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FLUOMETURON

DRAFT

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.

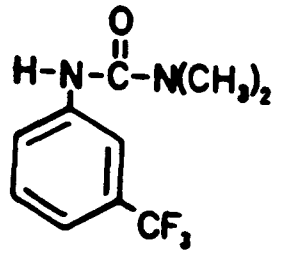
Health Advisories serve as informal technical guidance to assist Federal, State and local officials responsible for protecting public health when emergency spills or contamination situations occur. They are not to be construed as legally enforceable Federal standards. The HAs are subject to change as 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. 2164-17-2

Structural Formula



N,N-Dimethyl-N-(3-(trifluoromethyl)phenyl)-urea

Synonyms

° C 2059; Cotoron; Cottonex; Lanex (Meister, 1983).

Uses

° Herbicide (Windholz et al., 1983).

Properties (Windholz et al., 1983; CHEMLAB, 1985; TDB, 1985)

Chemical Formula	$C_{10}H_{11}ON_2F_3$
Molecular Weight	232.21
Physical State (25°C)	White crystals
Boiling Point	--
Melting Point	163-164.5°C
Density	--
Vapor Pressure (20°C)	5×10^{-7} mm Hg
Specific Gravity	--
Water Solubility (25°C)	80 mg/L
Octanol/Water Partition Coefficient	1.88 (calculated)
Taste Threshold	--
Odor Threshold	--
Conversion Factor	--

Occurrence

° Fluometuron was not found in any of 31 ground water samples analyzed from 29 locations (STORET, 1987). No surface water samples were tested.

Environmental Fate

° ^{14}C-Fluometuron (test substance not characterized) was intermediately mobile (R_f = 0.50) in a silty clay loam soil (2.5% organic matter) based on thin-layer chromatography (TLC) tests of soil (Helling, 1971; Helling et al., 1971).

- ^{14}C-Fluometuron (test substance not characterized), at various concentrations, was very mobile in a Norge loam soil (1.7% organic matter) with a Freundlich-K of 0.31 (Davidson and McDougal, 1973). Freundlich-K values, determined in soil:water slurries (5-10 g/100 mL) treated with ^{14}C-fluometuron (test substance not characterized) at 0.05 to 10.0 ppm, were 0.37 for Uvrier sand (1% organic matter), 1.07 for Collombey sand (2.2% organic matter), 1.66 for Les Evouettes loam (3.6% organic matter), 3.16 for Vetroz sandy clay loam (5.6% organic matter), and 1.36 for Illarsatz high organic soil (22.9% organic matter) (Guth, 1972).

- Fruendlich-K values were positively correlated with the organic matter content of the soil. Fluometuron (test substance not characterized), at 10 to 80 uM/kg, was adsorbed at 10 to 51% of the applied amount to a loamy sand soil (1.15% organic matter) and 16 to 67% of the applied to a sandy loam soil (1.9% organic matter) in water slurries during a test period of 1 minute to 7 days, with adsorption increasing with time (LaFleur, 1979). Approximately 22% of the applied fluometuron desorbed in water from the loamy sand soil and 15% desorbed from the sandy loam soil during a 7-day test period.

- Fluometuron (50% wettable powder, WP) dissipated from the 0- to 5-cm depth of a sandy clay loam soil (3.2% organic matter) in central Europe with a half-life of less than 30 days (Guth et al., 1969). Fluometuron residues (not characterized) dissipated with a half-life of 30 to 90 days.

III. PHARMACOKINETICS

Absorption

- Boyd and Foglemann (1967) reported that fluometuron is slowly absorbed from the gastrointestinal (GI) tract of female CFE rats (200 to 250 g). Based on the radioactivity recovered in the urine and feces of four rats given 50 mg ^{14}C-labeled fluometuron after a 2-week pretreatment with 1,000 ppm unlabeled fluometuron [estimated as 100 mg/kg/day, assuming 1 ppm equals 0.1 mg/kg/day in the young rat (Lehman, 1959)], the test compound appears not to have been fully absorbed within 72 hours. Of an orally administered dose (50 mg/kg), up to 15% was excreted in the urine and 49% in the feces.

Distribution

- Boyd and Foglemann (1967) detected radioactivity in the liver, kidneys, adrenals, pituitary, red blood cells, blood plasma and spleen 72 hours after oral administration of ^{14}C-labeled fluometuron at dose levels of 50 or 500 mg/kg in rats. The highest concentration was detected in red blood cells.

Metabolism

- Boyd and Foglemann (1967) concluded that, by thin-layer chromatographic analysis, the urine of rats in their study contained m-trifluoromethyl-aniline, desmethyl-fluometuron, demethylated fluometuron, hydroxylated

desmethyl-fluometuron, hydroxylated demethylated fluometuron, and hydroxylated aniline.

- Lin et al. (1976) reported that after incubation of $^{14}CF_3$-labeled fluometuron with cultured human embryonic lung cells for up to 72 hours, 95% of the compound remained unchanged. Human embryonic lung cell homogenate metabolized small amounts of fluometuron through oxidative pathways to N-(3-trifluoromethylphenyl)-N-formyl-N-methylurea, N-(3-trifluoromethylphenyl)-N-methylurea, and N-(3-trifluoromethylphenyl) urea.

Excretion

- Boyd and Foglemann (1967) reported that urinary excretion of radioactive label peaked at 24 hours after administration of ^{14}C-fluometuron (50 mg/kg) and decreased during the remaining 48 hours. Seventy-two hours after oral administration of the radioactive label, up to 15% of the administered dose was eliminated in the urine.

- In the study by Boyd and Foglemann (1967), fecal excretion of fluometuron peaked by 48 hours postdosing and decreased over the remaining 24 hours. Forty-nine percent of the administered dose (50 mg/kg) was eliminated in the feces.

IV. HEALTH EFFECTS

Humans

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

Animals

Short-term Exposure

- NIOSH (1985) reported the acute oral LD_{50} values of fluometuron as 6,416, 2,500, 900 and 810 mg/kg in the rat, rabbit, mouse and guinea pig, respectively.

- Sachsse and Bathe (1975) reported an acute oral LD_{50} value of 4,636 mg/kg for both male and female Tif RA1 rats.

- Foglemann (1964a) reported the acute oral LD_{50} values for CFW albino mice as 2,300 mg/kg in females and 900 mg/kg in males.

Dermal/Ocular Exposure

- Siglin et al. (1981) conducted a primary dermal irritation study in which undiluted fluometuron powder (80%) was applied to intact and abraded skin of six young adult New Zealand White rabbits for 24 hours. The test substance was severely irritating, with eschar formation observed at 24 and 72 hours.

- Foglemann (1964b) exposed the skin of eight albino rabbits (four/sex) to a 10% aqueous suspension of fluometuron (applied under rubber dental damming) for 6 hours/day for 10 days. No contact sensitization developed during the exposure period. Weight depression at day 130 was evident in the treated group.

- Galloway (1984) reported no sensitizing reactions in Hartley albino guinea pigs exposed to undiluted fluometuron on alternate days for 22 days and on day 36.

- Technical fluometuron was not found to be an eye irritant in rabbits (Foglemann, 1964c).

Long-term Exposure

- Foglemann (1965a) conducted a 90-day feeding study in which CFE rats (15/sex/dose) were administered technical fluometuron (purity not specified) in the diet at dose levels of 100, 1,000 or 10,000 ppm (reported as 7.5, 75 or 750 mg/kg/day). Following exposure, various parameters including hematology, clinical chemistry and histopathology were evaluated. Enlarged, darkened spleens were observed grossly in male rats given 75 mg/kg/day. At the highest dose level, a depression in body weight and congestion in the parenchyma of the spleen, adrenals, liver and kidneys were evident. A mild deposition of hemosiderin in the spleen was also evident. Spleens were large and dark; livers were brownish and muddy colored; and kidneys were small with discolored pelvises in high-dose males. Histopathological findings were confined to mild congestion in various organs and mild hemosiderin deposits in the spleens of high-dose rats. No effects were evident in rats given the 7.5 mg/kg/day dose level for any parameter measured. This dose level was identified as the No-Observed-Adverse-Effect-Level (NOAEL) for this study.

- Foglemann (1965b) administered technical fluometuron (purity not stated) in feed to three groups of beagle pups (three/sex/dose) at dose levels of 40, 400 or 4,000 ppm (reported as 1.5, 15 or 150 mg/kg/day) for 90 days. At 150 mg/kg/day, mild inflammatory-type reactions and congestion in the liver and kidneys and mild congestion and hemosiderin deposits in the spleen were observed. Also at this high dose, the spleen to body weight ratio was slightly increased. No adverse systemic effects were observed in dogs administered 1.5 or 15 mg/kg/day (NOAEL).

- In the NCI (1980) study, B6C3F_1 mice and F344 rats (10 of each sex) were given fluometuron (>99% pure) in the diet for 90 days to estimate 1,000, 2,000, 4,000, 8,000, and 16,000 ppm. Decreased body weight gain (>10%) was apparent with doses above 2,000 ppm. Treatment-related splenomegaly was found in rats with doses above 1,000 ppm. Microscopic examination was done on spleens only from rats given more than 2,000 ppm, and this assessment indicated dose-related changes including hyperemia of red pulp with atrophy of Malpighian corpuscles and depletion of lymphocytic elements. Body weight gain was reduced (>10%) in male and female mice given more than 2,000 ppm. Assuming

that 1 ppm in the diet equals 0.10 mg/kg/day in the young rat and 0.15 mg/kg/day in the mouse (Lehman, 1959), 1,000 ppm (NOAEL) corresponds to 100 mg/kg/day in rats and 2,000 ppm (NOAEL) corresponds to 300 mg/kg/day in mice.

- Hofmann (1966) administered 0, 3, 10, 30 or 100 mg/kg technical fluometuron (Cotoron = C-2059, purity not specified) as a suspension in 1% Mulgafarin six times per week for 1 year by pharnyx probe to four groups of Wistar rats (25/sex/dose). Following treatment, general behavior, mortality, growth, food consumption, clinical chemistry, blood, urine, and histopathology were evaluated. Males dosed with 30 or 100 mg/kg/day and females dosed with 100 mg/kg/day showed significant ($p < 0.05$) reductions in body weight at the end of the study compared to controls. No toxicological effects were observed in rats administered 3 or 10 mg/kg/day (NOAEL).

- In the NCI (1980) study, F344 rats (10 of each sex) were given fluometuron (>99% pure) at dietary levels of 250, 500, 1,000, 2,000 and 4,000 ppm in a repeat of the 90-day study to examine splenic effects more closely. Splenomegaly in all treated groups was noted. A dose-related increase in spleen weights and a dose-related decrease in circulating red blood cells was observed in females fed 250 ppm and higher. Increased spleen weights were evident in males given doses above 500 ppm. However, statistical analysis of the data was not done. Stated in the report without presentation of data is the observation of a dose-related increase in red blood cells with polychromasia and anisocytosis in male and female rats and congestion of red pulp with corresponding decrease of white pulp in spleen. Assuming that 1 ppm equals 0.10 mg/kg/day in the young rat (Lehman, 1959), a Lowest-Observed-Adverse-Effect-Level (LOAEL) of 250 ppm (25 mg/kg/day) is suggested in this study.

- No noncarcinogenic effects (survival, body weight and pathological changes) in $B6C3F_1$ mice and F344 rats were found in the NCI (1980) bioassay discussed under Carcinogenicity.

Reproductive Effects

- No information was found in the available literature on the effects of fluometuron on reproduction.

- A reproduction study with technical fluometuron in rats is in progress to satisfy U.S. EPA Office of Pesticide Programs (OPP) data requirements.

Developmental Effects

- Fritz (1971) reported a teratology study in rats in which dams were given C-2059 suspension in carboxymethylcellulose during days 6 through 15 of gestation. Offspring were removed on day 20 of gestation for examination. The NOAEL was indicated as 100 mg/kg/day, and higher doses reduced fetal body weight. However, this study was invalidated by the U.S. EPA OPP because of inadequate reporting.

- A teratology study in which pregnant Spf New Zealand rabbits were given technical fluometuron (purity not specified) by gavage at dose levels of 50, 500, and 1,000 mg/kg/day during gestation days 6 through 19 was reported by Arhur and Triana (1984). Does were examined for body weight, food consumption and pathological and developmental effects, and laparohysterectomy was done on gestation day 29 for pathological evaluation of fetuses. Increased liver weights and increased mean number of resorptions were found with all doses ($p < 0.05$ at the low and mid doses; insufficient number of fetuses for statistical analysis at the high dose). A LOAEL of 50 mg/kg/day was identified. Reductions in body weights and food consumption occurred in does given 500 and 1,000 mg/kg/day. Deaths, abortions and perforated stomachs were observed in does given 1,000 mg/kg/day.

Mutagenicity

- In bacterial assays (Dunkel and Simmon, 1980), fluometuron (6.6 mg/plate) was not mutagenic in Salmonella strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100, either with or without metabolic activation.

- Seiler (1978) reported that fluometuron (2,000 mg/kg bw) given as a single oral dose of an aqueous suspension by gavage resulted in a strong inhibition of mouse testicular DNA synthesis in mice killed 3.5 hours after treatment. Results were inconclusive in a subsequent micronucleus test.

- In yeast assays (Seibert and Lemperle, 1974), a commercial formulation of fluometuron was ineffective in inducing mitotic gene conversion in Saccharomyces cerevisiae strain D4 without exogenous metabolic activation.

Carcinogenicity

- In a long-term bioassay (NCI, 1980), fluometuron was administered in feed to F344 rats and $B6C3F_1$ mice. Groups of rats (50/sex/dose) were fed diets containing 125 or 250 ppm fluometuron for 103 weeks. Mice (50/sex/dose) were fed 500 or 1,000 ppm for an equivalent period of time. Assuming that 1 ppm equals 0.05 mg/kg/day in the older rat and 0.15 mg/kg/day in the mouse (Lehman, 1959), 125 and 250 ppm equaled 6.25 and 12.5 mg/kg/day in rats and 500 and 1,000 ppm equaled 75 and 150 mg/kg/day in mice. Results based on survival, body weights, and nonneoplastic pathology (including spleen) were negative in rats. Following treatment, there were no significant increases in tumor incidences in male or female F344 rats or in female $B6C3F_1$ mice compared to controls. In male $B6C3F_1$ mice, an increased incidence of hepatocellular carcinomas and adenomas was noted. The incidences were dose-related and were marginally higher than those in the corresponding matched controls or pooled controls from concurrent studies [matched control, 4/21 or 19%; low dose, 13/47 or 28%; high dose, 21/49 or 43% ($p = 0.049$); pooled controls, 44/167 or 26%]. NCI (1980) concluded that additional testing was needed because of equivocal findings for male mice and because both rats and mice may have been

able to tolerate higher doses. The NOAELs identified for rats and mice are 12.5 and 75 mg/kg/day, respectively.

- Chronic feeding studies with technical fluometuron in rats and mice are ongoing to satisfy OPP data requirements.

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:

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

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 the One-day HA value for fluometuron. The teratology study by Arhur and Triana (1984) was not selected because a NOAEL was not identified. It is therefore recommended that the Longer-term HA value for a 10-kg child (1.5 mg/L, calculated below) be used at this time as a conservative estimate of the One-day HA value.

Ten-day Health Advisory

No information was found in the available literature that was suitable for determination of the Ten-day HA value for fluometuron. The teratology study by Arhur and Triana (1984) was not selected because a NOAEL was not identified. It is therefore recommended that the Longer-term HA value for a 10-kg child (1.5 mg/L, calculated below) be used at this time as a conservative estimate of the Ten-day HA value.

Longer-term Health Advisory

The 90-day feeding study in dogs by Foglemann (1965b) has been selected to serve as the basis for the Longer-term HA value for fluometuron. In this

study, dogs given technical fluometuron at dose levels of 0, 1.5, 15 or 150 mg/kg/day in the diet for 90 days showed pathological effects in spleen, liver and kidney at the highest dose and no observable effects at the lower doses. The 90-day feeding studies with rats by Foglemann (1965a) and NCI (1980) were not selected because the 15 mg/kg/day NOAEL in the Foglemann (1965b) study was below the lowest doses of 75 mg/kg/day in the Foglemann (1965a) and 25 mg/kg/day (estimated) in the NCI (1980) repeat 90-day study where effects were noted. Additionally, pathological changes in spleen found with the lowest dose (250 ppm) in the repeat NCI (1980) study in rats were not found with this dose in the initial 90-day study and in the 2-year bioassay in rats by the NCI (1980). Because 7.5 mg/kg/day in the Foglemann (1965a) study and 12.5 mg/kg/day (estimated) in the NCI (1980) carcinogenicity bioassay were NOAELs, it is concluded that 15 mg/kg/day would be consistent with a NOAEL in these 90-day studies in rats. The study by Hofmann (1966) in which rats were given technical fluometuron as a suspension by gavage at dose levels of 0, 3, 10, 30 and 100 mg/kg, six times per week for 1 year, was not selected because feeding the substance in the diet is preferred over giving it as a suspension by gavage for estimating exposure from drinking water, although the 10 mg/kg NOAEL in this study approximates the 15 mg/kg/day NOAEL in the Foglemann (1965b) study. The 90-day feeding study in mice by NCI (1980) was not selected because the NOAEL of 300 mg/kg/day (estimated) is above the effect levels in the other studies considered. The 15 mg/kg/day dose level in dogs was, therefore, identified as the NOAEL.

Using a NOAEL of 15 mg/kg/day, the Longer-term HA for a 10-kg child is calculated as follows:

$$\text{Longer-term HA} = \frac{(15 \text{ mg/kg/day})\ (10 \text{ kg})}{(100)\ (1 \text{ L/day})} = 1.5 \text{ mg/L } (1{,}500 \text{ ug/L})$$

where:

15 mg/kg/day = NOAEL, based on absence of pathological changes in the spleen, liver and kidneys of dogs exposed to the test substance in 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.

The Longer-term HA for a 70-kg adult is calculated as follows:

$$\text{Longer-term HA} = \frac{(15 \text{ mg/kg/day})\ (70 \text{ kg})}{(100)\ (2 \text{ L/day})} = 5.3 \text{ mg/L } (5{,}300 \text{ ug/L})$$

where:

15 mg/kg/day = NOAEL, based on absence of pathological changes in the spleen, liver and kidneys of dogs exposed to the test substance in 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 NCI (1980) carcinogenicity bioassay in F344 rats has been selected to serve as the basis for determination of the Lifetime HA value for fluometuron. Rats were exposed to dose levels of 0, 125 and 250 ppm fluometuron in the diet (estimated as 6.25 and 12.5 mg/kg/day) for 103 weeks. No observable effects were evident in this study. Although pathological changes in spleens of rats given 250 ppm fluometuron in the diet (estimated as 25 mg/kg/day) were noted in the repeat 90-day study in rats by NCI (1980), it appears that splenic lesions were either not evident or were able to reverse in the rats given the 250-ppm dietary level for 2 years (only one rat died by 1 year into the bioassay). Furthermore, pathological changes in the spleen were not evident with doses below 2,000 ppm in the initial 90-day study in F344 rats by NCI (1980). The 90-day and 1-year studies discussed under Longer-term Health Advisory have not been selected for calculation of a Lifetime HA because of their short duration compared to the 103-week NCI (1980) bioassay and because, although not as many end points were assessed in the NCI (1980) bioassay compared to these studies, major effects observed in these studies (pathology, body weight) were evaluated in the NCI (1980) bioassay. The NCI (1980) bioassay in $B6C3F_1$ mice was not considered because higher dose levels (500 and 1,000 ppm, estimated as 75 and 150 mg/kg/day) were used.

Using the NCI (1980) bioassay in rats with a NOAEL of 12.5 mg/kg/day, the Lifetime HA is calculated as follows:

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{(12.5 \text{ mg/kg/day})}{(100)(10)} = 0.0125 \text{ mg/kg/day}$$

where:

12.5 mg/kg/day = NOAEL, based on absence of observable effects in rats exposed to fluometuron in the diet for 103 weeks.

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

10 = additional uncertainty factor used by U.S. EPA OPP to account for data gaps (chronic feeding studies in rats and dogs, reproduction study in rats, teratology studies in rats and rabbits).

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

$$DWEL = \frac{(0.0125 \text{ mg/kg/day})\ (70 \text{ kg})}{(2 \text{ L/day})} = 0.438 \text{ mg/L (438 ug/L)}$$

where:

0.0125 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 = (0.438 mg/L) (20%) = 0.09 mg/L (90 ug/L)

where:

4.38 mg/L = DWEL.

20% = assumed relative source contribution from water.

Evaluation of Carcinogenic Potential

- NCI (1980) determined that fluometuron was not carcinogenic in male and female F344 rats and female mice ($B6C3F_1$). The marginal increase in the incidence of hepatocellular carcinomas and adenomas in male $B6C3F_1$ mice was concluded to be equivocal evidence in the NCI (1980) report on its bioassay.

- IARC (1983) has classified fluometuron in Group 3: This chemical cannot be classified as to its carcinogenicity for humans.

° Applying the criteria described in EPA's guidelines for assessment of carcinogenic risk (U.S. EPA, 1986), fluometuron 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

° The U.S. EPA/OPP previously calculated an ADI of 0.008 mg/kg/day based on a NOAEL of 7.5 mg/kg/day in a 90-day feeding study in rats (Foglemann, 1965a) and an uncertainty factor of 1,000 (used because of data gaps). This has been updated to 0.013 mg/kg/day, based on a 2-year feeding study in rats using a NOAEL of 12.5 mg/kg/day and an uncertainty factor of 1,000.

° Tolerances have been established for negligible residues of fluometuron in or on cottonseed and sugar cane at 0.1 ppm (U.S. EPA, 1985a). A tolerance is a derived value based on residue levels, toxicity data, food consumption levels, hazard evaluation and scientific judgment, and it is the legal maximum concentration of a pesticide in or on a raw agricultural commodity or other human or animal food (Paynter et al., undated).

VII. ANALYTICAL METHODS

° Analysis of fluometuron is by a high-performance liquid chromatographic (HPLC) method applicable to the determination of certain carbamate and urea pesticides in water samples (U.S. EPA, 1985b). This method requires a solvent extraction of approximately 1 liter of sample with methylene chloride using a separatory funnel. The methylene chloride extract is dried and concentrated to a volume of 10 mL or less. HPLC is used to permit the separation of compounds, and measurement is conducted with a UV detector. The method detection limit for fluometuron is 11.1 ug/L.

VIII. TREATMENT TECHNOLOGIES

° Available data indicate that granular activated carbon (GAC) adsorption will remove fluometuron from water.

° Whittaker (1980) experimentally determined adsorption isotherms for fluometuron 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, fluometuron breakthrough (when effluent concentration equals 10% of influent concentration) occurred after 1,640 bed volumes (BV). When a bi-solute solution of fluometuron diphenamide was passed over the same column, fluometuron breakthrough occurred after 320 BV.

- GAC adsorption appears to be the most promising treatment technique for the removal of fluometuron from contaminated water. However, selection of individual or combinations of technologies to attempt fluometuron removal from water must be based on a case-by-case technical evaluation, and an assessment of the economics involved.

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