DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Agency for Toxic Substances
and Disease Registry

Memorandum

Date: July 21, 2011

From: Agency for Toxic Substances and Disease Registry

Subject: Comments on EPA's Toxicological Review of Tetrachloroethylene

To: Environmental Protection Agency

We appreciate the opportunity to review EPA's Toxicological Review of Tetrachloroethylene as well as the accompanying review by the NRC's Committee to Review EPA's Toxicological Assessment of Tetrachloroethylene. Overall we found the IRIS Toxicological Review and fact sheet to be well-written, comprehensive and fully supported by the studies cited.

We consider the RfC of 0.04 mg/m^3 that EPA obtains to be acceptable and strongly supported by the scientific literature. EPA focuses on the same studies that ATSDR evaluated in our 1997 toxicological profile (as well as a few newer studies) and, via a meta-like analysis, EPA averages three select studies to arrive at a point of departure (POD) value not very different from the POD cited in the ATSDR tox profile. EPA does include one additional uncertainty factor of 10 to give a final value that is tenfold lower than ATSDR's chronic MRL (0.3 mg/m^3 or 0.04 ppm). In other words, EPA uses a total uncertainly factor of 1000, whereas ATSDR uses 100. Thus, the difference in final values is methodological in that EPA has simply added an additional uncertainty factor of 10 for 'database uncertainty.' This results in their final RfC value being just an order of magnitude lower than ATSDR's chronic inhalation MRL.

EPA's RfD of 0.006 mg/kg/day is obtained using a route-to-route extrapolation of the same three inhalation studies mentioned above. We find this to be supported by EPA's PBPK assessment. ATSDR did not derive a chronic oral MRL in our 1997 profile.

We agree with the EPA statement that tetrachloroethylene is "likely to be carcinogenic to humans by all routes of exposure." This statement is based upon EPA's assessment of the numerous studies cited to show that, in humans, tetrachloroethylene is strongly associated with bladder cancer, non-Hodgkin lymphoma and multiple myeloma and, in animals, it causes an increase in the incidence of hepatocellular adenomas and carcinomas.

There are two apparent errors noted by our reviewers in the section on derivation of the oral slope factor: an error in congruence and an apparent typo. First, the Interagency Summary document (page 17) and the full Toxicological Review (page 5-98 and 6-23) list the oral slope factor as $6 \text{ X } 10^{-2}$ per mg/kg-day, whereas the Fact Sheet shows the oral slope factor as $5 \text{ X } 10^{-2}$ per mg/kg-day (page 6). Additionally, in the Interagency Summary document (page 17, section II.B.1.1) there is an equation shown which is supposed to arrive at the $6 \text{ x } 10^{-2}$ value, but the result is shown as 0.1 / (1.7 mg/kg-day) equaling $1 \text{ X } 10^{-2}$ rather than the value of $6 \text{ X } 10^{-2}$ shown in the section title.