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DRAFT

METRIBUZIN

Health Advisory
Office of Drinking Water
U.S. Environmental Protection Agency

I. INTRODUCTION

The Health Advisory (HA) Program, sponsored by the Office of Drinking Water (ODW), provides information on the health effects, analytical methodology and treatment technology that would be useful in dealing with the contamination of drinking water. Health Advisories describe nonregulatory concentrations of drinking water contaminants at which adverse health effects would not be anticipated to occur over specific exposure durations. Health Advisories contain a margin of safety to protect sensitive members of the population.

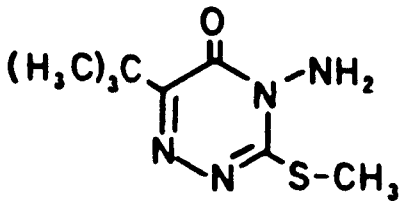
Health Advisories serve as informal technical guidance to assist Federal, State and local officials responsible for protecting public health when emergency spills or contamination situations occur. They are not to be construed as legally enforceable Federal standards. The HAs are subject to change as new information becomes available.

Health Advisories are developed for one-day, ten-day, longer-term (approximately 7 years, or 10% of an individual's lifetime) and lifetime exposures based on data describing noncarcinogenic end points of toxicity. Health Advisories do not quantitatively incorporate any potential carcinogenic risk from such exposure. For those substances that are known or probable human carcinogens, according to the Agency classification scheme (Group A or B), Lifetime HAs are not recommended. The chemical concentration values for Group A or B carcinogens are correlated with carcinogenic risk estimates by employing a cancer potency (unit risk) value together with assumptions for lifetime exposure and the consumption of drinking water. The cancer unit risk is usually derived from the linear multistage model with 95% upper confidence limits. This provides a low-dose estimate of cancer risk to humans that is considered unlikely to pose a carcinogenic risk in excess of the stated values. Excess cancer risk estimates may also be calculated using the One-hit, Weibull, Logit or Probit models. There is no current understanding of the biological mechanisms involved in cancer to suggest that any one of these models is able to predict risk more accurately than another. Because each model is based on differing assumptions, the estimates that are derived can differ by several orders of magnitude.

II. GENERAL INFORMATION AND PROPERTIES

CAS No. 21087-64-9

Structural Formula



4-Amino-6-(1,1-dimethylethyl)-3-methylthio-1,2,4-triazin-5(4H)-one

Synonyms

- Bayer 6159; Bayer 6443H; Bayer 94337; Lexone; Sencor; Sencoral; Sencorer; Sencorex

Uses

- Herbicide used for the control of a large number of grass and broadleaf weeds infesting agricultural crops (Meister, 1983).

Properties (CHEMLAB, 1985)

Chemical Formula	$C_8H_{14}ON_4S$
Molecular Weight	214.28
Physical State (at 25°C)	white crystalline solid
Boiling Point	--
Melting Point	125-126°C
Density	--
Vapor Pressure (25°C)	10^{-5} mmHg (20°C)
Specific Gravity	--
Water Solubility (25°C)	1,200 mg/L
Log Octanol/Water Partition Coefficient	-5.00 (calculated)
Taste Threshold	--
Odor Threshold	--
Conversion Factor	--

Occurrence

- Metribuzin has been found in 1,517 of 3,580 surface water samples analyzed and in 54 of 240 ground water samples (STORET, 1987). These samples were collected at 407 surface water locations and 204 ground water locations; metribuzin was found in 14 states. The 85th percentile of all nonzero samples was 4.79 ug/L in surface water and 0.1 ug/L in ground water sources. The maximum concentration found in surface water was 22.79 ug/L and in ground water, 1.25 ug/L.

- Metribuzin has been found in Iowa ground water resulting from agricultural uses; typical positives were 1 to 4.3 ppb (Cohen et al., 1986).

Environmental Fate

- The rate of hydrolysis of metribuzin is pH dependent. During a 28-day test, little or no degradation was observed at pH 6 or 9 at 25°C, or at pH 6 at 37°C or 52°C (Day et al., 1976).

- ^{14}C-Metribuzin on silty clay soil degraded, with a half-life of 15 days, when exposed to natural sunlight (Khasawinah, 1972). The half-life in control samples kept in the dark was 56 days. After 10 weeks, 20.6, 6.5 and 7.0% of the applied radioactivity was present in the irradiated soil as 6-t-butyl-1,2,4-triazin-3,5-(2H,4H)-dione (DADK), 6-t-butyl-3-(methylthio)-1,2,4-trizin-5(4H)-one (DA) and parent compound, respectively. A substantial portion of the applied radioactivity (56%) was bound to the soil. In the dark control, 4.6, 16.9, 44.0 and 34% of the applied radioactivity was present as DADK, DA, parent or bound compound, respectively.

- Under aerobic conditions, metribuzin at 10 ppm degraded with a half-life of 35-63 days in silt loam and sandy loam soils treated with a 50% wettable powder (WP) formulation, and 63 days in soils treated with a 4-lb/gal FlC formulation (Pither and Gronberg, 1976). Degradates found were: 6-t-butyl-1,2,4-triazin-3,5-(2H,4H)-dione (DADK); 4-amino-6-butyl-1-2,4,-triazin-3,5-(2H,4H)-dione (DK); and 6-t-butyl-3-(methylthio)-1,2,4-triazin-5-(4H)-one (DA).

- ^{14}C-Metribuzin residues degraded slowly in silty clay soil under anaerobic conditions with a half-life of more than 70 days (Khasawinah, 1972). After 10 weeks of incubation, 10, 10.9, 57, and 19% of the applied radioactivity was present as DADK, DA, parent compound or bound to the soil, respectively.

- Metribuzin adsorption was significantly correlated to soil organic matter, clay and bar soil water contents (Savage, 1976). Calculated K_d values ranged from 0.27 for a sandy loam soil (0.75% organic matter, 11% clay and 12% of 0.33 bar soil water content), to 3.41 for a clay soil (42% organic matter, 71% clay and 42% of 0.33 bar soil water content).

- ^{14}C-Metribuzin residues were very mobile in Amarillo sandy loam and Louisiana Commerce silt loam soils; after leaching 12-inch soil columns with 20 inches of water, 96.6 and 91.6% of the applied radioactivity, respectively, was found in the leachate (Houseworth and Tweedy, 1973). ^{14}C-Metribuzin residues were relatively immobile in Indiana silt loam and New York muck soils; after leaching 12-inch soil columns, 90.6 and 89.4% of the applied radioactivity was detected in the top 3 cm of the Indiana silt loam and New York muck, soil columns, respectively. No radioactivity was detected in column leachates.

- ^{14}C-Metribuzin residues (test substance not characterized) aged 30 days were moderately mobile in an Amarillo sandy loam soil column; after leaching a 12-inch column with 22.5 inches of water, 7.3% of the applied radioactivity was found in the leachate (Tweedy and Houseworth, 1974). In the soil column, 85.2% of the applied radioactivity remained within the top 2 inches.

- ^{14}C-Metribuzin residues (test substance not characterized) were intermediately mobile in sandy clay loam and silt loam soils (R_f 0.61 to 0.62) and mobile in sandy, sandy loam, and two silty clay soils (R_f 0.68 to 0.77), based on soil thin-layer chromatography (TLC) tests (Thornton et al., 1976). ^{14}C-Metribuzin residues (test substance not characterized) were intermediately mobile in sand (R_f 0.61), sandy clay loam (R_f 0.64), two silty clay soils (R_f 0.62 and 0.71), silt loam (R_f 0.66) and sandy loam (R_f 0.82) soils, based on soil TLC tests (Obrist and Thorton, 1979). ^{14}C-Metribuzin (purity not specified) at 1.5 ug/spot had low mobility (R_f 0.13 to 0.26) in two muck soils and intermediate mobility (R_f 0.42 to 0.53) in six mineral soils ranging in texture from sand to clay, based on soil TLC plates developed in water (Sharon and Stephenson, 1976).

- In the field, metribuzin dissipates with half-lives of less than 1 month to 6 months. Three metribuzin degradates were detected: 6-t-butyl-1,2,4-triain-3,5-(2H,4H)-dione (DADK); 4-amino-6-t-butyl-1,2,4-triazin-3,5-(2H,4H)-dione (DK); and 6-t-butyl-3-(methylthio)1,2,4-triazin-5-(4H)-one (DA). Soil type and characteristics, chemical formulation or application rates did not discernibly affect the dissipation rate of metribuzin (Stanley and Schumann, 1969; Finlayson, 1972; Rockwell, 1972a; Rockwell, 1972b; Rockwell, 1972c; Rowehl, 1972a; Rowehl, 1972b; Schultz, 1972; Mobay Chemical, 1973; Fisher, 1974; Murphy, 1974; United States Borax and Chemical Corp., 1974; Potts et al., 1975; Analytical Biochemistry Laboratories, 1976; Ballantine, 1976; and Ford, 1979).

III. PHARMACOKINETICS

Absorption

- A study was conducted in four dogs using oral dosing of radiolabeled metribuzin (Khasawinah, 1972) to evaluate absorption, distribution and metabolites. Analysis of blood samples showed a peak level at 4 hours.

Distribution

- No information was found in the available literature on the distribution of metribuzin.

Metabolism

- No information was found in the available literature on the metabolism of metribuzin.

Excretion

- Khasawinah (1972) reported that 52 to 60% of the administered dose of metribuzin in dogs was excreted in the urine and 30% in the feces.

IV. HEALTH EFFECTS

Humans

No information was found in the available literature on the health effects of metribuzin in humans.

Animals

Short-term Exposure

- Crawford and Anderson (1974) reported the acute oral LD_{50} values following the administration of technical metribuzin to guinea pigs and rats as 245 and 1,090 mg/kg, respectively, for male animals, and 274 and 1,206 mg/kg, respectively, for females.

- Mobay Chemical (1978) reported the acute oral LD_{50} values for a wettable granular formulation of metribuzin to be 2,379 and 2,794 mg/kg for male and female rats, respectively.

- Mobay Chemical (1978) reported the acute dermal LD_{50} for a wettable granular formulation of metribuzin to be >5,000 mg/kg for both male and female rats.

- Mobay Chemical (1978) reported the acute (1-hour) inhalation LC_{50} in rats for a wettable granular formulation to be >20 mg/L.

Dermal/Ocular Effects

- In studies conducted by Mobay Chemical (1978), metribuzin (wettable granular) was determined to be a very slight irritant to rabbit eyes and skin.

Long-term Exposure

- Loser et al. (1969) administered metribuzin to Wistar rats (15/sex/dose) for 3 months in their feed at levels of 0, 50, 150, 500 or 1,500 ppm (about 2.5, 7.5, 25 or 75 mg/kg/day, based on calculations in Lehman et al., 1959). Following treatment, food consumption, growth, body weight, organ weight, clinical chemistry, hematology, urinalysis and histopathology were measured. No significant efects on these parameters were observed in either sex at 50 ppm (2.5 mg/kg/day). Among females, enlarged livers were found in the 150, 500 or 1,500 ppm (7.5, 25 or 75 mg/kg/day) dosage groups ($p < 0.05$), and thyroid glands were also enlarged in the 500 or 1,500 ppm (25 or 75 mg/kg/day) groups ($p < 0.05$ and $p < 0.01$, respectively). In the males, enlarged thyroids were reported among the 500 (25 mg/kg/day) ($p < 0.05$) and 1,500 ppm

(75 mg/kg/day) ($p < 0.01$) dosage groups, while an enlarged heart was reported at 1,500 ppm (75 mg/kg/day) ($p < 0.05$). At 1,500 ppm (75 mg/kg/day), lower body weights ($p < 0.01$) were reported in both sexes when compared to untreated controls.

- In studies conducted by Lindberg and Richter (1970), beagle dogs (four/sex/dose) administered oral doses of 50, 150 or 500 ppm (about 1.25, 3.75 or 12.5 mg/kg/day, based on calculations in Lehman et al., 1959) technical metribuzin for 90 days showed no significant differences in body weights, food consumption, behavior, mortality, hematologic findings, urinalysis, gross pathology or histopathology.

- Loser and Mirea (1974) reported that dietary concentrations of 1.5, 2 or 20 mg/kg/day metribuzin did not significantly affect physical appearance, behavior, mortality, hematologic clinical chemistry, urinalysis or histopathology in rats (40/sex/dose) fed technical metribuzin in the diet for 24 months. The body weights of females at the 20 mg/kg/day dose level were usually lower ($p < 0.05$) than those of controls; at the end of the test period, however, no significant differences were noted.

- Hayes et al. (1981) administered technical metribuzin in the diet to albino CD mice (50/sex/dose) at 200, 800 or 3,200 ppm (about 30, 120 or 480 mg/kg/day, based on calculations in Lehman et al., 1959) for 24 months. Following treatment, feed consumption, general behavior, body and organ weights, mortality, hematology and histopathology were analyzed. No adverse effects were observed in these parameters in either sex at 800 ppm (120 mg/kg/day). However, a significant ($p < 0.05$) increase in absolute and relative liver and kidney weights was observed in female mice receiving 3,200 ppm (480 mg/kg/day).

- In studies conducted by Loser and Mirea (1974), four groups of beagle dogs (four/sex/dose) were administered metribuzin in the diet at dose levels of 0, 25, 100 or 1,500 ppm (about 0, 0.625, 2.5 or 37.5 mg/kg/day, based on calculations in Lehman, 1959) for 24 months. Following treatment, food consumption, general behavior and appearance, clinical chemistry, hematology, urinalysis, body and organ weights and histopathology were evaluated. No toxicologic effects were reported in animals administered 100 ppm metribuzin (2.5 mg/kg/day) or less for any of the parameters measured. Necrosis of the renal tubular cells, slight iron deposition as well as slight hyperglycemia and temporary hypercholesterolemia were noted in animals administered 1,500 ppm (37.5 mg/kg/day).

Reproductive Effects

- In a 3-generation reproduction study, Loser and Siegmund (1974) administered technical metribuzin in the feed at dose levels of 0, 35, 100 or 300 ppm (about 0, 1.75, 5 or 15 mg/kg/day, based on calculations in Lehman et al., 1959) to FB30 (Elberfeld breed) rats during mating, gestation and lactation. Following treatment, fertility, lactation performance and pup development were evaluated. No treatment-related effects were reported at any dose tested.

Developmental Effects

- Unger and Shellenberger (1981) administered technical metribuzin by gastric intubation to pregnant female rabbits (16 to 17/dose) on days 6 through 18 of gestation at daily doses of 15, 45 or 135 mg/kg/day. Following treatment, there was a statistically significant ($p < 0.05$) decrease in body weight gain in the high-dose does (135 mg/kg). No maternal toxicity was reported in animals administered metribuzin at levels of 45 mg/kg/day or less. No treatment-related effects were reported at any dose level in fetuses based on gross, soft tissue and skeletal examinations.

- Machemer (1972) reported no maternal toxicity, embryotoxicity or teratogenic effects following oral administration (via stomach tube) of technical metribuzin to FB30 rats (21 to 22/dose) on days 6 through 15 of gestation at dose levels of 5, 15, 50 or 100 mg/kg/day.

Mutagenicity

- Metribuzin showed no mutagenic activity in several bacterial assays (Inukai and Iyatomi, 1977; Shirasu et al., 1978) or in dominant lethal tests in mice (Machemer and Lorke, 1974, 1976). The results of microbial point mutation assays (Machemer and Lorke, 1974) did not indicate a mutagenic potential for metribuzin in the test systems utilized. The results of dominant lethal mutations in mice or chromosomal aberrations in hamster spermatogonia at dose levels of 300 mg/kg and 100 mg/kg, respectively, did not indicate any mutagenic effects of metribuzin.

Carcinogenicity

- Hayes et al. (1981) conducted studies in which technical metribuzin was administered in the diet to albino CD-1 mice (50/sex/dose) at 200, 800 or 3,200 ppm (30, 120 or 380 mg/kg/day) for 24 months. Minimal toxic effects were observed at the high-dose level in the form of increased liver weight and changes in the hematocrit and hemoglobin measurements. Although some increase in the number of tumor-bearing animals was observed in low- and mid-dose animals, significant increases in the incidence of specific tumor types were not observed at any dose level. It was concluded that, under the conditions of the test, there was no increase in the incidence of tumors in mice.

V. QUANTIFICATION OF TOXICOLOGICAL EFFECTS

Health Advisories (HAs) are generally determined for one-day, ten-day, longer-term (approximately 7 years) and lifetime exposures if adequate data are available that identify a sensitive noncarcinogenic end point of toxicity. The HAs for noncarcinogenic toxicants are derived using the following formula:

$$HA = \frac{(NOAEL \text{ or } LOAEL) \times (BW)}{(UF) \times (___ \text{ L/day})} = ___ \text{ mg/L } (___ \text{ ug/L})$$

where:

NOAEL or LOAEL = No- or Lowest-Observed-Adverse-Effect-Level in mg/kg bw/day.

BW = assumed body weight of a child (10 kg) or an adult (70 kg).

UF = uncertainty factor (10, 100 or 1,000), in accordance with NAS/ODW guidelines.

___ L/day = assumed daily water consumption of a child (1 L/day) or an adult (2 L/day).

One-day Health Advisory

No information was found in the available literature that was suitable for determination of a One-day HA for metribuzin. It is therefore recommended that the Ten-day HA value for a 10-kg child (4.5 mg/L, calculated below) be used at this time as a conservative estimate of the One-day HA value.

Ten-day Health Advisory

The study by Unger and Shellenberger (1981) has been selected to serve as the basis for determination of the Ten-day HA for metribuzin. In this study, pregnant rabbits (16 or 17/dose) that were administered technical metrizubin by gastric intubation at dosage levels of 0, 15, 45 or 135 mg/kg/day on days 6 through 18 of gestation showed a statistically significant ($p < 0.05$) decrease in body weight gain at the 135-mg/kg dose. No maternal toxicity was reported at or below the 45-mg/kg dose. No treatment-related effects were reported at any dose level in fetuses based on gross, soft tissue and skeletal examinations. The NOAEL identified in this study was, therefore, 45 mg/kg/day. While a reproductive end point is not the most appropriate basis for derivation of an HA for a 10-kg child, this study is the only one available for the appropriate duration.

Using a NOAEL of 45 mg/kg/day, the Ten-day HA for a 10-kg child is calculated as follows:

$$\text{Ten-day HA} = \frac{(45\ \text{mg/kg/day})\ (10\ \text{kg})}{(100)\ (1\ \text{L/day})} = 4.5\ \text{mg/L}\ (4{,}500\ \text{ug/L})$$

where:

45 mg/kg/day = NOAEL, based on absence of body weight reduction in rabbits exposed to metribuzin via gastric intubation on days 6 through 18 of gestation.

10 kg = assumed body weight of a child.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

1 L/day = assumed daily water consumption of a child.

Longer-term Health Advisory

The study by Loser et al. (1969) has been selected to serve as the basis for the Longer-term HA for metribuzin. In this study, rats (15/sex/dose) were fed diets containing metribuzin at doses of 50, 150, 500 or 1,500 ppm (about 2.5, 7.5, 25 or 75 mg/kg/day based on calculations in Lehman et al., 1959) for 90 days. Thyroid glands were enlarged in males in the 500 or 1,500 ppm (25 or 75 mg/kg/day) dosage groups, while the heart was enlarged at the 1,500 ppm (75 mg/kg/day) dose level. In females, enlarged livers were detected in the 150, 500 or 1,500 ppm (7.5, 25 or 75 mg/kg/day) dosage groups, and the thyroid was enlarged in the 500 or 1,500 ppm (25 or 75 mg/kg/day) dosage groups. Body weights were reduced in both sexes at 1,500 ppm (75 mg/kg/day), compared to untreated controls. The NOAEL identified in this study was, therefore, 50 ppm (2.5 mg/kg/day). Lindberg and Richter (1970) determined a NOAEL of 12.5 mg/kg/day in dogs; however, this study was not chosen, since the NOAEL was higher than the LOAEL of 7.5 mg/kg/day identified by Loser et al. (1969) in the rat.

Using a NOAEL of 2.5 mg/kg/day, the Longer-term HA for a 10-kg child is calculated as follows:

$$\text{Longer-term HA} = \frac{(2.5\ \text{mg/kg/day})\ (10\ \text{kg})}{(100)\ (1\ \text{L/day})} = 0.25\ \text{mg/L}\ (250\ \text{ug/L})$$

where:

2.5 mg/kg/day = NOAEL, based on absence of increased absolute organ weights in rats exposed to metribuzin via the diet for 90 days.

10 kg = assumed body weight of a child.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

1 L/day = assumed daily water consumption of a child.

Using a NOAEL of 2.5 mg/kg/day, the Longer-term HA for a 70-kg adult is calculated as follows:

$$\text{Longer-term HA} = \frac{(2.5\ \text{mg/kg/day})\ (70\ \text{kg})}{(100)\ (2\ \text{L/day})} = 0.875\ \text{mg/L}\ (875\ \text{ug/L})$$

where:

2.5 mg/kg/day = NOAEL, based on absence of increased absolute organ weights in rats exposed to metribuzin via the diet for 90 days.

70 kg = assumed body weight of an adult.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

2 L/day = assumed daily water consumption of an adult.

Lifetime Health Advisory

The Lifetime HA represents that portion of an individual's total exposure that is attributed to drinking water and is considered protective of noncarcinogenic adverse health effects over a lifetime exposure. The Lifetime HA is derived in a three-step process. Step 1 determines the Reference Dose (RfD), formerly called the Acceptable Daily Intake (ADI). The RfD is an estimate of a daily exposure to the human population that is likely to be without appreciable risk of deleterious effects over a lifetime, and is derived from the NOAEL (or LOAEL), identified from a chronic (or subchronic) study, divided by an uncertainty factor(s). From the RfD, a Drinking Water Equivalent Level (DWEL) can be determined (Step 2). A DWEL is a medium-specific (i.e., drinking water) lifetime exposure level, assuming 100% exposure from that medium, at which adverse, noncarcinogenic health effects would not be expected to occur. The DWEL is derived from the multiplication of the RfD by the assumed body weight of an adult and divided by the assumed daily water consumption of an adult. The Lifetime HA is determined in Step 3 by factoring in other sources of exposure, the relative source contribution (RSC). The RSC from drinking water is based on actual exposure data or, if data are not available, a value of 20% is assumed for synthetic organic chemicals and a value of 10% is assumed for inorganic chemicals. If the contaminant is classified as a Group A or B carcinogen, according to the Agency's classification scheme of carcinogenic potential (U.S. EPA, 1986), then caution should be exercised in assessing the risks associated with lifetime exposure to this chemical.

The study by Loser and Mirea (1974) has been selected to serve as the basis for the Lifetime HA for metribuzin. In this study, dogs (four/sex/dose) were administered metribuzin in the diet at dose levels of 0, 25, 100 or 1,500 ppm (0, 0.625, 2.5 or 37.5 mg/kg/day) for 24 months. Necrosis of the renal tubular cells was reported as well as slight and temporary changes in certain clinical chemistry parameters (e.g., blood glucose and cholesterol) at the high-dose level. No other toxicologic effects were reported. Based on this information, a NOAEL of 100 ppm (2.5 mg/kg/day) and a LOAEL of 1,500 ppm (37.5 mg/kg/day) were reported. Loser and Mirea (1974) reported a NOAEL of 20 mg/kg/day in rats. This study was not selected because no dose-related toxicologic responses were observed, and the rat may be less sensitive than the dog. Hayes et al. (1981) determined a NOAEL of 120 mg/kg/day in mice; however, this value exceeded the LOAEL (37.5 mg/kg/day) reported by Loser and Mirea (1974).

Using this study, the Lifetime HA is calculated as follows:

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{(2.5\ mg/kg/day)}{(100)} = 0.025\ mg/kg/day$$

where:

2.5 mg/kg/day = NOAEL, based on absence of organ toxicity and clinical chemistry effects in dogs exposed to metribuzin via the diet for 24 months.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

Step 2: Determination of the Drinking Water Equivalent Level (DWEL)

$$DWEL = \frac{(0.025\ mg/kg/day)\ (70\ kg)}{(2\ L/day)} = 0.875\ mg/day\ (875\ ug/L)$$

where:

0.025 mg/kg/day = RfD.

70 kg = assumed body weight of an adult.

2 L/day = assumed daily water consumption of an adult.

Step 3: Determination of the Lifetime Health Advisory

Lifetime HA = (0.875 mg/L) (20%) = 0.175 mg/L (175 ug/L)

where:

0.875 mg/L = DWEL.

20% = assumed relative source contribution from water.

Evaluation of Carcinogenic Potential

- In a study by Hayes et al. (1981), metribuzin was administered in the feed of mice (50/sex/dose) at dose levels of 200, 800 or 3,200 ppm (30, 120 or 480 mg/kg/day) for 24 months. Following treatment, the incidence of tumor formation was analyzed in a variety of tissues. Neoplasms of various tissues and organs were similar in type, localization, time of occurrence and incidence in control and treated animals. It was concluded that under the conditions of the test, there was no increase in the incidence of tumors in mice.

- The International Agency for Research on Cancer has not evaluated the carcinogenic potential of metribuzin.

- Applying the criteria described in EPA's guidelines for assessment of carcinogen risk (U.S. EPA, 1986), metribuzin may be classified in Group D: not classified. This category is used for substances with inadequate animal evidence of carcinogenicity.

VI. OTHER CRITERIA, GUIDANCE AND STANDARDS

- A Threshold Limit Value-Time-Weighted Average (TLV-TWA) of 5 mg/m^3 was determined, based on animal studies substantiated by repeated inhalation tests, a safety factor of 5, and assuming a total pulmonary absorption (ACGIH, 1984).

VII. ANALYTICAL METHODS

- Analysis of metribuzin is by a gas chromatography (GC) method applicable to the determination of certain organonitrogen pesticides in water samples (U.S. EPA, 1985). This method requires a solvent extraction of approximately 1 L of sample with methylene chloride using a separatory funnel. The methylene chloride extract is dried and exchanged to acetone during concentration to a volume of 10 mL or less. The compounds in the extract are separated by GC and measurement is made with a thermionic bead detector. The method detection limit for metribuzin is 0.46 ug/L.

VIII. TREATMENT TECHNOLOGIES

- Available data indicate that granular-activated carbon (GAC) adsorption and a conventional treatment scheme will remove metribuzin from water.

- Whittaker (1980) experimentally determined adsorption isotherms for metribuzin on GAC.

- Whittaker (1980) reported the results of GAC columns operating under bench-scale conditions. At a flow rate of 0.8 gpm/sq ft and an empty bed contact time of 6 minutes, metribuzin breakthrough (when effluent concentration equals 10% of influent concentration) occurred after 112 bed volumes (Bv).

- In the same study, Whittaker (1980) reported the results for four metribuzin bi-solute solutions when passed over the same GAC continuous flow column.

- Another study investigated the effectiveness of two different GAC columns in removing metribuzin from contaminated wastewater (Whittaker, et al., 1982). One type of GAC showed breakthrough for metribuzin (6 mg/L) from an initial concentration of 140 mg/L after 50 gallons of the wastewater had been treated. No pesticide was found in the effluent from the second type of GAC.

- Conventional water treatment, coagulation and sedimentation with alum and an anionic polymer removed more than 50% of the metribuzin present (Whittaker et al., 1980). The optimum alum dosage was 200 mg/L. Also equivalent dosages of ferric chloride were found to be equally effective.

- Treatment technologies for the removal of metribuzin from water are available and have been reported to be effective. However, selection of individual or combinations of technologies to attempt metribuzin removal from water must be by a case-by-case technical evaluation, and an assessment of the economics involved.

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