PUBLIC STAKEHOLDER WORKSHOP TO INFORM EPA'S UPCOMING IRIS TOXICOLOGICAL REVIEW OF INORGANIC ARSENIC

AGENDA

TUESDAY, JANUARY 8 – WEDNESDAY, JANUARY 9, 2013

U.S. EPA Auditorium C 111 • 109 T.W. Alexander Drive • Research Triangle Park, North Carolina 27711

Agenda in Brief

Tuesday, January 8	
8:00 am	Registration
8:30 am	Workshop begins
12:00–1:00 pm	Lunch
5:30 pm	Workshop adjourns

Wednesday, January 9	
8:30 am	Workshop begins
12:15–1:00 pm	Lunch
5:00 pm	Workshop adjourns

Scope and Objectives

This workshop is designed to inform the development of EPA's draft Toxicological Review of inorganic arsenic (iAs) (cancer and non-cancer effects), which EPA intends to post to the Integrated Risk Information System (IRIS) database. Workshop participants will be asked to highlight significant new and emerging research that could inform the development of the draft Toxicological Review, discuss methods for identifying the relevant literature, identify major areas of scientific controversy, identify data gaps, and discuss potential approaches for characterizing dose-response.

Workshop Goals:

- Ensure that EPA provides the public an opportunity to inform the Toxicological Review.
- Transparently communicate how EPA will produce a Toxicological Review that meets the needs of the Agency and the public.

Workshop participants are encouraged to think broadly about the body of iAs scientific evidence and how it can best be used in a draft Toxicological Review. Attendees are invited to participate in an open dialogue regarding ways in which the data would most effectively be used in the Toxicological Review that will serve as part of the scientific and technical foundations for the Agency's decisions on iAs. Specifically, workshop discussions will provide important input as EPA considers the design, scope, and methods used to develop the draft Toxicological Review. The Toxicological Review, in turn, will inform risk management decisions by Agency stakeholders and partners. Panelists participating in the workshop represent a range of scientific expertise (e.g., epidemiology, human and animal toxicology, systematic review, risk assessment, dose-response, and mode of action).

The outcome of the workshop will inform EPA's planning for the Toxicological Review and an upcoming National Academy of Sciences (NAS) public workshop on iAs. Development of the draft Toxicological Review will be informed by the key issues and recommendations from the public NAS and EPA meetings. In addition to conducting a workshop, the NAS will also conduct a review of the draft Toxicological Review. Throughout the process, the public is encouraged to take advantage of the opportunities to review and comment on the draft Toxicological Review. The draft Toxicological Review will be revised in response to the NAS and public review comments. The Toxicological Review will be finalized as expeditiously as possible after the NAS review.

Workshop Structure

The workshop will begin with an introductory session in which EPA will highlight the approaches under consideration for identifying and evaluating literature for the development of the draft Toxicological Review. The panel sessions, each facilitated by two co-chairs, will then address the following topic areas:

Session 1: Applying Systematic Review to the iAs Toxicological Review

- Scoping and Problem Formulation Overview
- Systematic Review
- Methods for Identifying, Evaluating, and Synthesizing Literature

Session 2: Hazard Identification for iAs—Noncancer and Cancer Effects

- Noncancer and Cancer Effects – Identifying health effects and susceptible populations for hazard identification
- Mode of Action Evidence – Noncancer and cancer effects

Session 3: Dose Response

- Identifying Factors Relevant to the Dose Response
- Approaches to Dose-Response Analysis
- Extrapolation Approaches

Session 4: Roundtable Discussion on Planning and Scoping

- Identifying Stakeholder Needs
- Recommended Revisions to the Draft Planning and Scoping Summary

Session 5: Opportunity for Additional Public Comment

The co-chairs will begin Sessions 1–3 by highlighting appropriate background information and policy issues, and lead discussants will provide opening comments on the topic. Other panel members and interested participants will then be invited to join a structured discussion of the topic. Sessions 4 and 5 on Day 2 are structured to provide additional opportunities for stakeholder input regarding their needs for the Toxicological Review of iAs and suggested revisions to the draft planning and scoping summary. The co-chairs or moderators will facilitate each session to ensure the discussion remains focused on providing useful information that will inform the development of the draft Toxicological Review.

The charge questions presented for each Session Panel Discussion provide a starting point for the discussion in each session. These questions are not intended to be prescriptive or limit discussion of other relevant issues. Rather, it is understood that some issues will warrant more discussion time than others and that the agenda could change during the course of the workshop as panel members and other participants offer input and respond to the issues raised.

Day 1: Tuesday, January 8, 2013

8:00 am	**Registration**
8:30 am	**Welcome and Overview** **Reeder Sams** Deputy Division Director (Acting), U.S. EPA National Center for Environmental Assessment
8:45 am	**Introductory Remarks – Partnerships and Approaches for the Future of IRIS Assessments** **Ken Olden** Director, U.S. EPA National Center for Environmental Assessment
9:15 am	**EPA Draft Planning and Scoping Summary for the Toxicological Review** **John Cowden** Co-Chemical Manager for Arsenic, U.S. EPA National Center for Environmental Assessment

SESSION 1: APPLYING SYSTEMATIC REVIEW TO THE iAs ASSESSMENT

Co-Chairs: **Andy Rooney,** National Institute of Environmental Health Sciences
Roberta Scherer, Johns Hopkins University

Panelists: **Janice Lee**, U.S. EPA National Center for Environmental Assessment
Warner North, North Works, Inc.
Beth Owens, U.S. EPA National Center for Environmental Assessment
Craig Steinmaus, CalEPA, University of California–Berkeley, University of California–San Francisco

9:30 am	**Elements of Systematic Review** **Andy Rooney**
9:45 am	**Options for Literature Search Strategies** **Janice Lee**
10:00 am	**Break**
10:15 am	**Methods for Identifying, Evaluating, and Synthesizing Literature** 1.1. What approaches could EPA use to identify relevant literature for the development of a Toxicological Review of iAs? What approaches could EPA use to transparently communicate results of its literature search and screening strategy? **Lead Discussants: Beth Owens, Andy Rooney**

10:15 am	**Methods for Identifying, Evaluating, and Synthesizing Literature (continued)** 1.2. What approaches are available to evaluate the quality of individual studies? What aspects of epidemiological studies could be considered in such an evaluation? **Lead Discussants: Andy Rooney, Craig Steinmaus** 1.3. What approaches are available to synthesize the available evidence on iAs? **Lead Discussants: Warner North, Roberta Scherer**
11:15 am	**Discussion (open to all on-site and virtual participants)**
12:00 pm	**Lunch**

SESSION 2: APPROACHES FOR HAZARD IDENTIFICATION FOR iAs – NON-CANCER AND CANCER

Co-Chairs: **Ken Cantor,** National Cancer Institute
David Thomas, U.S. EPA National Health and Environmental Effects Research Lab

Panelists: **Vasken Aposhian,** University of Arizona
Rory Conolly, U.S. EPA National Health and Environmental Effects Research Lab
Craig Steinmaus, CalEPA, University of California–Berkeley, University of California–San Francisco
Mirek Styblo, University of North Carolina
Mike Waalkes, National Institute of Environmental Health Sciences
Tim Wade, U.S. EPA National Health and Environmental Effects Research Lab
Doug Wolf, U.S. EPA National Health and Environmental Effects Research Lab

1:00 pm	**Noncancer and Cancer Effects – Identifying health effects and susceptible populations for hazard identification** 2.1. What data are available to identify noncancer effects following iAs exposure (oral or inhalation)? **Lead Discussants: Mirek Styblo, Tim Wade** 2.2. What data are available to identify cancer effects of iAs exposure (oral or inhalation)? **Lead Discussants: Ken Cantor, David Thomas** 2.3. What data are available to identify differences in susceptibility to the effects of iAs? **Lead Discussants: Craig Steinmaus, Mike Waalkes**

2:30 pm	Discussion (open to all on-site and virtual participants)
3:15 pm	**Break**
3:30 pm	Mode-of-Action Evidence – Noncancer and cancer effects 2.4. What data are available to identify mode(s) of action for the health effects of iAs (e.g., key toxicokinetic/toxicodynamic events, inter-species or inter-individual differences)? Lead Discussants: Vasken Aposhian, Doug Wolf 2.5. What data are available to identify common toxic moieties and mode(s) of action for multiple health effects (noncancer and cancer) from iAs exposure? Lead Discussants: Rory Connolly, Mirek Styblo
4:30 pm	Discussion (open to all on-site and virtual participants)
5:30 pm	**Day 1 Adjourns**

8:30 am **Welcome and Overview**

John Cowden
Co-Chemical Manager for Arsenic, U.S. EPA National Center for Environmental Assessment

SESSION 3: DOSE RESPONSE

Co-Chairs: **Weihsueh Chiu**, U.S. EPA National Center for Environmental Assessment

William Cullen, University of British Columbia

Panelists: **Karen Bradham,** U.S. EPA National Exposure Research Laboratory

Ken Cantor, National Cancer Institute

Hisham El-Masri, U.S. EPA National Health and Environmental Effects Research Lab

Jeff Gift, U.S. EPA National Center for Environmental Assessment

Bill Mendez, ICF International

Warner North, North Works, Inc.

8:35 am **Identifying Factors Relevant to Dose Response**

3.1. What types of exposure could contribute to the aggregate dose, and in what ways might this impact how an iAs dose-response characterization is used/applied? How can we estimate impact of drinking water exposure alone vs. aggregate exposure on possible effects of iAs exposure?

Lead Discussants: Karen Bradham, Bill Mendez

3.2. What kinds of endpoints may be useful for characterizing risk (e.g., precursor key events, clinical disease endpoints)? How are these endpoints linked to estimates of iAs dose or biomarkers (e.g., metabolites) in exposed populations?

Lead Discussants: Ken Cantor, William Cullen

3.3. What kinds of dose-response characterization may be needed (e.g., reference value, incremental change in risk with dose, probabilistic risk at dose) for aggregate (e.g., urine, blood) and source-specific (e.g., food, water) dose metrics?

Lead Discussants: Ken Cantor, Weihsueh Chiu

9:20 am	**Approaches to Dose-Response Analysis**

3.4. What kinds of approaches are available to analyze dose-response data (e.g., statistical models, non-parametric approaches)?

Lead Discussants: Weihsueh Chiu, Jeff Gift

3.5. What are factors (e.g., toxicokinetics, bioavailability, water consumption rates, background exposure, susceptibility) that can impact the dose-response analysis, and how could these factors be transparently accounted for?

Lead Discussants: William Cullen, Hisham El-Masri

3.6. EPA has traditionally addressed uncertainty in modeling dose-response data by using a statistical lower confidence bound on the benchmark dose. What other approaches are available to address and transparently convey the impact of uncertainty on the dose-response analysis?

Lead Discussants: Bill Mendez, Warner North

10:20 am Break

10:35 am	**Extrapolation Approaches**

3.7. What kinds of extrapolations are needed (e.g., interspecies, exposure route, human variability, low-dose/effect)?

Lead Discussants: Bill Mendez, Warner North

3.8. What approaches are available for such extrapolations (e.g., PBPK modeling, uncertainty factors, probabilistic factors, linear/non-linear dose-response)?

Lead Discussants: Hisham El-Masri, Jeff Gift

3.9. EPA has traditionally addressed uncertainty via the application of uncertainty factors. What other approaches may be available to address and transparently convey the impact of uncertainty on these extrapolations?

Lead Discussants: Ken Cantor, Weihsueh Chiu

11:20 am Discussion (open to all on-site and virtual participants)

12:15 pm Lunch

SESSION 4: ROUNDTABLE DISCUSSION ON PLANNING AND SCOPING

Moderator: **Reeder Sams**, U.S. EPA National Center for Environmental Assessment

Discussants: **Sam Cohen**, University of Nebraska

Vincent Cogliano, U.S. EPA National Center for Environmental Assessment

Suzanne Fitzpatrick, U.S. Food and Drug Administration

Deborah McKean, U.S. EPA Region 8

Michele Roberts, Advocates for Environmental Human Rights

Mike Waalkes, National Institute of Environmental Health Sciences

1:00 pm	**Discussion of Key Themes from Sessions 1–3** Roundtable discussion followed by questions and comments from on-site and virtual participants
2:30 pm	**Recommendations for Revision to the Planning and Scoping Summary** Roundtable discussion followed by questions and comments from on-site and virtual participants
3:30 pm	**Break**

SESSION 5: OPPORTUNITY FOR ADDITIONAL PUBLIC COMMENT

Moderator: **Janice Lee**, U.S. EPA National Center for Environmental Assessment

3:45 pm	**Discussion (open to all on-site and virtual participants)**
4:45 pm	**Concluding Remarks and Next Steps** **Vincent Cogliano** IRIS Division Director, U.S. EPA National Center for Environmental Assessment
5:00 pm	**Workshop Adjourns**