



THE ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OCT 13 2015

Michael Dourson, Ph.D.  
Chairman  
Chemical Assessment Advisory Committee  
Augmented for the IRIS Ammonia Assessment Review Panel  
Science Advisory Board  
U.S. Environmental Protection Agency  
1200 Pennsylvania Avenue, NW  
Washington, D.C. 20460

Dear Dr. Dourson:

Please accept my gratitude for your August 6, 2015, letter providing the Science Advisory Board review panel's comments on the U.S. Environmental Protection Agency's draft Integrated Risk Information System Toxicological Review of Ammonia that was released for external peer review in August 2013.

The EPA appreciates the panel's thorough review and constructive recommendations. We are pleased that the SAB panel commended the agency for the progress made on addressing the recent National Research Council's recommendations for developing clearer and more consistent IRIS toxicological reviews. It also is gratifying that the SAB agreed with key decisions in the draft assessment, including the following:

- the conclusion that ammonia induces significant respiratory effects in humans and animals and the use of this endpoint as a point of departure for deriving the reference concentration
- the use of the Holness et al. (1989) study for the development of the RfC; and
- the conclusion that there is inadequate information to assess the carcinogenic potential of ammonia.

Your letter also included several SAB recommendations that will enhance the clarity of the EPA's assessment and strengthen the scientific basis for its conclusions. The EPA will carefully consider the SAB report and make revisions to the assessment that will address these recommendations. Some of the key SAB recommendations that we will address include:

- an expanded rationale for excluding ammonium salts from the assessment;
- a more detailed evaluation of the chemical reactions and pathways of ammonia generation that may impact gastrointestinal endpoints;
- further discussion of the potential implications of reversibility and long-term attenuation of effects through acclimatization or the healthy-worker effect that may lead to an underestimation of risk;
- a determination of whether alternative points of departure could be identified in the Holness et al. (1989) study;
- further consideration of a cumulative effect of ammonia if corroborated by other studies;

- development of an expanded discussion on the endogenous production of ammonia; and
- inclusion of concentration ranges for typical indoor and ambient concentrations of ammonia.

The SAB panel also offered recommendations on the overall structure of the IRIS toxicological review, the clarity of the preamble, the transparency of integrative approaches and incorporation of other features of systematic review that will benefit both the ammonia assessment and future IRIS assessments. The EPA is working to respond to these recommendations and to finalize the assessment as quickly as possible.

In the meantime, I thank you again for the SAB and the Chemical Assessment Advisory Committee panel's thoughtful review of the EPA's draft IRIS Toxicological Review of Ammonia. The SAB's efforts are invaluable to ensuring that the EPA uses the best available science in finalizing this critical health assessment.

Sincerely,

A handwritten signature in black ink, appearing to read "Gina McCarthy", written in a cursive style. The signature is positioned above the printed name "Gina McCarthy".

Gina McCarthy



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Peter S. Thorne, Ph.D.  
Chairman  
Science Advisory Board  
U.S. Environmental Protection Agency  
1200 Pennsylvania Avenue, NW  
Washington, D.C. 20460

Dear Dr. Thorne:

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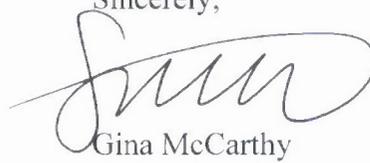
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Gina McCarthy