MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

January 20, 2016

TO: File for Trans-1,2-dichloroethylene (CAS# 156-60-5)

FROM: Mike Depa, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level

The Initial Threshold Screening Level (ITSL) for trans-1,2-dichloroethylene is 200 µg/m³ with annual averaging time.

A literature review was done previously to find toxicological data to develop a screening level (Depa, 1998).

The current review found that the U.S. Environmental Protection Agency (EPA) derived a Reference Dose (RfD) for trans-1,2-dichloroethylene (trans-1,2-DCE) of 0.02 mg/kg/day. The following excerpts from EPA (2010) were selected as a summary of how the RfD was derived.

> The critical effect for the RfD for trans-1,2-DCE is based on decreased antibody production directed against sRBCs in male mice (Shopp et al., 1985). The AFC[1] response exhibited a dose response. EPA determined that the 26% suppression in the number of sRBC[2]-specific AFCs per 106 spleen cells of male mice in Shopp et al. (1985) is a biologically significant measure indicating suppressed antibody response associated with oral exposure to trans-1,2-DCE that is not contradicted by a lack of observed change in the hemagglutination assay to sRBCs or proliferative response to LPS. Suppression of T-cell-dependent antibody response as determined by the AFC assay to sRBCs is a well-validated endpoint that is highly predictive for immunotoxicity (Herzyk and Holsapple, 2007; Luster et al., 1992). Support for this critical effect can be found in the decreased thymus weight in the Barnes et al. (1985) study. Decreased thymus weight can be a good indicator of immunotoxicity and, when accompanied by decreased AFC response in the absence of general toxicity, serves as a predictor of immunotoxicity (Luster et al., 1992). In the case of trans-1,2-DCE, it should be noted, however, that decreased thymus weight was observed in female mice, whereas decreased AFC response was observed in male mice. Confidence in the critical effect for the trans-1,2-DCE RfD would be increased if the positive immune response reported by Shopp et al. (1985) was corroborated by similar findings in a second study. EPA (2010)

To derive an RfD for trans-1,2-DCE, the BMDL1SD[3] (POD[4]) of 65 mg/kg-day (Shopp et al., 1985) was divided by a composite UF of 1,000. The composite UF of 1,000 includes factors of 10 to protect sensitive individuals, 10 to extrapolate from animals to humans, and 10 for use of a study of subchronic duration. Note that EPA (2010) used a total (composite) UF of 3,000 to obtain an RfD of 0.02 mg/kg/day (i.e., RfD = 65/3000). EPA (2010) used a database (DB) uncertainty factor (UF) of 3 which was determined to be unnecessary because there was no chemical-specific or toxicity-specific reason that a database UF was justified and appropriate.

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[1] antibody-forming cells
[2] Spleen red blood cells
[3] Benchmark dose lower 95% confidence limit at the 1-standard deviation effect level
[4] POD = point of departure; experimental data point at which low-dose extrapolation occurs

After removing the DB UF of 3, the composite UF of 1000 was used to derive the RfD. The RfD is recalculated as follows:

RfD = (POD)/(UF1 x UF2 x UF3)

Where POD = point of departure, the BMDL1SD of 65 mg/kg/day
UF1 = 10 to protect sensitive individuals,
UF2 = 10 to extrapolate from animals to humans,
UF3 = 10 for use of a study of subchronic duration

RfD = (65 mg/kg-day)/(10 x 10 x 10)
RfD = 0.065 mg/kg/day

The ITSL for trans-1,2-DCE was based on the recalculated oral RfD, pursuant to Rule 229(2)(b) as follows:

ITSL = RfD x 70kg/20m^3
ITSL = 0.065 mg/kg/day x 70kg/20m^3 x 1000µg/mg
ITSL = 228 mg/m^3; rounded to 1 significant figures to get 200 µg/m^3

The current file review concludes that the AT may appropriately be set at annual, based on the nature and duration of the key study and the ITSL value derivation, as allowed under Rule 229(2)(b). Therefore, the AT is set to annual.

References

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