

Trifluralin Risk Assessment Overview

(August 30, 2004)

Introduction

This document summarizes EPA's human health and environmental fate risk finding for the pre-emergence herbicide trifluralin. These findings are presented fully in the HED human health risk assessment document "*Trifluralin: Human Health Risk Assessment*" dated May 7, 2004; and the EFED water assessment document "*Trifluralin - Drinking Water Assessment for Tolerance Reassessment Eligibility Decision*", dated December 3, 2003.

The purpose of this overview is to assist the reader in understanding the conclusions reached in the risk assessments by identifying the key features and findings of each.

Use Profile

- Herbicide: Trifluralin is a selective, pre-emergence, dinitroaniline herbicide primarily used in soybeans and cotton. Additionally, trifluralin is used on residential lawns, landscape ornamentals, trees, and vegetable gardens and is also marketed for use by professional applicators on residential turf, on golf courses, other turf such as recreational/commercial areas, and on ornamental plantings. Important markets for trifluralin usage include: soybeans, cotton, wheat, alfalfa, sunflowers, and dry beans/peas. However, use of this chemical is also important for minor crops such as peas, okra, sunflower, asparagus, peanuts, vegetables, tomatoes and beans.
- Targeted Pest: Registered products containing trifluralin are intended for the control of annual grasses and certain broadleaf weeds.
- Formulations: Trifluralin is formulated as a dust, emulsifiable concentrate, granular, emulsifiable concentrate/liquid, and soluble concentrate. Trifluralin end-use products for food and feed crops include emulsifiable concentrates (EC, 36.4, 50.8% ai) and a granular formulation, (G,10%),(EC, 43% ai). For residential and other non-agricultural uses, trifluralin is formulated as a granular (G, 0.17 - 2.0% ai), which is the only formulation used on turf for this usage, and an emulsifiable concentrate liquid (EC, 43% ai).

- Method of Application: Currently, trifluralin may be applied: dormant, semi-dormant, pre-plant, pre-transplant, pre-emergence, post-emergence, lay-by or post-harvest (as a soil incorporated treatment), liquid sprays of water or liquid fertilizer, or impregnated on dry bulk fertilizer or clay granules. Trifluralin is generally applied once per growing season on all registered crops and sites. However, there are exceptions for sugarcane and cotton. Additionally, trifluralin is soil incorporated into the top 2-3 inches of soil within 24 hours of application and can be applied via chemigation on: alfalfa, field corn, cotton, grain sorghum (milo), potatoes, tree and vine crops, and soybeans. The maximum amount of trifluralin per acre per year that can be applied depends on the site of use. For homeowner use, trifluralin may be in a granular or liquid form, and applied via belly grinder, push-type spreader, shaker can (by hand), hose-end sprayer, low pressure handwand, backpack sprayer, and impregnated fabric squares to soil at various rates from 3 lbs ai/A on turf, to 20 lbs ai/A on ornamental beds.
- Use Summary: The top six uses of trifluralin include soybeans, cotton (75% of the volume is applied to soybeans and cotton), wheat, alfalfa, sunflowers, and dry beans/peas, and accounts for 93% of total trifluralin ai applied in the US. However, turf uses pre-dominate with approximately 75% of use on turf occurring in the North, 20% in the South, and 5% used elsewhere. Based on 1997-2001 data, the Agency estimates that approximately 18 million pounds of trifluralin ai is used per year for agricultural production in the United States. The majority of the agriculture use is in the Midwest, High Plains, Mid-South and Central Valley regions. Additionally, more than 50% of the acreage planted in tomatoes and carrots is treated with trifluralin.

The label rate for agricultural uses is 1 to 2 lbs ai/acre, with a maximum rate of 4 lbs ai/acre on sugarcane, whereby the registrant reports a typical use rate of 1lb ai/acre, or less.

- Technical Registrant: Dow AgroSciences

EPA does not have, at this time, available data to determine whether trifluralin has a common mechanism of toxicity with other substances. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to trifluralin and any other substances. For purposes of this tolerance action, therefore, EPA has not assumed that trifluralin has a common mechanism of toxicity with other substances.

Hazard Characterization

The Trifluralin toxicology database is sufficient for tolerance reassessment and adequate for Food Quality Protection Act (FQPA) consideration. The Agency determined that since the dose

response was well characterized, the developmental effects were only seen in the presence of maternal toxicity, and clear No Observable Adverse Effect Levels (NOAELs) were established for developmental and maternal toxicities, thus the concern for increased susceptibility for children was low.

The FQPA Safety Factor recommendation by the Hazard Identification Assessment and Review Committee (HIARC) assumed that the exposure databases (food, drinking water, and residential) are complete and the risk assessment for each exposure scenario includes all metabolites and/or degradates of concern, and the assessment does not underestimate the potential risk for infants and children. Upon review of the trifluralin toxicity data, the HIARC selected the appropriate studies, endpoints, and dose levels for human health risk assessment (see Table 1 below).

Table 1: SUMMARY OF TOXICOLOGY ENDPOINT SELECTION
Summary of Toxicological Dose and Endpoints for Trifluralin

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF* Target MOE	Study and Toxicological Effects
Acute Dietary (Females 13-50 years of age)	NOAEL = 100 mg/kg/day UF = 100 Acute RfD = 1.0 mg/kg/day	FQPA SF = 1 aPAD = 1.0 mg/kg/day	Developmental Toxicity Study - Rat LOAEL = 500 mg/kg/day based on increased total litter resorptions.
Acute Dietary (All populations)	No appropriate single dose endpoint was selected for all populations except Females 13-50.		
Chronic Dietary (All populations)	NOAEL = 2.4 mg/kg/day UF = 100 Chronic RfD = 0.024 mg/kg/day	FQPA SF = 1 cPAD = 0.024 mg/kg/day	Chronic Toxicity (capsule) - Dog LOAEL = 40 mg/kg/day
Short-Term Incidental Oral (1-30 days)	NOAEL = 10 mg/kg/day	MOE = 100	Two-generation Reproduction Study - Rat LOAEL = 32.5 mg/kg/day based on decreased pup weights in both generations

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF* Target MOE	Study and Toxicological Effects
Intermediate-Term Incidental Oral, Dermal and Inhalation (1- 6 months)	NOAEL= 10 mg/kg/day (Dermal absorption rate = 3 % (Inhalation absorption rate = 100 %)	MOE = 100	Special Urinalysis Study - Rat LOAEL = 40 mg/kg/day
Short-Term Dermal (1 to 30 days)	No quantification required since there was no systemic toxicity at the limit dose in the dermal toxicity study. There are no developmental toxicity concerns.		
Long-Term Dermal (>6 months)	Oral study NOAEL= 2.4 mg/kg/day (dermal absorption rate = 3 % when appropriate) (Inhalation absorption rate = 100 %)	Residential MOE = 100	Chronic Toxicity (capsule) - Dog LOAEL = 40 mg/kg/day
Short-Term Inhalation (1 to 30 days)	Inhalation study NOAEL= 81 mg/kg/day	Residential MOE = 100	30-Day Inhalation Study - Rat LOAEL = 270 mg/kg/day
Cancer (oral, dermal, inhalation)	$Q_1^* = 5.8 \times 10^{-3} \text{ (mg/kg/day)}^{-1}$ Group C ("Possible" Human Carcinogen)		

UF = uncertainty factor, FQPA SF = FQPA safety factor, NOAL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, NA = Not Applicable

NOTE: Since a toxicological endpoint, based on dermal exposure, was not selected for trifluralin, only post-application incidental oral ingestion (i.e., soil, granule, and hand-to-mouth ingestion) exposures to children were calculated.

The Agency concluded that the FQPA Safety Factor should be removed (equivalent to a 1x Safety Factor) based on a conclusion of no concern for qualitative susceptibility seen for pre-and post-natal toxicities. However, the Agency remains concerned about dermal sensitization reactions to adults and children who are exposed to trifluralin in residential settings and recommends for labeling to this effect, on all products.

Human Health Risk Assessment

Acute Dietary (Food) Risk

Acute dietary risk is calculated considering the toxicity of a chemical, what is eaten by individuals in one day and residue values for various foods. A risk estimate that is less than 100% of the acute Population Adjusted Dose (aPAD) (the dose at which an individual could be exposed on any given day and no adverse health effects would be expected) does not exceed the Agency's risk concern.

An acute Population Adjusted Dose (aPAD) of 1.0 mg/kg/day was established for females of child-bearing age based on the No Observable Adverse Effect Level (NOAEL) of 100 mg/kg/day observed in the rat developmental study. The Dietary Exposure Evaluation Model (DEEM™) analysis evaluated the individual food consumption as reported by respondents in the USDA 1994-1996 and 1998 Nationwide Continuing Surveys of Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity. Additionally, acute risks were also estimated using the Lifeline model (version 2.0). Lifeline converts the raw agricultural commodity (RAC) residues into food residues by randomly selecting a RAC residue value from the user defined residue distribution (created from the residue, percent crop treated, and processing factors data), and calculating a net residue for that food based on the ingredient's mass contribution to that food item. The Lifeline model estimated acute exposure based on the acute 1-day dietary dose drawn randomly from an age-specific seasonal exposure profile of 1000 individuals.

An acute dietary assessment was not conducted for the general U.S. population or infants and children because there was no appropriate single dose endpoint for this population sub-group. The acute dietary risk estimates are below the Agency's level of concern (<100% aPAD) at the 99.9th exposure percentile for the females 13 - 49 years of age (<1% aPAD), the population subgroup of concern. Results of the Lifeline analysis are fully consistent with DEEM-FCID results (See Table 2 below).

Table 2. Results of Acute Dietary Exposure Analysis Using both DEEM FCID and Lifeline Softwares				
Population Subgroup	aPAD (mg/kg/day)	Model	99.9th Percentile	
			Exposure (mg/kg/day)	% aPAD
Females 13-49 yrs	1	DEEM-FCID	0.000262	0.03
		Lifeline	0.000311	0.03

Chronic and Cancer Dietary (Food and Water) Risk

Trifluralin is classified as a Group C possible human carcinogen with carcinogenic risk quantified by the Q_1^* approach. Carcinogenic dietary risk is based on the chronic exposure estimate for the general U.S. population derived from the same residue, percent use, and averaged consumption data. Chronic dietary risk is calculated by using the average consumption value for food and average residue values on those foods over a 70-year lifetime. A risk estimate that is less than 100% of the chronic RfD (the dose at which an individual could be exposed over the course of a lifetime and no adverse health effects would be expected) does not exceed the Agency's risk concern. Estimated chronic dietary risk is below the Agency's level of concern for all populations (<1% of cPAD; 0.005 mg/kg/day). The estimated exposure of the general U.S. population to trifluralin is 0.000028 mg/kg/day for both dietary risk assessment models. Applying the Q_1^* of 5.8×10^{-3} (mg/kg/day)⁻¹ to the exposure value results in a cancer risk estimate of 1.64×10^{-7} (DEEM-FCID) and 1.13×10^{-7} (Lifeline), which is also below the Agency's level of concern.

Drinking Water Dietary Risk

Drinking water exposure to pesticides can occur through groundwater and surface water contamination. EPA considers both acute (one day) and chronic (multiple year) drinking water risks, and uses either modeling or actual monitoring data, if available, to estimate those risks. Modeling is designed to provide a high-end estimate of exposure. The Agency lacks sufficient data to accurately determine dietary exposure from drinking water. Therefore, residues for trifluralin in drinking water are refined by PRZM-EXAMS modeling. The drinking water assessment is based on modeling and monitoring data. Modeling was completed for parent as well as combined trifluralin residues observed in fate studies.

Since trifluralin is registered on several crops, Tier II modeling crop scenarios were selected to reflect crops with the highest uses of trifluralin (soybeans and cotton), the maximum application rate (sugarcane), and availability of scenarios. The maximum daily peak concentration of trifluralin from PRZM/EXAMS simulation (38.1 ppb) is greater than the highest concentration in the USGS/National Water Quality Assessment (NAWQA) monitoring database (1.74 ppb) for surface water. However, the maximum annual average trifluralin concentration in surface water (1.9 ppb) is comparable to time weighted annual means (TWAM) concentrations in USGS monitoring studies (0.618 ppb). Additionally, the maximum trifluralin concentration in shallow ground water (0.035 ppb), as predicted through SCI-GROW, is lower than the 99.8 percentile concentration in the NAWQA ground water monitoring database (0.012 ppb).

Residential Risk

Residential risk assessment considers potential pesticide exposure, other than dietary and occupational exposure. Exposure may occur during and after application at homes; or after applications at golf courses, parks, schools, etc. Each route of exposure (oral, dermal, inhalation) is assessed, where appropriate, and risk is expressed as a Margin of Exposure (MOE), which is

the ratio of estimated exposure to an appropriate No-Observed-Adverse-Effect-Level (NOAEL) dose. Based on its uses, trifluralin is assessed for the residential applicator (or “handler”), for children’s post-application oral exposure that may occur from turf contact, and for post-application dermal contact. Additionally, carcinogenic risk is also estimated by the Q_1^* approach.

Residential exposure scenarios were developed for trifluralin and based on the use sites, formulations, application rates, and the various equipment that could be used during applications. Residential risk estimates are also based on estimates (and assumptions) regarding the body weight of a typical homeowner/applicator, the area treated per application, and the seasonal duration (in days) of exposure. Note also that residential applicators are assumed to complete all elements of an application (mix/load/apply) without use of protective equipment (assessments are based on an assumption that individuals will be wearing short-sleeved shirts and short pants).

Short-term inhalation risks to residential handlers and dermal and inhalation cancer risks to residential handlers were calculated using surrogate data. For short-term non-cancer risks to residential handlers, a margin of exposure (MOE) of less than 100 exceeds the Agency’s level of concern. For residential handlers, the calculations of short-term inhalation non-cancer risk indicate that the MOEs are greater than 100 for all residential handler scenarios.

For residential handler scenarios, cancer risks greater than 1×10^{-6} are considered to be of concern. The calculations of residential handler cancer risk indicate that all scenarios have a cancer risk of less than 1×10^{-6} .

Post-Application Risk Estimates

Exposure to trifluralin occurs in the residential environment following applications by professionals, or non-professionals, to lawns and ornamentals. Exposure to trifluralin also occurs following applications by professionals to private or public areas such as golf courses, parkland, etc. For this assessment, children are the population group of concern. Since *systemic* toxicity was not observed in a dermal toxicity study, up to a dose level of 1,000 mg/kg/day, the only risk scenario addressed in this assessment is the possible oral exposure of small children from treated turf, or from treated soil (i.e., soil ingestion, granule ingestion, and hand-/object-to-mouth). A Margin of Exposure of 100 (or more) is considered adequately protective for this assessment.

For non-cancer post-application risks, since there is no short-term dermal toxicological endpoint of concern for trifluralin and no intermediate-term dermal exposure is anticipated, the only assessment is for incidental ingestion by toddlers by hand-to-mouth and object-to-mouth exposure scenarios. These scenarios produce MOEs greater than 100, therefore risks are not of concern to the Agency.

Since there was no dermal endpoint identified, short-term post-application risks are based on incidental oral exposures. For residential post-application, the calculations of non-cancer risk based on the incidental oral NOAEL endpoint indicate that the MOEs were more than 100 for residential post-application scenarios.

In addition, the Agency determined that in order to complete the residential non-cancer post-application risk assessment a combined risk assessment would be required. In doing so, the Agency combines risk values resulting from separate post-application exposure scenarios, when it is likely that they can occur simultaneously based on the use pattern and the behavior associated with the exposed population. For trifluralin, the Agency combined risk values for post-application exposures to toddlers associated with turf applications by combining risks from oral exposures via transfer of residues from hands-to-mouth, object-to-mouth, and incidental soil ingestion. The combined MOE for these scenarios is greater than 100 and is not considered a risk concern.

Carcinogenic risk estimates are based, in part, on estimates of days per year that persons are exposed to treated areas following trifluralin use. Based on the transferable residue study, post-application exposure to residential turfgrass and golf course turfgrass will occur on the day of application (day zero) following two applications, each year. As with residential applicators, the assessment is based on 50 years of trifluralin use and exposure. Cancer risks are 5×10^{-10} and are therefore, not of concern.

Exposure estimates are also based on data that measured the transfer of residue (any chemical) from the surface of treated turf to persons while doing specific activities. As in the post-application oral assessment, the transferable residue estimate (0.0033 ug/cm^2) is taken from the trifluralin-specific study and is the average transferable residues at day 0 (after day 0, no residues were detectable) and accounts for the 3 lb ai/A application rate used on turf. These estimates form the basis for the “Lifetime Average Daily Dermal Dose”, or LADD, used with the Q_1^* to estimate (lifetime) carcinogenic risk for trifluralin users.

The Agency has determined that there are potential post-application cancer risks for adults in residential areas treated with trifluralin. The following scenarios were assessed: (1) dermal exposure to residue on lawns, (2) dermal exposure to golf course turfgrass, and (3) dermal exposure to residue on home gardens. For residential post-application scenarios, cancer risks greater than 1×10^{-6} are considered to be of concern. The calculation of residential post-application cancer risk indicate that all scenarios have a cancer risk of less than 1×10^{-10} and are not considered a risk concern.

For the residential turfgrass scenario, the Agency combined the cancer risks for residential handlers applying granular formulation to lawns with post-application cancer risks to adults from exercising on just-treated lawns. The combined handler plus post-application cancer risk associated with applications to residential turfgrass is 5.4×10^{-7} . This is below EPA’s level of concern for cancer. (Note: combining short-term risks was not done, since there are no short-term post-application risks because there is no short-term dermal endpoint of concern.)

Aggregate Risk

Aggregate exposure assessment is based, in part, on the same assumption that there is a predictable level of chronic pesticide exposure, attributable to food and drinking water, and this level is estimated on a per day basis (mg/kg/day) by using averaged estimates of residue, use, and consumption. For trifluralin, homeowner use is highly seasonal (mostly early Spring) and this exposure will likely be acute (one day of golf) or short-term (multiple residential applications). The route of exposure may be oral (children on turf), dermal (at application or post-application), or by inhalation (at application).

Aggregate Short-Term Risk: The aggregate (3 specific exposure scenarios) incidental oral exposure estimate for children on turf is 0.00009 mg/kg/day. When combined with the estimated chronic dietary exposure (0.000051 mg/kg/day) for children 1-2 years old, the sum is 0.00014 mg/kg/day. Compared to the appropriate dose (10 mg/kg/day) for short-term incidental oral risk assessment, this aggregate exposure estimate is much greater than the target MOE of 100, and a conclusion of safety can be made.

Aggregate Carcinogenic Risk: When using the Q_1^* approach to assess a pesticide, the Agency considers all exposure to be additive to aggregate carcinogenic risk, regardless of exposure route or exposure duration (per season). For trifluralin, this means that the chronic exposure from foods (0.000022 mg/kg/day) is added to chronic exposure due to drinking water (0.000008 mg/kg/day), which is added to exposure estimated for residential use. Based on this assumption, carcinogenic risk estimates are made for those applying trifluralin themselves, each season, throughout adulthood (50 years).

As previously noted, the exposure and carcinogenic risk estimates for residential applicators varies significantly depending on the application *method*, even if other inputs (rate and area treated) remain the same. Since carcinogenic risk assessment attempts to reflect long-term exposure, the most appropriate exposure estimate would be based on the most common application method; the push-type spreader. The Lifetime Average Daily Dose estimated for this application method is negligible (0.0000006 mg/kg/day), and when added to the chronic dietary (food and water) exposure the aggregate carcinogenic risk estimate is 2×10^{-7} .

Recommendations

In addition to being classified as a possible human carcinogen trifluralin is also classified as a skin sensitizer. EPA has no method of quantifying risk due to skin sensitization and remains concerned about *dermal sensitization* reactions to adults and children who are exposed to trifluralin in residential settings. Therefore, it is recommended that all products containing trifluralin be labeled as “SENSITIZER” and state that “skin contact should be avoided”.

Tolerance Reassessment

Currently, there are 35 tolerances (majority at 0.05 ppm) established for residues of trifluralin in or on raw agricultural commodities. However, there is no tolerance for trifluralin in or on raw agricultural commodities for mint oil. Available data show that residues of trifluralin in foods prepared with mint oil will not exceed the existing raw agricultural commodity tolerance. As a result, the Agency has made a safety finding that trifluralin is safe as currently used in pesticide products. Therefore, the Agency will be proposing, via a Federal Register (FR) notice, to establish a permanent tolerance of 2.0 ppm for mint oil. Additionally, existing tolerances for residues of trifluralin do not exceed the Agency's risk concern and will be considered reassessed under section 408(q) of the FFDCA.