MICHIGAN DEPARTMENT OF ENVIRONMENT, GREAT LAKES, AND ENERGY

INTEROFFICE COMMUNICATION

TO: File for 1,2-Benzisothiazol-3(2H)-one (CAS # 2634-33-5)

FROM: Keisha Williams, Air Quality Division

DATE: August 6, 2019

SUBJECT: Rescind Screening Level for 1,2-Benzisothiazol-3(2H)-one

The Initial Threshold Screening Level (ITSL) for 1,2-benzisothiazol-3(2H)-one of 0.1 µg/m³ with annual averaging time is being rescinded.

After reviewing the basis of the 1,2-benzisothiazol-3(2H)-one ITSL, it was determined that the default ITSL may not be health protective due to the sensitization hazard associated with 1, 2-benzisiothiazol-3(2H)-one exposure. 1, 2-Benzisiothiazol-3(2H)-one will be reviewed on a case-by-case basis until toxicity information is available to derive a screening level.

KW:lh

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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TO: File for 1,2-Benzisothiazol-3(2H)-one (CAS # 2634-33-5)

FROM: Keisha Williams, Air Quality Division

DATE: December 21, 2018

SUBJECT: Screening Level Derivation for 1,2-Benzisothiazol-3(2H)-one

The initial threshold screening level (ITSL) for 1,2-benzisothiazol-3(2H)-one is 0.1 µg/m^3 (annual averaging time) based on the Michigan Department of Environmental Quality (MDEQ), Air Quality Division (AQD) Rule 336. 232 (1) (i) and (2) (c).

The following references or databases were searched to identify data to determine the screening level: United States Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS), 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, Agency for Toxic Substances and Disease Registry (ATSDR) Minimal Risk Levels (MRLs), International Agency for Research on Cancer (IARC) Monographs, Health Effects Assessment Summary Tables (HEAST), National Toxicology Program (NTP) Status Report, the American Chemical Society's SciFinder database, EPA Superfund Provisional Peer Reviewed Toxicity Values, EPA Acute Exposure Guideline Levels (AEGLs) for Airborne Chemicals, EPA High Production Volume Database, United States Department of Labor Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs), Spacecraft Maximum Allowable Concentrations (SMACs), California Office of Environmental Health Hazard Assessments Reference Exposure Levels, Texas Commission on Environmental Quality (TCEQ) Effects Screening Levels (ESLs), German maximale Arbeitsplatz-Konzentration (MAK) values, and European Chemicals Agency Registered Substances Dossiers.

Background Information

1,2-Benzisothiazol-3(2H)-one, which is also known as BIT (Figure 1) is "a preservative and antimicrobial agent in industrial and consumer products such as cosmetics and paints. It is also an ingredient in some fungicides, microbiocides, disinfectants and pesticides. Benzisothiazolinone is used as a slimicide in the manufacture of powder-free polyvinyl gloves. It is a component of air fresheners, printer inks, household cleaners and laundry products" (HSDB, 2015). Chemical properties are listed in Table 1.

Figure 1. Chemical structure for BIT

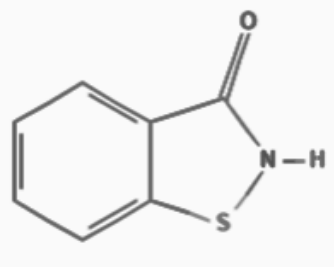

Table 1. Chemical properties of BIT

Molecular weight: 151.183 grams/mole
Melting point: 156.6 °C
Boiling point: 327.6 °C
Vapor pressure: 2.78 x 10^{-6} mmHg at 25°C
Physical state at room temperature: solid

Reference: PubChem Compound Database

Epidemiological and case studies have shown an association between BIT exposure and skin/respiratory sensitization (HSDB, 2015; TSCA, 2018). BIT has been shown to be an eye irritant in *in vivo* studies (ECHA, 2018). Furthermore, potential portal of entry effects have been seen with stomach hyperplasia after oral administration in *in vivo* studies (ECHA, 2018). Since BIT may be a portal of entry irritant, route to route extrapolation from oral studies would not be appropriate for the derivation of an acute ITSL. Unfortunately, there is a lack of inhalation studies on which to derive an ITSL. As a result, the default ITSL, 0.1 µg/m^3 (annual averaging time), will be applied to this toxic air contaminant (TAC) to be health protective. If inhalation studies become available, this ITSL should be re-evaluated.

No studies were identified in which BIT was evaluated for carcinogenicity. As a result, this TAC is not classifiable as a carcinogen.

Since an oral, two-generation reproductive toxicity study is available, a potential ITSL was derived for comparison to the default ITSL. This will give an estimation of the level of health protection provided by the default ITSL for BIT. The original study was not obtained, but this study was summarized in sufficient detail for ITSL derivation in the REACH dossier (ECHA, 2018). Briefly, male and female rats were administered 0, 250, 500 or 1000 ppm BIT (N=24 for male and 25 for female) in their diet for 10 weeks before mating. From mating through pregnancy and weaning, this parent (P) generation of females continued to receive BIT. This was estimated to give approximately 19 weeks of exposure to the P generation. In the same way, 24 “animals of each sex were randomly selected from each group to form the filial (F1) generation” and given the same BIT dosing per group as seen with the P generation. Clinical signs were monitored, body and organ weights were collected, food consumption was monitored, gross pathology was examined at necropsy, and histopathology was examined following necropsy.

The lowest observable adverse effect level (LOAEL) was seen with “hyperplasia of the limiting ridge of the stomach” in the P generation at the 500 ppm level (“mean dose of 37.2 mg/kg/day” in males and “54.2 mg/kg/day” in females). Developmental toxicity, as seen with decreased pup survival and decreased weight gain, was also observed in F1 generation males and females,

but at the 1000 ppm level. A potential ITSL can be derived from the NOAEL from this study (250 ppm, or 18.5 mg/kg per day) as shown in Equation 1 per AQD Rule 336.1232 (1) (b).

Equation 1.

$$Potential\ ITSL = RfD\ x \frac{70\ kg}{20\ m^3}$$

Where

$$RfD = \frac{POD_{HED}}{UFs}$$

$$POD_{HED} = Point\ of\ Departure_{Human\ Equivalent\ Dose}$$

$$POD_{HED} = POD_{animal} x \left(\frac{Body\ weight_{animal}}{Body\ weight_{human}}\right)^{0.25}$$

$$POD_{animal} = no\ observable\ adverse\ effect\ level\ in\ P\ generation\ males = 18.5 \frac{mg}{kg} per\ day$$

$$body\ weight_{animal} = 0.470\ kg\ as\ noted\ in\ memo\ to\ file\ from\ Butterfield\ (1996)$$

$$body\ weight_{human} = 70\ kg$$

$UFs = uncertainty\ factors$

UF=10 for intraspecies extrapolation
UF=3 for interspecies extrapolation
UF=10 for duration from subchronic to chronic exposure

$$POD_{HED} = 18.5 \frac{mg}{kg} per\ day\ x \left(\frac{0.470\ kg}{70\ kg}\right)^{0.25} = 5.295679373 \frac{mg}{kg} per\ day$$

$$RfD = \frac{5.295679373 \frac{mg}{kg} per\ day}{10\ x3\ x\ 10} = 0.01752265 \frac{mg}{kg} per\ day \approx 0.02\ \frac{mg}{kg} per\ day$$

$$Potential\ ITSL = 0.02 \frac{mg}{kg} per\ day\ x \frac{70\ kg}{20\ m^3} x \frac{1000 \mu g}{mg} = 70\ \frac{\mu g}{m^3}, annual\ averaging\ time$$

The default ITSL will be used for BIT, since the default ITSL was derived with some consideration for health protection regarding chemicals with either chronic or acute ITSLs (MDEQ, 1997). This is especially important because BIT has the potential to be a respiratory sensitizer and an acute, portal of entry irritant. Furthermore, the default will be used, since the default ITSL is lower than the ITSL derived from developmental study.

References

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