

New York State Department of Environmental Conservation

Division of Solid & Hazardous Materials

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Alexander B. Grannis
Commissioner

April 17, 2009

CERTIFIED MAIL **RETURN RECEIPT REQUESTED**

Ms. Marie Maks
Senior Manager, Regulatory Affairs
Nichino America, Inc.
4550 New Linden Hill Road, Suite 501
Wilmington, Delaware 19808

Dear Ms. Maks:

Re: Registration of a Major Change in Labeled (MCL) Use Pattern for Fenpyroximate (Chemical Code 129131) as Contained in the Pesticide Product Portal (EPA Reg. No. 71711-19)

The New York State Department of Environmental Conservation (Department) has reviewed your application, received August 28, 2008, and additional information received November 6, 2008, to register the new pesticide product Portal (EPA Reg. No. 71711-19) in New York State.

This product contains the active ingredient fenpyroximate which is currently registered in New York State for the control of spider mites on greenhouse and indoor ornamental, floral and foliage crops. Portal is labeled for the control of leafhoppers, mealybugs, mites, and psylla on pome fruit, citrus, cotton, nonbearing deciduous fruit and nut trees, vines, and tree nuts. The additional proposed use of fenpyroximate on food crops and cotton represents a major change in labeled use pattern for this active ingredient in New York State.

The New York State Department of Health (DOH), the Department's Bureau of Habitat (BOH) and the Department's groundwater staff reviewed the application and supporting data submitted by Nichino America, Inc., to register the pesticide products Portal (EPA Reg. No. 71711-19) in New York State.

Toxicological Risk Assessment:

DOH previously reviewed fenpyroximate in the pesticide products Akari 5SC Miticide/Insecticide, and Fujimite 5EC Miticide/Insecticide. The formulated product Portal (which is identical in formulation to FujiMite 5EC Miticide/Insecticide) was not very toxic in acute oral, dermal or inhalation exposure studies in laboratory animals. It, however, was moderately to severely irritating to the skin and eyes (tested on rabbits), but was not a skin sensitizer (tested on guinea pigs).

Fenpyroximate caused some health effects in laboratory animal studies. This compound was moderately toxic by the oral and inhalation routes of exposure and slightly toxic by the dermal route of exposure in acute toxicity laboratory animal studies. Fenpyroximate was not irritating to the skin or eyes (tested on rabbits). It was a slight to moderate skin sensitizer (tested on guinea pigs) by one test method, but was not a sensitizer by another test method. Fenpyroximate caused some effects in subchronic and chronic toxicity studies, and also caused some developmental effects. It was not oncogenic or genotoxic and consequently was classified by the United States Environmental Protection Agency (USEPA) as “not likely to be a human carcinogen.” The USEPA Office of Pesticide Programs established an oral reference dose (RfD) for fenpyroximate of 0.01 milligrams per kilogram body weight per day (mg/kg/day) based on a no-observed-effect level (NOEL) of 0.97 mg/kg/day from a chronic feeding/oncogenicity study in rats (decreased body weight) and an uncertainty factor of 100.

A current search of the toxicological literature did not find any significant new information on the toxicity of fenpyroximate in laboratory animals or humans. However, some scientific articles mention fenpyroximate as being one of the many naturally occurring and commercial chemicals that can inhibit Complex I of the mammalian electronic transfer chain. There is some evidence to suggest that Complex I may have a role in Parkinson's disease and other neurodegenerative disorders. DOH did not locate any direct evidence that fenpyroximate can cause such neurological disorders, and toxicological studies conducted in laboratory animals have not identified neurotoxicological effects following subchronic or chronic exposures. Thus, the relevance, if any, of fenpyroximate's reported inhibitory potential on Complex I and the use of this compound on crops is not known.

The USEPA established tolerances for fenpyroximate residues in or on a number of crops including pome fruit at 0.4 parts per million (ppm) and grapes at 1.0 ppm. The chronic population adjusted dose (cPAD) for fenpyroximate residues is 0.01 mg/kg/day and has the same basis as the RfD. The USEPA estimated that chronic dietary exposure to these residues from all food crops for which there are tolerances and from water would be 9.8% of the cPAD for the general U.S. population, 20% for all infants less than one year old, and 34% for children one to two years old. This chronic exposure analysis is based on the conservative assumptions that 100% of the currently registered crops are treated and contain tolerance level residues.

The USEPA conducted an occupational risk assessment for dermal and inhalation exposures to fenpyroximate. For determining margins of exposure (MOEs) for workers handling fenpyroximate at the maximum labeled application rate of 0.2 pounds per acre, the USEPA compared estimated short-term and intermediate-term dermal exposures to a NOEL of 300 mg/kg/day from a 21-day dermal toxicity study in rabbits (reduced body weights and body weight gain, increased absolute liver weights). Short-term inhalation exposures were compared to a NOEL of 2 mg/kg/day from a rat multigeneration reproduction study (parental decreases in body weight gain). For mixer/loaders, MOEs were 23,000 and 2,950 for short-term dermal and inhalation exposures, respectively. For applicators applying by air-blast sprayer, MOEs were 11,000 and 3,900 for dermal and inhalation exposures. For these estimates, it was assumed that workers wore long-sleeved shirt, long pants, shoes plus socks and chemical-resistant gloves as required by the Portal label. The MOE for post-application occupational exposure from agricultural activities such as hand thinning fruit was estimated to be 2,000. The USEPA

considers MOEs of 100-fold or greater to provide adequate worker protection from fenpyroximate exposures.

There are no chemical specific federal or New York State drinking water/groundwater standards for fenpyroximate. Based on its chemical structure, fenpyroximate falls under the 50 microgram per liter New York State drinking water standard for “unspecified organic contaminants” (10 NYCRR Part 5, Public Water Systems).

The available information on fenpyroximate and the Portal product indicates that overall neither the active ingredient nor the formulated product was very acutely toxic in laboratory animal studies. Furthermore, fenpyroximate was not carcinogenic in rats or mice. The Portal product, however, has moderate to severe eye and skin irritating properties. To mitigate these adverse effects to the eye and skin (as well as systemic effects), the product label requires that applicators and other handlers must wear personal protective equipment which includes protective eyewear, long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves and for overhead use, chemical-resistant headgear. Mixer/loaders and those cleaning equipment must wear a chemical-resistant apron. In addition, the label has the precautionary statement: “Causes substantial but temporary eye injury.” Although data from subchronic/chronic and developmental/reproductive studies showed that fenpyroximate has the potential to cause some toxicity, the expected exposures from the labeled use of this active ingredient in the Portal product should not pose a significant risk to workers or the general public. Given the above, DOH does not object to the registration of Portal in New York State.

Environmental Fate Risk Assessment:

Portal is a contact miticide labeled for control of leafhoppers, mealybugs, mites and psylla on pome fruit, citrus, cotton, nonbearing deciduous fruit and nut trees, and vines and tree nuts. It is to be used in rotation with other products to provide resistance management. Portal contains 5% by weight fenpyroximate (0.4 lb ai/gallon). The maximum application rate is 0.2 lb ai/a/season. The inerts do not appear to be solvent carriers.

Transformation products:

M1 - [tert-)utyl (Z) - α -(1,3-dimethyl-5-phenoxy-pyrazol-4-yl)methyleneamino-oxy-p-toluate]
M3 - [(E)-4-((1,3-dimethyl-5-phenoxy-pyrazole-4-yl)-methyleneamino-oxymethyl)benzoic acid]
M8 - [1,3-dimethyl-5-phenoxy-pyrazole-4-carboxylic acid]
M11 - (1,3-dimethyl-5-phenoxy-pyrazole-4-carbonitrile)
M16 - α -hydroxy-p-toluic acid

Technical Review

Hydrolysis: USEPA found this study acceptable. Fenpyroximate had half-lives of 180, 226 and 221 days, pHs 5, 7, and 9, respectively.

Solubility: Fenpyroximate has a solubility of 14.7 ppb.

Aqueous Photolysis: USEPA found this study acceptable (MRID 44781016). Aqueous photolysis is a major degradative pathway. The half-life is very short at 1.5 hours. Two major transformation products were found, M-1 and M-11, at 59.8% and 22.2% respectively. M-1 then degraded with a half-life of 12.7 hours.

Soil Photolysis: In an acceptable study (MRID 45649705) in a sandy loam soil, in both ring-labeled studies the half-life was 24 days with one major degradate M-1. The half-life of the parent and the M-1 isomer was 109 days in the [pyrazole-3-14C] fenpyroximate labeled study and 76 days in the [benzyl-14C] fenpyroximate labeled study.

Anaerobic Soil Metabolism: USEPA found this study acceptable (MRID 45649707). In the pyrazole-labeled ring using a sandy loam flooded with irrigation water, the half-life in the soil and in the soil:water system was 39 days. The half-life of metabolite M3 in the soil:water system was 214 days. Major transformation products included M3, M8, M11, M16. In the benzyl-labeled ring, the half-life in water was not determined. The half-life in the entire system was 32 days. The half-life of M3 was not calculated. Major transformation products included M3 and M16.

Aerobic Soil/Water Metabolism: In a study that USEPA found acceptable (MRID 45734202), the half-life in a river water:sandy loam sediment system was 33.3 days in the entire system, 2.6 days in the water and 38.1 days in the soil. Major transformation products were M8 and M11. In a pond water:silt loam sediment system, the half-life in the entire system was 19.9 days, 2.8 days in pond water and 20.8 days in the sediment. Major transformation products were M8 and M11.

Aerobic Soil Metabolism: (MRID 46158501) USEPA found this study supplemental and scientifically valid, and together with the other submitted studies (MRIDs 44781017 and 44847910), it fulfilled the Subdivision N guidelines. The half-life of fenpyroximate parent was 77 and 93 days in the pyrazole and benzyl labeled rings in a sandy loam soil (pH 8.6 %OM 0.8). Major degradates M-3 at 15.1% and M-8 at 12.1% were found. Aerobic Soil Metabolism of M3: As calculated from MRID 46158501, the half-life is 160 days. Aerobic Soil Metabolism of M8: As calculated from MRID 46158501, the half-life is 111 days. The pH of the sandy loam soil is quite high when compared with the pH and percent organic carbon of Riverhead type soils (loamy sand soil, 5.0 to 5.5, %OC <1.0). However, these are the only values provided with the application.

Adsorption/Desorption: In an unacceptable study (MRID 44847911), the soils were autoclaved to sterilize them, and this is not an acceptable procedure. However, the adsorption Kocs of the soils were 40,000, 50,000, 40,000 and 44,000 for sand, sandy loam, clay loam and loam, respectively. The desorption Kocs were 37,000, 44,000, 64,000 and 37,000 for sand, sandy loam, clay loam and loam, respectively. Sterilization has been shown to alter the physical and chemical properties of the soil that affect the adsorption and desorption of chemicals, but with

Kocs ranging from 37,000 to 64,000, even a significantly lower Koc would still have the chemical in the immobile range.

In a second study (MRID 45649709) which USEPA found supplemental, the adsorption Kocs were 41,429, 18,600, 58,333, 44,302 and 7,545 in a silt loam, loamy sand, loamy sand, clay loam and sand soil, respectively. The desorption Kocs were 82,429, 44,600, 114,000, 126,226, and 11,091 in a silt loam, loamy sand, loamy sand, clay loam and sand soil, respectively. The test substance was unstable; however, since the results were similar to the study in MRID 4487911, the USEPA considers the 163-1 requirement satisfied.

Adsorption/Desorption of M3: In an acceptable study (MRID 45649708), the adsorption Kocs were 764, 610, 440, 1308, and 124 in silt loam, loamy sand, loamy sand, clay loam and sand soils, respectively. The desorption Kocs were 353, 692, 1914, 171, and 51 in silt loam, loamy sand, loamy sand, clay loam and sand soils, respectively. M3 was not observed to leach in the field.

Adsorption/Desorption of M8: In a study from the registrant completed July 30, 2008, the Kocs were 10, 169, 66 and 102 in a sandy clay loam, a sand, a sandy loam and a clay loam.

Aged Leaching: Three aged leaching studies were submitted (MRIDs 44781018, 44781019, and 44781020). All three studies were unacceptable and did not meet Subdivision N Guidelines 163-1 for several reasons. No mobility data were presented in the summary. The Notice of Registration, dated September 27, 2000, indicated that this study had to be provided by September 27, 2003 [3 years].

Terrestrial Field Dissipation: According to the June 7, 2004 letter from the USEPA to Nichino America, Inc., the status of the terrestrial field dissipation data requirement depends on the results of a well conducted aerobic soil metabolism study that contains both adequate material balance and complete metabolite balance. Then the terrestrial field dissipation data requirement may be considered satisfied.

Drinking Water: According to the DOH, there are no chemical specific federal or State drinking water/groundwater standards for fenpyroximate. Based on its chemical structures, fenpyroximate falls under the 50 microgram per liter ($\mu\text{g/L}$) New York State drinking water standard for "unspecified organic contaminants" (10 NYCRR Part 5, Public Water Systems).

Computer Modeling: Modeling was run on fenpyroximate using Riverhead soil, a Koc of 37,000, a half-life of 93 days and an application rate of 0.2 lb ai/a/yr. The modeling projected no leachate.

Running degredate M3 using a Koc of 610, a half-life of 160 days and an application rate of 15.1% of 0.2 lb ai/a/yr, the model projected peaks of up to 0.005 ppb. Running degredate M8 using a Koc of 66, a half-life of 111 days and an application rate of 12.1% of 0.2 lb ai/a/yr, the model projected cyclic peaks of up to 0.75 ppb.

Label Language: "This chemical can contaminate surface water through spray applications.

Under some conditions, it may also have a high potential for runoff into surface water after application. These include poorly drained or wet soils with readily visible slopes toward adjacent surface waters, frequently flooded areas, areas overlaying extremely shallow groundwater, areas with in-field canals or ditches that drain to surface water, areas not separated from adjacent surface waters with vegetated filter strips, and areas over-laying tile drainage systems that drain to surface waters.”

E-fate Summary: Based on the high K_{oc} and low application rate of the parent, as well as the K_{ocs} and half-lives of the degradates, it does not appear that this product will significantly impact groundwater when used as labeled. Therefore, groundwater staff does not object to the registration of this product as labeled.

Ecological Risk Assessment:

All toxicity, use, chemical, and environmental fate information contained herein was obtained from the fenpyroximate data package submitted by Nichino America, Inc.

Use Profile: Portal is labeled for control of leafhoppers, mealybugs, pear psylla, and mites on pome fruits, cotton, grapes, and nonbearing fruit and nut trees and vines. These are the first outdoor uses for products containing this active ingredient (ai).

Applications of 1 to 2 pints Portal per acre, 0.05-0.1 lbs. ai/acre, are made to all labeled crops using water as the carrier. Two applications may be made per season as long as no more than 2 pints of formulation are applied per acre per season.

Although 2 applications per season are allowed, the Resistance Management section of the label recommends that for best results no more than one application of Portal should be used per season. It also states that Portal must not be used in sequential applications but rather be rotated with products that have a different mode of action.

Portal may not be applied aerially or through any type of irrigation equipment. It may not be applied within 75 feet of any aquatic area or be used on cotton east of the Mississippi River. The label includes extensive instructions on spray drift management. Portal may not be applied within 14 days of harvest on any crop.

Chemical Description & Mode of Action: Portal is 5% fenpyroximate, *Tert*-butyl(E)-a-(1,3-dimethyl-5-phenoxy-pyrazol-4-ylmethyleneaminoxy)-p-toluate, a substituted pyrazole contact acaricide/insecticide.

Fenpyroximate has a relatively low water solubility of 23.1 ug/L at pH 7.0. Its octanol/water partition coefficient, K_{OW}, is 102,330, log K_{OW} = 5.01, indicating a potential to bioaccumulate. No acceptable fish bioaccumulation study was submitted. With its low vapor pressure, 5.6x10⁻⁸ mmHg, post-application volatilization will not be a significant route of fenpyroximate dissipation. Soil organic carbon partitioning coefficients, K_{OC}, for 9 soils ranged from 7,545-58,333 mL/g with a geometric mean of 33,460 mL/g, indicating low or no potential for mobility in soil following application.

Fenpyroximate inhibits mitochondrial electron transport at the NADH-CoQ reductase site, disrupting ATP formation.

Toxicity & Environmental Fate: Fenpyroximate is moderately toxic to mammals on an acute basis. Long-term exposure can result in chronic toxicity. It is practically nontoxic to birds on an acute basis but can produce chronic toxicity at residue levels only slightly higher than those expected on food items when Portal is applied as labeled. It is very highly toxic to all vertebrate and invertebrate aquatic organisms for which study results were submitted. Only one (mysid shrimp) of the required marine/estuarine species toxicity studies was submitted. The results of that study were nearly identical to the freshwater Daphnid results. Marine/estuarine species are assumed to be at least as sensitive to fenpyroximate as freshwater species. Fenpyroximate appears to be selectively toxic to several mite taxa and homopteran insects, it is practically nontoxic to honey bees. Acute contact toxicity studies were submitted for 5 beneficial arthropod taxa including predatory mites, lacewings, ladybugs, and predacious thrips. Fenpyroximate did not affect the test species when exposed directly to recommended application concentrations.

Fenpyroximate degrades readily following application. Dissipation will be primarily via microbial metabolism. It is resistant to hydrolysis, half-lives, $T_{1/2}$ s, in pH 5, 7, and 9 aqueous buffer solutions were 180, 226, and 221 days, respectively. Its aqueous photolysis $T_{1/2}$ is roughly 1.5 hours, the soil surface rate is much slower with a $T_{1/2}$ of 24 days. Laboratory aerobic soil metabolism $T_{1/2}$ s ranged from 35-161 days with a mean of 60 days. Fenpyroximate degrades rapidly in the water column, $T_{1/2}$ 2.6 days in river water and 2.8 days in pond water, but more slowly in sediments $T_{1/2}$ 21-38 days. It degrades more slowly under anaerobic conditions. A water/sediment system laboratory study yielded system $T_{1/2}$ s of 32-39 days. Terrestrial field dissipation studies showed a bi-phasic pattern of residue decline with a rapid initial phase and a slower secondary decline. Initial $T_{1/2}$ s calculated using data from day 0 to day 3 and 7 were 3.4 and 2.8 days, respectively. Degradation slowed thereafter, subsequent $T_{1/2}$ s ranged from 14-31 days. In 4 German soils, DT_{50} s (time to 50% dissipation) were 1, 10, 12, and 24 days, corresponding DT_{90} s were 6, 27, 32, and 48 days. In the studies conducted in U.S. soils, all of the applied material remained in the top 6 inches of the study plot soil. In 3 of the 4 German soils, all the applied material stayed within the top 4 inches of soil. At the last location, the parent compound was detected once each at depths of 4-8 inches and 8-16 inches.

Exposure & Risk Assessment: Screening level modeling was conducted to estimate nontarget organism exposure through terrestrial food item residues and surface water concentrations.

At the maximum application rate, terrestrial food item residue levels are below all mammalian toxicity thresholds. No avian acute thresholds were exceeded. At Upper Limit residue concentrations, the highest possible immediately following application, the avian reproductive NOEL was exceeded on the 4 food groups with the highest expected concentrations.

When more typical, or average, residue levels are used, only the 2 highest concentrations exceed the NOEL.

PONDTOX lists the results of modeling that estimates surface water concentrations resulting from precipitation runoff from treated areas. The 0.25%, 0.5%, and 1.0% runoff rates are based on fenpyroximate's K_{OW} . Given the limited mobility exhibited in field dissipation and laboratory mobility studies, the lower 2 rates are likely more representative of fenpyroximate mobility under actual use conditions. At those rates, using standard pome fruit cultural parameters of 60% target plant interception and 60% of runoff reaching the model pond, there are several instances of aquatic toxicity NOECs being exceeded. The fish chronic LOEC threshold is also exceeded at the higher of the 2 rates in the shallowest water depth considered. Due to fenpyroximate's relatively rapid dissipation rate, a runoff event would have to occur shortly following application to achieve these concentrations. Should this occur, it would be of brief duration due to this ai's short water column residence times.

Conclusion:

The Department concludes that Portal (EPA Reg. No. 71711-19) should not pose a significant risk to workers or the general public, the fish and wildlife resources, or to the ground and surface water of New York State when used as labeled. Therefore, the Department hereby accepts this product for general use registration in New York State.

Enclosed for your files is a copy of the New York State stamped "ACCEPTED" label and Certificate of Pesticide Registration for Portal (EPA Reg. No. 71711-19).

Nichino America, Inc., is reminded that if New York State registration is requested for this product or for any other product which contains an increased application rate and/or expanded use sites for fenpyroximate, the application will be considered a Major Change in Labeling and the Department will require an extensive review.

If you have any questions, please contact Cyndi Crowley, of our Pesticide Product Registration Section, at (518) 402-8768.

Sincerely,

Maureen P. Serafini

Maureen P. Serafini
Director

Bureau of Pesticides Management

Enclosures

ecc: w/enc. - A. Grey/E. Horn, NYSDOH
R. Mungari, NYS Dept. of Ag. & Markets
W. Smith, Cornell University, PMEP