Department of Defense Comments on the Revised IRIS Toxicological Review of cis- and trans-1,2-Dichloroethylene (DCE) dated August 2009		
Comments submitted by: Office of the Secretary of Defense, Chemical Material Risk Management Directorate.	Organization: Department of Defense	Date Submitted: 18 August 2009

*Comment categories: Science or methods (S); Editorial, grammar/spelling, clarifications needed (E); or Other (O). Also please indicate if Major i.e. affects the outcome, conclusions or implementation of the assessment.

Comment No.	Section	Page & Paragraph (Enter Global if not specific)	Comment	Suggested Action, Revision and References (if necessary)	Category*
1	Section 5.1.1.1	Reference Dose (RfD) for cis-DCE, Choice of Principal Study and Critical Effect With Rationale and Explanation, pg.80	Page 80 states that "*McCauley et al. (1990, 1995) is the only published oral toxicity study of cis-1,2-DCE...Relative liver weight was significantly increased in male and female rats at doses >97 mg/kg-day and relative kidney weight was significantly increased in male rats at all doses levels*". ..."*As discussed in Section 4.2.1.2.1, some errors and inconsistencies were identified upon examination of the unpublished (McCauley et al., 1990) and published (McCauley et al., 1995) versions of the study, principally related to the documentation of administered doses by the study authors, inconsistencies in reporting of methods, and in some transcription or calculation errors in the unpublished report and published paper. These errors and inconsistencies suggest issues with the quality of the report writing, but not with the study findings themselves. As the only repeat-dose study of cis-1,2-DCE toxicity, this study was used as the basis for the oral RfD [reference dose]*." Page 81 states, *"Therefore, change in relative liver weight is identified as the critical effect and serves as the basis for the point of departure (POD) for the RfD for cis-,2-DCE." (Bench Mark Dose Modeling).*	We believe that the errors and inconsistencies that USEPA notes are associated with the McCauley et al. studies strongly suggest issues with the study findings themselves and not just the "report writing" as USEPA has stated, and should be confirmed prior to basing the cis-1,2-DCE RfD on the increase in liver weight noted. For the sake of transparency, the USEPA should clearly state their supporting evidence that these errors and inconsistencies merely reflect poor report writing. Also, we believe that the apparent lack of pathological findings for the relative liver weight change is significant and thus, the change in the relative liver weight noted may be more reflective of a precursor effect and not an "adverse effect" in and of itself. We appreciate the fact that the database is limited for this isomer but believe that the USEPA should present further evidence to support the change in liver weights are adverse effects and not precursor effects.	M
2	Sections 5.1.2.1 and	Trans-1,2-DCE, Choice of Principal	The USEPA has selected Shopp et al. (1985) in place of the NTP (2002) study as the "critical study" for derivation of the RfD, reversing their previous decision to base the	We agree with the previous agency position that the relevance of the Shopp study is uncertain and believe that these	M

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	5.1.2.3.	Study and Critical Effect- with Rationale and Explanation. RfD derivation-including application of uncertainty factors. Pgs. 84, 103-104.	RfD for trans-1,2-DCE on the liver effects (NTP, 2002) as noted in the 2007 Interagency Review draft version of the document. This Shopp et al. (1985) study apparently was not only available at the time of the current IRIS assessment for 1,2-trans-DCE, but it is discussed in the current USEPA IRIS database for trans-1,2-DCE as a supporting study. The latter portion of the current IRIS text states the following, *"The significance of the decrease inform [antibody-forming cell] AFC/spleen in male mice at all three dose levels is uncertain. This decrease is seen at only the 175 and 387 mg/kg/day dose levels when the data were calculated on the basis of spleen cells. Furthermore, two other measures of humoral immune status, hemagglutination titers and spleen cell response to LPS, were not affected. Accordingly, this parameter will not be used to set a RfD, but will be used as supportive data."* Thus, one can conclude that that USEPA dismissed the Shopp et al. (1985) study in the previous IRIS assessment as not acceptable for deriving an oral RDF for the trans-,2-DCE isomer, but now the agency has changed their position on the relevance of the study.	data should be set aside until the strength of the weight-of-evidence for these effects is more robust through publication of additional studies. Selection of Shopp et al. 1985 after 20 years since its last consideration in IRIS (last revised 1989) is not appropriate without stronger evidence to support it.	
3	Section	Trans-1,2-	We recommend that the USEPA provide additional clarification as to the significance of the immune findings; in the current version of the document the	We suggest that discussion be included regarding how the findings of the Shopp et al. study may be related to human	S

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	5.1.2.1	DCE, pg. 84	significance is not transparent.	immune response issues and overall human health from exposure to low concentrations of 1,2-DCE in the environment.	
4	5.2.2.3. RfC Derivation—Including Application of Uncertainty Factors	Pg. 94	USEPA did not develop a reference concentration for trans 1,2-DCE due to the associated uncertainty being 10,000, above their policy level of 3000. We have not seen minimal data values published before and are unclear regarding how such values will be used in the current hierarchy for selecting toxicity values in site-specific risk assessments. We are also concerned that there will be confusion regarding their use "in limited circumstances, for example, in screening level risk assessments or to rank relative risks". We believe that many agencies will be confused that may screen a site with the value but may not use it to quantify risk; the apparent limitations may pose similar challenges for risk communication. In several paradigms we have seen screening levels translate into regulatory values and believe that use of this minimal data value will be confused as well.	We would prefer that USEPA continue their practice of stating that additional data are necessary to publish a reference concentration with no publication of a minimal data level. Given the large uncertainty value placed upon the minimal data level for trans 1,2-dichloroethylene and the lack of guidance of how to use such a value, we request that USEPA reconsider their publication of the value in this IRIS assessment.	M
5	List of Acronyms	viii	List of acronyms is not complete.	Insure that list of acronyms is complete and includes recently inserted text such as "benchmark dose modeling" etc.	E