MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

March 19, 2001

TO: File for Benzothiozole (CAS No. 95-16-9)

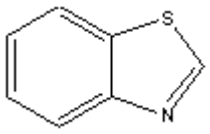
FROM: Michael Depa, Toxics Unit, Air Quality Division

SUBJECT: Development of the Screening Level

The initial threshold screening level (ITSL) for benzothiozole is 1 µg/m³ (annual averaging time).

The following references or databases were searched to identify data to determine the screening level: Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS), the Registry of Toxic Effects of Chemical Substances (RTECS), the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), National Institute of Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online (1967- September 2000), National Library of Medicine (NLM), Health Effects Assessment Summary Tables (HEAST), and National Toxicology Program (NTP) Status Report. The EPA has not established a reference concentration (RfC) or reference dose (RfD) for benzothiozole. The ACGIH and NIOSH have not established Occupational Exposure Limits (OELs). The molecular weight is 135.18 g, and the molecular formula is C7H5NS. The molecular structure is pictured in Figure 1. The melting point is 2ºC. Benzothiozole is a liquid at standard temperature and pressure.

Figure 1. Molecular Structure of Benzothiazole



Acute Toxicity

An LD50 of 492 mg/kg was reported (Younger Laboratories, 1964). The author also reported the lower and upper limit of 405 to 605 mg/kg. respectively. The authors stated that, "The compound was classed as mildly toxic by oral ingestion in male and female rats." Data that was not provided included, number and strain of rats used, method of LD50 calculation, number of mortalities per dose group and quantity of dose per group. Because of these shortcomings, this study was deemed unacceptable to use to derive an ITSL.

In another LD50 study, groups of 10 (5 male and female) Swiss Webster mice were dosed with unspecified doses of benzothiazole and observed for 14 days (Moran, et al., 1980). The LD50 was reported as 900 mg/kg with a 95% confidence interval of 803-1008. The authors referenced the Litchfield Wilcoxon method for determining the LD50.

In another LD50 study, groups of 2 or 3 male and 2 or 3 female Sprague-Dawley rats (5 in each dose group) were dosed with 251, 316, 398 or 501 mg/kg benzothiazole and observed for 14 days (Younger Laboratories, 1976). Mortalities included 0/5, 1/5, 3/5 and 5/5 in each respective dose group. The LD50 was determined to be 380 mg/kg (95% Confidence Limit = 340-420 mg/kg. Most deaths occurred within one day of dosing. Signs of intoxication included: reduced appetite and activity (one to two days in survivors), increasing weakness, ocular discharge, collapse, and death. Gross autopsy findings included lung and liver hyperemis and gastrointestinal inflammation. The viscera of the survivors appeared normal.

In another LD50 study, groups of 5 male and 5 female Fischer F-344 rats (10 rats in each dose group) were dose by gavage with 398, 501 and 631 mg/kg benzothiazole and observed for 14-days (Reddy *et al*., 1986). The LD50 was determined to be 493.3 mg/kg for males, 465.6 mg/kg for females, and 478.6 mg/kg for combined sexes. All mortalities occurred within 2 days of dosing. Body weight gain was observed in rats dosed with the low and mid-dose groups but not the high dose group. Clinical signs observed with all dose levels during the study included: lethargy, ataxia, prostration, lacrimation, squinting, body cool to touch, loose stool, few stools or no stools, crusty eye, crusty muzzle, and yellow/brown stained or damp fur in the perianal region. Necrocropsy of animals found dead revealed: dark content of stomach and small intestine, multiple focal black discoloration of glandular stomachs, diffuse pale discoloration of livers, diffuse pale or red discoloration of lungs and distended urinary bladder. Necropsy of terminal sacrifice animals revealed: enlarged hard red spleens, an ovarian cyst, a diaphragmatic hernia, and small testes.

Derivation of the Screening Level

Two of the LD50 studies were considered to adequate to derive the ITSL: Younger Laboratories (1976) and Reddy *et al*. (1986). The 1976 Younger Laboratories study was used because it provided more dose groups, statistical analysis and a dose-response slope. The screening level was calculated according to Rule 232(h).

The average body weight (W_a) and the inhalation rate (I_a) of male and female Sprague-Dawley rats were obtained from EPA, 1988.

$ITSL = 1/(500 \times 40 \times 100) \times LD50/(0.167) \times W_a/I_a$

$ITSL = (5 \times 10^{-7}) \times (380\ mg/kg)/(0.167) \times (0.475\ kg)/(0.434\ m^3)$

$ITSL = 1.25 \times 10^{-3}\ mg/m^3$

$ITSL = 1\ \mu g/m^3$ (annual averaging time)

The ITSL for benzothiazole is 1 $\mu g/m^3$ based on annual averaging time.

REFERENCES

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Reddy G, Mayhew D. 1992. Acute oral toxicity (LD50) study in rats with benzothiazole. Journal of American College of Toxicology. 11(6):666.

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Younger Laboratories. 1976. Initial Submission: Toxicologic investigation of benzothiazole (7/76) (Final Report) with cover letter dated 112691. US EPA microfiche # 88-920000373.