MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

_____

INTEROFFICE COMMUNICATION

_____

January 25, 2016

TO: 1,2-Dichloroethylene File (CAS # 540-59-0)

FROM: Mike Depa, Air Quality Division, Toxics Unit

SUBJECT: Screening level for 1,2-dichloroethylene

The Initial Threshold Screening Level (ITSL) for 1,2-dichioroethylene is 18 µg/m³ with annual averaging time.

The ITSL is based on an EPA (2010) Integrated Risk Information System (IRIS) Reference Dose (RfD). However, instead of using EPA's IRIS RfD of 0.002 mg/kg/day for cis-1,2-dichloroethylene, a new RfD was calculated using the same study and point of departure as EPA, but removing an uncertainty factor (UF) of 3 for database deficiencies (UF_{db}). EPA (2010) used a total UF of 3000. A new RfD of 0.0051 mg/kg/day was calculated using a total UF of 1000. The new RfD was used to calculate the ITSL.[1] (See attached memo from Mike Depa, dated January 20, 2016.)

Previously, the averaging time (AT) assigned to 1,2-dichioroethylene was 24 hours, as per the default methodology. See the attached memo (Attachment) from Gary Butterfield dated August 29, 2006 (hereafter: Butterfield, 2006). 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.

1,2-Dichioroethylene (CAS # 540-59-0) is a mixture of cis-1,2-dichloroethylene (CAS # 156-59-2), and trans-1,2-dichloroethylene (CAS # 156-60-5). Butterfield (2006) based the ITSL for the mixture on the Reference Dose (RfD) for cis-1,2-dichloroethylene. This approach is maintained for the current ITSL for the mixture.

Reference

EPA, 2010. Toxicological Review of cis-1,2-dichloroethylene and trans-1,2-dichloroethylene (CAS Nos. cis: 156-59-2; trans: 156-60-5; mixture: 540-59-0) In Support of Summary Information on the Integrated Risk Information System (IRIS), September 2010, U.S. Environmental Protection Agency Washington, DC. EPA/635/R-09/006F. www.epa.gov/iris http://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0418tr.pdf

[1] RfD x 70kg/20m³ = 0.0051 mg/kg x 3.5 x 1000µg/mg= 17.8 µg/m³ or 18 µg/m³ (rounded to 2 significant figures)

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

_____

INTEROFFICE COMMUNICATION

_____

TO: 1,2-dichioroethylene file (CAS # 540-59-0)

FROM: Gary Butterfield

SUBJECT: Screening level for 1,2-dichloroethylene

DATE: August 29, 2006

1,2-Dichloroethylene (CAS # 540-59-0) is mixture of trans-1,2-dichloroethylene (CAS # 156-60-5) and cis-1,2-dichloroethylene (CAS # 156-59-2). It is also known as dichloroethene. It is a colorless liquid. The molecular formula is C2H2C12. The molecular weight is 96.95 g/mol. The vapor pressure at 20 degrees C for cis-1,2-dichloroethylene is 180 mmHg, and for the trans-1,2-dichloro-ethylene it is 265 mmHg. It is reported that the trans-1,2-dichloroethylene is the most frequently used form of the 1,2-dictiloroethylene isomers by industry.

The following references or databases were searched to identify data to determine the screening level: U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH) Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), Michigan Department of Environmental Quality (DEQ) library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online (1968 - Jan 2005), National Library of Medicine (NLM) - Toxline, and National Toxicology Program (NTP) Status Report.

The CAS and NLM on-line literature searches were conducted on Jan 18, 2005. There were no toxicity studies located that have tested exposure to the 1,2-dichloroethylene mixed isomers. There are several studies that have tested the toxicity of either trans- or cis- isomer. Critical toxicity studies conducted with 1,2-dichlrorethylene have been identified by 1) EPA IRIS, which has established an RfD for trans-1.2-dichloroethylene based on Barnes et al (1985) a 90-day mouse drinking water study; 2) EPA HEAST with an RfD for cis-1,2-dichloroethylene based on McCauley et al (1995) - 90-day rat gavage study; and 3) ATSDR, which has established acute and intermediate inhalation MRLs for trans-1,2-dichlrorethylene based on Freundt et al (1977) a 14-day rat inhalation study.

There appears to not be any data to indicate that oral route to inhalation route extrapolation is inappropriate. This material is readily absorbed through the oral, inhalation and dermal routes of exposure leading to similar adverse effects (including liver changes, and clinical chemistry changes) caused by each of those exposure routes. In the past, the AQD developed an ITSL for cis-1,2-dichloroethylene of 35 µg/m^3 with 24-hour averaging time (based on the HEAST RfD of 10 µg/kg), and an ITSL for trans-1,2-dichioroethylene of 70 µg/m^3 with 24-hour averaging (based on the IRIS RfD of 20 µg/kg).

Although there is no available toxicity information on mixed isomer 1,2-dichloroethylene for the purpose of setting a screening level, it is considered most appropriate to use the lower ITSL of the cis- and trans- isomer screening levels for the mixture ITSL. Thus, the ITSL for 1,2-dichloroethylene (CAS # 540-59-0) is being set at 35 µg/m^3 with 24-hour averaging time based on the ITSL for cis-1,2-dìchlrorethylene.

References:

ATSDR. 1996. Toxicological profile for I ,2-dichloroethene
Barnes et al. 1985. Toxicology of trans-I ,2-dichlorethylene in the mouse. Drug and Chemical Toxicology 8(5): 373-392

EPA. 1997. HEAST document

EPA. 2006. Integrated Risk Information System (IRIS). On-line at www.EPA.govÍiris.
Freundt et al. 1977. Toxicity studies of trans-1,2-dichloroethylene. Toxicology 7:141-1 53.

McCauley et al. 1995. The effects of subacute and subchronic oral exposure to cis-1 ,2-dichloroethylene In Sprague-Dawley rats. Drug and Chemical Toxicology 18(2&3): 171-184.

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[2] 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.
>
> The POD[3] for the RfD for cis-1,2-DCE was chosen as 5.1 mg/kg-day, the lower of the male and female BMDL10[4] values. Applying a composite UF[5] 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).

[2] Blood urea nitrogen
[3] Point of departure
[4] Benchmark dose of 10% response, lower 95% confidence limit
[5] 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 mg/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

Depa, 1997. Memo to the File for cis-1,2-dichloroethylene, dated March 22, 1997. Michigan Department of Environmental Quality, Air Quality Division, Toxics Unit.

EPA, 2010. Toxicological Review of cis-1,2-dichloroethylene and trans-1,2-dichloroethylene (CAS Nos. cis: 156-59-2; trans: 156-60-5; mixture: 540-59-0) In Support of Summary Information on the Integrated Risk Information System (IRIS), September 2010, U.S. Environmental Protection Agency Washington, DC. EPA/635/R-09/006F. www.epa.gov/iris
http://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0418tr.pdf

McCauley, PT; Robinson, M; Daniel, FB; et al. (1990) The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in rats. Health Effects Research Laboratory, U.S. Environmental Protection Agency, Cincinnati, OH and Toxic Hazards Division, Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH; unpublished report.

McCauley, PT; Robinson, M; Daniel, FB; et al. (1995) The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug Chem Toxicol 18:171–184.

NTP (National Toxicology Program). (1991a) Range finding studies: developmental toxicity 1,2-dichloroethylene when administered via feed in Swiss CD-1 mice. Public Health Service, U.S. Department of Health and Human Services; NTP TRP 91022. Available from the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

NTP. (1991b) Range finding studies: developmental toxicity 1,2-dichloroethylene when administered via feed in CD Sprague-Dawley rats. Public Health Service, U.S. Department of Health and Human Services; NTP TRP 91032. Available from the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

NTP. (1991c) Range finding studies: developmental toxicity 1,2-dichloroethylene (repeat) when administered via feed in CD Sprague-Dawley rats. Public Health Service, U.S. Department of Health and Human Services; NTP TRP 91033. Available from the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Shopp, GM, Jr; Sanders, VM; White, KL, Jr; et al. (1985) Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug Chem Toxicol 8:393–407.