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RECORD NO.

9-23-91

121701
SHAUGHNESSEY NO.

REVIEW NO.

EEB REVIEW

DATE: IN 4-12-91 OUT SEP 23 1991

FILE OR REG. NO 62552-R;-E;-G

PETITION OR EXP. NO.

DATE OF SUBMISSION 4-12-91

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TYPE PRODUCT(S) : I, D, H, F, N, R, S Biochemical

DATA ACCESSION NO(S). 416264-22,-23,-24,-25

PRODUCT MANAGER NO. P.Hutton/W.Nelson (PM-18)

PRODUCT NAME(S) Azadirachtin (Azatin Technical™, Azatin EC™ and Azatin-Plus EC™)

COMPANY NAME Native Plants Incorporated

SUBMISSION PURPOSE Section 3 Registration

SHAUGHNESSEY NO.	CHEMICAL, & FORMULATION	
122701	Azatin Technical™	10.0 %
	Azatin EC™	3.0 %
	Azatin-Plus EC™	3.0 %

EEB REVIEW

Pesticide Name Azatin Technical™, Azatin EC™ and Azatin-Plus EC™

100.0.0 Submission Purpose and Label Information

100.1.0 Submission Purpose and Pesticide Use

Native Plants Incorporated (NPI) has requested a Section 3 Registration for azadirachtin as the active ingredient for control of a variety of insect pests on flowers, ornamentals, turf, trees and shrubs.

The active ingredient in Azatin is a natural insecticidal mixture extracted from seeds of the neem tree Azadiracta indica Juss. The major insecticidal principle in this mixture is the limonoid azadirachtin. Azadirachtin acts as an insect growth inhibitor against immature representatives of lepidopteran, coleopteran, dipteran, thysanopteran, orthopteran, and homopteran insects. It also acts as a feeding deterrent against immature and adult stages of several representative species in the insect orders listed above.

100.2.0 Formulation Information

Azatin Technical™

ACTIVE INGREDIENT: Azadirachtin*	10.0 %
Other Neem plant compounds	90.0 %
	100.0 %

Azatin EC™

ACTIVE INGREDIENT: Azadirachtin**	3.0 %
Other Neem plant compounds	27.0 %
INERT INGREDIENTS	70.0 %
	100.0 %

Azatin-Plus EC™

ACTIVE INGREDIENT: Azadirachtin**	3.0 %
Piperonyl Butoxide (synergist)	12.0 %
INERT INGREDIENTS	85.0 %
	100.0 %

* Contains 0.1 pounds (45.5 grams) of azadirachtin per pound of Technical

** contains 0.265 pounds (120 grams) of azadirachtin per gallon

100.3.0 Application Methods, Directions, Rates (Azatin EC™ and Azatin-Plus EC™)

A. Potted or Flowering Plants, Bedding Plants, Foliage Plants, Trees and Ornamentals:

1. SPRAY. Apply using suitable hand or power-operated spray equipment diluted in water at a rate of 8.0 fluid ounces per 100 gallons. Repeat application every seven days as needed. Apply a maximum of 21 ounces per acre.

2. DRENCH (injection irrigation or hand applied). Dilute in water at a rate or 8-21 fluid ounces per acre, not exceeding 21 ounces per acre.

B. Turf grass:

Apply at a rate of 0.5 fluid ounces per 1,000 square feet. Use 1-15 gallons of water to obtain good coverage.

100.4.0 Target Organisms

Ants, Aphids, Armyworms, Bagworms, Beetles and Weevils, Borers, Budworms, Bugs, Cankerworms, Caterpillars, Centipedes, Chafers, Crickets, Cutworms, Fungus Gnats, Greenhouse Leaf Tier, Grasshoppers and Locusts, Leafhoppers, Leafminers, Leafrollers, Loopers, Marsh Crane Flies, Mealybugs, Midges, Millipedes, Mites, Moths, Psyllids, Sawflies, Scales, Sowbugs, Thrips, Webworms, Whiteflies.

100.5.0 Precautionary Labeling

The label contains the following precautions:

WARNING: KEEP OUT OF REACH OF CHILDREN

HAZARDS TO HUMANS (AND DOMESTIC ANIMALS): (adequate)

ENVIRONMENTAL HAZARD STATEMENT: This pesticide is toxic to fish. Keep out of lakes, ponds and streams. Do not contaminate water by cleaning equipment or disposing of waste.

(Pesticide and container disposal directions are adequate)

101.0.0 Hazard Assessment

101.1.0 Discussion

The studies supplied with this submission will be considered supplemental because of a low test concentration. The results indicate that Azatin is highly toxic to freshwater fish and moderately toxic to aquatic invertebrate species. The avian testing indicates that this product is practically nontoxic to birds. These conclusions were based on testing a technical grade active ingredient (TGAI) that contains only 10% azadirachtin. However, for the purpose of making a risk assessment, the LD_{50} and LC_{50} values were adjusted (divided by 10) to take into account this discrepancy. The adjusted values indicate that Azatin is very highly toxic to freshwater fish, moderately toxic to aquatic invertebrate species, moderately toxic to quail through dietary exposure, and highly toxic to quail on an acute basis.

EEB is aware that this product is a natural plant compound and is formulated as a mixture of undifferentiated compounds extracted from Neem seed. Since the azadirachtin is not used in a pure form but in a mixture of other plant compounds, it was decided to allow the registrant to use the Neem seed extract, that will be used to formulate the actual product, as the TGAI. The amount of azadirachtin will vary depending on the potency of the Neem seeds and the effectiveness of the extraction process. Since, the 10% level in the test material is representative of the TGAI that will be used to formulate this product, these results should be adequate for assessing the risk this product may pose to nontarget organisms. However, the adjusted LD_{50} and LC_{50} values will be used to make the risk assessment.

Due to the highly toxic nature of this product to aquatic organisms (EC_{50} < 1 mg/L for invertebrates and < 0.048 mg/L for fish) the registrant will need to complete additional testing. Since the product is a molting inhibitor, the chronic effect of this product on aquatic invertebrates will need to be determined. Therefore, the Daphnia Magna Life-Cycle (21-Renewal) Chronic Toxicity Test (72-4) will be required before a complete risk assessment can be made. In addition, because of Azatin's proposed use on turf, the registrant will need to submit an Estaurine and Marine Animal Study using mollusc, estaurine fish and shrimp (72-3). The submitted data, even after taking into account the level of a.i., should present minimal risk to avian species. The product will not pose a risk to wild mammal species.

Because of the wide susceptible insects host range, risk to nontarget insects can be anticipated.

101.2.0 Likelihood at Adverse Effects to Nontarget Organisms

Avian Studies

A submitted study entitled "An Acute Oral Toxicity Study with the Northern Bobwhite" (MRID #416264-22) shows that the acute oral LD_{50} value for northern bobwhite exposed to NPI-720 as a single encapsulated oral dose was greater than 225 mg/kg the highest dose tested (highly toxic). The no observed effect dosage was 29.2 mg/kg based upon a possible reduction in body weight gain observed in males at the 48.6 mg/kg dose.

In a study entitled "A Dietary LC_{50} study with the Northern Bobwhite" (MRID #416264-23) the dietary LC_{50} value for northern bobwhite exposed to NPI-720 was determined to be greater than 562 ppm, the highest concentration tested (moderately toxic). The no observed effect concentration was 316 ppm based on a reduction in body weight gain and feed consumption at the 562 ppm concentration.

The results of these studies may be questioned because the concentration of active ingredient tested was not at the usual high levels (considered supplemental). However, because of the nature of the product (a mixture of natural plant components), a low use rate, and non toxic mode of action, these studies should be acceptable for assessing adverse effects to avian species.

Fish Studies

In a study entitled "Acute Flow-Through Toxicity of NPI-720 to Rainbow Trout" (MRID #416264-24) the 96 hour LC_{50} was calculated to be 0.048 mg a.i./L. The slope of the 96-hour dose-response line was 7.0. The 96 hour NOEL was 0.016 mg a.i./L based on a lack of sublethal responses at this concentration.

The above data indicate that Azatin is highly toxic to freshwater fish species.

Mammalian Wildlife

The data submitted to the toxicology branch indicate that there is no significant toxicity to rodents from acute oral testing at the maximum hazard dose. In light of the above results risk to mammalian wildlife is expected to be minimal to nonexistent.

Aquatic Invertebrate Studies

In a study entitled "Acute Flow-Through Toxicity of NPI-720 to Daphnia magna." (MRID #416264-25) the 48-hour LD_{50} was 1.0 mg a.i./L (confidence limits 0.86-1.3 mg/L). The NOEL was considered to be 0.13 mg a.i./L. The dose response slope was calculated to be 1.7.

The above data indicate that Azatin is moderately toxic to aquatic invertebrate species.

Estuarine and Marine Animal Studies

None submitted. These studies will need to be submitted prior to the registration of this product because of its use on turf.

Nontarget Plant Studies

None submitted. Plant testing of biochemical pest control agents is conditionally required when there is published evidence that the compound is toxic to plants. Azadirachtin is not known to be toxic to plants at the proposed use rates.

Honey Bee Studies

None submitted. In view of the wide insect host range supplied by the registrant (see section 100.4.0), it is likely that honey bees may also be affected. In view of this a honey bee hazard statement should be included on the label until honey bee toxicity studies are received and reviewed by EEB.

101.3.0 Endangered Species Considerations

Terrestrial endangered Lepidoptera and Coleoptera species will be exposed to the larvicide under the proposed use patterns. Aquatic vertebrate and invertebrate nontarget testing does indicate a hazard to aquatic animals, no exposure to aquatic animals, however, is anticipated from the proposed uses of this product. No risk to endangered avian species is expected from the use of this product.

101.4.0 Adequacy of Toxicity Data

(See the Generic Data Table)

The registrant has addressed the data requirements outlined in the Pesticide Assessment Guidelines, Subdivision M. However, because of the high level of toxicity to aquatic organisms demonstrated by this

testing, additional chronic testing will be required before a complete risk assessment can be made. A honey bee hazard statement will have to appear on the label unless the registrant chooses to submit honey bee toxicity data, and the product proves to be harmless to honey bees.

Generic Data Requirements For Azatin™

Data Requirement	Test[1] Substance	Use[2] Patterns	Does EPA Have Data?	Bibliographic Citation	Must Additional Data Be Submitted?
§158.740 Microbial Pesticide Nontarget Organism - Tier I					
Avian Testing					
154-6 Avian Acute Oral					
- upland gamebird	TGAI	B,G,H	Yes	416264-22	No[3]
154-7 Avian Dietary					
- upland gamebird	TGAI	B,G,H	Yes	416264-23	No[3]
Aquatic Organism Testing					
154-8 Freshwater Fish LC_{50}					
- rainbow trout	TGAI	B,G,H	Yes	416264-24	No
154-9 Freshwater Invertebrate					
- Daphnia magna	TGAI	B,G,H	Yes	416264-25	No
72-3 Estuarine and Marine					
- estuarine fish	TGAI	B,G,H	No	---	Yes[5]
- shrimp	TGAI	B,G,H	No	---	Yes[5]
- mollusc	TGAI	B,G,H	No	---	Yes[5]
154-13 Aquatic animal testing (Tier III)					
- Daphnia magna life-cycle (72-4)	TGAI	B,G,H	No	---	Yes[6]
Additional Testing					
154-10 Nontarget plant studies					
- terrestrial	TGAI	B,G,H	No	---	No
- aquatic	TGAI	B,G,H	No	---	No
154-11 Nontarget insect testing					
- honey bee	TGAI	B,G,H	No	---	Yes[4]

1/ TGAI = Technical Grade of the Active Ingredient; TEP = Typical End-Use Product.

2/ The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Nonfood; C = Aquatic, Food Crop; D = Aquatic, Nonfood; E = Greenhouse, Food Crop; F = Greenhouse, Nonfood; G = Forestry; H = Domestic, Outdoor; I = Indoor.

3/ The concentrations of active ingredient tested were not high enough to show that the test material is not toxic to birds. The only information that can be extracted from these data is that the compound is not highly toxic to birds.

4/ A honey bee hazard statement should be included on the label until honey bee toxicity studies are received and reviewed by EEB.

5/ Due to the product's use on turf, Estuarine and Marine Organism Testing will be required (72-3/Subdivision E).

6/ Due to the high toxicity demonstrated in the fish and invertebrate testing, the registrant will need to submit a Daphnia magna Life-Cycle (21-Day Renewal) Chronic Toxicity Test (72-4/Subdivision E).

101.5.0 Adequacy of Labeling

The precautionary labeling (see sec. 100.5.0) needs to have the following additions/modifications:

For MANUFACTURING-USE PRODUCTS:

"This pesticide is toxic to fish and aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or public water unless this product is specifically identified and addressed in an NPDES permit. Do not discharge effluent containing this product to sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA.

For END-USE PRODUCTS:

"This pesticide is toxic to fish and aquatic invertebrates. Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high-water mark. Drift and runoff may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water when disposing of equipment washwater or rinsate."

"Do not apply this product while bees are actively visiting the treatment area."

Endangered Species Labeling:

Endangered species labeling is deferred until the Technical Bulletin information is made available by OPP.

102.0.0 Classification: Not for aquatic, estuarine or marine uses

103.0.0 Conclusions

EEB has reviewed the proposed Section 3 Registration of Azatin™ by Native Plants Incorporated (NPI) for control of a variety of insect pests on flowers, ornamentals, turf, trees and shrubs.

The studies supplied with this submission, which are considered supplemtntal, indicate that Azatin is very highly toxic to freshwater fish and moderately toxic to aquatic invertebrate species. Due to the toxic nature of this product and the fact that it is an insect molting inhibitor, the registrant will be required to submit a Daphnia magna Life-Cycle (21-Day Renewal) Chronic Toxicity Test (72-4). In addition, due to its use on turf, the registrant will be required to submit Acute Toxicity Tests for Estuarine and Marine Organisms (72-3) using mollusc, shrimp and estuarine fish, before a complete risk assessment can be made.

Even though the amount of a.i. tested was not at the normal level for testing, the submitted data will be sufficient with adjustment to assess the level of toxicity to avian wildlife. The nature of this product will allow the test data to be used and indicates that Azatin should not present a risk to avian species.

The product will not pose a risk to wild mammal species.

Because of the wide susceptible insect host range, risk to nontarget insects can be anticipated. The product must not be used where honey bees are actively foraging until honey bee toxicity data are submitted and reviewed by EEB.

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