NIEHS/NTP Comments on Draft 1,1,2,2-Tetrachloroethane IRIS Document

We find the document well prepared, the authors have addressed most of the comments made by the external review panel, and made necessary revisions. We have a few comments for further consideration:

- 1. The statements on the information about the mode of action (MOA) for this chemical are confusing, in some places it is stated that there is no information and in other places it implies as if there is some information available to speculate the possible mode of action. We do not find any relevant information that can be used to explain the toxicity of the chemical.
- 2. The use of NTP studies is appropriate for derivation of sub-chronic oral RfD, but using it for chronic oral RfD with a very high uncertainty factor of 1000 lacks scientific justification. The increase in liver weight effect as an endpoint of toxicity is considered as adaptable effect by some of our scientific community and may not be an appropriate endpoint for setting of chronic RfD. In our opinion the sub-chronic RfD derived with an uncertainty factor of 300 should be protective enough for chronic oral exposures as well.
- 3. We tend to disagree with the elevation of concern from "possible carcinogenic to humans" to "likely to be carcinogenic to humans" for 1,1,2,2-tetrachloroethane because of the limited data available to support the change in classification to a higher level. The derivation of chronic RfD with an uncertainty factor of 1000 itself is suggestive that more convincing information is needed for reclassification. Furthermore, there is hardly any information on the MOA that would support the change in classification.

Submitted by:

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