National Institute of Environmental Health Science (NIEHS)/National Toxicology Program (NTP) Comments on the final Agency/Interagency Science Discussion Draft IRIS Toxicological Review of Hexachloroethane (dated April 2011)

NIEHS/NTP Comments on Hexachloroethane (HCE) Draft Document

The authors have addressed most of the comments raised by the External Peer Review Panel while revising this document. The document is clearly written and flows logically. We have the following comments for consideration:

The selection of Gorzinski study for derivation of chronic oral RfD is preferable because it provided NOAEL while the NTP studies did not. The dose levels used in the Gorzinski studies were 0, 1.0, 15 or 62 mg/kg. The difference between low and mid dose is 15 fold. This very wide dose spacing is not common in toxicology studies. Based on these studies the NOAEL could lie somewhere between 1.0 and 15 mg/kg for male rats. The authors may consider bringing this point up in their discussion on selection of a principal study.

The derivation of RfC is based on a single six week inhalation toxicity study, the top dose had clinical signs of CNS toxicity, and there were no effects in the lower two dose groups. HCE is considered as a systemic acting gas but did not induce any other systemic toxicity. Kidney is the major and most sensitive target of HCE mediated toxicity as shown by a number of oral studies. One would expect some effects on kidney in inhalation studies based on the chemical properties of HCE. There are a number of uncertainties because of very limited data base and it can be argued not to derive RfC for TCE. But one can also argue for it to have some numbers for guidance since the chances of having additional inhalation studies are not very promising.

Submitted by:

Rajendra S. Chhabra, BVSc.,PhD.,DABT

NIEHS/NTP