Memo to: Environmental Protection Agency

From: NCEH/ATSDR, Centers for Disease Control and Prevention

Regarding: Interagency review of EPA's Final Draft Toxicological Review and IRIS Summary for cis- and

trans-1,2-dichloroethylene

Date: August 31, 2010

CDC's National Center for Environmental Health (NCEH) and the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the final draft Toxicological Review and IRIS Summary for cisand trans-1,2-dichloroethylene. We appreciate the opportunity to comment on these documents as well as the report from EPA's External Peer Review Meeting.

NCEH/ATSDR derived an MRL of 0.2 ppm for both acute-duration exposure (14 days or less) and intermediate-duration inhalation exposure (15-365 days) to trans-1, 2 dichloethylene based on a study by Freundt et al. (1977) that found fatty degeneration of the liver. The acute MRL is based on an LOAEL of 200 ppm over an 8-hour period, and the intermediate MRL is based on an LOAEL of 200 ppm for 8 hours per day, 5 days per week for 9 or 16 weeks.

Oral MRLS for both acute-and intermediate-duration exposure were derived. For acute oral exposure, data supported the derivation of an MRL, for cis-1, 2-dichloroethylene of 1 mg/kg/day; however, no acute-duration MRL was derived for trans 1, 2-dichloroethylene. The acute oral MRL for cis-1,2-dichloroethylene is based on a study by McCauley et al. (1990) that found hematological effects at 200 mg/kg/day and reported a NOAEL of 97 mg/kg/day.

Intermediate-duration oral exposed MRLS were derived for both cis and trans isomers. The intermediate duration oral MRL for cis-1, 2-dicloroethylene is 0.3 mg/kg/day based on a hematological study (McCauley et al. 1990). For trans-1, 2-dichloroethylene, the intermediate oral is 0.2mg/kg/day based on hepatic effects (Barnes et al. 1985).

## **Comments on critical studies**

NCEH/ATSDR did use the Freundt et al (1977) study for both acute and intermediate duration inhalation exposure. We agree that the study is quite old, but for both acute and intermediate durations showed exposure levels associated with liver and lung toxicity.

The DuPont (1998) study was not included in the 1, 2-DCE profile because the last update was 1996. The absence of adverse hepatic effects in the study would not justify its use as a principal study.

The Barnes et al. (1985) should be considered as a principal study for the derivation of the oral RfD for trans-1, 2-DCE. The study clearly identified the hepatic endpoint as the most sensitive.

Shopp et al. (1985) was considered as the principal study for the oral MRL for trans 1, 2-DCE but was not used because, although there appeared to have been immune suppression, it was not clear if it were due to the administered 1, 2-DCE.

McCauley et al. (1990, 1995) - This study should be retained as the principal study for the derivation of the RfD for cis-1,2-DCE. Even though we were concerned about the gavage using corn oil, however, the study showed clear dose-related hematoxicity.

## **Chemical-specific charge comments**

Uncertainty factors (UFs) used in RfD derivation:

No comment.

## **Additional studies**

A high incidence of lymphosarcoma in the lungs and histopathological lesions in the spleen and kidneys was reported in the rats after 60 days of oral treatment with trans-1, 2 DCE (Witmer et al. 1990. Absorption of trans 1, 2-DCE studied in rats after intravenous and oral applications was reported (Manning et. al. 1990).