

Memorandum

Date:	November 8, 2011	
From:	Agency for Toxic Substances and Disease Registry	
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Subject: Comments on EPA's Toxicological Review of Ammonia

To: Environmental Protection Agency

ATSDR's Division of Toxicology and Environmental Medicine (DTEM) has completed a review of the IRIS toxicological review of ammonia. We appreciate the opportunity to comment. Overall, EPA's document is very thorough and well written; therefore we have only a few minor comments.

ATSDR has a Toxicological Profile for Ammonia that was published in 2004. ATSDR has two inhalation Minimal Risk Levels (MRLs) for ammonia: an acute inhalation MRL of 1.7 ppm and a chronic inhalation MRL of 0.1 ppm. While ATSDR has an acute inhalation MRL, EPA has not developed an acute RfC. ATSDR's chronic MRL is based on the same study (Holness et al. 1989) that EPA used to base their proposed chronic RfC of 0.3 mg/m³ (0.4 ppm). For the chronic MRL, ATSDR used the mean TWA ammonia concentration of 9.2 ppm from the Holness et al. (1989) study, adjusted for continuous exposure and divided by an uncertainty factor of 10 for protection of sensitive individuals and a modifying factor of 3 for lack of reproductive and developmental studies. EPA's proposed RfC is based on the high exposure category of 12.5 ppm (8.8 mg/m³) from the Holness et al. (1989) study, adjusted for continuous exposure and divided by an uncertainty factor of 10 to account for potentially susceptible individuals. Overall, the values use a slightly different NOAEL but the EPA chronic RfC is similar to the ATSDR chronic MRL for ammonia. Therefore, we have no objections to EPA's conclusions.

Specific Comments:

Page 8, Line 30 – Souba 1987 is cited referring to Figures 3-1 and 3-2. Should this citation be Nelson and Cox (2008) as stated in the footnote for these two figures?

Page 16, Line 35 – Add 40 ppm to list of exposure levels. See page C-35.

Page 17, Line 7 – Consider adding "However, brief exposure to 150-200 ppm produced lacrimation and transient discomfort", as stated on page C-33.

Page 28, Line 24 – Suggest replacing "over a long period of time" with "duration not specified".

Page 38, Section 4.3 Reproductive/Developmental Studies – Consider adding Minana et al. 1995 to discussion. Miñana MD, Marcaida G, Grisolia S, et al. 1995. Prenatal exposure of rats to ammonia impairs NMDA receptor function and affords delayed protection against ammonia toxicity and glutamate neurotoxicity. J Neuropathol Exp Neurol 54(5):644-650.

Overall, we consider the questions in the Charge to External Reviewers appropriate.