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DRAFT

TERBUFOS

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.

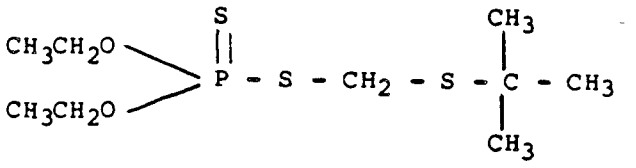
Health Advisories serve as informal technical guidance to assist Federal, State and local officials responsible for protecting public health when emergency spills or contamination situations occur. They are not to be construed as legally enforceable Federal standards. The HAs are subject to change as 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. 13071-79-9

Structural Formula



S-[[(1,1-Dimethylethyl)thio]methyl]O,O-diethyl phosphorodithioate

Synonyms

- Counter; Contraver (Meister, 1986).

Uses

- Control of corn rootworm and other soil insects and nematodes infesting corn. Control of sugarbeet maggots in sugarbeets; green bug on grain sorghum (Meister, 1986).

Properties (Windholz et al., 1983; Meister, 1986)

Chemical Formula	$C_9H_{21}O_2PS_3$
Molecular Weight	288.41
Physical State (room temp.)	Clear, slightly brown liquid
Boiling Point	69°C/0.01 mm Hg
Melting Point	-29.2°C
Density (24°C)	1.105
Vapor Pressure (25°C)	34.6 mPa
Specific Gravity	--
Water Solubility (25°C)	15 mg/L
Log Octanol/Water Partition Coefficient	595
Taste Threshold	--
Odor Threshold	--
Conversion Factor	--
Technical	87 to 97% pure

Occurrence

- Terbufos has been found in 444 of 2,016 surface water samples analyzed and in 9 of 283 ground water samples (STORET, 1987). Samples were collected at 55 surface water locations and 261 ground water locations, and terbufos was found in 5 states. The 85th percentile of all nonzero samples was .10 ug/L in surface water and 3 ug/L in ground water sources. The maximum concentration found was 2.25 ug/L in surface water and 3 ug/L in ground water.

Environmental Fate

Forthcoming from OPP, EPA

III. PHARMACOKINETICS

Absorption

° North (1973) reported that 83% of a single oral dose of technical 14C-terbufos (0.8 mg/kg) was excreted in the urine of rats 168 hours after dosing. (The carbon atom of the thiomethyl portion of terbufos was radiolabeled.) An additional 3.5% was recovered in feces. This study indicates that terbufos was well absorbed (about 80 to 85%) from the gastrointestinal tract.

Distribution

° North (1973) reported that maximum residues of cholinesterase-inhibiting compounds (phosphorylated metabolites), resulting from a single oral dose of technical ^{14}C-terbufos (0.8 mg/kg) given to rats, were found in rat liver (0.08 ppm) 6 hours after dosing. In the same study, residues of hydrolysis (nonphosphorylated metabolites) products reached a maximum in rat kidney 12 hours after dosing (0.9 ppm). After 168 hours, each body tissue in the rat contained less than 0.1 ppm radiolabeled) terbufos.

Metabolism

° North (1973) reported that terbufos was extensively metabolized in the rat. ^{14}C-Radiolabeled terbufos was administered in a single dose to 16 male Wistar rats at a dose level of 0.8 mg/kg via gavage. Examination of urine extracts by thin-layer chromatography (TLC) showed the presence of 10 radiometabolites in the rat urine. Approximately 96% of the radioactivity present in the urine was composed of an S-methylated series of metabolites, which result from the cleavage of the sulfur-phosphorus bond, methylation of the liberated thiol group and oxidation of the resulting sulfide to sulfoxides and sulfones. Of the remaining radioactivity, about 2% was composed of various oxidation products of the intact parent organophosphorus compound and 2% was an unknown metabolite.

Excretion

° North (1973) reported that technical terbufos and its metabolites were rapidly excreted in the urine of the rat. Radiolabeled terbufos was administered in a single dose to male Wistar rats at a dose level of 0.8 mg/kg by gavage. Of all the radioactivity recovered in the urine, 50% was excreted after 15 hours. After 168 hours, the termination of the test, 83% of the terbufos was excreted via the urine and 3.5% was recovered in the feces.

IV. HEALTH EFFECTS

Humans

- Peterson et al. (1984) reported the results of farm worker exposure to Counter 15-G (a 15% granular formulation of terbufos). Five farmers (one loader, one flagger and three scouts) were exposed for varying time periods (loader, 5 minutes; flagger, 15 minutes; scouts, twice for 30 minutes) during a typical workday while Counter 15-G was applied aerially to a young corn crop. The mean exposure via inhalation was <0.25 ug/hour, the sensitivity of the monitoring method, for all samples collected. The exposure values for the five farm workers were: 331 ug/hour for the loader, 0 ug/hour for the flagger, 381 ug/hour for scouts (after 3 days) and 250 ug/hour for scouts (after 7 days). All of the farm workers were men and weighed between 65.9 and 90.9 kg. Analysis of urinary metabolites showed no indication of any adverse effects to any of the exposed workers. All urinary alkyl phosphate analyses were negative (detection level, 0.1 ppm), indicating no significant absorption of terbufos. Plasma and red blood cell cholinesterase values of the exposed workers showed no significant (95% confidence level) decrease in activity when compared to pre-exposed samples, indicating no adverse physiological effects from exposures.

- Devine et al. (1985) reported results similar to Peterson et al. (1984) for 11 farmers who were exposed to terbufos during a typical workday while planting corn and applying Counter 15-G. The average estimated dermal exposure was 72 ug/hour, and the estimated respiratory exposure was 11 ug/hour. The results of urinary alkyl phosphate analyses were all negative, showing no detectable absorption of terbufos. Plasma and red blood cell cholinesterase (ChE) values of the exposed farmers showed no significant difference in activity when compared to pre-exposure or control values, indicating no adverse physiological effects from the exposure. The report concluded that, based on the study results, the use of Counter 15-G does not present a significant hazard, in terms of acute toxicity, to farmers using this product for the control of corn insects.

Animals

Short-term Exposure

- Parke and Terrell (1976) reported that the acute oral LD_{50} value of technical-grade (86%) terbufos in Wistar rats was 1.73 mg/kg. Terbufos was administered in doses of 1.0 to 3.0 mg/kg via gavage in corn oil to a total of 50 rats (10/sex/dose). Average weight of the rats ranged from 200 to 300 g. The lowest dose (1.0 mg/kg) did not result in any mortality. Observed effects to the rats were: respiratory depression, piloerection, cloric convulsions, exophthalmus, ptosis, lacrimation, hemorrhage and decreased motor activity.

- Consultox Laboratories (1975) reported that the acute oral LD_{50} value of technical-grade (86%) terbufos in male Wistar rats was 1.5 mg/kg.

Terbufos was administered by gavage in doses of 0.50 to 2.5 mg/kg to a total of 50 rats (10/sex/dose) at an average weight of 200 ± 20 g. No mortality was reported at the low dose (0.50 mg/kg). Ten percent mortality was reported at the 0.75-mg/kg dose. Other effects reported were: salivation, diuresis, diarrhea, disorientation, chromodocryorrhea, piloerection and body tremors.

- American Cyanamid (1972a) reported acute oral LD_{50} values (for 96.7% technical-grade terbufos) in dogs, mice and rats of 4.5 mg/kg (male)/ 6.3 mg/kg (female), 3.5 mg/kg (male)/9.2 mg/kg (female), and 4.5 mg/kg (male)/ 9.0 mg/kg (female), respectively. No details were given as to age, weight or route of exposure.

- American Cyanamid (1972b) reported additional acute oral LD_{50} values in male Wistar rats and female CF1 mice of 1.6 mg/kg and 5.0 mg/kg, respectively. Other effects reported included cholinesterase inhibition in both sexes.

- Berger (1977) reported that plasma ChE was inhibited by as much as 79% in eight beagle dogs that were dosed via corn oil with 0.05 mg/kg/day technical terbufos for 28 days. Red blood cell ChE was not inhibited at the dose tested.

Dermal/Ocular Effects

- Kruger et al. (1973) conducted a subacute dermal toxicity test in New Zealand White rabbits. Technical-grade terbufos was administered at doses varying from 0.004 to 0.1 mg/kg to the shaved, abraded backs of male and female rabbits (2.5 to 3.5 kg). All animals survived the 30-day test and showed no adverse effects with regard to food and water intake, elimination, behavior, pharmacological effects and weight gain differences. There were no observed changes in hematological determinations (hematocrit, total erythrocyte and total leukocyte levels). Minor changes reported were increased numbers of eosinophils and basophils in all groups, occasional minimal edema that abated by day 21, and occasional mild erythema. All observed changes occurred on intact and abraded skin sites.

- American Cyanamid (1972a,b) conducted a series of tests with 96.7 and 85.8% terbufos using New Zealand White rabbits. Twenty male rabbits (2.56 to 2.73 kg) were administered doses of 0.4 to 3.5 mg/kg terbufos to their shaved backs. Dermal contact with terbufos was maintained for 24 hours. The dermal LD_{50} value was 1.0 mg/kg. An acute dermal test with 96.7% terbufos resulted in an LD_{50} of 1.1 mg/kg in male rabbits (no other details were given). In another test with 96.7% terbufos, 0.5 mL (500 mg) of terbufos was applied to the backs of rabbits; all of these animals died within 24 hours after dosing.

- American Cyanamid (1972a) reported the results of an application of 0.1 mg of technical-grade (96.7%) terbufos to the eyes of New Zealand albino rabbits. All animals died within 2 to 24 hours after dosing.

Long-term Exposure

° Daly et al. (1979) administered terbufos (90% active ingredient (a.i.)) in the diet to groups of male and female Sprague-Dawley rats (10/sex/group, 24 to 39 days old, 95 to 150 g) at levels of 0, 0.125, 0.25, 0.5 or 1.0 ppm (estimated doses of 0, 0.01, 0.02, 0.04 or 0.08 mg/kg/day based on feed conversions given by the authors) for 90 days. Body weights and food consumption were measured weekly. Blood samples were obtained weekly and analyzed for plasma, erythrocyte and brain ChE. Body organs were weighed and analyzed for histopathology. The No-Observed-Adverse-Effect-Level (NOAEL) was determined to be 0.02 mg/kg/day, based on the absence of effects on ChE. The statistically significant Lowest-Observed-Adverse-Effect-Level (LOAEL) was determined to be 0.046 mg/kg based on the observed 17% decrease in plasma ChE in females. There were no depressions of erythrocyte or brain ChE at the highest dose tested (0.09 mg/kg/day). In addition, gross postmortem observations and histopathologic evaluation of selected tissues revealed no findings related to the test substance. Systemically, the LOAEL for increased liver weight in females and for a dose-related increase in liver extra-medullary hematopoiesis was 0.046 mg/kg/day. The systemic NOAEL based on absence of liver effects was determined to be 0.02 mg/kg in this study.

° Morgareidge et al. (1973) administered technical-grade terbufos in the diet to groups of male and female beagle dogs (four/sex/group, 10 to 13 months old, 9.0 to 13.8 kg) at levels of 0.0025, 0.01 and 0.04 mg/kg/day, 6 days a week for 26 weeks. Plasma, red blood cell and brain ChE levels, body weight and food, urinalysis, gross necropsy examination and histopathology were evaluated. Observed effects included a decrease in ChE activity in plasma at all dose levels; however, decreased ChE activity was statistically significant only for doses of 0.01 mg/kg/day and above. At 0.01 mg/kg/day, plasma ChE was inhibited by 26% and red blood cell ChE was inhibited by 14%. The systemic NOAEL was determined to be greater than the highest dose tested (0.04 mg/kg/day). No statistical analyses were performed on body weight changes, food consumption, hematology, clinical chemistry, urinalyses and organ weight data. The LOAEL (based on ChE effects) determined by the study was 0.01 mg/kg/day and the NOAEL was determined to be 0.0025 mg/kg/day.

° Rapp et al. (1974) administered technical-grade terbufos in the diet to groups of Long-Evans rats (six/sex/dose, weanlings, 122 to 138.8 g) at levels of 0.25, 1.0, 2.0, 4.0, and 8.0 ppm for 2 years. These doses correspond to 0.0125, 0.05, 0.1, 0.2 and 0.4 mg/kg/day (Lehman, 1959. The original high doses (2.0 ppm) were increased to 4.0 and then to 8.0 ppm for males, and were increased from 2.0 to 4.0 to 8.0 and then reduced to 4.0 ppm for females. Body weight and food consumption were measured weekly. Hematology, clinical chemistry and urinalyses were also performed. Red blood cell ChE and brain ChE were significantly inhibited at 0.05 mg/kg/day (20% inhibition for brain ChE and 43% for red blood cell ChE in females) and above. Red blood cell ChE was also inhibited at 0.0125 mg/kg/day (12% in males and 15% in females).

At the high dose (0.1 to 0.4 mg/kg/day), there was a noticeable inhibition in mean body weight and mean food consumption. Mortality rates were 24 and 27% (males and females, respectively) at the high dose, 19% (males) at the mid-dose and 10% (males) at the low dose. The incidence of exophthalmia was in high-dose females (exophthalmia was also noted in low- and mid-dose control females). This study did not establish a NOAEL. The LOAEL was equivalent to the lowest dose tested (0.0125 mg/kg/day).

° McConnell (1983) administered technical-grade terbufos in the diet to groups of Long-Evans rats (60/dose/sex) at levels of 0.25, 1.0, 2.0, 4.0 and 8.0 ppm for 2 years. These doses are equivalent to 0.0125, 0.05, 0.1, 0.2 and 0.4 mg/kg/day (Lehman, 1959). The original high dose (2.0 ppm) was increased to 4.0 and then 8.0 ppm for males after the first 3 months, and increased from 2.0 to 4.0 to 8.0 and then reduced to 4.0 ppm for females after the first 3 months. At the end of the 2-year study, tissues were prepared for microscopic examination. Mortality occurred in all groups (control and test) due to bronchopneumonia, with mortality rates ranging from 17 to 35% in controls and low-dose groups, respectively. Mortality rates at the high dose (0.4 mg/kg/day) were 58% and 43% in male and female rats, respectively. Other effects reported were gastric ulceration and/or erosion of glandular and nonglandular stomach mucosa in high-dose rats. No similar effect was seen in lowand mid-dose rats. Acute bronchopneumonia and granuloma of lungs occurred in high-dose rats more frequently than in low-dose, mid-dose or control rats. The authors reported that lung inflammation did not appear directly associated with the compound. No LOAEL or NOAEL was established in this study.

° Shellenberger (1986) administered technical-grade terbufos (89.6% a.i.) in capsule form to groups of beagle dogs (six/sex/dose, 6.8 to 7.5 kg, 5 to 6 months old) at doses of 0, 0.015, 0.060, 0.090, 0.120, 0.240 and 0.480 mg/kg/day for 1 year. High doses were eventually reduced to 0.090 and 0.060 mg/kg/day after the 8th week of the study. Body weight and food consumption were measured together with assessment of urinalyses, organ weights and cholinesterase levels. One male and one female at the high dose and one female at 0.240 mg/kg/day were found dead. At the two highest doses (0.240 and 0.480 mg/kg/day), decreased body weights and food consumption were observed. Mean erythrocytic parameters of high-dose males and females were significantly reduced at 3 months but not at 6 months or at termination of the study. Plasma ChE activity was significantly inhibited to 55% of controls at 0.015 mg/kg/day. Slight inhibition of erythrocyte ChE activity occurred at 0.120 mg/kg/day in females but not in males. No inhibition of erythrocyte ChE in males or females was observed at the lower doses. Brain ChE activities were similar for both sexes at all dose levels. Urinalyses and organ weight data revealed no significant differences. The report suggests that the NOAEL was 0.120 mg/kg/day in males and 0.090 mg/kg/day in females.

Reproductive Effects

° Smith and Kasner, (1972a) administered technical terbufos via the diet to Long-Evans and Blue Spruce rats (10 males/dose, weighing 276.3 g; 20

females/dose, weighing 185.6 g) for a period of 6 months at levels of 0, 0.25 and 1 ppm. These levels correspond to doses of 0, 0.0125 and 0.05 mg/kg/day, based on a conversion factor of 0.05 for rats (Lehman, 1959). The first parental generation (F_0) was dosed for 60 days. No reproductive effects were observed in males or females at any dose tested. The authors concluded that the reproductive NOAEL was greater than 0.05 mg/kg/day, the highest dose tested.

Developmental Effects

- MacKenzie (1984) administered terbufos (87.8% a.i.) by gavage to groups of 18 female New Zealand White rabbits (3.5 kg) at levels of 0, 0.1, 0.2 and 0.4 mg/kg/day on days 7 to 19 of gestation. Reproductive indices monitored were female mortality, corpora lutea or implants, sex ratio, implantation efficiency, fetal body weight, fetal mortality and skeletal development. Cesarean sections were performed on day 29 of gestation. Survival of adult female rabbits was 100% in controls and in the 0.2-mg/kg/day dose group; 89% in the 0.1-mg/kg/day dose group; and 67% in the high-dose (0.4 mg/kg/day) group. There were no statistically significant dose-related differences in mean body weight, weight changes or gravid uterine weights, mean number of corpora lutea, implantation efficiency, sex ratio, fetal body weight or number of live or resorbing fetuses. The incidence of fetuses with accessory left subclavian artery was significantly greater in the high-dose (0.4 mg/kg/day) group. The incidence of an extra unilateral rib and of chain fusion of sternebrae was significantly lower in the high-dose group than in the controls. According to the author, terbufos appears to be maternally toxic at 0.4 mg/kg/day, the highest dose tested.

- Rodwell (1985) administered terbufos (87.8% a.i.) via gavage to groups of 25 Charles River female rats (226 to 282 g, 71-days old) at doses of 0.05, 0.10 and 0.20 mg/kg/day on days 6 to 15 of gestation. Cesareans sections were performed on day 20; half of the fetuses were stained for skeletal evaluation. Parent survivability, body weight and embryonic and fetal development were all assessed. All parents survived the test. No changes in general appearance or behavior were observed. Slightly decreased mean body weights were observed during days 12 to 16 and following treatment in the 0.10- and 0.20-mg/kg/day dose groups. The study demonstrates that terbufos is slightly maternally toxic at dose levels of 0.10 and 0.20 mg/kg/day. A NOAEL of 0.05 mg/kg/day, the lowest dose tested, was identified.

Mutagenicity

- Thilager et al. (1983) reported that Chinese hamster ovary cells tested with and without S-9 rat liver activation at concentrations of 100, 50, 25, 10, 5 and 2.5 nL/mL (ppm) terbufos did not cause any significant increase in the frequencies of chromosomal aberrations. Only a concentration of 100 nL/mL proved to be cytotoxic.

- Allen et al. (1983) conducted mutagenicity tests with terbufos (87.8% a.i.) in the presence of metabolic activation and Chinese hamster ovary cells and in the absence of S-9 activation. Initial tests were conducted with doses of 100 to 10 ug/L, and then followed up with activation at doses of 50, 42, 33, 25, 10 and 5 mg/ml. Terbufos proved to be cytotoxic at 75 to 100 ug/mL with activation and at 50 to 70 mg/mL without activation. There were no increases in the frequency of chromosomal aberrations. The authors concluded that terbufos reflected a negative mutagenic potential.

- Godek et al. (1983) conducted a rat hepatocyte primary culture/DNA repair test with terbufos (87.8% a.i.) at doses ranging from 100 to 33 ug/well (a well contains 2 mL of media). Unscheduled DNA repair synthesis was quantified by a net nuclear increase of black silver grains for 50 cells/slide. This value was determined by taking a nuclear count and three adjacent cytoplasmic counts (100 ug/well was cytotoxic). The results for terbufos were negative in the rat hepatocyte primary culture/DNA repair test. These findings are based on the inability of terbufos to produce a mean grain count of 5 or greater than the vehicle-control mean grain count at any level. The authors concluded that terbufos reflected a negative mutagenic potential.

Carcinogenicity

- Smith and Kasner (1972b) administered technical terbufos in the diet to groups of mice (15/sex/dose) at levels of 0, 0.5, 2.0 and 8.0 ppm for 18 months. These doses correspond to 0.075, 0.3 and 1.2 mg/kg/day (Lehman, 1959). The authors reported no signs of tumors or neoplasia. Effects noted include alopecia and signs of ataxia; exophthalmia in males, corneal cloudiness and opacity and eye rupture. Organ tissues examined were liver, kidney, heart and lung. No pathological changes in these four organs were observed.

- Rapp et al. (1974) administered technical terbufos in the diet to groups of Long-Evans rats (six/sex/dose) at levels of 0, 0.25, 1.0, 2.0, 4.0 and 8.0 ppm for 2 years. These doses correspond to 0.0125, 0.05, 0.1, 0.2 and 0.4 mg/kg/day (Lehman, 1959). There were no indications of tumorigenic effects at any dose tested.

  McConnell (1983) administered technical terbufos in the diet to groups of Long-Evans rats (60/sex/dose) at levels of 0, 0.25, 1.0, 2.0, 4.0 and 8.0 ppm for 2 years. These doses correspond to 0, 0.125, 0.05, 0.1, 0.2 and 0.4 mg/kg/day (Lehman, 1959). The author concluded that the compound had no effect on tumorigenesis.

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 the determination of the One-day HA value for terbufos. It is, therefore, recommended that the Ten-day HA value for a 10-kg child (0.005 mg/L, calculated below) be used at this time as a conservative estimate of the One-day HA value.

Ten-day Health Advisory

The teratogenicity study in rats by Rodwell (1985) has been selected to serve as the basis for the Ten-day HA value for terbufos. Pregnant rats administered terbufos via gavage at a level of 0.05 mg/kg/day showed no clinical signs of toxicity in the adult animals and no reproductive or teratogenic effects in the fetuses. The study identified a NOAEL of 0.05 mg/kg/day. These results are supported by the results of studies by MacKenzie (1984) with rabbits and by Smith and Kasner (1972a) with rats.

Using a NOAEL of 0.05 mg/kg/day, the Ten-day HA for a 10-kg child is calculated as follows:

$$\text{Ten-day HA} = \frac{(0.05 \text{ mg/kg/day}) (10 \text{ kg})}{(100) (1 \text{ L/day})} = 0.005 \text{ mg/L } (5 \text{ ug/L})$$

where:

0.05 mg/kg/day = NOAEL, based on the absence of clinical signs of toxicity and the lack of reproductive or teratogenic effects in rats exposed to terbufos via gavage for 10 days during 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 Advisories

No suitable studies were available to serve as the basis for the Longer-term HA value for terbufos. It is recommended, however, that the modified Drinking Water Equivalent Level (DWEL) (adjusted for a 10-kg child) be used as a conservative estimate for a longer-term exposure. Accordingly, the Longer-term HA for a 10-kg child is 0.00025 mg/L and the Longer-term HA for an adult is 0.00088 mg/L.

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, 1986a), then caution should be exercised in assessing the risks associated with lifetime exposure to this chemical.

The 6-month feeding study in beagle dogs by Morgareidge et al. (1973) has been selected to serve as the basis for the Lifetime HA value for terbufos. In this study, beagle dogs were administered terbufos in the diet at doses of 0.0025, 0.01 and 0.04 mg/kg/day. At 0.01 mg/kg/day and above, plasma and red blood cell ChE activity were significantly inhibited. At 0.01 mg/kg/day, plasma ChE was inhibited by 26% and red blood cell ChE was inhibited by 14%. These effects were not observed at 0.0025 mg/kg/day, which was identified as the NOAEL. Other studies were not selected because a clear NOAEL was not identifed or the respective NOAELs/LOAELs were an order of magnitude higher than the NOAEL derived from the Morgareidge et al. (1973) study.

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

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{(0.0025 \text{ mg/kg/day})}{(100)} = 0.000025 \text{ mg/kg/day}$$

where:

0.0025 mg/kg/day = NOAEL, based on absence of inhibition of cholinesterase in beagles exposed to terbufos in the diet for 6 months (180 days).

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)

$$DWEL = \frac{(0.000025 \text{ mg/kg/day})\ (70 \text{ kg})}{(2 \text{ L/day})} = 0.00088 \text{ mg/L/day } (0.88 \text{ ug/L})$$

where:

0.000025 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 = (0.00088 mg/L) (20%) = 0.00018 mg/L (0.18 ug/L)

where:

0.00088 mg/L = DWEL.

20% = assumed relative source contribution from water.

Evaluation of Carcinogenic Potential

- The International Agency for Research on Cancer has not evaluated the carcinogenic potential of terbufos.
- The U. S. EPA's Cancer Assessment Group (CAG) has assessed the carcinogenic potential of terbufos and has concluded that there are not enough data to determine whether terbufos is carcinogenic.
- Applying the criteria described in EPA's guidelines for assessment of carcinogenic risk (U.S. EPA, 1986a), terbufos may be classified in Group E: no evidence of carcinogenicity for humans. This group is for substances that show no evidence of carcinogenicity in at least two adequate animal tests in different species or in both epidemiologic and animal studies. The studies by Smith and Kasner (1972b) on mice and by Rapp et al. (1974) and McConnell (1983) on rats reported no statistically significant influence on the incidence of neoplasms or tumors at any dose level tested.

VI. OTHER CRITERIA, GUIDANCE AND STANDARDS

- No other criteria, guidance or standards were found in the available literature.

VII. ANALYTICAL METHODS

- Analysis of terbufos is by a gas chromatographic (GC) method applicable to the determination of certain nitrogen-phosphorus containing pesticides in water samples (U.S. EPA, 1986b). In this method, approximately 1 liter of sample is extracted with methylene chloride. The extract is concentrated and the compounds are separated using capillary collumn GC. Measurement is made using a nitrogen-phosphorus detector. The method detection limit has not been determined for this compound but it is estimated that the detection limits for the method analytes are in the range of 0.1 to 2 ug/L.

VIII. TREATMENT TECHNOLOGIES

- No data were found for the removal of terbufos from drinking water by conventional treatment.

- No data were found on the removal of terbufos from drinking water by activated carbon adsorption. However, due to its low solubility and high molecular weight, terbufos probably would be amenable to activated carbon adsorption.

- No data were found on the removal of terbufos from drinking water by ion exchange. However, the structure of this ester indicates that it is not ionic and thus probably would not be amenable to ion exchange.

- No data were found for the removal of terbufos from drinking water by aeration. However, the Henry's Coefficient can be estimated from available data on solubility (10 to 15 mg/L) and vapor pressure (0.01 mm Hg at 69°C). Terbufos probably would not be amenable to aeration or air stripping because its Henry's Coefficient is approximately 12 atm.

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