MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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TO: File for 2-Mercaptobenzothiazole (CAS # 149-30-4)

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: May 13, 2016

SUBJECT: Screening Level for 2-Mercaptobenzothiazole (CAS # 149-30-4)

The initial risk screening level (IRSL) for 2-mercaptobenzothiazole (CAS # 149-30-4) is 0.54 µg/m^3 annual averaging time and the secondary risk screening level (SRSL) is 5.4 µg/m^3 annual averaging time.

2-Mercaptobenzothiazole (2-MBT) is also known as 2-thiobenzothiazole and captax. It is a pale yellow to tan crystalline powder with a pungent odor and a molecular weight of 167.2513 g/mol. Even though it has a melting point of 180.2 °C, it is readily soluble in alcohol, ether, acetone, benzene, and in alkali and alkali carbonate solutions. 2-Mercaptobenzothiazole is used: as an antifungal agent; microbiocide; as a copper corrosion inhibitor in circulating cool water systems; in veterinary ointments and lotions for canine dermatoses and on teats of cows; in water based adhesives; in wood preservatives; as an accelerator for the vulcanization of rubber; and was historically used in rubber baby bottle nipples (Pubchem, 2016).

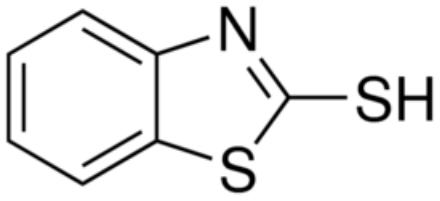

Figure 1. Structure of 2-mercaptobenzothiazole.

A literature review was conducted to determine an initial risk screening level (IRSL) for 2-MBT. The following references and databases were searched to derive the above screening level: CCD, 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) 2014 Guide, National Toxicology Program (NTP) Study Database, International Agency for Research on Cancer (IARC), Acute Database, Chemical Abstract Service (CAS) Online (SciFinder) [CAS search performed on 5/10/16], National Library of Medicine (NLM)-online, EPA Aggregated Computational Toxicology Resource (ACToR) Database, and EPA Toxic Substance Control Act Test Submission Database (TSCATS).

IRSL Derivation:

In a study by the National Toxicology Program (NTP, 1988), male F344 rats and male and female B6C3F$_1$ mice (50 per sex, species, and exposure group) "were administered 0, 375, or 750 mg/kg 2-mercaptobenzothiazole in corn oil by gavage, 5 days per week for 103 weeks. Groups of 50 female rats were administered 0, 188, or 375 mg/kg 2-mercaptobenzothiazole in corn oil by gavage on the same schedule" (NTP, 1988). "All animals were observed two times per day, and clinical signs were recorded once per week. Body weights by cage were recorded once per week for the first 12 weeks of the study and once per month thereafter. Mean body weights were calculated for each group. Animals found moribund and those surviving to the end of the studies were humanely killed. A necropsy was performed on all animals including those found dead, unless they were excessively autolyzed or cannibalized, mis-sexed, or found missing. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study" (NTP, 1988). "Mean body weights of dosed male rats were similar to or greater than those of the vehicle controls. Mean body weights of dosed female rats were generally greater (up to 11%) than those of the vehicle controls. Rats were lethargic after they were dosed" (NTP, 1988). "Under the conditions of these 2-year gavage studies, there was some evidence of carcinogenic activity of 2-mercaptobenzothiazole for male F344/N rats, indicated by increased incidences of mononuclear cell leukemia, pancreatic acinar cell adenomas, adrenal gland pheochromocytomas, and preputial gland adenomas or carcinomas (combined). There was some evidence of carcinogenic activity for female F344/N rats, indicated by increased incidences of adrenal gland pheochromocytomas and pituitary gland adenomas" (NTP, 1988).

Table 1. Lesions in Rats in the Two-Year Gavage Study of 2-Mercaptobenzothiazole.

	Control	Low Dose	High Dose
Male Rats			
Adrenal gland pheochromocytomas	18/50	25/50	22/49
Mononuclear cell leukemia	7/50	16/50	3/50
Pancreatic acinar cell adenomas	2/50	13/50	6/49
Preputal gland adenomas or carcinomas (combined)	1/50	6/50	5/50
Female Rats			
Adrenal gland pheochromocytomas	1/28	3/31	5/25
Pituitary gland adenomas	15/49	24/50	25/50

(Note: Week of first tumor incidence was used to determine whether to use overall tumor rates or terminal rates. Female rat adrenal gland pheochromocytomas first week of tumor incidence occurred on week 96 when the number of surviving animals was closer to the terminal rate surviving animal numbers. All other tumor incidences occurred when the number of surviving animals was closer to the overall tumor rate surviving animal numbers.)

Each tumor incidence was run on the EPA's Benchmark Dose Software (version 260.1) using the multi-stage cancer model. A linear extrapolation from the lower 95% confidence limit on dose as the point of departure to zero response at zero dose. The cancer slope factor was then calculated from this benchmark dose lower confidence limit (BMDL) and the benchmark dose associated with 10% extra risk (BMR) as shown below:

$$Cancer\ slope\ factor = \frac{BMR}{BMDL} = q_1^*$$

After reviewing the results, the best statistical fit was for the female rat pituitary gland adenomas giving a benchmark dose lower confidence limit (BMDL) of 60.1415 mg/kg as the point of departure and a cancer slope factor of 0.00166275 when BMR is 0.1. Rule 231(3)(f) can be used to derive an inhalation slope factor from an oral slope factor by using the following equation:

$$q_1^*(^{\mu g}/_{m^3})^{-1} = q_1^* (^{mg}/_{kg})^{-1} \times \frac{20\ m^3}{70\ kg} \times \frac{1\ mg}{1000\ \mu g} \times \frac{a}{b}$$

Where:
a = absorption efficiency by inhalation route of exposure.
b = absorption efficiency by oral route of exposure.

In the absence of absorption efficiency data the value for a/b = 1. To determine q_1^* ($^{mg}/_{kg}$), the oral slope factor for humans, the following equation is used:

$$q_1^*\ animal \times T = q_1^*\ human$$

To determine T, the interspecies scaling factor, the following equation is used:

$$T = (\frac{W_H}{W_A})^{\frac{1}{4}} = (\frac{70\ kg}{0.31\ kg})^{\frac{1}{4}} = 3.8764$$

Where:
W_H = Average weight of an adult human and assumed to be 70 kilograms.
W_A = Body weight of male rat in kilograms.

The mean body weight for the female F344/N rats in this study was 0.31 kg. Adding the information to the above equation gives a T of 3.8764. The T value from the above equation and the q_1^* animal value (which is the multi-stage cancer slope factor of 0.00166275 per mg/kg from the BMDS multi-stage cancer model) were to determine the q_1^* for humans as follows:

$$q_1^*\ human = 0.00166275\ (^{mg}/_{kg})^{-1} \times 3.8764 = 0.006446\ (^{mg}/_{kg})^{-1}$$

Inserting the value of q_1^* human oral slope factor in $(mg/kg)^{-1}$ into the equation to determine the q_1^* inhalation in $(\mu g/m^3)^{-1}$ found in Rule 231(3)(f) above gives:

$$q_1^*\ (^{\mu g}/_{m^3})^{-1} = 0.006446\ (^{mg}/_{kg})^{-1} \times \frac{20\ m^3}{70\ kg} \times \frac{1\ mg}{1000\ \mu g} \times \frac{1}{1} = 0.00000184(^{\mu g}/_{m^3})^{-1}$$
$$= 1.84E^{-6}\ (^{\mu g}/_{m^3})^{-1}$$

Rule 231(1) was used in the equation below to develop the IRSL:

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

Where:
Unit Risk = Additional lifetime cancer risk occurring in a population in which all individual are exposed continuously for life to a concentration of 1 microgram per cubic meter of the chemical in the air they breathe.
Unit Risk = q_1^*.

$$IRSL = \frac{1 \times 10^{-6}}{1.84E^{-6}(^{\mu g}/_{m^3})^{-1}} = 0.5435\,^{ug}/_{m^3} = 0.54\,^{\mu g}/_{m^3}$$

The initial risk screening level (IRSL) for 2-mercaptobenzothiazole (CAS# 149-30-4) is 0.54 µg/m^3 annual averaging time and the secondary risk screening level (SRSL) is 5.4 µg/m^3 annual averaging time.

References:

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

NTP. 1988. NTP Technical Report on the Toxicology and Carcinogenesis Studies of 2-Mercaptobenzothiazole (CAS No. 149-30-4) In F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). National Toxicology Program. Box 12233 Research Triangle Park, North Carolina 27709. NTP Publication No. 88-2588. NTP TR 332.

Pubchem. 2016. 2-Mercaptobenzothiazole. PubChem Open Chemistry Database. Accessed on 5/9/2016. Available online at: https://pubchem.ncbi.nlm.nih.gov/compound/2-Mercaptobenzothiazole#section=Top

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