MEMORANDUM

DATE: June 17, 2014

SUBJECT: Removal of the *trans*-1,2-Dichloroethylene (CASRN 156-60-5) Provisional Peer-Reviewed Toxicity Value (PPRTV) assessment from the Electronic Library

FROM: Scott Wesselkamper
Director, Superfund Health Risk Technical Support Center (STSC)
EPA/ORD/NCEA

TO: Michele Burgess (OSWER/OSRTI)
Lynn Flowers (NCEA)
Teresa Shannon (NCEA)
The File

It was brought to the attention of the STSC that there is an inconsistency in the conclusions regarding the derivation of a reference concentration (RfC) for *trans*-1,2-Dichloroethylene (DCE) between the 2006 PPRTV assessment and the 2010 IRIS assessment (http://www.epa.gov/iris/toxreviews/0418tr.pdf) for this chemical. The 2006 PPRTV assessment derived a chronic p-RfC of 0.06 mg/m^3 based on pulmonary and liver effects observed in the principal study by Freundt et al. (1977). No subchronic p-RfC was derived. The 2010 IRIS assessment found Freundt et al. (1977), a study by the National Toxicology Program (NTP, 2002), and an unpublished study by DuPont (1998) to be insufficient to support derivation of an RfC value for *trans*-1,2-DCE. Thus, there appears to be a fundamental difference in how the principal study and critical effect(s) used to derive the chronic p-RfC in the 2006 PPRTV assessment were evaluated compared to what was more recently done by IRIS. It is important to note that there are some differences in the respective decision-making processes for developing PPRTV and IRIS assessments, specifically with the IRIS Program having a more extensive review process (e.g., agency and interagency review steps, a public comment period, etc.) than that utilized for developing PPRTV assessments.

Pertinent information from the 2010 IRIS Toxicological Review on *trans*-1,2-DCE that outlines why the Freundt et al. (1977) study was discounted and no RfC value was derived is excerpted and italicized below:

"The finding of lung effects in the Freundt et al. (1977) study is difficult to interpret as this study is the only report of lung pathology in animals exposed to trans-1,2-DCE, a small number of animals were examined, several of the controls also developed this effect, and the upper respiratory tract was not examined for pathology."

"For each of the exposure durations, there was no statistically significant difference between the controls and the exposed groups with respect to the incidence of liver effects (fat accumulation). In general, however, the incidence and severity of fat accumulation increased with increasing exposure duration. Although Freundt et al. (1977) reported histopathologic changes in the liver of rats, the DuPont (1998) study did not corroborate the Freundt et al. (1977) study findings. DuPont (1998) reported relatively small increases in relative and absolute liver weight (1–8%) and no gross or microscopic changes of the liver attributable to trans-1,2-DCE at an exposure concentration 20-fold higher than that

used in the Freundt et al. (1977) study. NTP (2002a) similarly found no histopathologic changes in the liver when trans-1,2-DCE was administered for 90 days by the oral route at dietary concentrations as high as 50,000 ppm. In light of the results of DuPont (1998) and NTP (2002a), it is difficult to explain the liver findings in the single-exposure concentration study by Freundt et al. (1977). Given the limitations of the Freundt et al. (1977) study (i.e., small sample size, use of only one exposure concentration, and observation of fatty accumulation in the liver lobules and Kupffer cells in control animals at some exposure durations) and lack of corroboration from other studies, the Freundt et al. (1977) study was not used as the basis for deriving an RfC for trans-1,2-DCE."

"In summary, the available inhalation data from DuPont (1998) and Freundt et al. (1977) were considered insufficient to support reference value derivation and, therefore, an RfC for trans-1,2-DCE was not derived."

Current practice by the PPRTV Program states that once an IRIS assessment becomes available for any given chemical, the PPRTV assessment for that chemical is removed from the PPRTV electronic library. Thus, based on this practice and the rationale outlined above, it is recommended that the conclusions presented in the IRIS assessment for *trans*-1,2-DCE be presently adhered to, and the *trans*-1,2-DCE PPRTV assessment has been removed from the electronic library. Any additional questions regarding *trans*-1,2-DCE should be directed to the IRIS Hotline at (202) 566-1676 or http://www.epa.gov/iris/contact_hotline.htm.

References:

Freundt, K.J., G.P. Liebaldt and E. Lieberwirth. 1977. Toxicity studies on trans-1,2-dichloroethylene. Toxicology. 7: 141-153.

NTP (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Public Health Service, U.S. Department of Health and Human Services; NTP TR 55. Available from the National Institute of Environmental Health Sciences, Research Triangle Park, NC and online at http://ntp.niehs.nih.gov/ntp/htdocs/ST_rpts/tox055.pdf