

Planning and Scoping Summary for the Toxicological Review of Inorganic Arsenic

Exposure to inorganic arsenic may be associated with increased long-term risks for both cancer and non-cancer endpoints. Exposure to inorganic arsenic may occur through contaminated air, food, water, soil, and dust as well as through occupational settings or consumer goods. Given the breadth of potential human exposure, a Toxicological Review of inorganic arsenic is important to several offices and regions within the U.S. Environmental Protection Agency (EPA), as well as government partners and public stakeholders outside of the Agency. EPA has held scoping meetings to determine the needs of partners and stakeholders.

Partner and Stakeholder Needs

Partners and stakeholders have requested a toxicological review that evaluates potential health effects from both oral and inhalation exposure for hazard identification. In evaluating endpoints for hazard identification, the need for mode of action analyses has been emphasized. In addition, partners and stakeholders have indicated that measures of exposure, bioavailability, and arsenic speciation are relevant considerations for risk management decisions. Partners and stakeholders have indicated the need to estimate excess risk (i.e., risk above naturally occurring background levels) at potential exposure levels for cancer and non-cancer endpoints, including any potential risk at naturally occurring background levels of inorganic arsenic. Partners and stakeholders have indicated that potential increased risk to sensitive populations and the impact of uncertainties on the dose-response analyses are important considerations for risk management decisions. To address the needs of the partners and stakeholders, EPA's Integrated Risk Information System (IRIS) Program will develop a state-of-the-science toxicological review to serve as a decision-support product for partners and stakeholders.

Components of the Toxicological Review

The toxicological review of inorganic arsenic will consist of hazard identification and dose-response analyses. Exposure assessment and risk characterization are beyond the scope of this toxicological review. A cost-benefit analysis on the human health effects of reducing inorganic arsenic exposure or related mitigation efforts is outside the scope of this toxicological review; however, this toxicological review is anticipated to provide quantitative dose-response relationships that may be useful for estimating benefits of measures to reduce exposure to inorganic arsenic. Future regulatory actions that address inorganic arsenic will be able to use information in this toxicological review as part of the scientific basis for estimating avoided human disease that may result from mitigation efforts.

Temporal and Exposure Considerations	The toxicological review will evaluate the risks of chronic exposure to inorganic arsenic. In addition, the toxicological review will consider potential risks of exposure during susceptible life stages, including in utero and developmental exposures. The toxicological review will evaluate the human health risks of oral and inhalation exposure to inorganic arsenic. Exposure sources, including environmental sources and individual intake pathways, will only be considered as they impact the dose-response analysis. Options for mitigating exposure are beyond the scope of this toxicological review.
Scope of the Hazard Identification	The toxicological review will consider the cancer and non-cancer health effects of oral and inhalation exposure to inorganic arsenic; arsenic speciation data will be evaluated only as those data inform the health effects of inorganic arsenic exposure. Similarly, mode of action analyses will be limited to health effects associated with direct exposure to inorganic arsenic. The hazard identification will consider susceptibility, including stressors and potential biomarkers of at-risk populations. Uncertainties in the hazard identification will be fully characterized in the toxicological review. Based upon feasibility, the qualitative impact of these uncertainties will be discussed in the toxicological review. Health effects related to clinical or ecological mitigation efforts are outside the scope of this toxicological review.
Scope of the Dose-response Analyses	Dose-response analyses will indicate potential risks for health effects at potential exposure levels, including naturally occurring background levels of inorganic arsenic. Bioavailability and arsenic speciation data will be evaluated only as those data impact the dose-response analyses. Uncertainties in dose-response analysis will be fully characterized in the toxicological review. Based upon feasibility, the qualitative and quantitative impact of these uncertainties will be discussed in the toxicological review. Dose-response analyses for mitigation related health effects are outside the scope of this toxicological review.