

## Michigan Department of Natural Resources and the Environment

### Interoffice Communication

TO: File for Pentafluorobenzene (CAS #363-72-4)

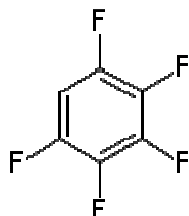
FROM: Doreen Lehner, Toxics Unit, Air Quality Division

SUBJECT: Correction of Screening Level for Pentafluorobenzene (CAS #363-72-4)

DATE: March 9, 2011

The initial threshold screening level (ITSL) for pentafluorobenzene (CAS #363-72-4) is  $10 \mu\text{g}/\text{m}^3$  with an annual averaging time. There is no change from the previous ITSL of  $10 \mu\text{g}/\text{m}^3$  even though there is a correction of a mathematical algorithm ( $I_A$ ) in the ITSL calculation. The correction was due to an error where a value in  $\text{m}^3/\text{kg}$  was used instead of the correct value in  $\text{m}^3/\text{day}$ .

Pentafluorobenzene is a colorless liquid with a molecular weight of 168.07 and is used primarily as an intermediate in organic synthesis in the pharmaceutical and other fine chemical industries. It is generally stable, though it is highly flammable and incompatible with strong oxidizing agents. Contact with salts or combustion may cause the production of toxic hydrogen fluoride gas.



A literature review was conducted to determine an initial threshold screening level (ITSL) for pentafluorobenzene. 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, US EPA TSCATS database, US EPA High Production Volume Information System (HPVIS), US EPA Health and Environmental Research Online (HERO), and Hazardous Substances Data Bank (HSDB).

An acute toxicity study performed on rats which showed an oral LD50 of 2,000 mg/kg (NTIS. OTS0559309. 1998). There was also a 28-day repeated-dose oral toxicity study of pentafluorobenzene in rats (6 rats/sex/group), 5 weeks old at the start of dosing. Pentafluorobenzene was probably given by gavage though the not specifically stated in

the study. The dose levels were 640, 160, 40, and 8 mg/kg/day and a vehicle control group. A 14-day recovery period was provided for the two highest dose levels and the vehicle control group. No deaths were associated with the test substance treatment and no abnormalities were noted in hematological examinations and urinalysis at the end of the dosing period. Many clinical signs associated with treatment-related changes were seen including: decreased spontaneous locomotion, salivation, whitish region in the incisor (160 and 640 mg/kg/day males and females); decreased respiration rate, lids closure (160 and 640 mg/kg/day males and 640 mg/kg/day females); lacrimation, unkempt hair, defect of the lower incisor tips, irregular surface of the lower incisors (640 mg/kg/day males and females); reddish tear (640 mg/kg/day males); diarrhea, staining around the nose and mouth, staining on the lower abdomen, moist hair on the chest, abdomen, and around the anus, and loss of hair on the femur (640 mg/kg/day females). Decreases or trends toward decreases in body weights were noted in the 160 mg/kg/day males for days 15-28 and in the 640 mg/kg/day males for days 3-28. At terminal examinations, an increase in total bilirubin level, a decrease in potassium level (640 mg/kg/day males), a decrease in cholinesterase level, increases in total cholesterol, total protein, and albumin levels (640 mg/kg/day females), and trends toward increases in GPT levels (640 mg/kg/day males and females) were noted. In organ weights, an increase in liver weight (160 and 640 mg/kg/day females and 640 mg/kg/day males) and brownish change of the liver (640 mg/kg/day females) were observed. In histopathological examinations, decreased iron pigments of the ameloblasts, irregular alignment, degeneration, and loss of the ameloblasts at the maturation stage, necrosis and cell infiltration of the pulp, proliferation of the papillary layer (640 mg/kg/day males and females), ground glass appearance and prominent nuclei of the hepatocytes (160 and 640 mg/kg/day males), and centrilobular swelling of the hepatocytes (160 and 640 mg/kg/day females and 640 mg/kg/day males) were noted. Based upon the results of this study, the NOEL (no-observed-effect-level) of pentafluorobenzene for the rat was considered to be 40 mg/kg/day (NTIS. OTS0559309. 1998).

### Determination of the ITSL

The NOEL of 40 mg/kg/day will be used to calculate the ITSL for pentafluorobenzene. Based on Rule 232 (1) (e) the ITSL is determined as follows:

$$ITSL = \frac{NOAEL(\text{mg}/\text{kg}/\text{day})}{35 \times 100} \times \frac{W_A}{I_A} \times \frac{b}{a}$$

Where:

$W_A$  = Body weight of experimental animal in kilograms (kg).

$I_A$  = Daily inhalation rate of experimental animal in cubic meters/day.

$b$  = Absorption efficiency by the oral route of exposure.

$a$  = Absorption efficiency by the inhalation route of exposure.

Since the value  $b/a$  is not known, the default for this value is 1.

The  $W_A$  is the default value for a non-gender rat is 0.395 kg. The  $I_A$  is determined by the following equation taken from EPA 1988 determined below:

$$I_A = 0.80 \times W^{0.8206}$$

Where:

I = Inhalation rates in m<sup>3</sup>/day

W = Body weight (kg)

$$I_A = 0.80 \times 0.395^{0.8206} = 0.373 \text{ m}^3/\text{day}$$

Adding the values to the above equation gives.

$$ITSL = \frac{40 \text{ mg/kg/day}}{35 \times 100} \times \frac{0.395 \text{ kg}}{0.373 \text{ m}^3/\text{day}} \times 1 = 0.012102642 \text{ mg/m}^3 = 10 \text{ } \mu\text{g/m}^3$$

According to Rule 232 (2) (c), the averaging time is annual.

Based on the above data, the ITSL for pentafluorobenzene (CAS #363-72-4) is 10  $\mu\text{g}/\text{m}^3$  with an annual averaging time.

#### References:

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

EPA. 1988. Recommendation for and documentation of biological values for use in risk assessment. PB 88-179874.

NTIS. OTS0559309. 1998. National Technical Information Service. Springfield, VA 22161. Initial submission: TSCA HLTH & SFTY study CVR SHT FR N.A. Indus inc. re 28-day repeated-dose oral tox study of pentafluorobenzene in rats W/ATTCHMT (SUMM), DT'D 5/13/98 (Sanitized).

DL:lh