

Additional Information from USDA
Comments on Interagency Science Consultation
Draft IRIS Toxicological Review of Inorganic Arsenic
November 2022
(Date Received January 26, 2023)

Thank you for an opportunity to respond to the additional questions asked at the Interagency Meeting on the draft IRIS Toxicological Review of Inorganic Arsenic (iAs) on January 18, 2023. Below is a summary of the USDA responses to EPA's questions.

USDA Summary of Verbal EPA Questions:

- When USDA said MOA was not considered, does that mean a modifying factor or a BMR?
- What is meant from “only some of the total body of information” was used. Can USDA describe what type of comparison would be needed/how would you like us to include the MOA data in our document?
- Do USDA epidemiologists have a process for using MOA and epi data?

USDA Response:

USDA was not referring specifically to the use of a modifying factor or a benchmark response (BMR) in its MOA comments. A variety of MOA studies are available, and EPA has focused its efforts on using the epidemiology data. Appendix A of Appendix A provides a summary of the analyses of mechanistic information that EPA reviewed and a case study using idiopathic bladder cancer; however, EPA has not fully explained why it is acceptable to not use the MOA data. Appendix A of Appendix A also notes that studies “on other potential MOAs (e.g., immune system surveillance, stem cell modification) were tagged during screening in literature search updates and are available in HERO. However, given the refined assessment focus on epidemiological studies for dose-response these studies were not further analyzed.” It would be beneficial to include in the MOA section a comprehensive discussion of the steps EPA took in response to the concerns raised in the National Academies of Sciences *Review of EPA's Updated Problem Formulation and Protocol for the Inorganic Arsenic IRIS Assessment* (2019) about EPA's decision to not use the MOA data.

USDA recommends that EPA seek additional input through its charge questions to the SAB and seek additional input from the public regarding use of the inorganic arsenic MOA data as part of the Step 4 review process.

At this time, the peer reviewers are not aware of USDA documentation of a process for using MOA and epidemiology data.