Department of Defense Comments on DCM_ToxReview_AR-IASD draft_6-29-11_CLEAN.pdf					
Comments submitted by: Chemical Material Risk Management Directorate			Organization: Department of Defense	Date Submitted: 7/25/2011	
*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**	**Pages**	**Comment**	**Suggested Action, Revision and References (if necessary)**	***Category**
1	Global, Cross-chemical issue	Global	Conclusions regarding the mode of action (MOA) appear to be inconsistent across chemicals. For example for tetrachloroethylene (PCE), EPA has concluded that it cannot determine the mode of action. For DCM, EPA has concluded that the chemical has a mutagenic mode of action, which do not agree with at low doses of DCM We also do not belive the MOA was well described and did not list key events. Yet it appears that there is more information for each of the issues regarding mode of action for PCE than for DCM, especially if one considers the amount of information of the very closely related chemical TCE.	EPA should evaluate the all chemicals by the same set of criteria. EPA should explain the specific data and inferences that allow it to determine that DCM has a mutagenic mode of action while it cannot determine the mode of action for PCE when the data appear very similar.	S/M
2	4.5.1. Genotoxicity Studies	167	EPA continues to discuss genotoxicity when the relevant data for determining a mutagenic MOA are mutagenicity data. The results presented are mixed, and those that are positive are generally positive only at very high levels that are unlikely to occur for ambient environmental	DoD recommends that, as encouraged by EPA's 2005 cancer guidelines, EPA differentiate the MOA for higher and lower levels of exposure and calculate toxicity values for both separtely.	S/M

			exposures. DoD believes that the data presented does not demonstrate that DCM is mutagenic at lower levels of exposure. As EPA's cancer guidelines encourages the use of different MOAs for different levels of exposure when the data indicate that such differences are likely, DoD suggests that EPA use this flexibility and state that a mutagenic MOA might occur at occupational levels but is not likely to occur at ambient environmental levels absent a nearby source.		
3	5	Table 5.5	One of the external peer reviewers questioned EPA's selection of hepatic vacuolation (Nitschke et al., 1988a) as the critical effect for deriving the DCM RfC. The reviewer notes that it appeared to be a high-dose effect in female rats only, the effect was incompletely reported in the male rat, and had no human correlate. We agree with this suggestion that these limitations should be discussed in the text, with EPA's response. EPA agreed that the Nitschke et al. study showed no linear dose-response across the experimental dose ranges (0 to 500 ppm). The incidence of 59% hepatic vacuolation for the controls (no DCM exposure) also is also of concern.	We concur with the external peer reviewer's recommendation to include a more thorough evaluation in the main section of the document (not just in Appendix A). Please follow the reviewer's recommendation and discuss the weaknesses of the Nitschke et al. (1988a) study related to the liver lesion data, this will give a more rigorous and balanced scientific discussion of the limitations of the critical study used to derive the RfC.	S
4	Appendix A	Page A-21, B5 Response	The text states that "A response that addresses the critical effect (hepatic vacuolization) is provided under RfD Charge Question B6. A response that addresses the recommendation for an exposure response array based on	It appears as if "RfD" should be changed to "RfC" as Question B-5 refers to the RfC.	E

			internal dose metrics is provided under RfD Charge Question B1.”		