Draft Charge to External Reviewers for the IRIS Toxicological Review of Ammonia

October 2011

Introduction

The U.S. Environmental Protection Agency (EPA) is seeking an external peer review of 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 the EPA's National Center for Environmental Assessment (NCEA) within the Office of Research and Development (ORD). The existing IRIS assessment for ammonia includes a chronic reference concentration (RfC) posted in 1991. The external review draft Toxicological Review of Ammonia includes an RfC and a qualitative cancer assessment.

Charge Questions

Below is a set of charge questions that address scientific issues in the draft Toxicological Review of Ammonia. Please provide detailed explanations for responses to the charge questions. EPA will also consider reviewer comments on other major scientific issues specific to the hazard identification and dose response assessment of ammonia. Please identify and provide the rationale for approaches to resolve the issues where possible. Please consider the accuracy, objectivity, and transparency of EPA's analyses and conclusions in your review.

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) Oral reference dose (RfD) for ammonia

1. An RfD was not derived for ammonia. Has the scientific justification for not deriving an RfD been clearly described in the document? Are there available data to support the derivation of an RfD for ammonia? If so, please identify these data.

(B) 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. Changes in lung function and respiratory symptoms in humans were concluded by EPA to be adverse effects and selected as the critical effect for the derivation of the RfC. Please comment on whether the selection of this critical effect and its characterization is scientifically supported and clearly described. If a different endpoint is recommended as the critical effect for deriving the RfC, please identify this effect 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.

(C) 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. Are there available data to support the derivation of a quantitative cancer risk estimate? If so, please identify these data.