Comments of Environmental Defense Fund on

Availability of the Draft IRIS Toxicological Review of Formaldehyde (Inhalation)

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Introduction

Environmental Defense Fund (EDF) commends EPA for developing the draft Integrated Risk Information System (IRIS) Toxicological Review of Formaldehyde (Inhalation).

Formaldehyde is subject to regulation under multiple environmental statutes. It is important that decisions made under these environmental statutes be based on the best available science. A cornerstone is an IRIS assessment that all EPA program offices and regions can rely upon. While these statutes vary in their requirements, the science used for decisions made pursuant to these discussions should not. Thus, the need for an Agency-level assessment.

An updated IRIS formaldehyde assessment is needed so that risk mitigation decisions will be made considering the full range of toxicities that formaldehyde can cause or exacerbate, such as asthma. This is important for vulnerable populations including frontline communities that may have higher incidences of asthma and face higher exposures to carcinogens.

Despite the well-documented health effects of formaldehyde, this assessment has been delayed for years, often because of specious claims by the regulated community about the quality of IRIS assessments, and political interference, particularly under the Trump Administration. This has impacted the robustness of these decisions. Given the critical need for the IRIS assessment, we urge EPA to resist further delays based on future specious claims by those who would benefit by further delay.

EDF applauds EPA's Office of Research and Development's IRIS program for a thorough, clear, well documented robust assessment that clearly demonstrates that the IRIS program

heeded the advice of the National Academies of Sciences, Engineering, and Medicine (NASEM) in their 2014[1] and 2018[2] reports on the IRIS program.

EDF looks forward to the NASEM review and supports the IRIS program in their efforts to finalize the IRIS assessment for formaldehyde as soon as possible. EDF offers the following specific comments on the assessment.

Specific Comments

1. **EDF recommends that EPA consider the risk to myeloid leukemia its inhalation cancer risk (IUR).**

Although the Draft IRIS Toxicological Review of Formaldehyde—Inhalation ("Draft Assessment") concludes that the "evidence demonstrates" that formaldehyde inhalation causes myeloid leukemia, the current inhalation unit risk (IUR) was derived solely on the basis of nasal cancers using human data on nasopharyngeal cancers. Specifically, the IUR was derived from a large National Cancer Institute (NCI) occupational epidemiology study conducted by Beane-Freeman et al., 2013. EPA thoroughly explains its decision to exclude myeloid leukemia from the cancer IUR by discussing the potential limitations and uncertainties associated with the data that would be used to inform the unit risk. EPA even calculates a myeloid leukemia specific IUR considering several quantitative risk assessment approaches, which is in line with recommendations from the National Academies on EPA's 2011 Draft IRIS Assessment of Formaldehyde.[3]

In its External Review Charge Questions for the Draft Assessment, EPA asked whether the unit risk estimate for myeloid leukemia should inform the IUR for cancer and, if it should, how specifically should the unit risk estimate for myeloid leukemia inform the estimate. EDF recommends that the agency consider using the unit risk for myeloid leukemia to inform the overall cancer IUR. As stated previously, EPA did conclude that the available scientific evidence "demonstrates" that formaldehyde inhalation causes myeloid leukemia. Furthermore, as EPA stated in the Draft Assessment, the public health burden should be considered; nasopharyngeal cancer is rare and, in comparison, myeloid leukemia is more prevalent (pg. 712). EDF does not have specific recommendations for how to include the unit risk of myeloid leukemia to that of the overall cancer IUR. Rather, we ask the agency to consider the following points as it reviews comments on how to potentially update the cancer IUR. When deciding if and how the unit risk for myeloid leukemia should inform the cancer IUR, EPA should consider the existing weakness associated with the current IUR. Our specific points to consider are as follows:

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[1] National Research Council. 2014. Review of EPA's Integrated Risk Information System (IRIS) Process. Washington, DC: The National Academies Press. https://doi.org/10.17226/18764

[2] National Academies of Sciences, Engineering, and Medicine. 2018. Progress Toward Transforming the Integrated Risk Information System (IRIS) Program: A 2018 Evaluation. Washington, DC: The National Academies Press. https://doi.org/10.17226/25086.

[3] National Research Council. 2011. Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde. Washington, DC: The National Academies Press. https://doi.org/10.17226/13142.

a. **Uncertainty with the exposure metric.** EPA acknowledged that one significant uncertainty associated with the current IUR for nasopharyngeal cancer is related to the exposure metric chosen to derive the IUR. EPA used the cumulative exposure metric to calculate the IUR, instead of the peak exposure metric which has the strongest exposure-response relationships (p. 667). EPA justified this decision by explaining that the potential for exposure misclassification was greater with the peak exposure metric. Additionally, EPA stated that it is "unclear how to extrapolate RR estimates based on peak exposure estimates to meaningful estimates of lifetime extra risk of cancer from environmental exposure" (p. 726). Similarly, the unit risk for myeloid leukemia, also derived from an updated analysis of the occupational epidemiology study of the NCI (Beane-Freeman et al. 2009), was based on the cumulative exposure metric. The reported relationship with cumulative exposure showed a statistically nonsignificant and small increase in risk for myeloid leukemia, while the relationship with the peak exposure metric was marginally significant.

b. **Potential bias associated with heterogeneity among the industrial plants included in the NCI studies.** The Beane-Freeman et al., 2013 study cohort included workers from ten industrial plants. Six of the ten deaths from nasopharyngeal cancers were from one plant in Connecticut, which may suggest that the excess nasopharyngeal cancer deaths were attributed to this plant being different from the others. Given that the unit risk for myeloid leukemia was also derived from updated analyses of the NCI cohort, EPA should be mindful of any clustering of cancer cases at a single plant.

The National Academies also flagged these similar concerns about the Hauptmann et al., 2004 study, which was used to derive the IUR for nasopharyngeal cancer in the 2011 draft formaldehyde assessment, in its review of the 2011 document.[4] We highlight these areas of uncertainty again as we believe they would be important to consider as EPA evaluates the benefit of considering myeloid leukemia in the cancer IUR.

Thank you for considering our comments.

[4] *Ibid*