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DRAFT

TRIFLURALIN

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.

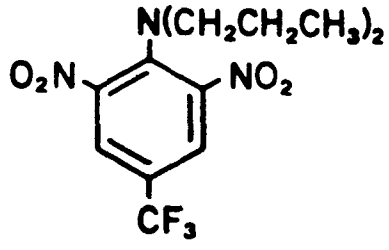
Health Advisories serve as informal technical guidance to assist Federal, State and local officials responsible for protecting public health when emergency spills or contamination situations occur. They are not to be construed as legally enforceable Federal standards. The HAs are subject to change as 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. 1582-09-8

Structural Formula



alpha, alpha, alpha-Trifluro-2,6-dinitro-N,N-dipropyl-p-toluidine

Synonyms

- 2,6-Dinitro-N, N-dipropyl-4-trifluoromethylaniline; Agreflan; Crisalin; Treflan; L-36352 Trifluralin (U.S. EPA, 1985a,b).

Uses

- A selective herbicide (preemergent) for control of annual grasses and broad-leafed weeds. Applied to soybean, cotton and vegetable crops; fruit and nut trees, shrubs; and roses and other flowers. Also used on golf courses, rights-of-way, and domestic outdoor and industrial sites (U.S. EPA, 1985b).

Properties

Chemical Formula	$C_{13}H_{16}F_3N_3O_4$
Molecular Weight	335.2
Physical State (25°C)	Orange, crystalline solid
Boiling Point	139 to 140°C
Melting Point	46 to 49°C
Density	--
Vapor Pressure (25°C)	1.1×10^{-4} mm Hg
Specific Gravity	--
Water Solubility (25°C)	0.3 mg/L
Log Octanol/Water Partition Coefficient	4.69
Taste Threshold	--
Odor Threshold	--
Conversion Factor	--

Occurrence

- Trifluralin is not a potential ground water contaminant due to its strong adsorption to soil and negligible leaching (U.S. EPA, 1985b).

- Trifluralin has been detected in finished drinking water supplies (NAS, 1977).

- Trifluralin has been found in 318 of 377 surface water samples analyzed and in 13 of 283 ground water samples (STORET, 1987). Samples were collected at 194 surface water locations and 251 ground water locations, and trifluralin was found in 9 states. The 85th percentile of all nonzero samples was 0.10 ug/L in surface water and .54 ug/L in ground water sources. The maximum concentration found was 16 ug/L in surface water and 0.54 ug/L in ground water.

Environmental Fate

- Trifluralin at 5 ppm degraded with 15% of the applied trifluralin lost after 20 days in a silt loam soil (aerobic metabolism) study (Parr and Smith, 1973). The samples were incubated in the dark at 25°C and 0.33 bar moisture.

- Trifluralin, applied alone or in combination with chlorpropham or chlorpropham plus PPG-124, dissipated with a half-life of 42 to 84 days in sandy loam or silt loam soil incubated at 72 to 75°F and 18% moisture content under laboratory conditions (Maliani, 1976).

- In an anaerobic soil metabolism study, trifluralin at 5 ppm degraded in nonsterile silt loam soil, with less than 1% of applied trifluralin detected after 20 days of incubation (0.33 bar moisture in the dark at 25°C; anaerobicity was maintained with nitrogen gas). Autoclaving and flooding the soil decreased the degradation rate of the compound (Parr and Smith, 1973).

- ^{14}C-Trifluralin at 1.1 kg/ha was relatively immobile in sand, sandy loam, silt, loam and clay loam soil columns (30-cm height) eluted with 60 cm of water, with more than 90% of the applied radioactivity remaining in the top 0- to 10-cm segment (Gray et al., 1982).

- Trifluralin concentrations in runoff (water/sediment suspensions) were less than 0.04% of the applied amount for 3 consecutive years following treatment at 1.4 kg/ha and 13 to 27 cm of rainfall (Willis et al., 1975). The field plots (silty clay loam soil, 0.2% slope) were planted with cotton or soybeans.

- In the field, ^{14}C-trifluralin (99% pure) at 0.84 to 6.72 kg/ha dissipated in the top 0- to 0.5 cm layer of a silt loam soil, with 14, 4, and 1.5% of the applied amount remaining 1, 2 and 3 years, respectively, after application (Golab et al., 1978). Approximately 30 minor degradates were identified and quantified; none represented more than 2.8% of the applied amount. Trifluralin (4 lb/gal EC) at 0.75 and 1.5 lb/A dissipated in a medium loam soil, with 20 and 32%, respectively, of the applied remaining 120 days after treatment (Helmer et al., 1969; Johnson, 1977).

- Trifluralin (4 lb/gal EC) dissipated from a sandy loam soil treated at 1.0 lb ai/A, with a half-life of 2 to 4 months (Miller, 1973).

- Trifluralin was detected in 107 soil samples taken nationwide at less than 0.01 to 0.98 ppm in fields treated with trifluralin at various rates for 1, 2, 3 or 4 consecutive years (Parka and Tepe, 1969).

- Trifluralin was detected in 12% of the soil samples taken from 80 sites in 15 states in areas considered to be regular pesticide-use areas based on available pesticide-use records (Stevens et al., 1970). Concentrations detected in soils ranged from less than 0.01 to 0.48 ppm. Trifluralin residues were detected in only 3.5% of the 1,729 agricultural soils sampled in 1969 (Wiersma et al., 1972).

- Trifluralin was detected at a maximum concentration of 0.25 ppm. Residues of volatile nitrosamines (dimethylnitrosoamine, N-nitro-sodi-propylamine, or N-butyl-N-ethyl-N-nitrosoamine) were not detected in water samples taken from ponds and wells located in or near fields that had been treated with trifluralin at various rates (Day et al., 1977).

III. PHARMACOKINETICS

Absorption

- Emmerson and Anderson (1966) indicated that trifluralin is not readily absorbed from the gastrointestinal (GI) tract and that the fraction that is absorbed is completely metabolized. Of an orally administered dose (100 mg/kg), only 11 to 14% was excreted in the bile after 24 hours, indicating low GI absorption.

Distribution

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

Metabolism

- Four metabolites of trifluralin were identified in rats. Twelve rats were given 100 mg/kg $^{14}CF_3$-trifluralin in corn oil by gavage for 2 weeks. The metabolites, identified by thin-layer chromatography, were produced by removal of both propyl groups or dealkylation and reduction of a nitro group to an amine (Emmerson and Anderson, 1966).

- An *in vitro* study using rat hepatic microsomes indicated that trifluralin undergoes aliphatic hydroxylation of the N-alkyl substituents, N-dealkylation and reduction of a nitro group (Nelson et al., 1976).

- There are insufficient data to characterize the general metabolism of trifluralin in animals (U.S. EPA, 1986a).

Excretion

- Rats given an oral dose (100 mg/kg) of $^{14}CF_3$-trifluralin excreted virtually all of the dose within 3 days. The radioactivity was excreted during the first 24 hours. Approximately 78% of the dose was eliminated in the feces and 22% in the urine (Emmerson and Anderson, 1966).

IV. HEALTH EFFECTS

Humans

Short-term Exposure

- The Pesticide Incident Monitoring System database revealed 105 incident reports involving trifluralin from 1966 to April of 1981. Of the 105 reports, 49 cases involved humans exposed to trifluralin alone. Twenty-seven cases involved human exposure to mixtures containing trifluralin. The remaining incidents involved nonhuman exposures (U.S. EPA, 1981a).

- Among reports of human exposure to trifluralin alone, one fatality was reported. A 9-year-old girl suffered cardiac arrest following the ingestion of an unknown amount of trifluralin (U.S. EPA, 1981a).

- Verhalst (1974) reported that the symptoms observed in trifluralin poisonings appeared to be related to the solvent used (e.g., acetone or xylene) rather than trifluralin itself.

Long-term Exposure

- The majority of reported trifluralin exposure cases were occupational in nature. Trifluralin exposure has resulted in dermal and ocular irritation in humans. Other reported symptoms include respiratory involvement, abdominal cramps, nausea, diarrhea, headache, lethargy and parasthesia following dermal or inhalation exposure. Specific exposure levels or durations were not reported (U.S. EPA, 1981a).

Animals

Short-term Exposure

- The acute oral toxicity of trifluralin is low. The following oral LD_{50} values have been reported: mice >5 g/kg; rats >10 g/kg; dogs, rabbits and chickens >2 g/kg (Meister, 1983; RTECS, 1985).

- An inhalation LC_{50} value (41% trifluralin; species not specified) of >2.44 mg/L/hour was reported (U.S. EPA, 1985c). No other information was available.

Dermal/Ocular Effects

- The results of a primary dermal-irritation study in the rabbit were negative. No dermal irritation was observed at 72 hours following application of a 41.2% trifluralin solution (U.S. EPA, 1985c).

- Treflan, containing 10% trifluralin, was tested for sensitization in female guinea pigs. A dose of 50 mg was applied to the skin of 12 animals, three times a week for 2 weeks. No dermal irritation or contact sensitization developed during this time (ELANCO, 1984a).

- In a similar study, a 95% technical trifluralin solution was shown to be a potential skin sensitizer in guinea pigs using the Buehler topical-patch method (U.S. EPA, 1985c).

- A 14-day study in which rabbits were exposed to 2 mL/kg trifluralin topically produced diarrhea and slight dermal erythema in exposed animals. No other effects were reported (ELANCO, 1979).

- Technical-grade trifluralin applied as a powder to rabbit eyes was reported as nonirritating. Slight conjunctivitis developed but cleared within a week (U.S. EPA, 1985c).

- When applied as a liquid to rabit eyes, technical trifluralin produced corneal opacity that cleared in 7 days (U.S. EPA, 1985c).

Long-term Exposure

- In a modified subacute study, female Harlan-Wistar rats were given 0, 0.05, 0.1 or 0.2% (0, 500, 1,000 or 2,000 ppm) trifluralin in their diet for 3 months. Assuming that 1 ppm in the diet of rats equals 0.05 mg/kg/day (Lehman, 1959), these levels correspond to doses of 0, 25, 50 and 100 mg/kg/day. Physical appearance, behavior, body and organ weights, mortality and clinical chemistries were monitored in progeny from 10 females. No significant effects were observed in survival or appearance. Liver weights in progeny continuously fed diets of 0.1% and 0.2% trifluralin were increased over those of control animals. The study identified a No-Observed-Adverse-Effect-Level (NOAEL) in progeny of 0.05% (25 mg/kg) trifluralin (ELANCO, 1977a).

- In a 90-day study, male F344 rats were fed dietary levels of 0 (n = 60), 0.005% (n = 60), 0.02% (n = 45), 0.08% (n = 45), 0.32% (n = 45) and 0.64% (n = 45). These concentrations are equivalent to dose levels of 0, 50, 200, 800, 3,200 and 6,400 ppm trifluralin, respectively (ELANCO, 1985). Assuming that 1 ppm in the diet of a rat equals 0.05 mg/kg/day (Lehman, 1959), these levels correspond to doses of 0, 2.5, 10, 40, 160 and 320 mg/kg/day. After 90 days, alpha-1, alpha-2 and beta-globulin levels were significantly increased in all treatment groups. Other effects included increased aspartate transaminase, urinary calcium, inorganic phosphorus and magnesium at levels $\geq$160 mg/kg/day. A Lowest-Observed-Adverse-Effect-Level (LOAEL) of 2.5 mg/kg/day (the lowest dose tested) can be identified from this study.

- Sixty weanling Harlan rats were fed 0, 20, 200, 2,000 or 20,000 ppm trifluralin in the diet for 729 days (24 months). Assuming that 1 ppm in the diet of a rat equals 0.05 mg/kg (Lehman, 1959), these concentrations correspond to doses of 0, 1, 10, 100 or 1,000 mg/kg/day. No significant effects were observed in growth rate, mortality or food consumption of treated animals at the three lower dose levels. Animals in the highest dose group (1,000 mg/kg/day) were significantly smaller than controls and ranked lower in food consumption. No effects on hematology were noted. Animals in the high-dose group displayed a slight proliferation of the bile ducts. No other histopathological effects were observed. A NOAEL of 2,000 ppm (100 mg/kg/day) was reported (ELANCO, 1966a).

- In a 2-year chronic carcinogenicity study with F344 rats, doses greater than 128 mg/kg/day in males and 154 mg/kg/day in females were reported to produce overt toxicity. Groups of 60 animals/sex/dose were fed dietary levels of 0.08, 0.3 or 0.65% (30, 128 or 272 mg/kg/day for males, and 37, 154 or 336 mg/kg/day for females) trifluralin. Body weights of the high-dose groups were significantly decreased in both sexes. This may be related to the decreased food consumption observed in those groups. Increased blood urea nitrogen (BUN) levels and increased liver and testes weights were note in the two high-dose groups. Kidney and heart weights were significantly decreased in females in the 0.3- and 0.65%-trifluralin groups. Other noncarcinogenic effects included decreased hemoglobin values and erythrocyte counts in both sexes of the high-dose group (ELANCO, 1980a). This study appears to identify a NOAEL of 0.08% trifluralin (30 to 37 mg/kg/day)

- B6C3F_1 mice (40/sex/group) were exposed to dose levels of 40, 180 or 420 mg/kg/day trifluralin in the diet for 2 years. Animals exposed to the two higher levels exhibited decreased body weight and renal toxicity. Other noncarcinogenic effects included decreased erythrocytic and leukocytic values in the high-dose group, increased BUN and alkaline phosphatase levels in the 180- and 420-mg/kg/day group, decreased kidney weights in the two high-dose groups and decreased spleen and uterine weights with increased liver weights in the high-dose group (ELANCO, 1980b). No effects were noted at the low-dose level (40 mg/kg/day).

- Occasional emesis and increased liver-to-body weight ratios were observed in dogs (three/sex/dose) fed 25 mg/kg/day trifluralin for 3 years. No adverse effects were observed in animals fed 10 mg/kg/day (Worth, 1970). An intermediate dose was not tested.

Reproductive Effects

- In a four-generation reproduction study (ELANCO, 1977b), rats were given 0, 200 or 2,000 ppm trifluralin in the diet (0, 10 or 100 mg/kg/day). A reproductive NOAEL of 200 ppm (10 mg/kg/day) was identified. The number of animals used in the study was not reported. However, a review of this study (U.S. EPA, 1985c) indicated that an insufficient number of animals were used and that several other deficiencies in the study may have compromised the integrity of the results.

- In a 3-year feeding study in dogs a NOAEL of 10 mg/kg/day was identified in adults (ELANCO, 1967). Dogs (three/sex/dose) were given 10 or 25 mg/kg/day trifluralin in the diet. When bred after 2 years of exposure, no differences in litter size, survival or growth of the pups were reported. An occasional emesis and increased liver weights were reported in adults in the 25-mg/kg/day group.

Developmental Effects

- Female rabbits (number not specified) were fed 0, 100, 225, 500, or 800 mg/kg/day by gavage during pregnancy (ELANCO, 1984b). No adverse

reproductive effects were observed at the two lower dose levels. The 500 and 800 mg/kg/day levels resulted in anorexia, aborted litters and decreased live births. The NOAEL for maternal effects was identified as 225 mg/kg/day.

- Rabbits (number not specified) exposed to 100, 225 or 500 mg/kg/day trifluralin during pregnancy exhibited anorexia and cachexia at all dose levels (U.S. EPA, 1985c). Aborted litters were observed at the two high-dose levels. Fetotoxicity as evidenced by decreased fetal weight and size was observed at the high-dose level.

- In a rabbit teratology study, a total of 32 mated females were given up to 1,000 mg/kg/day trifluralin by gavage (ELANCO, 1966b). Specific dose increments were not reported. Animals were dosed until the 25th day of gestation and then sacrificed. Does in the 1,000 mg/kg/day group weighed slightly less than controls. Two fetuses were found to be underdeveloped in the high-dose group; however, this was not considered by the investigators to be treatment related. Average litter size and weight were not significantly affected. The authors reported that their results identified a safe level of 1,000 mg/kg/day.

- Rabbit does (number per group not specified) were given 100, 225, 500 or 800 mg/kg/day trifluralin by gavage during pregnancy (ELANCO, 1984b). The 500 and 800 mg/kg/day levels resulted in decreased live births, cardiomegaly and wavy ribs in the progeny. No effects on progeny were observed at 225 mg/kg/day or less (ELANCO, 1984b).

Mutagenicity

- Anderson et al. (1972) reported that trifluralin did not induce point mutations in any of the three microbial systems tested. No further details were provided in the review.

- Trifluralin was tested for genotoxicity in several *in vivo* and *in vitro* systems (ELANCO, 1983). No reverse mutations were observed in *Salmonella typhimurium* or *Escherichia coli* when incubated with 25 to 400 mg trifluralin/plate without activation; trifluralin was also negative when tested at levels of 50 to 800 mg/plate with activation. Negative results were obtained in mouse lymphoma L5178Y TK^+ cells incubated with 0.5 to 20 ug/mL trifluralin with and without activation. An *in vivo* sister-chromatid exchange study in Chinese Hamster Ovary (CHO) cells following exposure to 500 mg/kg trifluralin was also negative.

Carcinogenicity

- NCI (1978) conducted bioassays on $B6C3F_1$ mice and Osborne-Mendel rats using technical-grade trifluralin (which contained 84 to 88 ppm of the contaminant dipropylnitrosamine). Two dietary levels were used in each bioassay. Mice (50/sex/group) were exposed to trifluralin at dose levels of 2,000 or 3,444 ppm (males) or 3,740 or 5,192 ppm (females) for 78 weeks and observed for an additional 13 weeks after exposure. A significant close-related increase in hepatocellular

carcinoma was observed in female mice (0/20 control, 12/47 low dose, 21/44 high dose). An increased incidence of alveolar/ bronchiolar adenomas was also observed (0/19 control, 6/43 low dose, 3/30 high dose) in female mice. Squamous cell carcinomas in the forestomach of a few treated female mice were also observed. Although the incidence of squamous cell carcinoma in the forestomach was not statistically significant when compared to pooled and matched controls, NCI deemed this finding to be treatment related, since it was an unusual type of lesion. Male mice were not significantly affected by trifluralin exposure.

- Rats (50/sex/group) were exposed to two levels of trifluralin in the feed (4,125 or 8,000 ppm for males; 4,125 or 7,917 ppm for females) for 78 weeks followed by a 33-week observation period (NCI, 1978). Assuming 1 ppm in the diet of rats equals 0.05 mg/kg/day (Lehman, 1959), these doses correspond to 206 or 400 mg/kg/day. Several neoplasms were observed and compared to pooled and matched controls. These neoplasm types were reported to occur spontaneously in the Osborne-Mendel strain and were not considered treatment related by NCI.

- In a 2-year feeding study, B6C3F_1 mice were given 563, 2,250 or 4,500 ppm trifluralin (assuming 1 ppm in the diet of a mouse equals 0.15 mg/kg/day, these doses correspond to 40, 180 or 420 mg/kg/day (Lehman, 1959) in the diet (ELANCO, 1980b). Levels of a nitrosamine contaminant of trifluralin, NDPA, were below the 0.01-ppm analytical detection limit. A total of 40 animals/sex/treatment group was used. At the lowest dose level, 40 mg/kg/day, no adverse effects were observed in either sex. Decreased body weight and renal effects were noted in mice in the mid- and high-dose groups. Pathology revealed progressive glomerulonephritis in females of the high-dose group. Hepatocellular hyperplasia and hypertrophy were also observed in the treated mice. The specific dose level was not reported. No evidence of increased incidence or decreased latency for any type of neoplasm was found in any of the mice.

- Trifluralin was administered to F344 rats (60/sex/group) at dose levels of 813, 3,250 or 6,500 ppm [assuming 1 ppm in the diet of a rat equals 0.05 mg/kg/day (Lehman, 1959), these doses correspond to 30, 128 or 272 mg/kg/day for males and 37, 154 or 336 mg/kg/day for females] in the diet for 2 years (ELANCO, 1980a). A significant increase in malignant renal neoplasms and thyroid tumors in male rats and in neoplasms of the bladder in both sexes was reported. A high incidence (20/30) of renal calculi was also observed in animals in the high-dose groups.

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 the One-day HA value for trifluralin. Therefore, it is recommended that a modified DWEL (0.025 mg/L, calculated below) for a 10-kg child be used as a conservative estimate for the One-day HA value.

For a 10-kg child, the adjusted DWEL is calculated as follows:

$$DWEL = \frac{(0.0025 \text{ mg/kg/day}) (10 \text{ kg})}{1 \text{ L/day}} = 0.025 \text{ mg/L}$$

where:

0.0025 mg/kg/day = Rfd (see Lifetime Health Advisory Section).

10 kg = assumed body weight of a child.

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

Ten-day Health Advisory

No information was found in the available literature that was suitable for determination of the Ten-day HA value for trifluralin. It is, therefore, recommended that a modified DWEL (0.025 mg/L) for a 10-kg child be used as a conservative estimate for the Ten-day HA value.

Longer-term Health Advisory

No information was found in the available literature that was suitable for determination of the Longer-term HA value for trifluralin. It is, therefore, recommended that a modified DWEL (0.025 mg/L) for a 10-kg child be used as a conservative estimate for a Longer-term exposure.

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 ELANCO (1985) study has been selected to serve as the basis for the Lifetime HA value for trifluralin. F344 rats were fed diets containing 0.005, 0.02, 0.08, 0.32 or 0.64% trifluralin (2.5, 10, 40, 160 or 320 mg/kg/day) for 90 days. Significant increases in urinary alpha-1, alpha-2, and beta-globulins were observed in all treated animals. A NOAEL was not identified. Other longer-term studies report NOAELs at higher doses.

Using a LOAEL of 2.5 mg/kg/day, the Lifetime HA is calculated as follows:

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{(2.5 \text{ mg/kg/day})}{(1{,}000)} = 0.0025 \text{ mg/kg/day}$$

where:

2.5 mg/kg/day = LOAEL, based on increased urinary globulins in rats consuming a trifluralin diet for 3 months.

1,000 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a LOAEL from an animal study.

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

$$DWEL = \frac{(0.0025 \text{ mg/kg/day}) (70 \text{ kg})}{(2 \text{ L/day})} = 0.088 \text{ mg/L } (87 \text{ ug/L})$$

where:

0.0025 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

$$\text{Lifetime HA} = \frac{(0.088 \text{ mg/L})\ (20\%)}{10} = 0.0017 \text{ mg/L } (2 \text{ ug/L})$$

where:

0.088 mg/L = DWEL.

20% = assumed relative source contribution from water.

10 = additional uncertainty factor per ODW policy to account for possible carcinogenicity.

Evaluation of Carcinogenic Potential

- Applying the criteria described in EPA's guidelines for assessment of carcinogenic risk (U.S. EPA, 1986b), trifluralin may be classified in Group C: possible human carcinogen. This category is used for substances that show limited evidence of carcinogenicity in animals and inadequate evidence in humans.

- In an NCI (1978) study of female B6C3F_1 mice, a significant dose-related increase in hepatocellular carcinomas and alveolar adenomas was observed when the animals were exposed to 33 or 62 mg/kg/day trifluralin in the diet for 78 weeks. The trifluralin used in this study contained 84 to 88 ppm dipropylnitrosamine. Male rats, when exposed to 30, 128 or 272 mg/kg/day trifluralin in the diet for 2 years, exhibited significant increases in the incidences in kidney, urinary bladder and thyroid tumors (ELANCO, 1980a).

- The evidence from the ELANCO (1980a) and NCI (1978) studies indicates that trifluralin has carcinogenic potential. Based on the results of the ELANCO (1980a) study, the U.S. EPA Carcinogen Assessment Group (CAG) has prepared a quantitative risk estimate of trifluralin exposure (U.S. EPA, 1981b). The CAG estimated a potency factor (q_1*) of 7.66 x 10^{-3} mg/kg/day based on the combined incidence of tumors in male rats. Assuming that a 70-kg human adult consumes 2 liters of water a day over a 70-year lifespan, the estimated cancer risk would be 10^{-4}, 10^{-5} and 10^{-6} at concentrations of 500, 50 and 5 ug/L, respectively.

VI. OTHER CRITERIA, GUIDANCE AND STANDARDS

- Residue tolerances from 0.05 to 2.0 ppm trifluralin have been established for a variety of agricultural commodities (U.S. EPA, 1985).

- NAS (1977) has calculated an ADI of 0.1 mg/kg bw/day with a Suggested-No-Adverse-Response-Level (SNARL) of 700 ug/L.

VII. ANALYTICAL METHODS

- Determination of trifluralin is by a liquid-liquid extraction gas chromatographic procedure applicable to the determination of organochlorine pesticides in water samples (Standard Methods, 1985). Specifically, the procedure involves extraction with a mixed solvent, diethyl ether/hexane or methylene chloride/hexane. The extract is concentrated by evaporation, and the compounds are separated by gas chromatography. Detection and measurement are accomplished by the use of an electron-capture detector. Additional confirmatory identification can be made through the use of two unlike columns or by mass spectrometry.

VIII. TREATMENT TECHNOLOGIES

- Available data indicate that reverse osmosis (RO), granular-activated carbon (GAC) adsorption conventional treatment and possibly air stripping will remove trifluralin from water.

- U.S. EPA investigated the amenability of a number of compounds, including trifluralin, to removal by GAC. No system performance data were given.

- Conventional water treatment techniques of coagulation with alum, sedimentation and filtration proved to be 100% effective in removing trifluralin from contaminated water (Nye, 1984).

- Sanders and Seibert (1983) determined experimentally water solubility, vapor pressure, Henry's Law Constant and volatilization rates for trifluralin; 100% of the compound volatilized under laboratory conditions.

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

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