

**OMB Staff Working Comments on EPA's Toxicological Review of cis and trans-1,2-Dichloroethylene (DCE) and draft IRIS Summary (dated Aug 2010)**

September 3, 2010

OMB staff focused this review on EPA's response to the external peer review. Where EPA agrees with the comments, we suggest that appropriate conforming changes be made in the main text of the toxicological review and the IRIS summary.

**General Science Comments:**

- Page A-4 and elsewhere, EPA states the critical effect for the cis-DCE RfD is now relative kidney weight and not relative liver weight. In 5.1.1.2 EPA discusses both endpoints as candidate critical effects. It is not clear in this section where EPA makes a decision and what the scientific basis is for the justification. Similarly, in 5.1.1.3, EPA does not verbalize which critical effect was chosen and why. If the change was partly in response to the comments raised by Dr. Longstreth regarding the liver endpoint, it would be helpful to explain this.
- It appears that the majority of reviewers suggested that EPA decrease the interspecies uncertainty factor for cis-DCE to 3 (rather than 10), but EPA has not adopted this recommendation. The reviewers provided a scientific rationale (as per pages 20-22 of the peer review report) for this suggestion. While EPA cites a lack of chemical specific data as a justification for keeping the 10x factor, it would be helpful if EPA could further respond to the rationale offered by the reviewers in explaining its decision not to adopt the recommendation.
- In describing the confidence in the RfD values for cis and trans-DCE, while we agree that the overall confidence in these values is low, it is unclear how the studies used could be of medium confidence. If these studies were of medium confidence for use in deriving the RfD, then it is not clear why EPA found it necessary to apply the maximum acceptable uncertainty factors (3000). Similarly, it is not clear how the database for these RfDs could be anything but low, rather than low to medium.
- In the body of the toxicological review, it would be helpful if EPA could provide data tables showing the results of the BMD modeling for the RfD endpoints including model fitting criteria (such as AIC values, p values, and others) in chapter 5. Further discussion of the decision criteria in choosing the best fitting model would also be helpful.

*Specific Comments on Appendix A:*

- Page A-1, in response to general question 1, it would be helpful if this response also captured and responded to some of the more critical general impressions of the reviewers (see pages 6-7 of the peer review report) as these do not appear to be discussed anywhere.
- Page A-3, it would be helpful to respond directly to peer reviewer concerns over the quality of the study and Dr. Longstreth's suggestion of not deriving an RfD for the cis 1,2-DCE due to these concerns.

*IRIS STEP 6 INTERAGENCY COMMENTS (OMB)*

- Page A-6, please verify that the first comment describing responses to question A3 adequately characterizes the reviewer comments. In the peer review report (page 18-19), only one reviewer mentions that it is scientifically justified and it is not clear that all reviewers found the approach reasonable (as per comments of Dr. Longstreth at page 19 of the peer review report). It would be helpful to respond specifically to the comments of Dr. Kodell (see page 16 of the peer review report) where he makes specific suggestions regarding the types of statistical tests that should be conducted and explain EPA's choice of 1 sd or a 10% response as it relates to kidney weight changes.
- Page A-6, in describing question A4, EPA states that three reviewers considered the intraspecies UF of 10 to be justified. By our reading, Drs. Bruckner and Kodell suggested it be reduced to 3, while Drs. Howd and Luster agreed with EPA's choice (but both did not necessarily say it was justified). Dr. Longstreth did not comment on it. It would be helpful if the document could more clearly respond to the reviewers who suggested reducing it to 3. A more robust scientific rationale is also suggested on page A-11 where EPA responds to similar comments regarding the UFs applied to trans-DCE.
- Page A-7, in responding to Dr. Bruckner's comment suggesting that the UF for subchronic to chronic extrapolation be reduced, it would be helpful if EPA responded directly to his scientific comment, rather than simply citing that there was not a chronic study. Dr. Bruckner was likely aware that there was no chronic study available when he made the recommendation.
- Page A-8, in describing comments on question B1, it would be helpful to respond to the comment by Dr. Longstreth who comments that the authors of the Shopp study did not find any compelling evidence suggesting that trans-DCE was responsive for any biologically significant adverse effects on the immune system.

*Specific Comments on the IRIS summaries:*

- The cis-DCE document should clearly present the gender chosen for the BMDL used as the point of departure.