MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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TO: File for 1,3-Dichloro-2-propanol [CAS# 96-23-1]

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: January 19, 2017

SUBJECT: 1,3-Dichloro-2-propanol [CAS# 96-23-1] ITSL change in the averaging time from 24 hours to annual

The current initial threshold screening level (ITSL) for 1,3-dichloro-2-propanol is 3 µg/m^3 based on an annual averaging time. The ITSL established on 7/12/2010 based on a 13-week gavage study in rats (NTIS. 1989). When the screening level was derived in 2010 the averaging time was set at 24 hours. As the basis for the screening level used a 13-week gavage study, the averaging time may appropriately be set at annual. Therefore, the averaging time is being changed from 24 hours to annual at this time.

References:

APCR. 2016. Air Pollution Control Rules, Promulgated pursuant to Part 55, Air Pollution Control, of the Natural Resources and Environmental Protection Act, Michigan Department of Environmental Quality. 1994. Act 451, as amended (NREPA).

NTIS. 1989. OTS0526377. 1,3-Dichloro-2-propanol: 13-Week Gavage Toxicity Study in Sprague-Dawley Rats (Final Report) with Cover Letter. National Technical Information Service. Springfield, VA 22161.

MICHIGAN DEPARTMENT OF NATURAL RESOURCES & ENVIRONMENT

INTEROFFICE COMMUNICATION

TO: File for 1,3-Dichloro-2-propanol (CAS #96-23-1)

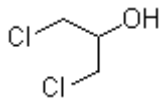
FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: July 12, 2010

SUBJECT: Screening Level for 1,3-Dichloro-2-propanol (CAS #96-23-1)

The initial threshold screening level (ITSL) for 1,3-dichloro-2-propanol is 3 µg/m^3 based on a 24-hour averaging time. The initial risk screening level (IRSL) for 1,3-dichloro-2-propanol is 0.07 ug/m^3 based on an annual averaging time. The secondary risk screening level (SRSL) for 1,3-dichloro-2-propanol is 0.7 ug/m^3 based on an annual averaging time.

1,3-Dichloro-2-propanol (CAS# 96-23-1) is a semi-volatile organic liquid that is soluble in water and most organic solvents. It is used in epichlorohydrin production and the production of 1,3-dichloropropene and 1,2,3-trichloropropane. Exposure to 1,3-dichloro-2-propanol (1,3-DCP) may occur from ingestion of food to which hydrochloric acid-hydrolyzed vegetable protein has been added or in drinking water in which epichlorohydrin polyamine polyelectrolytes are used as flocculants and coagulants for water purification. It is also used to manufacture lacquers, as a solvent for nitrocellulose and hard resins, and as a dye fixative/anti-fading agent in detergent formulations.



1,3-Dichloro-2-propanol

Structure taken from this source http://www.chemblink.com/products/96-23-1.htm

A literature review was conducted to determine an initial threshold screening level (ITSL) for aminoethylpiperazine. The following references and databases were searched to derive the above screening level: EPBCCD, United States Environmental Protection Agency (US EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH), American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values and Biological Exposure Indices (TLV/BEI) 2008 guide, National Toxicology Program (NTP) Study Database, International Agency for Research on Cancer (IARC), Acute Database, Chemical Abstract Service (CAS) Online, National Library of Medicine (NLM)-online, EPA Aggregated Computational Toxicology Resource (ACToR) Database, EPA Toxic Substance Control Act Test Submission Database (TSCATS) and Kirk-Othmer chemical encyclopedia.

There is a 13-week gavage toxicity study in Sprague-Dawley rats using 1,3-dichloro-2-propanol. This study was comprised of five groups of 10 male and 10 female rats in each group which were dosed at either 0, 0.1, 1, 10, or 100 mg/kg body weight/day, 5 days a week, for 13 weeks. The rats were observed for changes in body weight and body weight gain, feed consumption, hematology, urinalysis, clinical chemistry, organ weights, and gross and histopathologic

alterations. Gavage administration of 1,3-dichloro-2-propanol at 100 mg/kg/day produced decreases in body weight gain, feed consumption, and hematologic parameters (RBC, Hgb, PCV), increases in clinical chemistry values (total protein) and organ weights (kidneys and liver), gross pathologic changes in the stomach and histopathologic changes in the stomach, kidney, liver, and nasal tissue in male and female rats. At 10 mg/kg/day, increased liver weights in males and females and histopathologic changes in the stomach, kidneys, and liver in males were observed. No effects attributed to treatment were observed at 0.1 or 1 mg/kg/day in either males or females. It is concluded that under the conditions of this study, the no-observed-adverse-effect level (NOAEL) was 1 mg/kg/day for males and female rats.

There is a report of a 104-week chronic toxicity study with 1,3-dichloro-2-propanol using Wistar rats. The study was comprised of four groups each containing 80 male and 80 female rats. Group 1 was the control group while groups 2, 3, and 4 were administered 27, 80, and 240 mg/l of 1,3-dichloro-2-propanol in the drinking water. When the daily dose is adjusted according to body weight the doses become 0, 2.09, 6.25, and 19.31, respectively, in mg/kg for body weight/day for male rats and 0, 3.39, 9.63, and 29.83, respectively, in mg/kg body weight/day for female rats. The rats were observed for changes in food consumption, water consumption, body weight, hematology, clinical biochemistry, urinalysis, organ weights, and pathologic alterations. Renal adenomas and hepatic carcinomas were seen in both male and female rats. The incidences of hepatocellular carcinoma in male rats were 0/32 (0 mg/kg/day), 0/39 (2.09 mg/kg/day), 1/34 (6.25 mg/kg/day), and 3/18 (19.31 mg/kg/day) and incidences of renal adenoma in male rats were 0/32, 0/39, 0/34, and 1/18 respectively after 104 weeks. The incidences of hepatocellular carcinoma in female rats were 1/37 (0 mg/kg/day), 0/41 (3.39 mg/kg/day), 26/36 (9.63 mg/kg/day), and 0/23 (29.83 mg/kg/day) and incidences of renal adenoma in female rats were 2/37, 0/41, 1/36, and 0/23 respectively. The benchmark dose software calculation showed the best correlation with male rat renal adenoma. The study was performed in 1986 before the report of alpha$_{2\mu}$-globulin, an endogenous compound in male rats and it's association with renal neoplasia. Hence, there is no discussion in the report on hyaline droplet accumulation and granular casts in the kidney medulla, which would have been helpful in determining whether the renal neoplasia in the male rats is due to chemical induction or alpha$_{2\mu}$-globulin. It is important to note that both males and females developed renal adenomas, which points to chemical induction with the 1,3-dichloro-2-propanol.

Determination of the ITSL

The 13-week study NOAEL of 1 mg/kg/day was used to calculate the ITSL for 1,3-dichloro-2-propanol. The study only dosed animals 5 days a week. In order to adjust the dose to 7 days, an average daily dose needs to be calculated.

$$Adjusted\ldots average\ldots daily\ldots dose = NOAEL \times \frac{5 days}{7 days} = 1\,{}^{mg}\!/_{kg/day} \times \frac{5 days}{7 days} = 0.7143\,{}^{mg}\!/_{kg/day}$$

A 13-week study is the minimum length of study needed to develop an RfD. The EPA uses the following equation to determine an RfD from a NOAEL:

$$RfD = \frac{NOAEL}{(UF \times MF)} = \frac{NOAEL}{(UF_H \times UF_A \times UF_S \times MF)} = \frac{0.7143\,{}^{mg}\!/_{kg/day}}{(10 \times 10 \times 10 \times 1)} = 0.007143\,{}^{mg}\!/_{kg/day}$$

Where:

UF = The uncertainty factor used to account for differences between the available data and the possible effects in the human population, usually expressed as factors of 10.

UF_H = Uncertainty factor used to account for the variation in sensitivity among individuals of the human population.
UF_A = Uncertainty factor used to account for the extrapolation from animal data to humans.
UF_S = Uncertainty factor used to account for the extrapolation from less than chronic NOAELs to chronic NOAELs.

MF = The modifying factor which is an additional scientific uncertainty of the study not accounted for in the uncertainty factor, usually expressed as a value greater than 0 and less than or equal to 10.

Rule 232 (1) (b) uses an oral RfD to determine an ITSL using the following equation:

$$ITSL = Oral \ldots RfD \times \frac{70kg}{20m^3}$$

Where 70 kg is the value is the default body weight for the human and 20 m^3 is used to define the minute volume (default ventilation rate) for the human. Taking the oral RfD, which was determined to be 0.001 mg/kg/day above, this leads to the following equation:

$$ITSL = 0.007143 \, {}^{mg}\!/_{kg/day} \times \frac{70kg}{20m^3} = 0.025 \, {}^{mg}\!/_{m^3}$$

$$ITSL = 0.0025 \, {}^{mg}\!/_{m^3} \times \frac{1{,}000\mu g}{1mg} = 2.5 \, {}^{\mu g}\!/_{m^3} = 3 \, {}^{\mu g}\!/_{m^3}$$

Therefore the ITSL is 3 ug/m^3. According to Rule 232 (2) (b) an 24-hour averaging time period is used for the ITSL.

Determination of the IRSL and SRSL

The United States Environmental Protection Agency Benchmark Dose Software (BMDS) version 2.1.2 was used to determine an IRSL using a Benchmark Dose Response of 10% (BMR_{10}), which is a default value in the software. The software was run using dichotomous data utilizing the multistage-cancer model.

BMDS Data Run	Chi^2	p-Value	AIC	Multistage Cancer Slope Factor
Hepatocellular Carcinoma	1.07	0.5864	25.8152	0.010117
Renal Adenoma	0.82	0.6645	36.5995	0.0146377

After reviewing the benchmark dose data generated from the multistage cancer model using dichotomous data, the best goodness of fit using p-values, and chi^2 it was determined that the male rat renal adenoma was the best fit. The multistage cancer slope factor of 0.0146377 (mg/kg)$^{-1}$ was used as the unit risk in assessing the cancer risk screening methodology for determining an IRSL.

Using the equation listed under R 336.1231 on part 3 (c) was used to calculate the equivalent human dose from animal data, it is assumed that milligram/surface area/day is an equivalent dose between species. To make this adjustment, the multistage cancer slope factor in units of (milligram/kilogram/day)$^{-1}$, is multiplied by factor (T). Using the most current EPA method for using this calculation, the EPA now uses ¾ power in their calculation, so this equation has been changed to ¼ to reflect this update.

$$T = (\frac{W_H}{W_A})^{\frac{1}{4}}$$

Where WH = Average weight of an adult human (assumed to be 70 kg).
WA = Body weight of the male Wistar rat (control group at 104 weeks).

$$T = (\frac{70kg}{0.5578kg})^{\frac{1}{4}} = 125.4930^{\frac{1}{4}} = 3.347$$

The multistage cancer slope factor of 0.0146377 (mg/kg)$^{-1}$ for rats needs to be converted to a human cancer slope factor by multiplying the T factor above.

Human cancer slope factor = rat cancer slope factor x 3.347
Human cancer slope factor = 0.0146377 (mg/kg)$^{-1}$ x 3.347 = 0.04899 (mg/kg)$^{-1}$

The oral human cancer slope factor is in (mg/kg) units need to be converted to µg/m^3.

$$\frac{0.04899}{\frac{mg}{kg}} \times \frac{1}{\frac{1000\mu g}{mg} \times \frac{70kg}{20m^3}} = \frac{0.04899}{3500\frac{\mu g}{m^3}} = 0.000013997\frac{\mu g}{m^3}$$

The equation listed under R 336.1231 part 1 was used to derive an IRSL using the human cancer slope factor as the unit risk value.

$$IRSL = \frac{1\times10^{-6}}{unit\ldots risk} = \frac{1\times10^{-6}}{0.000013997\,{}^{\mu g}\!/_{m^3}} = 0.07\,{}^{ug}\!/_{m^3}$$

IRSL = 0.07 ug/m^3
And the SRSL is defined as:

$$SRSL = \frac{1\times10^{-5}}{unit\ldots risk} = \frac{1\times10^{-5}}{0.000013998\,{}^{\mu g}\!/_{m^3}} = 0.7\,{}^{\mu g}\!/_{m^3}$$

Therefore the SRSL is 0.7 ug/m^3. According to Rule 231 (4) an annual average time period is used for the IRSL and SRSL.

The Initial Threshold Screening Level (ITSL) for 1,3-dichloro-2-propanol is 3 µg/m^3 based on a 24-hour averaging time. The Initial Risk Screening Level (IRSL) for 1,3-dichloro-2-propanol is 0.07 µg/m^3 based on an annual averaging time. The Secondary Risk Screening Level (SRSL) for 1,3-dichloro-2-propanol is 0.7 µg/m^3 based on an annual averaging time.

References:

AQD. 1994. Act 451, Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environmental Quality

EPA. 1991. United States Environmental Protection Agency Risk Assessment Forum EPA/625/3-91/019F $Alpha_{2\mu}$-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Male Rat.

EPA. 1994. Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry. EPA/600/8-90/066F. United States Environmental Protection Agency. Office of Research and Development Washington DC 20460. October 1994.

NTIS. OTS0518517. 1989. National Technical Information Service. Springfield, VA 22161. 104 Week Chronic Toxicity and Oncogenicity Study with 1,3-Dichloropropan-2-ol in the Rat (Part I) with Cover Letter Dated 080389.

NTIS. OTS0526377. 1989. National Technical Information Service. Springfield, VA 22161. 1,3-Dichloro-2-propanol: 13-Week Gavage Toxicity Study in Sprague-Dawley Rats (Final Report) with Cover Letter.

Reference Dose (RfD): Description and Use in Health Risk Assessments. Last updated March 16, 2010. http://www.epa.gov/ncea/iris/rfd.htm

DL:lh