PUBLIC STAKEHOLDER WORKSHOP
TO INFORM EPA'S UPCOMING IRIS

TOXICOLOGICAL REVIEW OF INORGANIC ARSENIC

INTRODUCTION

Tuesday, January 8 &
Wednesday, January 9
RTP, North Carolina

HOSTED BY EPA'S NATIONAL CENTER
FOR ENVIRONMENTAL ASSESSMENT

EPA United States Environmental Protection Agency

Public Stakeholder Workshop –

Development of Toxicological Review of Inorganic Arsenic



USEPA / ORD / NCEA
Presented by: Reeder Sams II

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Welcome to the Public Stakeholder Workshop

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Why is EPA holding this workshop?

- Human health
- Most recent IRIS assessment completed in 1988
- Support and use in EPA's program / regional risk assessments and state / local government risk assessments
- Past human health assessment efforts for inorganic arsenic
- Stakeholder comments and requests
- Congressional Request (HR 2055; HR 112-151)
  - Review by National Academy of Sciences (NAS)
- Recommendations from the NAS

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Selected NAS Recommendations

From "Science and Decisions" (NAS 2009)

- Expand agency and interagency collaboration
- Implement scoping and problem formulation
- Consider feasibility/benefits of options in the design stages
- Uncertainty and variability into dose response analysis
- Incorporation of probabilistic and distributional methods into dose-response analysis
- Evaluate chemicals in terms of mode of action, background exposure, disease processes, and vulnerable populations
- Criteria to justify alternative assumptions in place of default assumptions

Selected NAS Recommendations

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- Literature search strategy and literature evaluation criteria (e.g., systematic review)
- Weight of evidence evaluation for non-cancer endpoints
- Use HERO database to capture study information and data
- Sensitivity analyses for reference values and effect of uncertainty factors
- Harmonize characterization of uncertainty and variability
- Unify outcome consideration around common modes of action

Common Themes

(NAS 2011, 2009; EPA, 2005, 2000)

- Transparency- Explicitness in the health assessment process
- Clarity- Health assessment is free from obscure language and is easy to understand
- Consistency- Conclusions of the health assessment are characterized in harmony w/ other EPA actions
- Reasonableness- Health assessment is based on sound judgment

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Workshop Goals

- Ensure that EPA provides the public an opportunity to inform the Toxicological Review.
  - Gather scientific information and public dialogue
  - Many opportunities beyond this workshop
    - Submit information to the docket
    - Future public meetings
    - Webinar series
- Transparently communicate how EPA will produce an assessment that meets the needs of the Agency and the public.
  - Presentations during this workshop
  - NCEA website
  - Other tools (e.g., IRIS List-serve, blogs, etc.)

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Workshop Logistics

- Workshop is organized into 5 sessions
  1) Applying Systematic Review to the iAs Toxicological Review
  2) Hazard Identification for iAs
  3) Dose Response
  4) Roundtable Discussion on Planning and Scoping
  5) Opportunity for Additional Public Comment and Workshop Summary
- General format for each session
  - Panel Discussion (*State of the Science*)
  - Opportunity for Public Comment (Webinar & In Person)

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Workshop Logistics

- Webinar Participants
  - Please submit comments or questions at any time during the workshop. Comments or questions from webinar participants will be during the Discussion section for each session as indicated on the agenda.
  - If you experience technical difficulties, please type this in as a comment on the webinar or email: EPA_arsenic@icfi.com
- RTP Facility (in-person participants)
  - Comments and question from in-person participants will alternate with comments from the webinar

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Thank You…

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EXTRA SLIDES

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Past Efforts for the Toxicological Review of Inorganic Arsenic

- ☑ **First arsenic assessment posted to IRIS database in 1988**
- ☑ **National Research Council (NRC)/National Academy of Sciences (NAS) review of scientific information: 1999**
- ☑ **Science Advisory Board completes review of EPA Arsenic Rule: 2001**
- ☑ **EPA establishes Primary Drinking Water Standard for Arsenic: 2001**
- ☑ **NRC assessment and review of EPA Drinking Water Standard: 2001**
- ☑ **EPA implements NRC 2001 recommendations in draft arsenic IRIS assessment and submits for Science Advisory Board review: 2005**
- ☑ **Science Advisory Board completes review of EPA 2005 draft: 2007**
- ☑ **Science Advisory Board completes review of EPA 2010 draft: 2011**

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Common Themes

(NAS 2011, 2009; EPA, 2005, 2000)

Principal	Definition	Criteria for a human health assessment
Transparency	Explicitness in the risk assessment process	-Describe assessment approaches, assumptions, extrapolations and model use -Describe plausible alternative assumptions -Identify data gaps -Distinguish science from policy -Describe uncertainty -Describe relative strength of assessment
Clarity	Assessment is free from obscure language and is easy to understand	-Employ brevity -Use plain English -Avoid technical terms -Use simple tables, graphics, equations

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Common Themes Continued

(NAS 2011, 2009; EPA, 2005, 2000)

Principal	Definition	Criteria for a human health assessment
Consistency	Conclusion of the risk assessment are characterized in harmony w/ other EPA actions	-Follow statutes -Follow Agency Guidance -Use Agency information systems -Define level of effort -Use review by peers
Reasonableness	Risk assessment is based on sound judgment	-Use review by peers -Use best available scientific information -Use good judgment -Use plausible alternatives

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iAs Human Health Assessment -Considerations

- NAS recommendations for human health assessments (2011; 2009)
- Common themes with guidance documents (EPA, 2005; EPA, 2000)
- Social, behavioral, and physical impacts (epigenome)
- Useful reviews and documents: SAB (2011, 2007, 2001) NAS (2001, 1999)

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Decision-Making Framework

(NAS 2009)

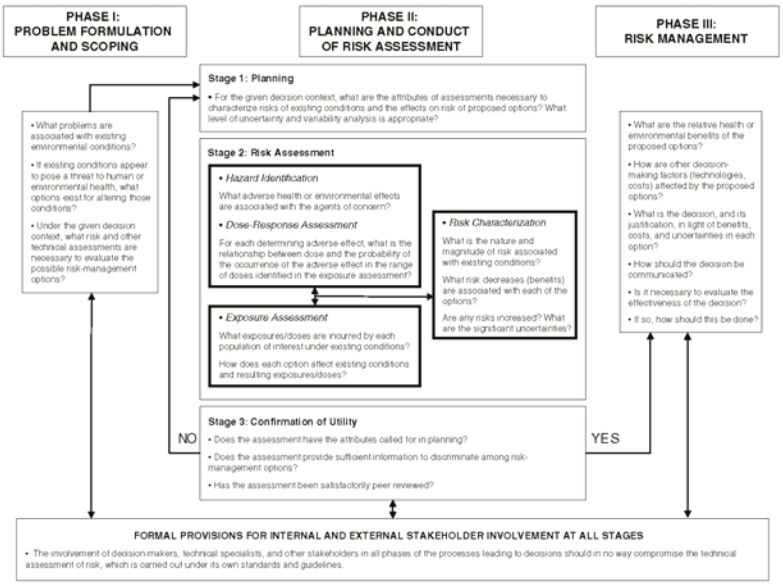

FIGURE S-1 A framework for risk-based decision-making that maximizes the utility of risk assessment.

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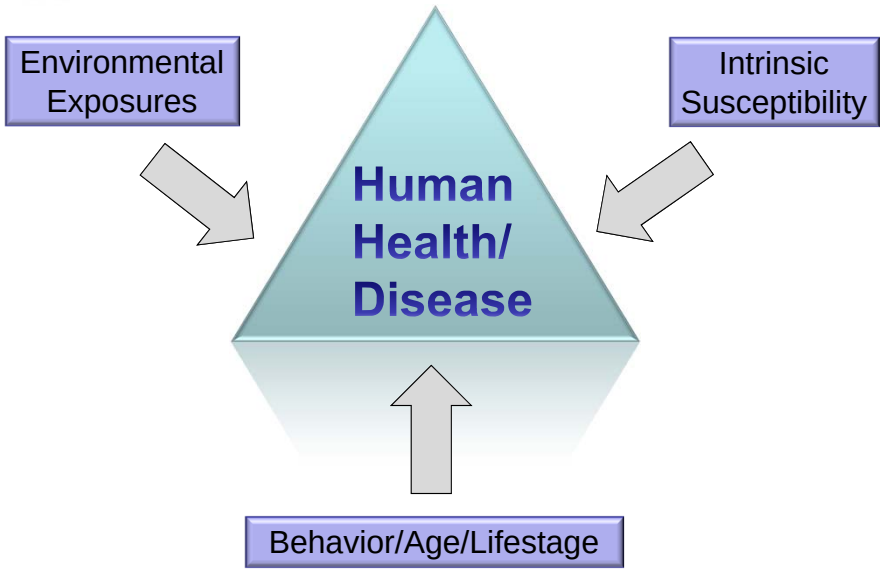

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Useful Reviews and Documents:

- SAB (2011; 2007) were reviews of existing EPA iAs cancer assessments
- NAS (2001) was a human health assessment; NAS (1999) was a review of the state of the science
- Recommendations should be utilized as appropriate throughout the development of a new integrated assessment (e.g., criteria categories for evaluating epi literature)
- Some recommendations may not be as informative for developing a new assessment compared to revising an existing assessment
- State of the science and human health assessment approaches are evolving

Workshop Goals

- Communication (throughout the development of the assessment)
  - Efficient and effective means
    - iAs human health assessment project page (internal and external)
    - Arsenic Communication Committee
  - List-serve
  - Ongoing dialogue
  - Assessment schedule
- Clear understanding of current regulatory practices and challenges across the Agency

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Workshop Goals

- Based upon the current regulatory practices and challenges, what are the needs of the Agency with respect to a new iAs human health assessment?
- Problem formulation / Scoping
- Provide input as to how the Agency can effectively engage outside stakeholders specifically for iAs
- Address how Agency partners can collaborate to develop an integrated assessment for iAs

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Selected SAB Recommendations

SAB Review of 2010 iAs Cancer Assessment (SAB 2011)

- Recommended EPA should more clearly state and utilize criteria to evaluate epidemiological data
- Improve the documentation of data sets utilized for sensitivity analyses;
- For complete EPA risk assessments provide context to the cancer risk estimate should be interpreted w/ respect to current cancer incidence in US populations
- Improve the documentation for selection and use of exposure assumptions for sensitivity analyses
- Commented on the importance of conducting integrated assessments (i.e., cancer and noncancer)

Selected SAB Recommendations

SAB Review of 2005 iAs Cancer Assessment (SAB 2007)

- Concluded that multiple modes of action are likely operable for the effects due to iAs
- Taiwanese dataset remains the most appropriate for dose-response analysis
- Epi studies of the US should be critically evaluated based upon a uniform set of criteria
- Information to determine a non-linear form of the dose-response and the linear default is most appropriate
- Recommendations regarding specific cancer modeling, exposure assumptions, and corresponding sensitivity analyses

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Risk Assessment Design

(NAS 2009)

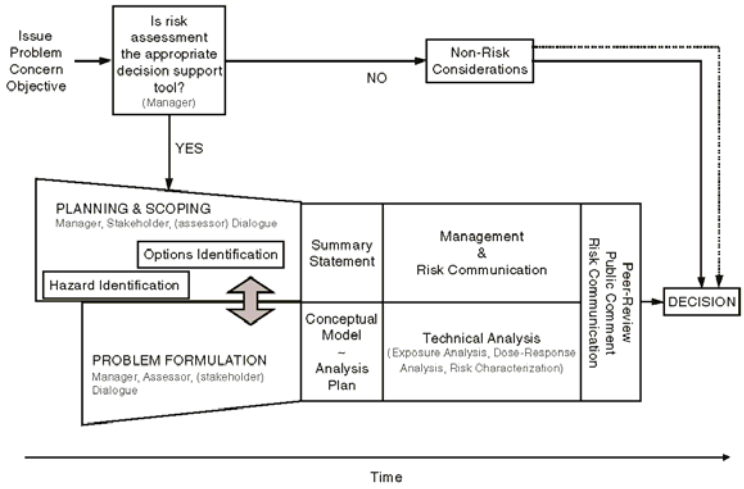

FIGURE 3-1 Schematic representation of the formative stages of risk-assessment design. Dotted line in figure denotes that decisions informed by risk assessment will be influenced by nonrisk considerations. Source: Adapted from EPA 1998, 2003.

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DRAFT PLANNING AND SCOPING SUMMARY

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Draft Planning and Scoping Summary for the Inorganic Arsenic (iAs) IRIS Assessment



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Research Triangle Park, NC

Office of Research and Development
National Center for Environmental Assessment

Disclaimer: the views expressed in this presentation are those of the speaker and do not necessarily represent the views or policies of the U.S. EPA.

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Key Terminology

IRIS Toxicological Review	Risk Assessment
• Hazard identification • Dose-response assessment	• Hazard identification • Dose-response assessment • Exposure assessment • Risk characterization

Planning and Scoping	Problem Formulation
• Establishes goals, breadth, depth, and focus of the toxicological review • Develops common understanding of why assessment is being developed, how assessment will be used, and data needed to answer key questions	• Describes specific technical details for the toxicological review • Consists of conceptual model and analysis plan

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NAS Guidance on Planning and Scoping

Scoping Elements	Considerations
Partner and Stakeholder needs	• Context and purpose • Areas of interest
Exposure	• Spatial and temporal considerations • Sources and source mitigation • Environmental exposure and exposure mitigation • Individual intake pathways and individual intake mitigations
Hazard Identification	• Direct and mitigation related hazards and stressors • Direct and mitigation-related adverse health outcomes • At-risk populations and populations at mitigation-related risk

Source: *"Science and Decisions: Advancing Risk Assessment;"* National Research Council of the National Academies, 2009

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Draft Planning and Scoping Summary

Considered	Limited Consideration	Outside the Scope
• Oral and inhalation exposure • Chronic exposure and exposure during susceptible life stages (e.g., in utero) • Cancer and non-cancer effects • Susceptibility – stressors and potential biomarkers of at-risk populations • Impact of uncertainty • Dose-response analysis indicating risk at potential exposure levels (including background levels)	• Exposure sources (e.g., environmental sources and individual intake pathways) – *as related to dose-response analysis* • Arsenic speciation data – *as data inform hazard identification, mode of action analyses, or dose response analyses* • Bioavailability – *as related to dose-response analysis*	• Options for mitigating exposure • Health effects related to clinical or ecological mitigation efforts • Dose-response analyses for mitigation related health effects • Cost benefit analysis on human health effects of iAs exposure or related mitigation efforts

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Developing the Toxicological Review

PROPOSED PROCESS	PROPOSED DATE
Scoping and Problem Formulation Workshop	**September 2012**
Public Stakeholder Workshop	**January 2013**
NAS Public Workshops	**January 24, 2013 April 4, 2013**
Interim NAS Report	**Fall 2013**
Completed Draft iAs Toxicological Review	**Spring 2014**
Complete Internal Agency Review	**Summer 2014**
Complete Interagency Science Consultation	**Summer 2014**
Release draft to External Peer Review (NAS Review)	**Fall 2014**
Complete NAS Review of the iAs Toxicological Review	**Winter 2015**
Complete Internal Agency Review/Interagency Science Discussion	**Spring 2016**
Post to IRIS Website	**Summer 2016**

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Conclusions

- **Planning and Scoping Summary**
  - DRAFT statement – discussion for Session 4
  - Context for discussions
- **Developing the IRIS Toxicological Review**
  - Multiple opportunities for public engagement
  - Importance of utility to partners and stakeholders
- **Next steps**
  - Meeting Report
  - Problem Formulation
  - NAS Public Meetings

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Additional Context: NAS Recommendations

From Formaldehyde review (NAS 2011)

- Literature search strategy and evaluation criteria (e.g., systematic review)
  - Use HERO database to capture study information and data
- Unify outcome consideration around common modes of action
- Weight of evidence evaluation for non-cancer endpoints
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- Harmonize characterization of uncertainty and variability

Additional context: NAS Recommendations (con't)

From "Science and Decisions" (NAS 2009)

- Expand collaboration
- Implement scoping and problem formulation
- Criteria to justify alternative assumptions in place of default assumptions
- Consider feasibility/benefits of options in the design stages
- Evaluate chemicals in terms of mode of action, background exposure, disease processes, and vulnerable populations
- Incorporation of probabilistic and distributional methods into dose-response analysis
- Develop process to communicate and incorporate uncertainty and variability into analysis

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Outline

- **Drafting the IRIS Toxicological Review**
  - Draft planning and scoping summary
- **Developing the IRIS Toxicological Review**
  - Proposed timeline

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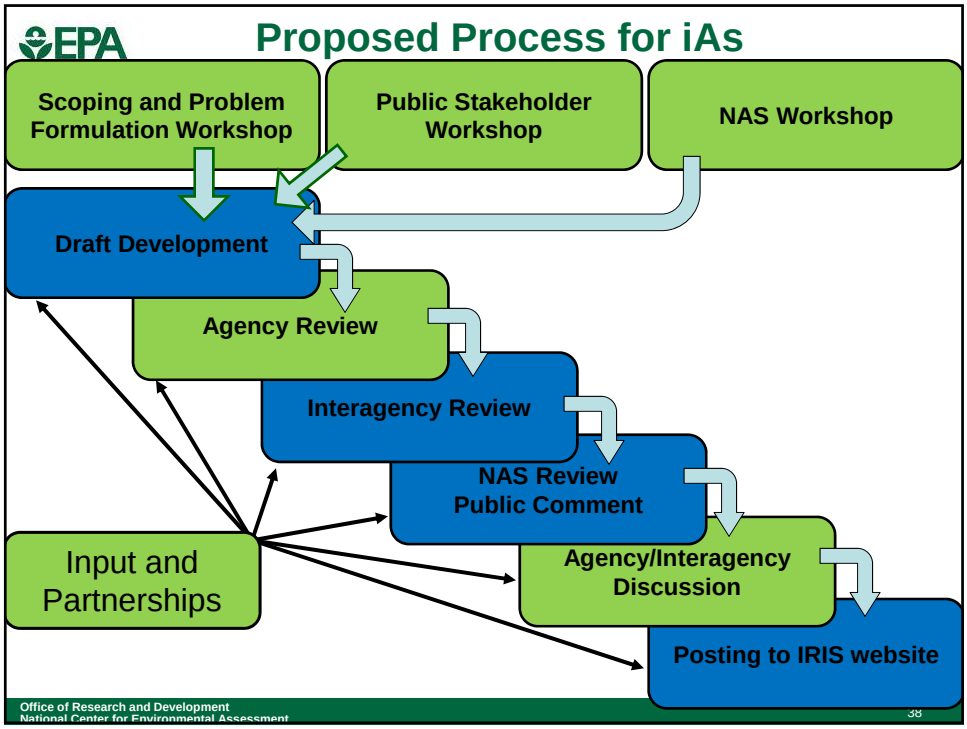
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Proposed Process for iAs
Scoping and Problem Formulation Workshop
Public Stakeholder Workshop
NAS Workshop
Draft Development
Agency Review
Interagency Review
NAS Review Public Comment
Agency/Interagency Discussion
Posting to IRIS website
Input and Partnerships
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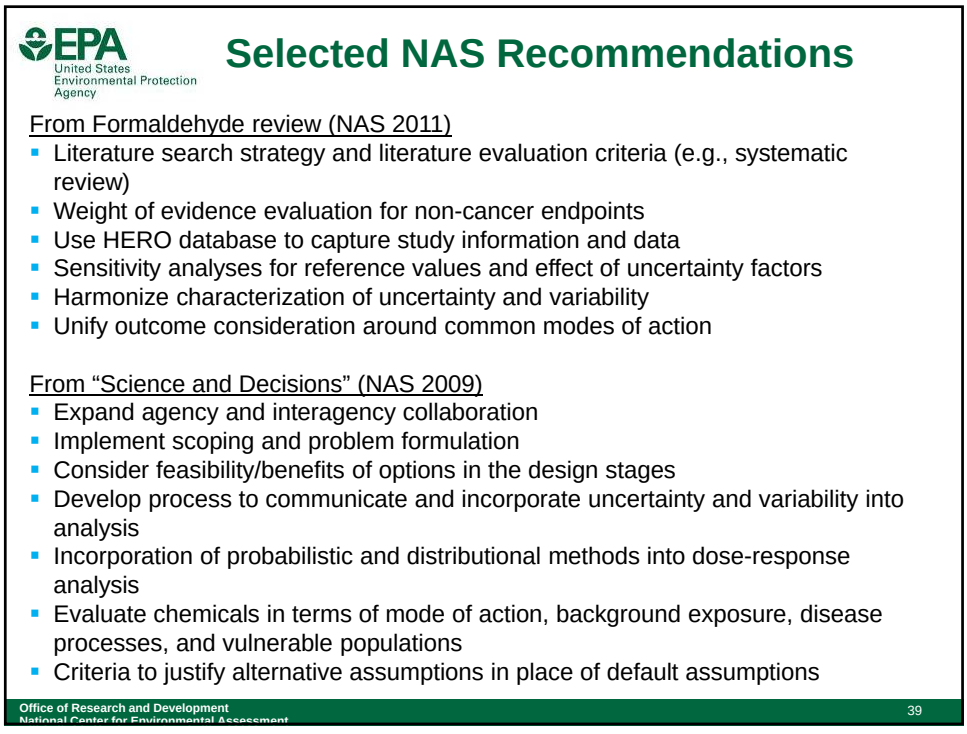
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Draft Planning and Scoping Summary

Scoping Elements	Considered	Limited Consideration	Beyond the Scope
Exposure	• Oral and inhalation exposure • Chronic exposure • Exposure during susceptible life stages (e.g., in utero)	• Exposure sources (e.g., environmental sources and individual intake pathways) – *as related to dose-response analysis*	• Options for mitigating exposure
Hazard Identification	• Cancer and non-cancer effects • Susceptibility – stressors and potential biomarkers of at-risk populations • Impact of uncertainty	• Arsenic speciation data – *as data inform hazard identification*	• Health effects related to clinical or ecological mitigation efforts
Dose-Response	• Dose-response analysis indicating risk at potential exposure levels (including background levels) • Impact of uncertainty	• Bioavailability – *as related to dose-response analysis* • Arsenic speciation – *as related to mode of action/dose-response analysis*	• Dose-response analyses for mitigation related health effects • Cost benefit analysis on human health effects of iAs exposure or related mitigation efforts

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