MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for 1,2,3,5-tetrachlorobenzene (TeCB) [CAS# 634-90-2]

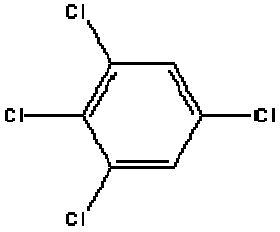
FROM: Margaret M. Sadoff, AQD, Toxics Unit

DATE: June 12, 2007

SUBJECT: Update of Screening Level related to DOW Permit #156-07

The final ITSL for 1,2,3,5-TeCB is 12 ug/m3 (24-hour average).

A search of the literature and the following databases was performed for information regarding 1,2,3,5-TeCB (1,2,3,5-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 CalEPA's Toxicity Values Database



1,2,3,5-TeCB [634-90-2]
MW=216 BP=246C
VP=0.073mmHg at 25C

PHYSICAL PROPERTIES, USE & ENVIRONMENTAL FATE

(Source: NLM Toxline Hazardous Substances Databank)
(Source: NTP (Oral) Toxicity Studies of 1,2,4,5-TECB in F344 Rats and B6C3F1 Mice, January 1991)

1,2,3,5-TeCB is a needle-like solid that has been produced commercially and used as a starting material and intermediate for fungicides, herbicides, insecticides and defoliants. It can also be found with PCBs in dielectric fluids for transformers and capicitators due to historical use. This may result in its release to the environment through various waste streams. 1,2,3,5-TeCB is a degradation byproduct of pentachlorobenzene and lindane and may enter the environment as a result of the microbial degradation of these compounds. Based on a vapor pressure of 0.073 mmHg at 25C, this chemical has low volatility but, if present, would be expected to exist as a vapor in ambient air. Vapor-phase 1,2,3,5-TeCB is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals with an estimated atmospheric half-life of 80

days. It is soluble in hot water (5.1 mg/L at 25C), ether, and benzene; slightly soluble in alcohol; and very soluble in carbon disulfide and petroleum ether.

Persistence and Bioaccumulation

1,2,3,5-TeCB is a metabolite of pentachlorophenol and lindane. It, in turn, metabolizes to 2,3,4,5- 2,3,4,6- and 2,3,5,6-TeCP. It has been detected in human blood, hair, adipose tissue and breast milk. Combined 1,2,3,5- and 1,2,4,5-TeCB isomers were detected in herring gull eggs from the Detroit River (mean= 0.01-0.45 ppm), near Lake Huron (mean=of 0.5-201 ng/g) and near Lake Superior (mean=0.004-0.01 ug/g). Combined 1,2,3,5- and 1,2,4,5-TeCB isomers were detected in eggs of terns (0.002 and 0.005 mg/kg), double-crested cormorant (0.003 mg/kg) and black-crowned night herons (0.005 and 0.002 mg/kg)(4).

Additionally, potential for interaction exists. Since TeCBs, in general, can induce metabolic detoxifying enzymes (e.g., cytochrome p450) exposure could potentially decreased or increase the pharmacologic or toxicologic activity of numerous other compounds. [USEPA; Ambient Water Quality Criteria Doc: Chlorinated Benzenes p.C-62 (1980) EPA 440/5-80-028]**PEER REVIEWED**

HUMAN TOXICITY/EXPOSURE DATA

(Source: NLM Toxline Hazardous Substances Databank)

Occupational exposure to 1,2,3,5-TeCB may be through inhalation and dermal routes at workplaces where this compound is produced or used. The general population may be exposed via inhalation of ambient air and ingestion of food. Individuals who suffer from skin, liver, kidney or chronic respiratory disease may be at increased risk if exposed to chlorobenzenes.

The World Health Organization (WHO) estimates the average daily intake of all TeCB isomers for humans is less than 0.1 ng/kg body weight(1).
[(1) Gunderson EL; J Assoc Off Anal Chem 71: 1200-1209 (1988)]**PEER REVIEWED**

Canada developed at TDI of 0.00041 mg/kg based on the Chu et al. NOAEL of 4.1 mg/kg/day and application of a total UF of 10,000.
Source: Priority Substances List Assessment Report. TeCBs. Environment Canada & Health Canada, 1993.

ANIMAL TOXICITY DATA

Toxicity by Inhalation

There are no inhalation data available for this chemical.

Acute Oral Toxicity

Chu et al. (1984) reported LD50s for male and female Sprague-Dawley rats fed a single dose of 1,2,3,5-TeCB in corn oil as 2297 mg/kg (1854-2828) and 1727 mg/kg (1396-2143), respectively. RTECs lists two rat LD50s as 1727 and 2297 mg/kg.
(Source: Chu et al. (1983). Comparative toxicity of 1,2,3,4-, 1,2,4,5-, and 1,2,3,5-TeCB in the rat: Results of acute and subacute studies. J Tox Environ Health 11: 663-677.)

Cancer/Genotoxicity Testing

1,2,3,5-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.*

Reproductive/Developmental Toxicity

Three TeCB (TECB) congeners (1,2,3,4-, 1,2,3,5-, and 1,2,4,-) were administered daily by gavage in corn oil 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 21 of gestation and the pups removed by cesarean section for teratological evaluation. Administration of 1,2,3,5-TECB failed to alter maternal body weight, organ weights, hematological, or the biochemical parameters. There was a decrease in the number of live fetuses at 200 mg/kg exposure. One pup from this group displayed anomalies at necropsy including edema of the head and neck, a clubfoot of the left hind limb and fusing of ribs on one side. Residue of the test substance was found in maternal and fetal tissues. 100 mg/kg/day could be considered a reproductive NOAEL based on this study. Since the point of the departure for the ITSL based on Chu is considerably lower (4.1 mg/kg/day for liver lesions), that ITSL will be protective of any potential reproductive effects. There were no treatment-related histopatholgical changes in either the adult rats or fetuses. Residues of all three congeners were found in maternal and fetal tissues. *(Source: Kacew et al. 1984 as reported in WHO IPCS Environmental Health Criteria 128. Chlorobenzenes other than Hexachlorobenzene (1991).This is DOW TSCATS submission OTS0533860)*

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.

Subchronic Oral Toxicity

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 (see next section). Gross observations, serum chemistry and histopathology of all major organs were performed. One male in the 0.5 ppm group died before conclusion of the study but the death was not believed to be attributable to the treatment. A separate metabolism study by this same research group showed approximately 46-51% of administered 1,2,3,5-TeCB was excreted in the urine within 48 hours.
(Source: Chu et al. 1984. Toxicity of 1,2,3,4- 1,2,3,5-, and 1,2,4,5-TeCB in the rat: Results of a 90-day feeding study. Drug & Chemical Toxicology 7(2): 113-127.)

ITSL DEVELOPMENT

The Chu 90-day feeding study is the best subchronic data available for 1,2,3,5-TeCB. Kidney and liver were the target organs in this study. In general, male rats were more susceptible to

the effects of TeCB than females. This study found increased kidney and liver weights and increased number and severity of lesions in male and female Sprague-Dawley rats, respectively, at the 500 ppm level. Although no statistical analysis was given, liver lesions in females exposed to 500 ppm (41 mg/kd/day) were 2-5 times higher than either controls or lower dose groups. Similarly, kidney lesions in males exposed to 500 ppm (34 mg/kg/day) were 2-5 times higher than either controls or lower dose groups. Therefore, 3.4 mg/kg/day could be considered a NOEL for screening level development based on males being the more sensitive sex. The ITSL calculation pursuant to R232(1)(b) is:

$$\frac{3.4 \text{ mg/kg/day}}{1{,}000^*} = 0.0034 \text{ mg/kg/day} \times (70\text{kg}/20\text{m}3) = 0.0119 \text{ mg/m3}$$ or **~ 12 ug/m3**

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

The final ITSL for 1,2,3,5-TeCB is 12 ug/m3 (24-hour average).
