

CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION
PUBLIC REPORT 2004-4
Pyraflufen-ethyl
Tracking ID Number 201510 N

DESCRIPTION OF ACTION

Nichino America, Inc. submitted an application seeking California registration of ET Herbicide/Defoliant, U.S. EPA Reg. No. 71711-7, for use as a defoliant/desiccant in cotton and potatoes, and to control certain broad-leaf weeds in various agricultural crops. This product contains the new active ingredient pyraflufen-ethyl.

The Department of Pesticide Regulation (DPR) evaluated the product label and scientific data supporting registration of the product and found them acceptable to support a conditional registration. The acute health risks from exposure to pyraflufen-ethyl are potentially significant due primarily to its corrosive nature to the eyes. However, the precautionary and first aid statements on the product label, as well as label directions requiring personal protective equipment (PPE) and other protective measures adequately mitigate the potential health risks to persons who may come in contact with the pesticide. DPR does not expect any significant adverse environmental impacts to result from registration of this product.

The United States Environmental Protection Agency (U.S. EPA) conditionally registered ET Herbicide/Defoliant on April 30, 2004. U.S. EPA is requiring the registrant to submit the following studies within three years or the product's registration will be subject to cancellation: (1) fourteen additional field trials to confirm that measurable residues of pyraflufen-ethyl will not be in wheat grown on treated ground; and (2) a detailed description of the methodology used to quantify residues of pyraflufen-ethyl in wheat.

BACKGROUND

Registrant:	Nichino America, Inc.
Common name:	Pyraflufen-ethyl
Chemical name:	Ethyl 2-chloro-5-(4-chloro-5-difluoromethoxy-1-methyl-pyrazol-3-yl)-4-fluorophenoxyacetate
Brand names:	ET Herbicide/Defoliant
Uses:	Defoliate cotton and potatoes, and control certain broad-leaf weeds in cotton, field corn, soybeans, wheat, and non-crop lands
Pests controlled:	Selected broad-leaf weeds
Type of registration:	Conditional for eighteen months

ET Herbicide/Defoliant is formulated as an emulsifiable concentrate with 0.208 lb. of pyraflufen-ethyl per gallon of product. Pyraflufen-ethyl is a protoporphyrinogen inhibitor that inhibits protoporphyrinogen IX oxidase causing cell membranes to become necrotic and die. Applied as a defoliant in cotton, it increases the production of ethylene and causes leaf abscission. ET Herbicide/Defoliant is applied at 0.5-2 oz. per acre as a pre-plant contact herbicide to control broadleaf weeds in field corn, cotton, soybeans, and

wheat. Post-emergent treatments are allowed in cotton. At non-crop and soil conservation sites, the product can be applied at 0.5-2.75 oz. per acre for weed control. When used as a cotton defoliant, ET Herbicide/Defoliant is applied at 1.5-2.75 oz. per acre. For desiccating potatoes, the product is applied at 2.75-5.5 oz.. The following maximum amounts of ET Herbicide/Defoliant can be applied per acre per crop during one growing season: field corn (2 oz.), cotton (8.5 oz.), potatoes (11 oz.), soybeans (2 oz.), wheat (2 oz.), non-crop areas (5.5 oz.), and soil conservation sites (5.5 oz.).

Applications can be made with ground and aerial application equipment. However, application of the product through any type of irrigation system is prohibited. Label directions prohibit the application of ET Herbicide/Defoliant within seven days of harvesting cotton or potatoes. Rotational crops other than cotton, corn, potatoes, soybeans or wheat cannot be planted within 30 days of a treatment. Livestock are not allowed to graze in any treated areas.

SCIENTIFIC REVIEW

A. Chemistry

1. Product Chemistry: DPR evaluated the submitted chemistry studies for ET Herbicide/Defoliant and summarized the results in the following table.

Table I. Physical and Chemical Properties of ET Herbicide/Defoliant

Properties	Values
Physical state	Light tan solid
Odor	Paraffin odor
Density	1.02 g/cm ³ at 20° C
Partition Coefficient*	Log P _{ow} of 3.49
Solubility (water)*	0.082 mg/L at 20° C
pH in water	7.78 at 22° C
Vapor pressure*	1.6 x 10 ⁻⁸ Pa at 25° C
Stability*	Stable two years at 20° C

* These properties were derived using pure grade pyraflufen-ethyl as the test substance.

DPR found the product chemistry data adequate to support a conditional registration of this product at this time.

2. Residues in Food and Animal Feed: The submitted residue studies support the harvest and use limitations listed on the ET Herbicide/Defoliant label for cotton, field corn, potatoes, soybeans and wheat. The residue levels are well within the tolerances established by the U.S. EPA for cotton, field corn, potatoes, soybeans and wheat. The established tolerances are listed in the following table.

Table II. Tolerances for Residues of Pyraflufen-ethyl

Commodity	Parts per Million
Cotton, undelinted seed	0.04
Cotton gin byproducts	1.50
Field corn (forage, grain, stover)	0.01
Potatoes	0.02
Soybeans (forage, hay, seed)	0.01
Wheat (forage, grain, hay, straw)	0.01

The wheat residue samples were stored for an extended period of time (500+ days). As a result, DPR is requiring the registrant to conduct a storage stability study to quantify the amount of pyraflufen-ethyl residues that may have been lost during storage.

3. Environmental Fate: The environmental fate data reviewed included studies on hydrolysis, photolysis (aqueous and soil), aerobic soil metabolism, anaerobic aquatic metabolism, soil adsorption and desorption, and field soil dissipation. The data indicate that pyraflufen-ethyl is stable in the environment under acidic conditions (pH 5), with an estimated half-life of 267 days. However, the chemical is rapidly hydrolyzed with neutral or alkali conditions with a half-life of 11 days (pH 7) and 6 hrs. (pH 9). Pyraflufen-ethyl is readily degraded by sunlight with a half-life of 1.25 days in water and 2.2 days on soil. With aerobic soil conditions, the half-life of pyraflufen-ethyl was less than one day. Similarly, in water with anaerobic soil conditions the chemical's half-life was also less than one day. Due to its instability, the soil adsorption/desorption of pyraflufen-ethyl was obtained using high pressure liquid chromatography (HPLC). The estimated value was 3.3, indicating the compound has low mobility in the soil. This physical property was evaluated further with a soil column leaching study utilizing radioactively labeled pyraflufen-ethyl. The majority (95%) of the radioactivity remained in the top 10 cm of soil indicating low mobility in soil. Soil dissipation of pyraflufen-ethyl in the field was evaluated in California and Washington. The results indicate pyraflufen-ethyl rapidly dissipates from the soil surface with a half-life of only a few hours.

The data indicate that the use of pyraflufen-ethyl is not likely to pose an unreasonable threat to the environment. The submitted studies were found to be adequate to support a conditional registration of ET Herbicide/Defoliant. This product may be registered, provided the registrant submits the complete study reports for the octanol-water partition coefficient, vapor pressure and the water solubility of pyraflufen-ethyl. The registrant is required to submit this information within six months.

B. Toxicology

DPR reviewed the toxicology studies submitted by Nichino America, Inc. and found them adequate to conduct a complete toxicological evaluation for ET Herbicide/Defoliant. DPR evaluated the data to ascertain the potential for acute adverse health effects from exposure. The acute toxicity parameters are summarized in Table III.

Table III. Acute Toxicity of ET Herbicide/Defoliant

Type of Study	Acute Toxicity Values	Acute Toxicity Category
Acute oral (rats)	>3300 mg/kg (M/F)	III
Acute dermal (rabbits)	>2000 mg/kg (M/F)	III
Acute inhalation (rats)	>2.03 mg/L	IV
Primary eye irritation (rabbits)	N/A	I
Primary dermal irritation (rabbits)	N/A	III
Dermal sensitization (guinea pigs)	N/A	Not a sensitizer
Signal word	N/A	DANGER

N/A-Not applicable.

DPR's evaluation of the acute toxicity studies indicates that exposure to concentrated ET Herbicide/Defoliant can cause irreversible damage to the eyes. The product label bears a warning statement identifying the product as being corrosive to the eyes and the "signal word," DANGER. The precautionary language on the product label adequately identifies all the acute toxicity hazards noted in the studies.

DPR found the submitted toxicology studies sufficient to satisfy the data requirements of the Birth Defects Prevention Act (Food and Agricultural Code section 13121 *et.al.*). Possible adverse health effects were observed in three of the toxicity studies. A combined chronic toxicity and oncogenicity study in rats indicated possible renal pathology. The mouse oncogenicity study noted an increased incidence of hepatocellular adenomas. One of the three gene mutation studies performed observed a possible adverse effect. A neurotoxicity study was not submitted. The Code of Federal Regulations (CFR 40 section 158.340) does not require this study if the compound is not an organophosphate compound, or does not cause cholinesterase depression.

DPR has not yet prioritized pyraflufen-ethyl for risk assessment. DPR prioritizes pesticide active ingredients for risk assessment based on the nature of the potential adverse health effects, number of potential adverse effects, number of species affected, no effect levels (NOELs), potential for human exposure, use patterns and similar factors. Based on these criteria, pesticides with the greatest potential for health problems are placed in high priority, with other chemicals being in moderate or low priority. The purpose of the risk assessment would be to appraise the potential for pyraflufen-ethyl to cause adverse health effects in humans if exposed to the pesticide as the result of a legal use. The potential for exposure from eating food crops treated with pyraflufen-ethyl will also be evaluated during the risk assessment. Further toxicity information is available in DPR's Summary of Toxicology Data for pyraflufen-ethyl, available on DPR public website at: <http://www.cdpr.ca.gov/docs/toxsums/pdfs/5865.pdf>.

C. Health & Safety

An evaluation of the medical management information on the to ET Herbicide/Defoliant label and the acute toxicity study results indicate the product label bears all of the required statements and warnings regarding safety for handlers

and other persons who may be exposed to the pesticide. The product label bears an adequate First Aid Statement. In addition, the product label requires persons handling and applying ET Herbicide/Defoliant to wear long-sleeved shirt and long pants, chemical-resistant gloves, protective eyewear, shoes plus socks and chemical-resistant head gear if overhead exposure can occur. Workers wearing only work clothing are not allowed to enter a treated field until 12 hours after an application. The product label requires that persons entering a treated area before the 12 hour restricted-entry interval (REI) has elapsed, must wear coveralls, chemical-resistant gloves, protective eyewear, and shoes plus socks if they are going to contact treated plants, soil or water.

D. Fish & Wildlife

The registrant submitted fish and wildlife toxicity studies, including studies on bluegill sunfish, honeybees, mallard duck, minnows, Mysid shrimp, northern bobwhite, oysters, rainbow trout, and rats. The submitted data are adequate to characterize the toxicity to wildlife and aquatic animals from an environmental exposure. Table IV summarizes the results of these studies.

Table IV. Summary of Toxicity Studies for Wildlife

Test Animal	Type of Study	Acute Toxicity Value ^a	Relative Toxicity
Rat (male, female)	Single acute oral dose	>5000 mg/kg(LD ₅₀)	Relatively non-toxic
Bluegill sunfish	Water exposure (96 hrs.)	>100 ug/L(LC ₅₀)	Highly toxic
Sheepshead minnow	Water exposure (96 hrs.)	>56 ug/L (LC ₅₀)	Extremely toxic
Rainbow trout	Water exposure (96 hrs.)	>100 ug/L (LC ₅₀)	Highly toxic
Mysid shrimp	Water exposure (96 hrs.)	>60 ug/L (LC ₅₀)	Extremely toxic
Oyster shell	Water exposure (96 hrs.)	>43 ug/L (LE ₅₀)	Highly toxic
Bobwhite quail	Single oral acute dose	>2000 mg/kg (LD ₅₀)	Slightly toxic
Bobwhite quail	Feeding study (5 days)	>5000 mg/kg (LC ₅₀)	Relatively non-toxic
Mallard duck	Feeding study (5 days)	>5000 mg/kg (LC ₅₀)	Relatively non-toxic
Honeybee	48 hr. contact dose	>100 ug/bee (LD ₅₀)	Relatively non-toxic

Values expressed as: 1. LD₅₀= lethal dose that will kill 50% of test population; 2. LC₅₀= lethal environmental concentration that will kill 50% of test population, and 3. EC₅₀. = concentration that caused some effect that can lead to death. The test substance used for the studies was technical pyraflufen-ethyl.

The data indicate pyraflufen-ethyl is relatively non-toxic to vertebrate animals, birds and honeybees, and highly to extremely toxic to aquatic organisms. The label bears adequate precautionary statements regarding the toxicity of the product to aquatic animals. In addition, the environmental fate data indicate that pyraflufen-ethyl is unstable in the environment and degrades rapidly. The water solubility is low with a very low vapor pressure indicating that movement of the chemical off-site should be minimal. The use of ET Herbicide/Defoliant in production agricultural sites is not expected to pose a threat to wildlife when used in accordance with label directions.

E. Efficacy

The submitted field studies were limited, but adequate to demonstrate the ability of ET Herbicide/Defoliant to control some of the weeds listed on the label. However, additional efficacy data are needed to support the use of the product on the full spectrum of weeds listed on the product label. The submitted data supports the label uses for defoliating cotton and desiccating potatoes. With regard to phytotoxicity, additional data are also needed to support label directions which indicate that buffer zones are not needed to protect sensitive crops from drift from aerial applications. The submitted data are adequate to support an eighteen month conditional registration in California.

ALTERNATIVES

ET Herbicide/Defoliant is a contact herbicide and is active on a wide range of broad-leaf weeds. With a maximum use rate of 2.75 oz. of product per acre, ET Herbicide/Defoliant can provide weed control at planting at much lower use rates than most conventional contact herbicides. Similarly, for use as a cotton defoliant and a potato desiccant, the application rates for ET Herbicide/Defoliant are much lower than currently registered products. Overall, its use can help to reduce the amount of herbicide needed for weed control in the labeled crops. Pyraflufen-ethyl also has the ability to control some weeds that have developed resistance to herbicides that are active as acetolactate synthase (ALS) inhibitors.

CONCLUSION

DPR evaluated the product label and scientific data submitted to support ET Herbicide/Defoliant and found them acceptable to support an eighteen month conditional registration. Although the acute health risks from exposure to pyraflufen-ethyl are potentially significant (corrosive to the eyes), the precautionary and first aid statements on the product label, as well as label directions requiring PPE and other protective measures, adequately protect persons who may be exposed to the pesticide. If, after a risk assessment, DPR determines that exposure to pyraflufen-ethyl may result in unacceptable margins of exposure, further restrictions will be placed on the use of pyraflufen-ethyl at that time. The submitted data also indicate significant adverse environmental impacts are not expected to occur from the use of ET Herbicide/Defoliant. When used in accordance with label directions, this product should be effective for the intended use.

DPR is proposing an eighteen month conditional registration of ET Herbicide/Defoliant. The registrant is required to conduct and/or submit the results of the following studies: (1) additional efficacy studies to support claims for control of the full spectrum of weeds listed on the label; (2) field phytotoxicity studies using sensitive crops to support the absence on the label of aerial application buffer zones for sensitive crops; (3) the complete octanol-water partition coefficient, vapor pressure and the water solubility studies; and (4) an extended storage stability wheat study.