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

February 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 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.

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 general guidelines for risk assessment set forth by the National Research Council (1983) and guidelines and technical reports published by EPA (see Preface). 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 reviewer panel 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.

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. Increased respiratory irritation and decreased lung function 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.