EPA Proposed Draft Charge to the SAB for the IRIS Toxicological Review of Ammonia

June 2012

Introduction

The U.S. Environmental Protection Agency (EPA) is seeking an external peer review of the scientific basis supporting the draft Toxicological Review of Ammonia that will appear on the Agency's online database, the Integrated Risk Information System (IRIS). IRIS is prepared and maintained by EPA's National Center for Environmental Assessment (NCEA) within the Office of Research and Development (ORD). An existing IRIS assessment for ammonia, which includes a chronic reference concentration (RfC), was posted to the IRIS database in 1991.

IRIS is a human health assessment program that evaluates qualitative and quantitative risk information on effects that may result from exposure to specific chemical substances found in the environment. Through the IRIS Program, EPA provides quality science-based human health assessments to support the Agency's regulatory activities. Combined with specific exposure information, government and private entities use IRIS to help characterize public health risks of chemical substances in site-specific situations in support of risk management decisions.

The external review draft Toxicological Review of Ammonia is based on a comprehensive review of the available scientific literature on the human and animal health effects of ammonia, and was developed according to guidelines and technical reports published by EPA (see Preamble). This draft IRIS assessment provides an overview of the data regarding the toxicokinetics of ammonia in humans and animals and characterizes the potential hazard posed by ammonia exposure for noncancer and cancer health effects, including the derivation of a chronic inhalation reference concentration (RfC). Additionally, the draft IRIS assessment includes a qualitative characterization of the human cancer potential.

Charge Questions

Below is a set of charge questions that address scientific issues in the draft IRIS Toxicological Review of Ammonia. Please provide detailed explanations for responses to the charge questions. EPA will also consider the Science Advisory Board review panel's comments on other major scientific issues specific to the hazard identification and dose-response assessment of ammonia. Please consider the accuracy, objectivity, and transparency of EPA's analyses and conclusions in your review.

In addition, in April 2011, the National Research Council (NRC) released its "Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde." In addition to offering comments specifically about EPA's draft formaldehyde assessment, the NRC included comments and recommendations to improve IRIS documents generally. The IRIS Program's implementation of the NRC

recommendations is following a phased approach. Phase 1 of implementation has focused on a subset of the short-term recommendations, such as editing and streamlining documents, increasing transparency and clarity, and using more tables, figures, and appendices to present information and data in assessments. Phase 1 also focused on assessments that had been near the end of the development process and close to final posting. The IRIS Program is now in Phase 2 of implementation, which addresses all of the short-term NRC recommendations. The Program is implementing all of these recommendations but recognizes that achieving full and robust implementation of certain recommendations will be an evolving process with input and feedback from the public, stakeholders, and external peer review committees. This phased approach is consistent with the NRC's "Roadmap for Revision" as described in Chapter 7 of the formaldehyde review report. The NRC stated that "the committee recognizes that the changes suggested would involve a multi-year process and extensive effort by the staff at the National Center for Environmental Assessment and input and review by the EPA Science Advisory Board and others."

General Charge Questions:

1. Is the Toxicological Review logical, clear and concise? Has EPA clearly presented and synthesized the scientific evidence for noncancer and cancer health effects of ammonia?

2. Please identify any additional peer-reviewed studies from the primary literature that should be considered in the assessment of noncancer and cancer health effects of ammonia.

Chemical-Specific Charge Questions:

(A) Hazard Identification for oral and inhalation exposure to ammonia

1. A synthesis of the evidence for ammonia toxicity is provided in Chapter 1, Hazard Identification. Please comment on whether the available data have been clearly and appropriately synthesized for each toxicological effect. Please comment on whether the weight of evidence for hazard identification has been clearly described and scientifically justified.

(B) Oral reference dose (RfD) for ammonia

1. An RfD was not derived for ammonia. Please comment on whether the scientific justification for not deriving an RfD is scientifically supported and clearly described. Please comment on whether data are available to support the derivation of an RfD for ammonia. If so, please identify these data.

(C) Inhalation reference concentration (RfC) for ammonia

1. An occupational epidemiology study of ammonia (Holness et al., 1989) was selected as

the basis for the derivation of the RfC. Please comment on whether the selection of this study is scientifically supported and clearly described. If a different study is recommended as the basis for the RfC, please identify this study and provide scientific support for this choice.

2. Decreased lung function and increased respiratory irritation in humans were concluded by EPA to be adverse effects and selected as the critical effects for the derivation of the RfC. Please comment on whether the selection and characterization of these critical effects is scientifically supported and clearly described. If a different endpoint(s) is recommended as the critical effect(s) for deriving the RfC, please identify and provide scientific support for this choice.

3. The NOAEL/LOAEL approach was used to identify the point of departure (POD) for derivation of the RfC. Please comment on whether this approach is scientifically supported and clearly described.

4. Please comment on the rationale for the selection of the uncertainty factors (UFs) applied to the POD for the derivation of the RfC. Are the UFs appropriate based on the recommendations described in *A Review of the Reference Dose and Reference Concentration Processes* (U.S. EPA, 2002; Section 4.4.5) and clearly described? If changes to the selected UFs are proposed, please identify and provide scientific support for the proposed changes.

(D) Carcinogenicity of ammonia

1. Under EPA's *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005; www.epa.gov/iris/backgrd.html), the draft Toxicological Review of Ammonia concludes that there is "inadequate information to assess the carcinogenic potential" of ammonia. Please comment on whether this characterization of the human cancer potential of ammonia is scientifically supported and clearly described.

2. The draft Toxicological Review of Ammonia did not derive a quantitative cancer estimate for ammonia due to the lack of available studies. Please comment on whether data are available to support the derivation of a quantitative cancer risk estimate.

(E) Endogenous production of ammonia

1. Ammonia is produced endogenously and has been detected in the expired air of healthy volunteers. Is the discussion of endogenous ammonia in Section 2.2.4 of the Toxicological Review scientifically supported and clearly described?