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

MAR 10 1994

MEMORANDUM

SUBJECT: Registration for Imidacloprid (NTN 33893)

..... DECISION MEMORANDUM .....

FROM: Stephen L. Johnson, Acting Director
Registration Division (7505C)

TO: Douglas D. Campt, Director
Office of Pesticide Program (7501C)

BACKGROUND

On March 25, 1992, Miles Inc. applied for registration of six pesticide products that contained the new active chemical Imidacloprid, 1-[(6-Chloro-3-pyridinyl) methyl)]-N-nitro-2-imidazolidinimine, (common name NTN 33893). The products were assigned the following EPA File Symbols.

Product Name	Propose Use	EPA File Symbol
NTN 33893 Technical 94%	Manufacturing Use Only	3125-URU
NTN 33893 Concentrate 75%	Formulating Use	3125-URL
MERIT 21.4% Flowable	Turfgrass and Ornamentals	3125-URI
MERIT 2.5% Granular	Ornamentals	3125-URT
MERIT 0.62% Granular	Ornamentals	3125-URA
MERIT 75%WP	Turfgrass and Ornamentals	3125-URE

An FR-Notice announcing receipt of the applications to register products containing the new active was published in the Federal Register on July 15, 1992. No comments were received with respect to this notice.

USE PATTERN AND PRODUCT LIMITATIONS

Imidacloprid is a systemic insecticide and the first of its chemical class, nitroguanidines. It exhibits a new mode of action. Imidacloprid attacks the cholinergic receptors of the insect's nervous system by competing with acetylcholine for available receptor sites, thereby rendering acetylcholine dysfunctional. Imidacloprid is to be applied to ornamentals and turfgrass such as home lawns, business and office complexes, golf courses, airports, cemeteries, parks, playgrounds, and athletic fields for the control of soil inhabiting pests. Application to turfgrass is by foliar spray only and cannot exceed a total of 0.4 lb of active ingredient per acre per year. Applications to ornamentals can be made by foliar application; soil applications such as soil injections, soil drenches and broadcast application. For outdoor ornamentals, broadcast application cannot exceed a total of 0.4 lb of active ingredient per acre per year.

SUMMARY AND STATUS OF DATA REQUIREMENTS

Agency reviews of product chemistry, toxicology, environmental fate and ecological effects have been completed. The available data support the conditional registration of Imidacloprid for the use-pattern discussed above. Data gaps exist in Toxicology for acute and subchronic neurotoxicity studies, Ecological Effects for a waterfowl reproduction monitoring study and Environmental Fate for validated analytical methods for the determination of Imidacloprid degradates of toxicological concern in ground and surface water samples.

The attached Data Tables list the data requirements for the disciplines of toxicology, environmental fate and ecological effects, for the proposed non-food uses, per 40 CFR 158. These tables also indicate whether or not the data requirements have been fulfilled.

Scientific Findings

I. Product Chemistry

Product chemistry data: product identity/composition, analysis/composition, analysis/certification of ingredients and physical/chemical characteristics have been reviewed and are acceptable.

II. Toxicology

The Toxicology Branch has concluded that the data submitted are adequate for the registration of these products for non-food uses.

The following acute studies required for the proposed products for use on turfgrass and ornamentals were reviewed and determined to be acceptable: Acute oral toxicity (rats), acute dermal toxicity, acute inhalation toxicity, primary eye irritation, primary dermal irritation and dermal sensitization. The primary eye irritation study indicated that NTN was not an ocular irritant. Based on these studies, the appropriate signal word is "CAUTION" (toxicity category III) for the proposed end use products.

The following acute studies required for the proposed Technical NTN 33893 formulation, were reviewed and determined to be adequate: Acute oral toxicity, acute dermal, acute inhalation, primary eye irritation, primary dermal irritation and dermal sensitization. Based on these studies, the appropriate signal word is "WARNING" (toxicity category II) based on acute oral LD_{50} mg/kg.

There were no teratogenic effects observed in the developmental toxicity studies with rats and rabbits. Embryotoxic effects were observed only at high, maternally toxic doses. In the reproduction study, reproductive effects were observed only at levels also otherwise toxic to animals.

Extensive mutagenicity studies investigating point and gene mutations, DNA damage chromosomal aberration, both using in vitro and in vivo test systems, showed NTN 33893 to be non-genotoxic.

In chronic toxicity/carcinogenicity studies no carcinogenic potential was observed at any dose, including some doses which exceeded the maximum tolerated dose. For chronic toxicity, the appropriate NOEL was 100 ppm (rat chronic study). Use of this NOEL with a 100-fold uncertainty factor yields a reference dose (or ADI) of 0.057 mg/kg weight per day.

Although there currently is no indication that NTN 33893 causes adverse effects to the nervous system, testing for neurotoxic effects is required in light of the chemical's mode of action. An acute neurotoxicity study as well as a 90-day neurotoxicity study are required. Both studies are in progress and expected to be submitted in March and June, 1994, respectively.

III. Environmental Fate Review

The environmental fate data are adequate to support the conditional registration of Imidacloprid non-food uses. The results of these studies are listed below:

Hydrolysis data indicate NTN 33893 is stable at pH 5 and 7, and showed some degradation at pH 9, $t_{1/2}$= 355 days.

Photodegradation in water - half-life of 1 hour in sterile aqueous buffer solutions (pH 7) that were continuously irradiated with an artificial light source (xenon lamp).

Photodegradation in soil - half-life 39 days (171 hours, theoretical half-life under natural sunlight) on sandy loam soil that was continuously irradiated with a UV-filter xenon light source for 15 days at 25 $\pm$ 2 C.

Aerobic soil metabolism - calculated half-life of > 1 year in sandy loam soil that was incubated in the dark at 22 $\pm$ 2°C and 75% of the 0.33 bar moisture. CO_2 was the major degradate.

Anaerobic Aquatic - half-life of 27 days in anaerobic silt loam sediment that was incubated in the dark at 22 $\pm$ 1 C for 1 year.

Leaching and adsorption/desorption - $K_{d(ads)}$ values ranged from 1.17 - 3.59. Sandy loam soil: 49% of applied was found in the aged sandy loam layer, 37% in the 0.5 cm layer, 11% in the 5-10 cm layer, 4.2% in the 10-15 cm layer, 1.8% was found in the 15-20 cm layer, 0.3% in the 20-30 cm layer, 0.14% was found in the leachate. The CO_2 level was 1.7% of applied after 30 days.

The bioccumulation study in fish is waived due to low octanol/water partition coefficient. The octanol/water partition coefficient for NTN 33893 is 3.7.

Based on the low vapor pressure of parent NTN 33893, volatilization from soils will not be an important dissipation mechanism. The low octanol/water coefficient suggests that parent NTN 33893 will have a low tendency to accumulate in fish.

In summary, EFGWB is concerned about surface water and ground water contamination because NTN has high water solubility and is persistent and moderately mobile based on Kd values. These are characteristics common to other pesticides that have been detected in groundwater. Repeated applications could cause saturation of soil sites thereby increasing desorption rates of future application of this chemical increasing its potential for ground water contamination. Also, if a heavy rainfall occurred following an application to a sandy soil with low organic matter content and the compound moved to an area below that of anaerobic microbial degradation, the resistance of NTN to hydrolysis coupled with its mobility could cause ground water contamination. Our concerns are based on the results of laboratory studies, the field dissipation studies are ambiguous.

Because of the concern about the persistence and mobility of NTN and the possiblity for ground water contamination, EFGWB initially concluded that two long term field dissipation studies

were needed. However, the need for these studies has since been reevaluated with the determination that the studies would probably only provide information that would confirm that NTN is both persistent and mobile, which we already know. We have therefore determined that the long term field dissipation studies are no longer needed.

The potential for NTN to contaminate ground water is still a concern. However, for the turf and ornamental uses we believe that a ground water advisory statement is sufficient to address our ground water concerns because of the limited uses, limited number of applications and low application rate. We have discussed with the registrant the limited information we believe the long term field dissipation studies will provide and requested that they consider starting a small scale prospective ground water study to support the pending food uses. At a meeting held in January 1994, Miles stated that they have started the long term field dissipation studies and will continue that work although it may be somewhat modified now because these studies are no longer required by the Agency. Miles also stated they would be willing to conduct a ground water study but first would like us to review a recently completed lysimeter study conducted in Germany before they initiate a ground water study. A lysimeter study is a modified field study that analyzes soil pore water similar to a ground water study. We have agreed to review the lysimeter study and provide feedback as to the need for a ground water study. Although we are concerned that based on lab studies NTN has potential to contaminate ground water, we do not believe as discussed above that ground water study is required to support the turf and ornamental uses.

The Agency proposed criteria for classifying pesticides for Restricted Use due to ground water concerns as a proposed rule in December 1991. The Agency published two options for public consideration and comment. One set of criteria included the measured persistence and mobility of an ingredient of a pesticide product and the detection of the ingredient in ground water in at least three different counties at levels greater than 10 percent of the Maximum Contaminant Level (MCL) or lifetime Health Advisory established under the Safe Drinking Water Act, or in 25 or more wells in 4 or more states. Under this option we also stated that we would use the persistence and mobility criteria to decide whether to classify a new chemical for restricted use without waiting for it to reach ground water. Based on laboratory studies NTN triggers the persistence and mobility criteria and would be a candidate for Restricted Use Classification.

We are not recommending that the turf and ornamental products be classified as Restricted Use products due to ground water concerns for several reasons. First, several of the proposed NTN products contain directions for use around the home and a Restricted Use Classification would not allow sale of these

products to the homeowner. Second, professional lawn care companies will be users of these products and they will not use a Restricted Use product. Third, when compared to other active ingredients registered for use on turf and ornamentals, such as diazinon and chlorpyrifos, NTN is used at a greatly reduced rate. For example, the turf recommendation for chlorpyrifos calls for 2 to 4 lbs/ai/A. The NTN rate is 0.4 lbs/ai/A. Fourth, NTN will reduce the need for multiple foliar application thereby decreasing the pesticide load in the environment. Finally, NTN is expected to replace currently used turf insecticides such as chlorpyrifos and diazinon and therefore likely represent significantly less toxicological and environmental risk than its alternatives.

Since the Agency is concerned about the persistence of NTN and the possible ground water contamination the following labeling ground water advisory statement is required:

"This chemical demonstrates the properties and characteristics associated with chemicals detected in ground water. The use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in ground water contamination." We are also requiring Miles to submit for EPA approval validated analytical methods for the determination of imidacloprid and degradates of toxicological concern in ground and surface water samples as a condition of registration. At present the Agency is not aware of any degradates of toxicology concern. These analytical method will be made available to any State Pesticide Lead Agency for inclusion in monitoring programs.

IV Ecological Effects

The data submitted are adequate to support the conditional registration of Imidacloprid non-food uses. The results of these studies are listed below:

Acute oral LD_{50} Bobwhite quail was determined to be 152.3 mg/kg. Dietary LC_{50} Bobwhite quail was determined to be 1535.787 ppm, based on these values NTN is classified as slightly toxic to Bobwhite quail.

Acute oral LD_{50} House sparrow is 41.0 mg a.i./kg based on NTN granular, the NOEC is 3.0 mg a.i./kg. Based on the LD_{50} NTN granular is classified as highly toxic to songbirds.

LC_{50} Mallard duck was determined to be > 4797 ppm, based on the LC_{50} NTN is classified as practically non-toxic to mallard ducks.

One-Generation Reproduction Bobwhite quail demonstrated an LEL of 243 mg a.i./L, NOEC was 126 mg a.i./L.

One-Generation Reproduction Mallard duck NOEC < 61 ppm based on eggshell thickness, LEL was 128 mg a.i./L and the NOEC was 61 mg a.i./L

Acute toxicity test for freshwater fish (Bluegill Sunfish) LC_{50} is > 105 ppm which classifies NTN as practically non-toxic to Bluegill and Sunfish.

Acute toxicity for freshwater fish (Rainbow trout) LC_{50} was determined to be > 83 mg/L, the highest concentration tested. NTN is classified as slightly to be practically non-toxic to cold-water, freshwater fish.

Acute toxicity test for freshwater fish 96 hours LC_{50} Rainbow trout is 229.1 mg/kg a.i. NTN is determined to be practically non-toxic to rainbow trout based on 96 hr LC_{50}.

Acute toxicity test for Daphnia magna EC_{50} was determined to be 85.2 ppm. NTN is classified as slightly toxic to Daphnia magna.

Acute toxicity test for Estuarine/Marine fish was determined to be 163.0 ppm. Based on the LC50 NTN is classified as practically non-toxic to sheepshead minnow.

Honey bee LD_{50} was 0.0.78 and 0.0039 ug/bee, based on this study NTN is determined to be highly toxic to honey bees.

Acute toxicity test for Mysid shrimp was determined to be 37.3 ug a.i./L. Based on the EC50 NTN is classified as very highly toxic to aquatic invertebrates.

In several preliminary reviews EEB determined that NTN 33893 could pose a hazard to aquatic invertebrates and birds due to the proposed non-food uses. Levels of concern were exceeded for acute effects to aquatic invertebrates and birds and chronic effects for waterfowl and aquatic invertebrates. These concerns were communicated to Miles early in the review process. Following the new paradigm instituted by the Eco-Risk Task Force, EEB identified potential risk mitigation measures that would limit the risk to non-target organisms. The risk mitigation measures proposed were Restricted Use classification, reduced application rate and label language revision. A meeting was held to discuss the registrant's response to the proposed risk mitigation measures. For turf, Miles proposed a 20% reduction in the application rate from 0.5 to 0.4 lbs/a.i./A. This rate reduction reduced the acute risk below the level of concern for both aquatic invertebrates and birds for the proposed turf use. For ornamentals, Miles proposed to reduce the acute and chronic risks to invertebrates below our levels of concerns by limiting the places where NTN 33893 could be applied

to ornamentals. The confined uses they proposed (commercial and residential landscape, interior plantscapes, nurseries and greenhouses) substantially reduced exposure to aquatic species and mitigated our concerns. However, the avian chronic concern still exists. The levels of concern for reproductive effects are exceeded. Miles proposed a waterfowl reproduction monitoring study as part of a conditional registration for NTN 33893 for use on turf and ornamentals. EEB believes that this study may sufficiently address the chronic avian concerns and has proposed that the study be at least 2 years in duration with testing conducted on multiple sites within the full geographic area of use using the mallard duck. A meeting was held on February 3, 1994 with Miles/EEB/RD to discuss a protocol. We are not recommending that the non-food use the products for NTN 33893 be classified as restricted use products for the same reasons as discussed earlier in the groundwater discussion.

Public Interest Finding

Miles Inc. submitted a document entitled "Biological and Economic Benefits Package on the Proposed Use of Imidacloprid (Merit(R)) (Provado(R)) on Ornamentals and Turfgrass." This document was submitted to assist the Agency in finding that the registration of Imidacloprid is in the public interest. The document has been reviewed and the conclusions from the review are stated as follows:

> "BEAD expects that Imidacloprid could play an important role in the overall scheme of pest control, especially, in the area of resistance management. Imidacloprid is systemic in plants and appears to have a fairly long residual life. BEAD believes that if Imidacloprid is used judiciously in rotation with other available insecticides, not only will it decrease the pesticide load in the environment, it will reduce the frequency and magnitude of resistant populations by further disrupting the resistant gene pool in insect pests; it would thereby delay the development of resistance."

In support of the registration of the use of Imidacloprid on turfgrass and ornamentals, the authors of the document identified the following benefits:

1. Based on a statistical analysis, ninety percent of these studies indicated that Imidacloprid was better than or equal to its alternatives in controlling insect pests on turf and ornamentals.

2. Imidacloprid appears to have a very broad pest control spectrum in that it has efficacy against insect pests from several different orders including Coleoptera, Homoptera, Diptera, Thysanoptera and Lepidoptera.

3. Imidacloprid's mode of action, its systemic properties and fairly long residual life, and its efficacy at a low rate, sets it apart from most of it alternatives.

Recommendation

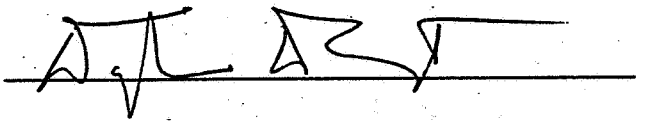
I recommend that you concur with the conditional registration of the proposed pesticide products containing Imidacloprid for use on turfgrass and ornamentals under Section 3(c)(7)(C) of the Act for the following reasons:

There is concern regarding the potential for NTN to contaminate ground water. There are also chronic avian concerns. However, we believe that NTN likely represents significantly less toxicological and ecological risk than most of the alternatives currently used on turf and ornamentals.

Miles has agreed to conduct acute and subchronic neurotoxicity testing. The acute study is scheduled to be completed in March 1994 and the subchronic to be completed by June 1994.

The registrant has agreed to submit a waterfowl reproduction monitoring study as part of the conditional registration. A pre-study meeting (in lieu of an actual review) of the protocol in order to provide suggestions and recommendations was held on February 3, 1994.

Miles has agreed to submit validated analytical methods for the determination of Imidacloprid and degradates of toxicological concern in ground and surface water samples.

CONCUR: 

DO NOT CONCUR: _____

DATE: MAR 14 1994