**MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY**

**INTEROFFICE COMMUNICATION**

TO: File for Dibromochloromethane [CAS # 124-48-1]

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: January 12, 2017

SUBJECT: Screening Levels for Dibromochloromethane [CAS # 124-48-1]

The initial threshold screening level (ITSL) for dibromochloromethane is 70 µg/m$^3$ based on an annual averaging time. The initial risk screening level (IRSL) for dibromochloromethane is 0.042 µg/m$^3$ and the secondary risk screening level (SRSL) is 0.42 µg/m$^3$ based on an annual averaging time.

Dibromochloromethane [CAS # 124-48-1] also known as chlorodibromomethane, monochloro-dibromomethane and DBCM, is a colorless to pale yellow liquid with a molecular weight of 208.28 g/mol. Dibromochloromethane is now used in laboratories, but was formerly used as a chemical intermediate in the production of fire extinguishing agents, aerosol propellants, refrigerants, and pesticides (ATSDR, 2005).

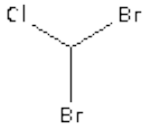


**Figure 1.** Structure of dibromochloromethane.

The following references and databases were searched to derive the above screening levels: United States Environmental Protection Agency (USEPA) Integrated Risk Information System (IRIS), American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values and Biological Exposure Indices (TLV/BEI) 2014 guide, National Toxicology Program (NTP) Study Database, EPA Aggregated Computational Toxicology Resource (ACToR) Database, Chemical Abstract Service Online (searched 11/22/16), and the Agency for Toxic Substances and Disease Registry Toxic Substances Database.

**ITSL Derivation:**

The USEPA's oral reference dose (RfD) was used to derive the ITSL. EPA's RfD used an National Toxicology Program (NTP) 1985 study. "Groups of 10 F344/N rats of each sex and 10 B6C3F1 mice of each sex were administered 0, 15, 30, 60, 125, or 250 mg DBCM/kg/day by gavage for 5 days/week for 13 weeks. At 250 mg/kg/day, male mice showed increased incidence of vacuolar change (fatty metamorphosis) in the liver and toxic nephrosis. Both sexes of rats showed increased incidences of liver vacuolar change, centrilobular necrosis, toxic nephropathy, and salivary gland inflammation and squamous metaplasia at 250 mg/kg/day. Vacuolar changes in the livers of lower-dose male rats were also increased. A Fisher Exact test

showed that incidences of these liver lesions at doses of 60 mg/kg/day or above were elevated relative to the vehicle controls, thus 30 mg/kg/day is the NOEL" (EPA, 1987).

"In the chronic bioassay portion of the NTP (1985) study, 50 F344/N rats of each sex were administered 0, 40, or 80 mg DBCM/kg/day by gavage for 104 weeks and 50 B6C3F1 mice of each sex were similarly treated with 0, 50, or 100 mg DBCM/kg/day for 105 weeks. Treatment was 5 days/week. A dose-related increase in liver fatty changes and ground glass cytoplasmic changes in treated rats of both sexes was reported. Treated female rats also had higher incidences of kidney nephrosis. Treated mice of both sexes exhibited higher incidences of hepatomegaly, fatty metamorphosis, calcification, and liver necrosis. The incidence of nephrosis was increased in dosed males and thyroid follicular cell hyperplasia was increased in dosed female mice. The LOAELs for this portion of the study are 40 mg/kg/day for rats and 50 mg/kg/day for mice" (EPA, 1987).

"The results in these chronic bioassays support the subchronic studies used as a basis of the RfD. In this case, the choice of the subchronic NOAEL as the basis of the RfD rather than the chronic LOAEL (either choice normally requires a 1000 UF, and the resulting RfDs are similar), reflects the slightly greater confidence in the subchronic NOAEL versus the chronic LOAEL that was associated with several adverse effects" (EPA, 1987). The USEPA used an uncertainty factor of 1000 (UF of 10 for subchronic to chronic extrapolation; UF of 10 for extrapolation from animal data; and an UF of 10 for protection of sensitive human subpopulations). This gives an oral RfD of 0.02 mg/kg/day.

Rule 232(1)(b) states that an RfD can be used to determine the ITSL using the following equation:

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

$$ITSL = 0.02\ {}^{mg}/_{kg/day} \times \frac{70\ kg}{20\ m^3} = 0.07\ {}^{mg}/_{m^3} = 70\ {}^{\mu g}/_{m^3}$$

According to Rule 232(2)(b) the averaging time for an ITSL based on an oral RfD is annual. Therefore, the initial threshold screening level (ITSL) for dibromochloromethane is 70 ug/$m^3$ based on an annual averaging time.

**IRSL Derivation:**

The USEPA (1987) has determined that dibromochloromethane is a Class C (possible human carcinogen) based on "inadequate human data and limited evidence of carcinogenicity in animals; namely, positive carcinogenic evidence in B6C3F1 mice (males and females), together with positive mutagenicity data, and structural similarity to other trihalomethanes, which are known animal carcinogens" (EPA, 1987). Dibromochloromethane is structurally similar to bromodichloromethane, bromoform, and chloroform, which the USEPA has classified as Class B2, (known animal carcinogens and possible human carcinogens). EPA (1987) derived a quantitative estimate of carcinogenic risk from oral exposure with an oral slope factor of 8.4E-2 per (mg/kg)/day using the dose-response data from the NTP (1985) study.

"In a 2-year carcinogenicity study, 50 F344/N rats/sex/dose were treated by gavage with dibromochloromethane (>98% pure) in corn oil at 0, 40, or 80 mg/kg, 5 days/week for 104 weeks (NTP, 1985). Groups of B6C3F1 mice (50/sex/dose) were similarly gavaged at doses of

0, 50, or 100 mg/kg, 5 days/week for 105 weeks. In rats, the final survival rates of all groups were comparable (approximately 76%); mean body weights were also comparable between dose groups in each sex, except for a decrease in high-dose males after week 20. No compound-related clinical signs were seen, and no evidence for carcinogenicity was seen in rats under these study conditions" (EPA, 1987).

"In mice, the mean body weights of both male and female high-dose groups were lower than those of their respective controls throughout the study. Mean body weight of the low-dose male mice was lower than the control group after both low-dose groups received an overdose of chemical in week 58. Survival of low- and high-dose males was significantly lower than the control group; the percent survival was 88, 14, and 58% in the control, low-, and high-dose groups, respectively (70% of the low-dose males were accidently killed). The survival rate in females was comparable for all groups (approximately 63%). In female mice, the incidence of hepatocellular adenomas and the combined incidence of hepatocellular adenomas and carcinomas were statistically increased in the high-dose group. The incidence of adenomas was 2/50, 4/49, and 11/50; the incidence of carcinomas was 4/45, 6/49, and 8/50; and the combined incidence was 6/50, 10/49, and 19/50 for female mice in the 0, 50, and 100 mg/kg dose groups, respectively. In high-dose male mice, there was a significantly increased incidence of hepatocellular carcinomas; however, the combined incidence of adenomas was 14/50, 5/50, and 10/50; the incidence of carcinomas was 10/50, 9/50, and 19/50; and the combined incidence of adenomas and carcinomas was 23/50, 14/50, and 27/50 for the 0, 50, and 100 mg/kg dose groups, respectively. Under the conditions of this study, NTP (1985) determined that there was equivocal evidence of carcinogenicity of dibromochloromethane in male mice, and some evidence of carcinogenicity in female mice" (EPA, 1987).

According to Rule 231, the IRSL can be determined using route-to-route extrapolation using the USEPA's quantitative estimate of carcinogenic risk from oral exposure to derive an inhalation unit risk (EPA, 2005).

$$IRSL = \frac{1 \times 10^{-6}}{Inhalation\ Unit\ Risk}$$

The inhalation unit risk can be calculated from the oral slope factor using the following equation:

$$Inhalation\ Unit\ Risk = oral\ cancer\ slope\ factor \times \frac{20\ m^3}{70\ kg} \times \frac{1\ mg}{1000\ \mu g}$$

$$Inhalation\ Unit\ Risk = 0.084\ ({}^{mg}/_{kg/day})^{-1} \times \frac{20\ m^3}{70\ kg} \times \frac{1\ mg}{1000\ \mu g} = 0.000024\ ({}^{m^3}/_{kg})^{-1}$$

$$IRSL = \frac{1 \times 10^{-6}}{Inhalation\ Unit\ Risk} = \frac{0.000001}{0.000024\ ({}^{\mu g}/_{m^3})^{-1}} = 0.041666667\ {}^{\mu g}/_{m^3} \approx 0.042\ {}^{\mu g}/_{m^3}$$

Rule 231(3) states that the averaging time for IRSLs and SRSLs is an annual averaging time. Therefore, the initial risk screening level (IRSL) for dibromochloromethane is 0.042 µg/m$^3$ and the secondary risk screening level (SRSL) is 0.42 µg/m$^3$ based on an annual averaging 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).

ATSDR. 2005. Toxicological Profile for Bromoform and Dibromochloromethane. U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry. Available online at: https://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=713&tid=128

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