MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

January 20, 2016

TO: File for Cis-1,2-dichloroethylene (CAS# 156-59-2)

FROM: Mike Depa, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level

The Initial Threshold Screening Level (ITSL) for cis-1,2-dichloroethylene is 18 µg/m^3 with annual averaging time.

A literature review was done previously to find toxicological data to develop a screening level (Depa, 1997).

The current review found that the U.S. Environmental Protection Agency (EPA) derived a Reference Dose (RfD) for cis-1,2-dichloroethylene (cis-1,2-DCE) of 0.002 mg/kg/day. The following excerpts from EPA (2010) were selected as a summary of how the RfD was derived.

> For cis-1,2-DCE, kidney effects were noted as the critical effect. Increases in relative kidney weight up to 27% in high-dose male rats and up to 23% in female rats occurred in the absence of renal histopathology, and BUN[1] and creatinine levels did not indicate renal dysfunction (McCauley et al., 1995, 1990). The biological significance of kidney weight changes in the absence of other histopathologic and clinical chemistry changes is difficult to interpret. Such increases in relative kidney weight could represent an early indicator of kidney toxicity. The absence of supporting evidence for kidney toxicity makes interpretation of the kidney weight findings difficult and the biological relevance of increased kidney weight uncertain.
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> The POD[2] for the RfD for cis-1,2-DCE was chosen as 5.1 mg/kg-day, the lower of the male and female BMDL10[3] values. Applying a composite UF[4] of 3,000 to the POD of 5.1 mg/kg-day yields an RfD of 0.002 mg/kg-day. The composite UF of 3,000 includes factors of 10 to protect sensitive individuals, 10 to extrapolate from animals to humans, 10 for use of a study of subchronic duration, and 3 to account for database deficiencies. Information was unavailable to quantitatively assess toxicokinetic or toxicodynamic differences between experimental animals and humans (applied a factor of 10) or the potential variability in human susceptibility (applied a factor of 10) to cis-1,2-DCE. In the absence of any chronic toxicity studies, an UF of 10 was used to account for extrapolating from a subchronic study to estimate chronic exposure conditions. An UF of 3 was used to account for deficiencies in the database, including lack of reproductive and developmental toxicity data for the cis- isomer. The potential for developmental toxicity of cis-1,2-DCE, however, is informed by a series of oral range-finding studies of the developmental toxicity of a mixture of 1,2-DCE isomers (composition of isomers unknown) (NTP, 1991a, b, c). No evidence of developmental toxicity was observed in mice or rats based on the parameters evaluated in these range-finding studies (gravid uterus weight, fetal body weight, and number of fetuses [live/dead], implantation sites, and resorptions).

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[1] Blood urea nitrogen
[2] Point of departure
[3] Benchmark dose of 10% response, lower 95% confidence limit
[4] Uncertainty Factor

> The cis- and trans-1,2-DCE database lacks a multigenerational study of reproductive toxicity by any route of exposure, and the cis-1,2-DCE database lacks studies of developmental toxicity. The absence of these studies introduces uncertainty in the RfDs. Uncertainty resulting from gaps in developmental toxicity data specific to the cis- and trans-1,2-DCE isomers was reduced by developmental toxicity studies of mixed 1,2-DCE isomers. Additionally, histopathology data from subchronic studies have shown that organs of the reproductive system are unlikely targets for 1,2-DCE toxicity. EPA (2010)

Because there was no indication that the oral-to-inhalation route extrapolation was inappropriate, EPA's RfD was used to derive the ITSL. However, EPA used a database 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. A composite UF of 1000 was used to derive the RfD. Therefore, the RfD is recalculated as follows:

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

Where POD = point of departure, the BMDL10 of 5.1 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 = (5.1 mg/kg-day)/(10 x 10 x 10)
RfD = 0.0051 mg/kg/day

The ITSL for cis-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 = 0.0051 mg/kg/day x 70kg/20m^3 x 1000µg/mg
ITSL = 18 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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