

## Peer Review Charge for

### 1,2,3-Trichloropropane Toxicological Profile - Draft for Public Comment

This toxicological profile is an update of a previous one published in 1992. This update has focused on Chapter 2, Health Effects, and resulted in the revision of the previous acute-duration inhalation MRL; and the addition of a new chronic-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 Chapter 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 the revision of the previously derived acute-duration inhalation MRL in the 1992 toxicological profile; and the addition of a new chronic-duration oral MRL.

#### MRLs:

**Acute-Duration Inhalation MRL:** A revised acute duration inhalation MRL of 0.001 ppm was derived based on decreased thickness of the nasal olfactory epithelium of rats. This MRL is based on a  $\text{NOAEL}_{\text{HEC}}$  of 0.03 ppm and a total uncertainty factor of 30 (3 for extrapolation from animals to humans with dosimetric adjustment and 10 for human variability).

The revised acute-duration inhalation MRL of 0.001 ppm has the same basis ( $\text{NOAEL}_{\text{HEC}}=0.03$ ) as the previously derived acute-duration inhalation MRL of 0.0003 ppm—the difference between the values is a decrease in the uncertainty factor for extrapolation from animals to humans. In deriving the revised MRL the uncertainty factor for interspecies variability was decreased from 10 to 3 to be consistent with current practices of using a partial factor when dosimetric adjustments are utilized for calculating a human equivalent concentration (HEC).

--Do you agree with the revised acute-duration inhalation MRL of 0.001 ppm? Explain. If you disagree, please specify the MRL that you propose.

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

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**Chronic-duration oral MRL:** A new chronic-duration oral MRL of 0.005 mg/kg/day was derived based on an increased incidence of bile duct hyperplasia in male rats. The MRL is derived from an adjusted  $\text{BMDL}_{10}$  of 0.47

mg/kg/day and a total uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability). A chronic-duration oral MRL was not derived in the 1992 toxicological profile due to the lack of chronic studies. Since that profile was published, NTP completed the 2-year study which serves as the basis for the new MRL.

--The new chronic-duration oral MRL is 0.005 mg/kg/day. Do you agree/disagree with this value? Explain. If you disagree, please specify the MRL value that you propose.

--In deriving the chronic-duration oral MRL, a rate of 10% was used as the bench mark response. Is this response rate appropriate? The point of departure used to derive this MRL was a BMDL<sub>10</sub> of 0.47 mg/kg/day for increased bile duct hyperplasia in male rats. Do you agree/disagree with the selection of this point of departure. Explain. If you disagree please specify the point of departure that you propose.

--In deriving the chronic-duration oral MRL a total uncertainty factor of 100 was applied. The individual components which comprise the total uncertainty value are:

10 for human variability

10 for extrapolation from animals to humans

In regards to each component which contributes to the total uncertainty factor, please answer the following: Do you agree/disagree with each component of the total uncertainty factor? Explain. If you disagree, please specify the uncertainty factor 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 worksheets based upon the questions provided above about the MRLs.

## APPENDIX B:

Please provide comments about the process utilized in this section.

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