public Commenting Group(s) Reflecting SACC Recommendation** |
|---|---|---|
| **Threshold Approach for Cancer:** Manage acute sensory irritation as a "treatment effect" that protects against all downstream events, including cancer. | **Implemented.** Transitioned to a **Threshold Mode of Action (MOA)** for cancer. | ACC Panels, Hexion, Wood Associations, industry toxicologists. |
| **Reduction of Uncertainty Factors:** Reduce the intrapopulation variability factor (*UFH*) to 1 or 3 for direct-acting portal-of-entry irritants. | **Implemented.** Reduced total *UFH* **to 1** (1 for toxicokinetics and 1 for toxicodynamics). | Composite Panel Association (CPA), ACC Panels, AWC. |
| **Abandonment of IRIS Values:** Discontinue reliance on the IRIS chronic RfC and cancer IUR, which some peer reviewers found "unreliable." | **Implemented.** The memo explicitly **no longer relies** on the EPA IRIS RfC or IUR. | ACC, manufacturing and chemical companies (Hexion, Bakelite), SBA. |
| **Distal Site Cancer Plausibility:** Acknowledge the lack of biological plausibility for | **Implemented.** Adopted threshold approach; **distal** | ACC Panels, wood associations, industry toxicologists. |

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|---|---|---|
| Myeloid Leukemia at distal sites due to rapid detoxification. | **cancer is not expected** if irritation is managed. | |
| **Acknowledgement of Endogenous Levels:** Factor in that formaldehyde is naturally produced and rapidly detoxified by the human body. | **Implemented (Qualitative).** Used to support the threshold MOA and POD reevaluation. | Wood product associations, chemical manufacturers. |
| **Quantitative Aggregate Assessment:** Perform a quantitative assessment rather than a qualitative discussion to avoid underestimating risk. | **Not Implemented.** EPA maintained there is **"too much uncertainty"** for quantification. | Earthjustice, Environmental Defense Fund (EDF), UCSF PRHE. |
| **Cumulative Risk Assessment:** Evaluate formaldehyde alongside shared-outcome carcinogens (e.g., 1,3-butadiene) as a chemical class. | **Not Implemented.** Deemed **beyond the scope** of the current risk evaluation. | Environmental Defense Fund (EDF), Earthjustice. |
| **Probabilistic Modeling:** Provide state-of-the-art probabilistic models for overall calculations rather than deterministic ones. | **Not Implemented.** The memo continues to rely on **deterministic** MOE calculations. | Academic experts, public health researchers. |
| **Vehicle Microenvironments:** Quantify exposure in vehicle cabins as a unique microenvironment with peak entry and durable voyage concentrations. | **Not Implemented.** Not added as a **new distinct quantitative scenario** in this specific update. | Academic scientists, bystander risk commenters. |
| **Challenged Urban Communities:"** Add a unique PESS community scenario for mixed-use urban areas where residential vents and industry are in close proximity. | **Not Implemented.** The memo did not implement this **specific community-level aggregation**. | Earthjustice, Boundless Community Action, fenceline community advocates. |

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|---|---|---|
| **Environmental Pathway Assessment:** Quantitatively assess releases to water and degradation products like **methylene glycol**. | **Not Implemented.** Memo focuses exclusively on **human health inhalation**. | Northwest Indian Fisheries Commissioner, National Aquaculture Association. |
| **Secondary Formation from Industry:** Quantitatively explore the 10-30% of secondary formaldehyde that comes from industrial precursor releases. | **Not Implemented.** Focused on **direct releases**; no quantitative secondary aggregation. | Fenceline community advocacy groups. |
| **EFAST Modeling for Water:** Use the EFAST model to provide conservative release estimates to water when monitoring data is missing. | **Not Implemented.** EPA maintains water/soil pathways are **negligible**. | *SACC technical recommendation—not reflected in public comments* |
| **Person-Oriented Modeling:** Adopt frameworks (like LifeLine) that aggregate risks across a person's lifetime and different population groups. | **Not Implemented.** Memo does not utilize **agent-based or person-oriented** modeling. | *SACC technical recommendation —not reflected in public comments.* |
| **Distribution Chain Exposures:** Assess workers in massive warehouses, distribution centers, and retail show rooms. | **Not Implemented.** Focus remains on **manufacturing and processing** scenarios. | *SACC technical recommendation —not reflected in public comments.* |
| **AMTIC Temporal Normalization:** Organize monitoring data by time of day and season to better align with POD studies. | **Not Implemented.** Used existing **ambient air datasets** without new statistical detrending. | *SACC technical recommendation —not reflected in public comments.* |
| **Children's Microenvironments:** More thoroughly address children's exposures in school buses and playgrounds covered in tire crumb rubber. | **Not Implemented.** No specific **new child-specific exposure scenarios** were quantified. | *SACC technical recommendation —not reflected in public comments.* |