

- 1) - One of the external reviewers (Allen) requested that further explanation regarding why the high incidence of liver tumors in all mouse groups in the NCI (1978) study precluded evaluation of noncancer effects in the liver. This specific text has been removed from Section 5.1.2.1 (it still appears in Table 4-20 though) and replaced with a NOAEL and LOAEL based on kidney effects in mice. The response that EPA has provided to this reviewer's comment does not directly address the comment provided. Specifically, were liver effects evaluated and/or observed in mice in the NCI study? Did the study authors indicate that the high incidence of tumors precluded evaluation of noncancer liver effects? If they were evaluated, why were they not considered in the selection of the LOAEL and NOAEL (i.e., did the study authors indicate that they were of questionable biological significance)? We suggest revision to the response provide clarification on these points regarding the hepatocellular tumors observed and their impact on the analysis of noncancer effects in the liver. Also, we suggest that the response indicate that the effects observed in this study were reconsidered and a NOAEL and LOAEL were identified (in this draft) based on kidney effects in mice.
- 2) - Two reviewers commented on the rationale presented for selection of liver weight changes as the critical effect for the RfD. Specifically, the reviewers commented that there is no scientific evidence to support the assertion that this effect may represent a sensitive endpoint that occurs early in the process leading to hepatocellular necrosis. There does not appear to be any chemical specific data that would support this statement. We suggest that EPA either clearly state that this is an assumption and/or that EPA has selected the most sensitive effect (i.e., lowest point of departure) as the critical effect for derivation of the RfD--recognizing that vacuolization occurred at the lowest dose but was not selected because the biological significance of the effect was not cleared (see discussion in 5.1.2.1).
- 3) - One reviewer, while agreeing with the selection of the NTP study as the principal study due to limitations with the Gulati study, commented on the modeling done for the Gulati data set. Specifically, the BMR of 5% should have been lower than 5%. This comment has not been addressed in Appendix A.
- 4) - The additional comment provided on Page 7 of the metabolism section (DeKant) regarding the support for the conclusion that tetrachloroethene is a metabolite of 1,1,2,2-tetrachloroethane has not been addressed. We suggest the addition of a response reference in the metabolism section where this is discussed.
- 5) - Page 4, Lines 11 – 13: It would be helpful to indicate why 1,1,2,2 tetrachloroethane is no longer used/registered as an insecticide, fumigant, weed killer or an ingredient in an insect repellent, i.e., was it found to be ineffective, was it expensive for companies, or were there environmental concerns?