



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 1 FEBRUARY 2006

SUBJECT: **TRIFLUMIZOLE** - Exposure/Risk Assessment for the FIFRA Section 18 Use of Triflumizole on Leafy Green Vegetables in Texas.

PC Code: 128879 DP Code: 325682

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INTRODUCTION

Under Section 18 of the Federal Insecticide, Fungicide and Rodenticide Act, (FIFRA) as amended, the State of Texas has requested the use of the fungicide triflumizole on leafy green vegetables (to include cilantro, collards, dandelion, kale, kohlrabi, mustard greens, Napa cabbage, parsley and Swiss chard) to control powdery mildew (*Erysiphe polygoni*). The product proposed for use is PROCURE[®] 50 WS Fungicide which is a 50 % by weight, active ingredient, dry powder formulation (EPA Reg. No. 400 - 431). This memorandum serves as HED's estimates of exposure and risk to occupational pesticide handlers and to agricultural workers from the proposed use on leafy green vegetables.

USE PATTERN SUMMARY

Chemically, triflumizole is known as [1-[1-((4-chloro-2-(trifluoromethyl)phenyl)imino)-2-propoxyethyl]-1H-imidazole]. The Section 18 supplemental labeling directs: "Use a minimum

of 20 gallons per acre spray volume for ground applications.” Aerial applications are not precluded on the label but there are no directions for use as an aerial spray. HED assumes only ground applications are intended. It may not be applied through any type of irrigation equipment. The rate of application is 0.1875 lb a.i./A. There is a maximum of 0.375 lb a.i./A/season that may be applied. No more than 2 applications per acre per year are permitted. Repeat applications of triflumizole must have a 10 - 14 day treatment interval. There is a 1 day preharvest interval (PHI). Applications should begin at the first indication of disease.

The request is for use on:

mustard greens	1,800 A
turnip greens	200 A
collards	1,200 A
broccoli	1,000 A
parsley	600 A
dandelion	150 A
Swiss chard	250 A
kohlrabi	300 A
Napa cabbage	150 A
kale	500 A
cilantro	<u>300 A</u>
	6,450 A

At an application rate of 0.1875 lb ai/A, approximately 1,209 lb ai will be required to treat all projected acres one time. Two applications would require approximately 2,418 lb ai.

See Table 1.0 for a summary of the proposed use pattern. The label requires applicators and other handlers to wear long-sleeved shirt, long pants, shoes plus socks and chemical resistant gloves made of any waterproof material.

Table 1.0 Summary of Proposed Section 18 Use of Triflumizole

Crop Site	Leafy green vegetables in Texas
Pest	powdery mildew <i>Erysiphe polygoni</i>
Formulation	PROCURE® 50 WS Fungicide; EPA Reg. No. 400 - 431; 50 % a.i. powder.
Application Method	groundboom
Application Rate	0.1875 lb a.i./A
Application Number	two applications/year
Application Maximum	0.375 lb a.i./A/yr.
Application Interval	10 - 14 days (do not apply more than 2 applications)
Pre-Harvest Interval	1 day
Maximum acres treated	6,450 acres possible
Maximum a.i. used	2,418 lb ai if 6,450 acres are treated two times at 0.1875 lb a.i./A
Manufacturer	Gowan Company

OCCUPATIONAL PESTICIDE HANDLER EXPOSURE

In this case, the most highly exposed occupational pesticide handlers are likely to be a mixer loader using open pour of wettable powder and an applicator using open cab ground boom equipment. Based upon the proposed use pattern, HED believes occupational pesticide handlers (i.e., mixers, loaders, applicators) will be exposed to short-term (1 - 30 days) duration exposures. Intermediate-term exposures (1 - 6 months) are not expected. Treatment blocks are expected to be small in comparison to typical field crops such as corn, wheat, cotton or soybeans. Although multiple applications are possible, they are separated by 10 - 14 days. It is expected that private (i.e., grower) applicators will treat the majority of acres needing treatment.

Private (i.e., grower) applicators may perform all functions, that is, mix, load and apply the material. The HED Science Advisory Council for Exposure (ExpoSAC) Standard Operating Procedure (SOP) Number 12 (29 March 2000) directs that although the same individual may perform all those tasks, they shall be assessed separately. "By separating the two job functions, (i.e., mixing/loading from application) HED determines the most appropriate levels of personal protection equipment (PPE) for each aspect of the job without requiring an applicator to wear unnecessary PPE that may be required for mixer/loaders (e.g., chemical resistant gloves may only be necessary during the pouring of a liquid formulation)."

Chemical specific data were not available with which to assess pesticide handler exposure.

Therefore surrogate data from studies in the Pesticide Handler Exposure Database Version 1.1 (August 1998) PHED SURROGATE EXPOSURE GUIDE were used to estimate mixer/loader and applicator exposure.

It is HED policy to assess handler exposure and risk using "baseline" Personal Protective Equipment (PPE) which is a single layer of work clothing comprised of long-sleeved shirt, long pants, and shoes plus socks and to assess "baseline" **plus the use of protective gloves** or other PPE as might be necessary or appropriate. The PROCURE® 50 WS label directs pesticide handlers to wear a long sleeved shirt, long pants, chemical resistant, water proof gloves and shoes plus socks.

On 7 February 2002 the HED Hazard Identification Assessment Review Committee (HIARC) met to review the adequacy of the toxicological database as it pertains to triflumizole. During that meeting the HIARC identified Short-term (1 - 30 days) exposure duration dermal and inhalation toxicological endpoints. The No Observable Adverse Effects Level (NOAEL) is 8.5 mg a.i./kg bw/day and is based on a rat developmental study. The effects seen were decreased body weight gains in pups during lactation. Therefore, a 60 kg body weight is used in the exposure calculations. The HIARC also identified a dermal absorption factor of 3.5%. Triflumizole is classified as a Group "E" (noncarcinogenic to humans) compound. Since the last HIARC meeting (2/7/2002), the registrant submitted acute rat neurotoxicity study (GLN 870.6200), and subchronic rat neurotoxicity study (GLN 870.6200). The acute and sub-chronic neurotoxicity studies have been reviewed by HED and determined to be acceptable (R. Fricke, TXR# 0052656). As a result the following has changed: 1) selection of an acute endpoint for the general U.S. population (including infants and children); and 2) the removal of the 3x database uncertainty factor (UF_{DB}). A Margin of Exposure (MOE) \geq 100 is adequate to protect pesticide handlers. The Margins of Exposure for inhalation and dermal routes of exposure are combined due to the same toxicological effect (i.e., decreased body weight gain in pups during lactation) being identified from the same multi-generation rat reproduction study. See Table 2.0 for a summary of estimated exposures and risks to occupational pesticide handlers. See the Attachment for a summary of toxicological endpoints used for risk assessment.

Table 2.0 Estimated Handler Exposure and Risk from the Use of Triflumizole on Leafy Green Vegetables					
Unit Exposure ¹ mg a.i./lb handled	Applic. Rate ²	Units Treated ³ Per Day	Average Daily Dose ⁴ mg a.i./kg bw/day	NOAEL ⁵ mg a.i./kg bw/day	MOE ⁶
<i>Mixer/Loader - Wettable Powder - Open-pour</i>					
Dermal: No Glove 3.7 LC With Glove 0.17 MC Inhal. 0.043 MC	0.1875 lb a.i./A	200A	Dermal: No Glove 0.081 W Glove 0.0037 Inhal 0.0269	8.5	No Glove 79 W Glove 278
<i>Applicator - Ground-boom - Open Cab</i>					
Dermal: No Glove 0.014 HC With Glove 0.014 MC Inhal 0.00074 HC	0.1875 lb a.i./A	200 A	Dermal: No Glove 0.00031 W Glove 0.00031 Inhal 0.00046	8.5	No Glove 11,000 W Glove 11,039

- Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing **No Gloves**; Single Layer Work Clothing **With Gloves**; Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.
- Applic. Rate. = Taken from the Texas Section 18 request.
- Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture", SOP No. 9.1. Science Advisory Council for Exposure, Revised 5 July 2000;
- Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated * absorption factor (3.5 % dermal; 100 % inhalation ÷ Body Weight (60 kg since NOAELs are identified from a developmental study with fetal effects).
- NOAEL = No Observable Adverse Effect Level (8.5 mg a.i./kg bw/day for short-term dermal and short-term inhalation)
- MOE = Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. Short-term dermal and short-term inhalation exposures are summed and divided into the NOAEL. The dermal and inhalation endpoints are the same and identified from the same study and have the same NOAELs.

A MOE of 100 is adequate to protect occupational pesticide handlers from short-term exposures to triflumizole. Therefore these exposures do not exceed HED's level of concern.

POST-APPLICATION EXPOSURE TO AGRICULTURAL WORKERS

There is a potential for agricultural workers to experience post-application exposures to pesticides during the course of typical agricultural activities. HED in conjunction with the Agricultural Re-entry Task Force (ARTF) has identified a number of post-application agricultural activities that may occur. HED has also identified Transfer Coefficients (TC) expressed as cm²/hr which describe the amount of foliar dislodgeable pesticide residue that is available to be transferred to agricultural workers during the course of post-application agricultural activities.

There were no chemical specific data with which to estimate post-application exposures of agricultural workers to dislodgeable residues of triflumizole. Therefore, theoretical estimates of

exposure, based on surrogate studies, have been conducted. The ExpoSAC (SOP 003.1, Rev. 7 Aug. 2000, Regarding Agricultural Transfer Coefficients; Amended ExpoSAC Meeting notes - 13 Sept 01) lists a number of possible post-application agricultural activities relative to leafy vegetables that result in pesticide exposure to agricultural workers.

The highest TC identified for collards and leafy green vegetables is 2,500 cm²/hr is for hand harvesting. For this assessment, HED uses the 2,500 cm²/hr TC as a Tier I, screening level figure.

The transfer coefficients used in this assessment are from an interim transfer coefficient procedure developed by HED's ExpoSAC using proprietary data from the Agricultural Re-Entry Task Force (ARTF) database (Standard Operating Procedure # 3.1). It is the intention of HED's ExpoSAC that this procedure will be periodically updated to incorporate additional information about agricultural practices in crops and new data on transfer coefficients. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.

Post-application worker exposure is estimated using HED procedure that assumes 20% of the application rate is available as dislodgeable foliar residue on the day of treatment. HED expects post-application agricultural exposures to scouts (i.e., crop advisors) or workers involved in irrigation would typically be short-term. The total number of acres treated per day is comparatively small and treatment is not expected to be necessary at the same time for all acres on a given farm, therefore scouting after treatment will occur in short-term periods of time.

$PDR_t = DFR_t * CF1 * Tc * ET$ where:

PDR_t = potential dose rate on day "t" (mg/day)

DFR_t = dislodgeable foliar residue on day "t" ($\mu\text{g}/\text{cm}^2$)

$CF1$ = weight unit conversion factor to convert μg units in DFR value to mg for the daily dose (0.001 mg/ μg)

TC = transfer coefficient (cm²/hr) (In this case 2,500 cm²/hr; ExpoSAC SOP 003.1 Rev. 7 Aug. 2000; amended 13 Sept 01 ExpoSAC meeting Notes).

ET = Exposure Time (hrs) (8)

and

$DFR_t = AR * F * (1-D)^t * CF2 * CF3$ where:

AR = Application rate (lb a.i./A) (0.1875 lb a.i./A)

F = fraction of a.i. retained on foliage (unitless)

D = fraction of residue that dissipates daily (unitless)

t = postapplication day on which exposure is being assessed

$CF2$ = weight unit conversion factor to convert the lbs a.i. in the application rate to μg for the

DFR value ($4.54 \times 10^8 \mu\text{g}/\text{lb}$)

CF3 = Area unit conversion factor to convert the surface area units (ft^2) in the application rate to cm^2 for the DFR value ($1.08 \times 10^{-3} \text{ft}^2/\text{cm}^2$ or $2.47 \times 10^{-8} \text{acre}/\text{cm}^2$ if the application rate is per acre).

$$\therefore \text{DFR} = 0.1875 \text{ lb a.i./A} * 0.20 * (1-0)^0 * 4.54 \times 10^8 \mu\text{g a.i./lb} * 2.47 \times 10^{-8} \text{A}/\text{cm}^2 = 0.42 \mu\text{g}/\text{cm}^2$$

$$\text{PDR} = 0.42 \mu\text{g}/\text{cm}^2 * 0.001 \text{ mg}/\mu\text{g} * 2,500 \text{ cm}^2/\text{hr} * 8 \text{ hr}/\text{day} = 8.4 \text{ mg a.i./day} * 3.5 \% \text{ dermal absorption} \div 60 \text{ kg bw} = 0.0049 \text{ mg a.i./kg bw/day}$$

Margin of Exposure (MOE) = NOAEL \div PDR

$$\therefore 8.5 \text{ mg a.i./kg bw/day} \div 0.0049 \text{ mg a.i./kg bw/day} = 1,734.$$

An MOE of 100 is adequate to protect agricultural workers from post-application exposure to triflumizole. The calculated MOEs $>$ 100 therefore this use does not exceed HED's level of concern.

ATTACHMENT

Acute Toxicity of Triflumizole

Guideline No.	Study Type	MRIDs #	Results	Toxicity Category
81-1	Acute Oral	00144463	LD ₅₀ = 1362 mg/kg	III
81-2	Acute Dermal	00144465	LD ₅₀ > 5000 mg/kg	IV
81-3	Acute Inhalation	00144466	LC ₅₀ > 3.2 mg/L	IV
81-4	Primary Eye Irritation	00144467	Slight ocular irritant	III
81-5	Primary Skin Irritation	00144468	Not a dermal irritant	IV
81-6	Dermal Sensitization	00144469	Mild dermal sensitizer	N/A

SUMMARY OF TOXICOLOGY ENDPOINT SELECTION

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary (Gen. Population)	No appropriate endpoint was available to determine the Acute RfD for the general population.		
Acute Dietary (Females 13-50)	NOAEL = 10 UF = 100	Decreased numbers of viable fetuses, increased dead or resorbed fetuses, increased numbers of late resorptions, decreased fetal body weight, and increased incidences of cervical ribs	Developmental Toxicity - Rat
Chronic Dietary	NOAEL = 1.5 UF = 100	Increased gestation length in the dams of the F _{3d} interval	Multi-generation Reproduction Study - Rat

Cancer	No quantification needed	"Group E" - No evidence of carcinogenicity in rats and mice	Combined Chronic Toxicity/Carcinog. Study - Rat Carcinogenicity Study - Mouse
Incidental Oral, Short-Term	NOAEL = 8.5	Decreased body weight gain noted in pups throughout lactation	Multi-generation Reproduction Study - Rat
Incidental Oral, Intermediate-Term	NOAEL = 8.5	Decreased body weight gain in pups during lactation and decreased body weight and body weight gain in parental animals	Multi-generation Reproduction Study - Rat
Dermal, Short-Term ^a	NOAEL = 8.5	Decreased body weight gain in pups during lactation	Multi-generation Reproduction Study - Rat
Dermal, Intermediate-/Long-Term ^a	NOAEL = 1.5	Increased gestation length in the dams of the F _{3a} interval	Multi-generation Reproduction Study - Rat
Inhalation, Short-Term ^b	NOAEL = 8.5	Decreased body weight gain in pups during lactation	Multi-generation Reproduction Study - Rat
Inhalation, Intermediate-/Long-Term ^b	NOAEL = 1.5	Increased gestation length in the dams of the F _{3a} interval	Multi-generation Reproduction Study - Rat

a Since an oral endpoint was selected, a dermal absorption factor of 3.5% should be used in route-to-route extrapolation.

b Since an oral endpoint was selected, an inhalation factor of 100% should be used in route-to-route extrapolation.

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