MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

April 4, 2016

TO: File for 1,2,3,4-tetrachlorobenzene (CAS No. 634-66-2)

FROM: Mike Depa, Air Quality Division, Toxics Unit

SUBJECT: Update to Screening Level for 1,2,3,4-tetrachlorobenzene

Previously, the averaging time (AT) assigned to 1,2,3,4-tetrachlorobenzene CAS# 634-66-2 was 24 hours, as per the default methodology (Rule 232(2)(b))(see attached memo from Margaret Sadoff dated June 12, 2007). 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.

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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TO: File for 1,2,3,4-tetrachlorobenzene CAS# 634-66-2

FROM: Margaret M. Sadoff, AQD, Toxics Unit

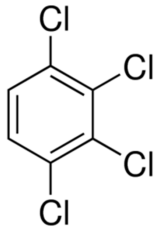
DATE: June 12, 2007

SUBJECT: Updated of Screening Level Related to DOW Permit #156-07

The final ITSL for 1,2,3,4-tetrachiorobenzene is 120 µg/m^3 (24-hour average).

A search of the literature and the following databases was performed for information regarding 1,2,3,4-tetrachlorobenzene (1,2,3,4-TeCB): American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values, National Institute for Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, EPA Integrated Risk Information System (IRIS), EPA High Production Volume Information System, Registry of Toxic Effects of Chemical Substances (RTECS), Environmental Protection Bureau Library, International Agency for Research on Cancer (IARC) Monographs, CAS Registry Online, Hazardous Substance Data Bank (HSDB), National Library of Medicine/Toxline, National Library of Medicine ToxSeek, Health Effects Assessment Summary Tables (HEAST), National Toxicology Program (NTP) Study Database, Entrez PubMed, Scirus, IPCS Intox Databank and CaIEPA's:Toxicity Values, Database

1,2,3,4-TeCB [634-66-2]
MW=216
BP=254C
VP 0.04mmHg at 25C



USE AND ENVIRONMENTAL FATE

(Secondary Source: NLM Toxiine Hazardous Substances Databank) (Source: NTP (Oral) Toxicity Studies of 1,2,4,5-TECB in F344 Rats and B6C3FI Mice, January 1991) 1,2,3,4-TeCB exists as a colorless, needle-like solid with a strong, unpleasant odor. It is minimally soluble in water, slightly soluble in ethanol, and very soluble in ether and carbon disulfide. 1,2,3,4-TeCB is used industrially as a component in the synthesis of dielectric fluids and as a chemical intermediate for pentachioronitrobenzene.

1,2,3,4-TeCB is a semivolatile organic compound with a vapor pressure of 0.04 mm Hg at 25C and a boiling point of 254C. If present, this chemical would be expected to exist as a vapor in ambient air. Vapor-phase 1,2,3,4-TeCB is degraded in the atmosphere by reaction with

photochemically-produced hydroxyl radicals. The atmospheric half-life for 1,2,3,4-TeCB is approximately 200 days which makes it a relatively persistent pollutant.

Persistence and Bioaccumulation

As a degradation byproduct of penta- and hexachlorobenzene, 1,2,3,4-TeCB may enter the environment as a result of microbial degradation. This chemical is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups.

Bioconcentration values suggest that accumulation in aquatic organisms is high. A wide range of concentrations has been found in Great Lakes wildlife and fish.

Although very low concentrations of tetrachlorobenzenes have been found in environmental media, all isomers have been found in human adipose tissue, breast milk, fish and wildlife. 1,2,3,4-TeCB was detected in human milk in Canada at 0.01 ng/g (whole milk) and 0.49 ng/g(milk fat). 1,2,3,4-Tetrachlorobenzene has been detected in 19 of 108 samples of human adipose tissue at a mean concentration of 67 ng/g. Combined trichlorobenzene and tetrachlorobenzene isomers were detected in human adipose tissue in Slovenia at a concentration of 60 ng/g and in human hair samples at 40 ng/g. 1,2,3,4-TeCB was also identified but not quantified in the adipose tissue of non-occupationally exposed individuals in Germany.

HUMAN TOXICITYIEXPOSURE DATA

There is no human toxicity data available for this particular isomer. There are no occupational exposure values but there are emergency inhalation values:

Values in mg/m^3: TEEL 0 = 12.5, TEEL 1 = 35, TEEL 2 = 250, TEEL 3 = 500

Canada has developed a tolerable daily intake (TDI) of 0.0034 mg/kg based on the Chu et al. NOAEL of 34 mg/kg/day and application of a total UF of 10,000. *Source: Priority Substances List Assessment Report. Tetrachiorobenzenes. Environment Canada Health Canada, 1993.*

Occupational exposure to 1,2,3,4-tetrachlorobenzene may occur through inhalation and dermal contact where this compound is produced or used. The general population may be exposed via inhalation of ambient air but more likely through the diet since this chemical is environmentally persistent and bioaccumulative. Individuals who suffer from skin, liver, kidney, or chronic respiratory disease may be at an increased risk if exposed to chlorobenzenes. The World Health Organization (WHO) estimates the average daily intake of all tetrachlorobenzene isomers for humans is less than 0.1 ng/kg body weight.

ANIMAL TOXICITY DATA

Inhalation Toxicity

There are no inhalation data available for this chemical.

Reproductive/Developmental Toxicity

RTECS lists two LOAELs for reproductive toxicity at 1500 and 2000 mg/kg/day. No details other than the toxic effect are given. Effects listed were reduced litter size, extra-embryonic structures, and fetotoxicity “other than death.”

To assess possible maternal hepatic and reproductive effects of 1,2,3,4-tetrachloro-benzene(TeCB) pregnant Sprague-Dawley rats were exposed to 0, 100, 300 or 1,000 mg/kg/day

1,2,3,4-TeCB via gavage (in 1.5% gum tragacanth) on gestation days 9-13. Animals were sacrificed on day 14 of gestation. Maternal mortality (7/19 rats) was increased and body weight gain was greatly decreased in the 1000 mg/kg/day TeCB group. Minimal to moderate hepatocellular hypertrophy (2/9) was reported at the highest dose level. Death (1/10) and minimal hepatocellular hypertrophy (2/9) were reported at 300 mg/kg. Embryonic growth was adversely affected by TeCB treatment at the 300 mg/kg level in which yolk sac diameter, embryonic crown-rump length and head length were all decreased. This 300 mg/kg/day dosage, however, did not significantly elevate the number of dead or abnormal embryos. *[Kitchin KT, Ebron MT; Toxicology 26 (3-4):243-256 (1983)]***PEER REVIEWED** *Source: Kitchin Ebron 1983 as reported in WHO IPCS Environmental Health Criteria 128. Chlorobenzenes other than Hexachlorobenzene (1991).*

Three tetrachlorobenzene (TeCB) isomers (1,2,3,4-, 1,2,3,5-, and 1,2,4,5-) were each administered daily in corn oil by gavage to 10/group female Sprague-Dawley rats at levels of 50, 100, or 200 mg/kg from day 6-15 of gestation. Pregnant dams were sacrificed on day 2i of gestation and the pups removed by cesarean section for teratological evaluation. Administration of 1,2,3,4- failed to alter maternal body weight, organ weights, hematological, or biochemical parameters. There was a decrease in the number of live fetuses at 200 mg/kg of 1,2,3,4- TECB but none of the congeners produced fetal anomalies. There were no treatment- related histopatholgical changes in either the mothers or fetuses. Residues of all three congeners were found in maternal and fetal tissues. *(Source: Kacew et aI. 1984 as reported in WHO IPCS Environmental Health Criteria 128. Chiorobenzenes other than Hexachlorobenzene (1991). This is DOW TSCATS submission OTS0533860)*

Summary: Studies of reproductive/developmental toxicity with exposure to tetrachlorobenzenes have not shown consistent dose-response relationships and have generally been associated with doses resulting in high maternal toxicity. In addition, since liver, kidney and thyroid effects have been demonstrated at even lower concentrations than those employed in these studies, protection of maternal toxicity (i.e. liver, kidney or thyroid effects) should be protective of potential effects to offspring.

Cancer/Genotoxicity Testing

1,2,3,4-TeCB did not show initiating activity in an in vivo rat liver foci bioassay. *(Source: Herren-Freund SL and Pereira MA. (1986). Carcinogenicity of by-products of disinfection in mouse and rat liver. EHP 69: 59-65.*

Acute Oral Toxicity

RTECS listed a rat LD50 (oral) of 1167 mg/kg and a mouse LD50 (ip) of> 500 mg/kg. Chu et al. (1984) reported LD50s for male and female Sprague-Dawley rats fed a single dose of 1,2,3,4-TeCB in corn oil as 1470 mg/kg (1186-1819) and 1167 mg/kg (934-1448), respectively.

Subchronic Oral Toxicity

A rat LOAEL for CNS effects is listed in RTECs as 5600 mg/kg/day for a 28-day intermittent study (no details given). A LOAEL of 575 mg/kg/day was also listed based on a 60-day intermittent study for lung and liver effects.

Dow reported results from a 30-day ad libitum feeding study in rats (10/sex/group) exposed to 0, 0.1, 0.03, 0.01, 0.003 and 0.001% 1,2,3,4-TeCB. At the 0.1% level, both sexes exhibited statistically significant increases in the average liver weight. Males also showed an increase in

average kidney weight at this dose level. Additionally, males showed increased liver weight as low as the 0.03% level.

Chu et al., 1984 performed a 90-day feeding study with 15 Sprague-Dawley rats/sex/group exposed to 0, 0.5, 5.0, 50 or 500 ppm 1,2,3,4-TeCB in corn oil (equates to 0, 0.034, 0.34, 3.4 and 34 mg/kg/day for males and 0,0.041,0.41,4.1 and 41 mg/kg/day for females). This study was used by EPA to derive an RfD value for the 1,2,4,5-TeCB isomer only. However, NOAELs for the other two isomers can be utilized to derive a de novo RfD from which an ITSL can be calculated. Gross observations, serum chemistry and histopathology of all major organs were performed. One female each in the 5 and 50 ppm groups died before conclusion of the study but the deaths were not attributable to the treatment. In a separate metabolism study by this same research group, approximately 46-51% of administered 1,2,3,4-TeCB was excreted in the urine within 48 hours.

Since no statistically significant effects were noted at any dose level for this isomer, a NOAEL of 34 mg/kg/day could be utilized. A total UF of 1,000 would be applied for intraspecies variation, interspecies variation and use of a less than chronic study. The ITSL calculation pursuant to R232(1)(b) is:

(34 mg/kg/day)/1000* = 0.034 mg/kg/day

0.034 mg/kg/day x (70kg/20m^3) = 0.119 mg/m^3 or ≈ 120 µg/m^3 (24 hr average)

*Total UF of 1,000 (10=interspecies; 10=intraspecies; 10= lack of chronic study)

The final ITSL for 1,2,3,4-tetrachlorobenzene is 120 µg/m^3 (24-hour average).