Peer Review Charge for

N-nitrosodi-n-propylamine Toxicological Profile - Draft for Public Comment

This toxicological profile is an update of a previous one published in 1989. This update has focused on Chapter 2, Health Effects, and resulted in the deletion of the previous acute-duration oral MRL.

Thus, we would like for you to focus on the specific chapters noted below, including the health effects section (Chapter 2), and the MRL issue presented below.

CHARGE TO REVIEWER:

CHAPTER 1:

Does Chapter 1 adequately summarize the published literature regarding the health effects present in Cpater 2 for this substance?

CHAPTER 2:

First, does Chapter 2 adequately reflect the published literature regarding health effects for this substance? Are you aware of any studies that are not included that may be relevant in the derivation of MRLs for this chemical?

Second, we would like you to focus on the current data assessment which resulted in deletion of the acute-duration oral MRL previously derived in the 1989 toxicological profile.

An acute-duration oral MRL of 0.095 mg/kg/day was derived in the 1989 toxicological profile. The MRL was based on a hepatic NOAEL of 9.5 mg/kg/day and a total uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability). A recently published study (Terashima et al. 2015) identified a LOAEL of 10 mg/kg/day for focal hepatocellular necrosis. Upon re-evaluation of the MRL, it was determined that the available database is limited and does not support the identification of a critical (most sensitive) effect since the liver was the only potential target tissue examined in the available studies. Because of the absence of toxicity data regarding other tissues the current database does not allow us to determine with certainty that the liver effect is the most sensitive end point. ATSDR policy requires that the critical effect utilized for MRL derivation must reflect the most sensitive toxicity end point.

-- Do you agree/disagree with the deletion of the acute-duration oral MRL of 0.095 derived in the 1989 toxicological profile? Explain. If you disagree, please specify the MRL value that you propose.

-- Please comment on any aspect of our MRL database assessment that you feel should be addressed.

CHAPTER 7:

We would like to know your thoughts on the regulations and guidelines that are presented and any that should be added or removed. Are you aware of any additional regulations or guidelines that we should add? Please provide citations. Are there any that should be removed? Explain.

APPENDIX A:

Please address the MRL worksheet based upon the questions provided above about the MRL.

APPENDIX B:

Please provide comments about the process utilized in this section.

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