



North American Metals Council

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March 1, 2021

Via Docket Submission

U.S. Environmental Protection Agency
EPA Docket Center (ORD Docket)
Mail Code: 28221T
1200 Pennsylvania Avenue N.W.
Washington, DC 20460

Re: Comments on Draft Staff Handbook for Developing Integrated Risk Information System Assessments; Docket Number EPA-HQ-ORD-2018-0654

Dear Sir or Madam:

The North American Metals Council (NAMC)¹ is pleased to submit these comments in support of the comments submitted by the Arsenic Science Task Force (ASTF) regarding the U.S. Environmental Protection Agency's (EPA) draft Staff Handbook for Developing Integrated Risk Information System (IRIS) Assessments, or IRIS Handbook (85 Fed. Reg. 76566 (Nov. 30, 2020)). NAMC applauds EPA's efforts in providing operating procedures for its staff in developing assessments and appreciates the opportunity to comment.

**Systematic Review in Considering Data for Making
Hazard Assessments Needs Revision**

While the draft IRIS Handbook codifies implicit decision-making processes and provides a means for documenting such processes, the Handbook seems overly reliant upon systematic review as a means to obtain quality data for making a hazard assessment. Systematic review can assist with obtaining the published information to ensure EPA has retrieved all articles of interest and undergone review for relevance to the risk assessment. The review as outlined in the draft IRIS Handbook, however, cannot determine high-quality studies or distinguish between studies that *appear* to be of high quality, but it allows for bias or inappropriately designed studies.

¹ NAMC is an unincorporated, not-for-profit organization serving as a collective voice for North American metals producers and users. NAMC is a leader for the metals industry on science- and policy-based issues affecting metals.



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NAMC believes that attention to data quality needs additional prominence and recognition and is as important as or of greater importance than the systematic review processes.

Terminology on the Use of Evidence Is Undefined

The IRIS Handbook uses the terms “weight of evidence” and “strength of evidence” interchangeably. NAMC urges EPA to provide clarity by defining both terms. The lack of definitions for these terms in the IRIS Handbook introduces ambiguity in the establishment of a consistent approach to systematic review processes.

Human Relevance Should Be of High Consideration in Hazard Assessments

NAMC believes that human relevance should be the most important consideration in the hazard assessment of a chemical or other agent. The IRIS Handbook should cite and encourage the use of the International Program on Chemical Safety’s (IPCS) Human Relevance Framework.² EPA should emphasize the Mode of Action (MOA) developed in the framework, which is both qualitatively and quantitatively relevant to human exposure scenarios.

The way in which a chemical causes an adverse outcome is critical to state-of-the-science hazard assessments. The IRIS Handbook fails to reinforce this key fact, which is an invaluable understanding even in instances where an abundance of human data seems to exist. NAMC notes a lack of consideration and weighting of MOA data in numerous instances within the IRIS Handbook.

MOA is essential to understanding the way that exposure to a chemical agent disturbs the biology of an organism and leads to a biological effect or multiple biological effects. Having an abundance of epidemiology data showing human responses at low doses when those responses are below the threshold for effects is why the MOA is needed in a hazard assessment.

² See [Boobis, A.R., Cohen, S.M., Dellarco, V., McGregor, D., Meek, M.E.B., Vickers, C., Willcocks, D., Farland, W. “IPCS framework for analyzing the relevance of a cancer mode of action for humans.” *Crit. Rev. Toxicol.* 2006, 36\(10\), 781-92. doi: 10.1080/10408440600977677. PMID: 17118728.](#)



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Language in the IRIS Handbook Encourages Concerning Biases

NAMC is concerned with certain language used in the IRIS Handbook because it seems to reflect and encourage certain biases. These biases are toward choices that are considered “conservative” and have become engrained in EPA’s philosophy as “default positions.” NAMC believes that such “default positions” often lead EPA to choose low-dose linearity for carcinogens. Consequently, these biases affect EPA’s approaches, resulting in an outdated process for hazard assessments.

NAMC observes that risk of biases in a study is not determined by the identity of the party that conducts or funds the study. There seems, however, to be an effort by the IRIS staff to de-emphasize publications by industry scientists or studies funded by industry. De-emphasizing or not using review articles that have undergone peer review is concerning because it implies that EPA refuses to look at the science as other stakeholders see it. As a result, EPA misses opportunities to learn from stakeholders’ efforts and implies lack of sound judgment on EPA’s part.

EPA Overemphasizes the Cancer or Non-Cancer Dichotomy Based on Hazard Identification

EPA’s emphasis on the existing cancer or non-cancer dichotomy is based on hazard identification only, an approach that has outlived its usefulness (Boobis *et al.* 2016).³ By focusing on a particular hazard rather than on what a chemical does, EPA misses an opportunity to understand better the actual or potential impacts that a chemical exposure may have on human health. Instead, NAMC believes that EPA should focus on cancer as one of a number of health endpoints that are potentially relevant to an exposure scenario.

³ Boobis, A.R., Cohen, S.M., Dellarco, V.L., Doe, J.E., Fenner-Crisp, P.A., Moretto, A., Pastoor, T.P., Schoeny, R.S., Seed, J.G., Wolf, D.C. “Classification schemes for carcinogenicity based on hazard-identification have become outmoded and serve neither science nor society.” *Regul. Toxicol. Pharmacol.* 2016, 82, 158–66. DOI: 10.1016/j.yrtph.2016.10.014.



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Thank you for the opportunity to submit these comments. Please contact Ligia Duarte Botelho, NAMC Manager, at lbotelho@bc-cm.com with any questions.

Sincerely,

William J. Adams, Ph.D.
NAMC Chair