

## **Summary of Meeting**

Event Title: Arsenic Task Force (ASTF) Stakeholder Meeting

Date: February 5, 2020

Time: 1:30 PM – 2:30 PM

Keyword: IRIS, inorganic arsenic, iAs

### **Attendees:**

Jennifer Orme-Zavaleta – US EPA, ORD

David Dunlap – US EPA, ORD

Bruce Rodan – US EPA, ORD

Lou D’Amico – US EPA, ORD

Lindsey Jones – US EPA, ORD

Samantha Jones – US EPA, ORD CPHEA

Emma Lavoie – US EPA, ORD CPHEA

Kris Thayer – US EPA, ORD CPHEA

Andrew Kraft – US EPA, ORD CPHEA

Allen Davis – US EPA, ORD CPHEA

Dahnish Shams – US EPA, ORD CPHEA

Vicki Soto – US EPA, ORD CPHEA

Wayne Cascio – US EPA, ORD CPHEA

Janice Lee – US EPA, ORD CPHEA

Greg Akerman – US EPA, OCSPP

Dana Vogel – US EPA, OCSPP OPP

Anna Lowit – US EPA, OCSPP OPP

Evisabel Craig - US EPA, OCSPP OPP

Julie Van Alstine – US EPA, OCSPP OPP

Rick Keigwin – US EPA, OCSPP OPP

David Fischer – US EPA, OCSPP –DAA

Joyce Tsuji – Exponent

Samuel Cohen – University of Nebraska

Patrick Quinn – The Policy Group/Wood Preservative Science Council

Seth Goldberg – Steptoe & Johnson/Wood Preservative Science Council

William Adams – Arsenic Science Task Force (Rio Tinto)

Charles Grizzle – The Grizzle Group/Organic Arsenical Products Task Force

LaJuana Wilcher – English, Lucas, Priest & Owsley/Organic Arsenical Products Task Force

Steve Hensley – National Cotton Council

Nick Skoulis – Steptoe & Johnson/Wood Preservative Science Council

Michal Eldan –Organic Arsenical Products Task Force

Allison Nyholm - Steptoe and Johnson/Wood Preservatives Science Council

Tawny Bridgeford – National Mining Association

Jane Luxton – Lewis Brisbois/Organic Arsenical Products Task Force

### **Summary of Meeting Activities:**

- **Introductions**
- **Welcome from Jennifer Orme-Zavaleta (US EPA) and David Dunlap (US EPA).**

- **ASTF Presentation – (See PowerPoint slides for more information)**
- **Discussion**

EPA stated the IRIS Program is working on completing the draft arsenic assessment and that an updated systematic review protocol will be released with the draft assessment.

ASTF, Prof. Sam Cohen, and Dr. Joyce Tsuji presented their concerns with the IRIS protocol. Their main concerns were the evaluation of study quality, its utilizing statistical modeling of the epidemiological studies, and perception that the IRIS Program was ignoring mode of action (MOA) analysis or consideration of a threshold for arsenic's carcinogenicity. ASTF believe mode of action studies in laboratory animals and *in vitro* support a threshold for adverse effects at human-equivalent drinking water concentrations of greater than 100 µg/L. Hence, ASTF posits there is no reason to expect a reliable dose-response below this level as indicated by statistical modeling of the epidemiological data at face value. ASTF believe the most plausible mode of action based on sound science involves sulfhydryl binding and cytotoxicity leading to regenerative hyperplasia and that other possible modes of action occur at test concentrations that would be lethal to humans and thus are not plausible. Consistent with the experimental animal and *in vitro* evidence on mode of action, Dr. Tsuji noted that epidemiology studies involving exposure to inorganic arsenic (iAs) overall indicate limited to no clear effects below 150 ppb in drinking water, involving lack of statistically significant risks and inconsistent dose-response relationships at low doses. Their presentation also noted that many studies regarded as low dose in fact included higher exposures or were insufficiently controlled for important confounding factors like smoking, folate deficiency, or recall bias for water intake. Dr. Tsuji emphasized that the EPA-IRIS observation that U.S. background exposures are within the range of doses associated with increased risks in epidemiological studies is based on modeling, not on the actual nature of the data at low exposures. It was pointed out that there is precedent in the Agency for concluding that certain carcinogenic substances have a threshold by a similar MOA involving cytotoxicity and regenerative hyperplasia, e.g., the Office of Pesticide Programs analysis of dimethyl arsenic acid (DMA) and the IRIS assessment of chloroform. ASTF also noted concerns about the different expertise represented in the NAS peer review committee compositions between the 2019 and the 2013 committees, as well as the lack of carryover of recommendations provided by the two committees. ASTF indicated a need for EPA-IRIS to provide evidence tables for studies included in the draft assessment in order to have a clear understanding of the studies that IRIS is relying upon. ASTF requested that key studies be identified prior to release of draft assessment.

EPA-IRIS reiterated that the proposed dose-response approach including the statistical model makes no assumptions on whether the shape of the dose-response is linear or threshold. Because there is an abundance of data from epidemiological studies, including those with exposures levels at or near the background exposure level of the United States, there is no need to extrapolate and the estimation of risk values will be based on data in the observed range of exposures. This approach was supported by the NAS, and the Academies recommended additional clarification on the dose-response methods to better make this point. EPA-IRIS noted that MOA analyses will be utilized to support modeling decisions for endpoints where epidemiological data is less robust, [as recommended by the NAS](#). EPA-IRIS will continue to work to ensure the MOA issues highlighted are addressed during the development of the assessment. Note: With respect to using MOA and mechanistic data to inform dose-response, EPA-IRIS has presented a significant amount of analyses of mechanistic information (see Appendix A of the Updated [Problem Formulation and Systematic Review Protocol](#)). Analysis of this information was also

used to support primary reliance on the epidemiological studies, similar to what has been done for prior assessments conducted by other organizations (see section 2.3.2).

EPA-IRIS also noted that the Agency was not involved in NAS committee member selection. The process is managed independently by the NAS. Additionally, the [proposed approaches and methodologies](#) for the arsenic IRIS assessment that were reviewed by the NAS in 2019 are responsive to recommendations provided by the [NAS committee in 2012 and 2013](#), including the recommendation to utilize [meta-regression and Bayesian methods](#). EPA-IRIS reiterated that the statistical approaches to be used within the assessment do not make any assumptions regarding linearity. EPA-IRIS indicated that only medium and high-quality studies would be utilized to support the dose-response analyses. EPA-IRIS and ASTF discussed the complexities of utilizing different dose metrics in relation to the proposed methodologies for the assessment.

**Action Items:**

- EPA will provide summary notes to participants followed by posting on the IRIS website [www.epa.gov/iris](http://www.epa.gov/iris).
- ASTF will provide an electronic version of the slides for posting on the IRIS website under Calendar “Stakeholder requested meetings” <https://cfpub.epa.gov/ncea/iris2/events.cfm#stakeholderMeetings>. (ASTF provided the slides and a follow-up letter dated 3-16-2020, both of which will be posted on the IRIS website)
- Next anticipated steps: Public comment draft projected release in FY21-Q4 and external peer review by the NAS projected for FY22-Q2.