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EEB REVIEW

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PETITION OR EXP. NO. \_\_\_\_\_

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TYPE PRODUCT(S) Herbicide

DATA ACCESSION NO(S) 405313-01, 02, 03, 04

PRODUCT MANAGER, NO. R. Mountfort (PM 23)

PRODUCT NAME(S) Isoxaben Technical: 1471-RLI

Gallery 75F: 1471-RLO

COMPANY NAME Elanco Products Company

SUBMISSION PURPOSE New Chemical Screen to follow-up

Previous Screen

SHAUGHNESSEY NO.	CHEMICAL	% A.I.
_____	_____	_____
_____	_____	_____
_____	_____	_____



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

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

May 23, 1988

SUBJECT: Addendum EEB Review of Isoxaben

FROM:

*Daniel Rieder* 5-23-88  
Daniel Rieder  
Ecological Effects Branch  
Hazard Evaluation Division

THRU:

*Norman J. Cook* 5.24.88  
Norman J. Cook, Head, Section 2  
Ecological Effects Branch  
Hazard Evaluation Division

THRU:

*James W. Akerman*  
James W. Akerman, Chief  
Ecological Effects Branch  
Hazard Evaluation Division TS-769C

TO:

Richard Mountfort PM 23  
Herbicide/Fungicide Branch  
Registration Division TS-767C

Attached is the addendum review of Isoxaben in Registration Standard format. It addresses the additional information submitted by Elanco Company for registering isoxaben technical and Gallery 75F (75% ai).

Isoxaben

Ecological Effects Topical Summary

Effects on Birds

Five Studies in two documents were evaluated under this topic. All studies were acceptable for use in a hazard assessment.

<u>Author</u>	<u>Date</u>	<u>Accession No.</u>
Lake and Kehr	1982	250793
Lake and Cochrane	1984	073292

In order to establish the toxicity of Isoxaben to birds, the following tests are required using the technical grade material: Two subacute dietary studies on one species of waterfowl (preferably mallard duck) and one species of upland game bird (preferably bobwhite quail or ring-necked pheasant); An avian single - dose oral study on one species (preferably mallard duck or bobwhite quail).

The acute oral toxicity test is acceptable for use in a hazard assessment and is described below:

<u>Species</u>	<u>T.M.</u>	<u>LD50</u>	<u>Author</u>	<u>Date</u>	<u>Acc. No.</u>	<u>Fulfills Req.</u>
Bobwhite	92.4%	>2000 mg/kg	Lake & Kehr	1982	250793	yes

The guideline requirement (71-1) for an avian acute oral study has been satisfied.

The acceptable subacute dietary toxicity studies for use in a hazard assessment are listed below:

<u>Species</u>	<u>T.M.</u>	<u>LD50</u>	<u>Author</u>	<u>Date</u>	<u>Acc. No.</u>	<u>Fulfills Req.</u>
Bobwhite quail	92.4%	>5000 ppm	Lake & Kehr	1982	250793	yes
Mallard Duck	92.4%	>5000 ppm	Lake & Kehr	1982	250793	yes

The guideline requirements (71-2) for avian subacute dietary toxicity tests have been satisfied.

There is sufficient information on Isoxaben to characterize it as practically nontoxic to birds.

Avian reproduction tests are required for an end-use pesticide when birds may be exposed to repeated or continuous residues through persistence, bioaccumulation or multiple applications or if mammalian reproduction tests indicate reproductive hazard. Since Isoxaben is extremely persistent in certain environmental compartments, avian reproduction tests are required for all outdoor uses including ornamental, turf and noncropland treatment. The following are acceptable avian reproduction tests:

<u>Species</u>	<u>T.M.</u>	<u>Results</u>	<u>Author</u>	<u>Date</u>	<u>Acc. No.</u>	<u>Fulfills Req.</u>
Mallard duck	95.5%	NOEL=300 ppm LEL=1000 ppm* *reduction in hatchability of eggs	Lake & Cochrane	1984	073292	yes
Bobwhite quail	95.5%	NOEL=1000 ppm (highest level tested)	Lake & Cochrane	1984	073292	yes

The avian reproduction guideline requirement (71-4) has been fulfilled.

#### Precautionary Labeling

Based on avian toxicity data, no label statement for birds is required.

Effects on Fish

Five studies in two documents were evaluated under this topic. All studies were acceptable for use in a hazard assessment.

<u>Author</u>	<u>Date</u>	<u>Accession No.</u>
Lake, Francis and Grothe	1984	252915
Lake, Sauter and Meyerhoff	1983	252915
Lake, Meyerhoff and Sauter	1983	252915
Lake, Grothe and Francis	1982	250793
Lake, Grothe and Francis	1982	250793

The minimum data requirements for establishing the acute toxicity to fish are the results from two 96-hour studies with the technical grade material. The studies are to be performed on one coldwater species (preferably rainbow trout) and one warmwater species. (preferably bluegill sunfish).

The acceptable acute toxicity studies are presented below:

<u>Species</u>	<u>T.M.</u>	<u>LC50</u>	<u>Author</u>	<u>Date</u>	<u>Acc. No.</u>	<u>Fulfill Req.</u>
Japanese carp ( <u>Cyprinum carpio</u> )	92.4%	>1.09 ppm	Lake, Francis and Grothe	1984	252915	partial <sup>1/</sup>

<sup>1/</sup> Inappropriate test species and low solubility.

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Rainbow trout ( <u>Salmo gairdneri</u> )	92.4%	>1.1 ppm	Lake, Grothe and Francis	1982	250793	partial <sup>1/</sup>
Bluegill sunfish ( <u>Lepomis macrochirus</u> )	92.4%	>1.1 ppm	Lake, Grothe and Francis	1982	250793	partial <sup>1/</sup>

There is sufficient information to characterize the toxicity of Isoxaben as no more than moderately toxic to fish. It does not have an observable acute effect at its level of maximum solubility. The guideline requirement for fish acute toxicity testing (72-1) has not been satisfied. However, these tests are adequate for risk assessments if aquatic exposure does not exceed 1 ppm.

Data from a fish early life stage test is required if an active ingredient is persistent in water. Isoxaben is persistent in water with no degradation after 32 days. The following tests are acceptable fish early life stage tests.

<u>Species</u>	<u>T.M.</u>	<u>Results</u>	<u>Author</u>	<u>Date</u>	<u>Acc No.</u>	<u>Fulfill Req.</u>
Fathead minnow ( <u>Pimephales promelas</u> )	95.5%	NOEL= 0.4 ppm*	Lake, Sauter and Meyerhoff	1983	252915	partial <sup>2/</sup>
Rainbow Trout ( <u>Salmo gairdneri</u> )	95.5%	NOEL= 0.42 ppm*	Lake, Meyerhoff and Sauter	1983	252915	partial <sup>2/</sup>

\* highest level tested.

The guideline requirement (72-4) has not been fulfilled, however, these data are adequate to show that Isoxaben has no apparent chronic effect on embryo-larval development at 0.4 and 0.42 ppm and could be used in a hazard assessment where chronic aquatic concentrations do not exceed these levels.

#### Precautionary Labeling

No toxicity statement for fish is required based on available data.

- 1/ Test material solubility was approximately 1.1 ppm. Test concentrations were measured, therefore, these tests fulfill the intent of the requirement by showing that Isoxaben is apparently not acutely toxic at its maximum solubility.
- 2/ An effect level was not determined.

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Effects on Freshwater Invertebrate

Two studies in two documents were evaluated. Both studies were acceptable for use in a hazard assessment.

<u>Author</u>	<u>Date</u>	<u>Accession No.</u>
Lake, Francis and Grothe	1984	252915
Lake, Francis and Grothe	1982	250793

The minimum date required to establish the acute toxicity to freshwater invertebrates is a 43-hr aquatic study with the technical material. The preferred test species is Daphnia magna. The acceptable toxicity test is presented below.

<u>Species</u>	<u>T.M.</u>	<u>LC50</u>	<u>Author</u>	<u>Date</u>	<u>Acc No.</u>	<u>Fulfill Req.</u>
<u>Daphnia magna</u>	92.4%	>1.3 ppm	Lake, Francis and Grothe	1982	250793	partial <sup>1/</sup>

This test does not fulfill the guideline requirement (72-2) for acute testing with aquatic invertebrates. It is adequate to assess risk provided aquatic exposure is unlikely to exceed 1.3 ppm. Isoxaben is no more than moderately toxic to aquatic invertebrates.

Data from an freshwater aquatic invertebrate life-cycle test are required if an active ingredient is persistent in water. Isoxaben is persistent in water with no degradation after 32 days. The aquatic invertebrate life-cycle test is required. The acceptable life-cycle test is provided below.

<u>Species</u>	<u>T.M.</u>	<u>Result</u>	<u>Author</u>	<u>Date</u>	<u>Acc No.</u>	<u>Fulfill Req.</u>
<u>Daphnia magna</u>	95.5%	NOEL= 0.69 LEL=1.01 ppm 2/	Lake, Francis and Grothe	1984	252915	yes

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1/ The test material was insoluble at above 1.3 ppm, which was the measured test concentration, nominal was 100 ppm.

2/ Statistically significant effects on growth and brood size.

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This test fulfills the requirement (72.4) for an aquatic invertebrate life-cycle test.

Precautionary Labeling

No precautionary label statement is required for aquatic invertebrates.

## 6.1

Effects on Estuarine Organisms

Three reports containing three studies on the toxicity of Isoxaben to estuarine organisms were received. All studies were used in the hazard assessment.

<u>Author</u>	<u>Date</u>	<u>MRID No:</u>
Grothe and Seacat	1987	40531304
Grothe and Mohr	1987	40531303
Dionne	1987	40531302

Acute testing of the technical grade of a chemical is required for estuarine and marine species (section 72-3) when an end-use product is intended for direct application to the marine or estuarine environment or is expected to reach this environment in significant concentrations when the product is used as directed. The following tests using the technical grade active ingredient are required to characterize the toxicity of Fenthion to estuarine and marine species.

1. A 96-hour LC50 study with an estuarine shrimp;
2. A 96-hour LC50 with an estuarine fish; and
3. Either a 48-hour EC50 study on oyster embryo-larvae or a 96-hour oyster shell deposition study.

The use of Isoxaben on noncroplands and turf is expected to result in exposure to marine and estuarine environments, therefore, these studies were required.

Technical Product Testing

The following studies indicated that Isoxaben is no more than highly toxic to shrimp, estuarine fish and mussels.

<u>Species</u>	<u>T.M.</u>	<u>EC50, LC50</u>	<u>Author</u>	<u>MRID No:</u>	<u>Fulfills Require.</u>
Quahog clam (embryo-larvae)	95.5%	>0.96 ppm* (40% effect at this level)	Dionne	40531302	yes**
Grass shrimp	95.5%	>1 ppm	Grothe & Mohr	40531303	yes**
Sheepshead	95.5%	>0.87 ppm	Grothe & Seacat	40531304	yes**

\* Maximum solubility attainable, nominal concentrations were 100 ppm.

\*\* These tests are adequate provided concentrations in estuaries are not expected to exceed the measured test concentrations for each test.

Formulation Testing

Direct application to water is not expected, so formulated product testing is not required.

Effects on Beneficial Insects

One study in one document was evaluated under this topic. The study was acceptable for use in a hazard assessment.

<u>Author</u>	<u>Date</u>	<u>Accession No.</u>
Akins	1984	073292

The minimum data requirement to establish the acute toxicity to honey bees is an acute oral LD50 study with the technical material. The acceptable test is presented below.

<u>Species</u>	<u>T.M.</u>	<u>LD50</u>	<u>Author</u>	<u>Data</u>	<u>Acc No.</u>	<u>Fulfills Req.</u>
Honey bee <u>Apis mellifera</u>	95.5%	>101.7 ug/Bee	Akins	1984	073229	yes

This test fulfills the requirement for acute toxicity testing with honey bees. There is sufficient information to characterize Isoxaben as practically nontoxic to bees.

Precautionary Labeling

Based on the above data, no toxicity statement is required.

Plant Protection

Two studies in two document were evaluated under this topic. They were considered acceptable.

<u>Author</u>	<u>Date</u>	<u>Accession No.</u>
Lake, Francis and Grothe	1982	250793
Saunders et al	1987	40531301*

\* Study submitted in response to previous review.

Tier I phytotoxicity data are required for terrestrial nonfood uses such as ornamentals and noncropland. The studies required are a seedling germination/seedling emergence, vegetative vigor and aquatic plant growth. The following study fulfills the requirement for a Tier I aquatic plant growth test (122.2).

<u>Species</u>	<u>T.M.</u>	<u>Results</u>	<u>Author</u>	<u>Date</u>	<u>Acc. No.</u>	<u>Fulfill Req.</u>
Algae ( <u>Selenastrum capricornutum</u> )	92.4%	NOEL=1.4 ppm (max. solubility)	Lake, Francis and Grothe	1982	250793	partial

The Tier I requirement for seedling emergence is fulfilled with the following study. It indicates that isoxaben reduces seeding germination at very low levels.

<u>Species</u>	<u>T.M.</u>	<u>Results</u>	<u>Author</u>	<u>Date</u>	<u>Acc. No.</u>	<u>Fulfill Req.</u>
see list below	75% DF	50% reduction of emergence at 0.05 to 1.3 ppm soil concentrations	Saunders et al.	1987	40531301	yes

The tier I data requirement for the vegetative vigor test has not been fulfilled. However, in the report cited above, there was mention (p 10) of a vegetative vigor type screening test in which adequate activity (herbicidal effect of isoxaben on emerged vegetation) at 8 lbs. ai per acre was inadequate to require retesting at lower rates. Additional information should be provided such as the species tested, percent ai or formulation, and the plant response. This test may fulfill the requirement for Tier I vegetative vigor testing if the response is such that EEB can evaluate potential hazard and conclude safety to nontarget plants at normal use rates.

annual ryegrass, barley, barnyardgrass, black nightshade, blackgrass, browntop panicum, cheatgrass, cocklebur, common ragweed, corn, cotton, cucumber, grain sorghum, green foxtail, jimsonweed, lambsquarters, morningglory, prickly sida, redroot pigweed, rice, socklepod, soybean, velvetleaf, wheat, wild oats

## 8.1

Since Isoxaben is a soil incorporation pre-emergent herbicide, it is likely that Tier II seed germination data would be required. This test has not been provided, however, it is possible that if the registrant has additional information on the seedling emergence test that this requirement could be fulfilled. The additional information required includes numbers of seeds planted and number that germinated at each treatment level. The species tested should also be identified.

The seed germination and vegetative vigor data may be submitted as part of a conditional registration.

Isoxaben Ecological  
Effects Disciplinary Review

I. Ecological Effects Profile

A. Manufacturing Use

1. Avian Studies

The avian acute oral LD50's of >2000 mg/kg (Bobwhite quail, Lake & Kehr, 1982, 250793) and the avian dietary LC50's of >5000 ppm for both Bobwhite quail and Mallards (Lake and Kehr, 1982, 250793) indicate that Isoxaben is practically non-toxic to birds. The avian reproductive NOEL and LEL for Mallards are 300 ppm and 1000 ppm, respectively, (Lake and Cochran, 1984, 073292). The reproductive NOEL for Bobwhite is 100 ppm (Lake and Cochran, 1984, 073292).

2. Aquatic Studies

The fish LC50 for Rainbow trout is > 1.09 ppm and for Bluegill it is >1.1 ppm (Lake, Grothe and Francis, 1982, 250793) indicating that Isoxaben is no more than moderately toxic to fish. The early life stage chronic NOEL's for Fathead minnow and Rainbow trout are 0.4 ppm and 0.42 ppm, respectively, (Lake, Sauter, and Sauter, 1983, 252915).

The LC50 of >1.3 ppm for Daphnia magna (Lake, Francis and Grothe, 1982, 250793) indicates that Isoxaben is no more than moderately toxic to aquatic invertebrates. The aquatic invertebrate life-cycle NOEL and LEL for Daphnia magna are 0.69 ppm and 1.01 ppm, respectively (Lake, Frances and Grothe, 1984, 252915).

Isoxaben is practically nontoxic to mammals with acute oral LD50's of >2000 mg/kg and >10,000 mg/kg for rat and mouse respectively. In a 3-generation rat reproduction study, the reproductive NOEL =2500 ppm and LEL = 12,500 ppm (Toxicology Branch One-Liner).

B. Formulated Product

No tests with formulated products are required nor have any been provided.

II Ecological Effects Hazard Assessment

A Use

Isoxaben is proposed for registration to control broad leaf weeds on established turf, landscape ornamentals, container grown ornamentals, ground covers, nursery stock, non-bearing fruit and nut crops, non bearing vineyards and noncropland. Noncropland is identified as industrial sites, utility substations, highway guard rails, sign posts and delineators. At higher use rates of 0.75 to 1 lb. ai/acre, some grasses are suppressed or partially controlled.

Prolan 75 Dry flowable contains 75% a.i. (Isoxaben) and is a preemergence herbicide. The label indicates it will not control established weeds. It is stable on soil surfaces but must be activated by one - half inch rainfall or irrigation to be effective.

The use categories for which Isoxaben is proposed are terrestrial food (non-bearing fruit and nut crops and vineyards) and terrestrial nonfood.

B Environmental Fate

1. Soil

The aerobic soil metabolism half-lives for clay loam, loam, and sandy loam are 4.3, 5.6 and 10.6 months, respectively. The octanal/water partition coefficient is 434.

2. Water

Isoxaben is stable to hydrolysis with no degradation after 32 days (various pH's).

3. Plant

No information was available on plant uptake or metabolism. There is no information on the photolysis of Isoxaben on surfaces.

10.1

Additional environmental fate data were also provided, including information on the fish bioaccumulation study previously submitted and determined to be only partially acceptable.

1. Fish Bioaccumulation Data: BCF after 28 days exposure was 14X, 134X and 70X in edible tissue, nonedible tissues, and whole fish. Depuration occurred within 14 days to 1.12X in edible, nonedible and whole fish. The test still only partially fulfills the Exposure Assessment Branch requirements. However, EEB is able to use the information to determine that Isoxaben does not bioaccumulate to a great extent in fish.

Accession/MRID No: 400595-09, partially fulfills requirement.

2. Terrestrial Field Dissipation: In clay loam soil (Illinois), Isoxaben dissipated with a half-life of 66-106 days. Maximum leaching depth for degradate (210469) was 24-30 inches with most remaining in the top 6 inches. Parent Isoxaben remained in the top 6 inches. Isoxaben does not tend to leach.

Accession/MRID No: 405321-02, partially fulfills requirement.

3. Hydrolysis: In light, hydrolytic half-life was 7-15 days. In the dark control, after 30 days, 94.4% of the original Isoxaben remained.

Accession/MRID Nos: 400976-01 and 400595-07, fulfills data requirement.

4. Aerobic Metabolism: Isoxaben degraded under aerobic conditions with a half-life of 4.3 months, 5.6 months and 10.6 months in clay loam, loam and sandy loam soils.

Accession/MRID Nos: 073607 and 002653-70, fulfills data requirement.

5. Leaching and Adsorption/Desorption: Based on the column leaching study, Kd values for the four soils tested ranged from 8.4 to 30.

Accession/MRID No: 00265730, partially fulfills requirement.

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C. Manufacturing-Use

The EEB does not perform a hazard assessment for manufacturing of pesticides.

D. End-Use Product

Prolan, which is 75% a.i. is the only end-use product proposed for registration.

1. Terrestrial

The maximum application rate is 1 lb ai/acre. At that rate the following residues (ppm) are expected on terrestrial food items.

	<u>Short</u> <u>grass</u>	<u>long</u> <u>grass</u>	<u>leafy</u> <u>crops</u>	<u>insects</u> <u>forage</u>	<u>seed</u> <u>Pods</u>	<u>Fruit</u>
maximum	240	110	125	58	12	7
typical	125	92	35	33	3	1.5

The maximum expected residue does not exceed the lowest avian reproductive NOEL of 300 ppm (Mallards, Lake & Cochrane, 1984, 073292).

This primary exposure is expected to cause minimal adverse acute and chronic effects to birds. Secondary exposure from accumulated residues is unlikely since bioaccumulation of isoxaben is expected to be minimal. Based on an LD50 of >2000 mg/kg for mice, a one day LC50 can be calculated.

$$\frac{20 \text{ grams (weight of mouse)} \times 2000 \text{ mg/kg (LD50)}}{3 \text{ grams (consumed per day)}} = 13,333 \text{ ppm}$$

No adverse acute effects to mammals are expected from primary exposure. The estimated residues are also on less than the mammalian reproductive NOEL of 2500 ppm. No chronic effects through primary or secondary exposure are expected.

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Based on the results of phytotoxicity data and the label, it is unlikely that isoxaben will impact emerged nontarget vegetation. This is based on a referenced screening study in which adverse impact to plants was not observed at 8 lbs. ai per acre (Saunders et al. 1987, 40531301, p 10) and the label which indicates that application to soil where emerged plants occur may be conducted without impacting these nontarget plants (such as ornamentals).

However, since isoxaben has preemergence activity, the impact would be to nontarget plant seedling emergence. Sensitive species would be impacted at soil concentrations as low as 0.05 ppm. Most of the proposed uses are conducive only to ground application, therefore, exposure (by drift) to nontarget areas would be unlikely and impact to nontarget plants should be minimal. If aerial application was conducted, 5% drift would result in 0.055 ppm in adjacent soils (2" deep). This could impact nontarget seedling emergence.

## 2. Aquatic

Because of its solubility, Isoxaben is expected to runoff to a moderate extent (1%) using the 10-acre treated field draining into a 1 acre pond 6 feet deep, the following estimated aquatic concentration is calculated:

$$10 \text{ acres} \times 1 \text{ lb ai/acre} \times 0.01 \text{ runoff} \times 61 \text{ ppb} = 6.1 \text{ ppb}$$

This estimated concentration is substantially lower than the fish chronic NOEL's of 0.40 and 0.42 ppm for minnow and Rainbow trout, respectively (Lake, Sauter, and Meyerhoff, 1983, 252915). It is also lower than the Daphnia magna life-cycle NOEL of 690 ppb (Lake, Francis and Grothe, 1984, 252915). Minimal adverse acute or chronic effects to aquatic organisms are expected from ambient exposure. Bioaccumulation potential in aquatic organisms is low and unlikely to result in hazards.

The uses for which Prolan 75 Dry Flowable is proposed are generally not considered conducive to aerial application. However, the label does not exclude this method, therefore, it will be addressed. If 5% of the aerially applied 1 lb ai/acre drifted into 6 inches of water, the resulting concentration would be 36.7 ppb. This is substantially less than the chronic NOEL's presented earlier. Minimal adverse effects from this exposure are expected.

## 3 Endangered Species

Residues on terrestrial food items are less than the chronic NOEL for birds, therefore, adverse effects to endangered birds from ingesting contaminated food items is not expected.

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Endangered mammals will not be exposed to residues exceeding the 3-generation reproduction NOEL of 2500 ppm. Therefore, no effects to endangered mammals through ingestion of contaminated food material are expected.

Potential for bioaccumulation is minimal based on the fish accumulation study results.

### Aquatic

Estimated residues from runoff or drift do not exceed aquatic organism chronic NOEL's. Adverse effects to endangered aquatic organisms through ambient exposure are not expected. The potential for bioaccumulation is minimal based on the bioaccumulation study data provided.

### Plants

Because it is a herbicide, Isoxaben is expected to adversely effect exposed endangered plant species. The only use where exposure is considered possible is the noncropland use which was addressed in the noncropland cluster already submitted to the USFWS. Their opinion will apply to Isoxaben. No labeling for protection of endangered plant species is required at this time.

### Risk Summary

Minimal adverse acute and chronic effects are expected to nonendangered and endangered terrestrial and aquatic organisms. Adverse effects to endangered plants are expected and will eventually require labeling to eliminate exposure potential.

## III. Precautionary Labeling

### A. Manufacturing-Use Product

The following statement is required:

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 into sewer systems without previously notifying the sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

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B. End-Use Product

Terrestrial food and Terrestrial nonfood

The following statement is required:

"Do not apply directly to water or wetlands (swamps, marshes, bogs, and potholes). Do not contaminate water by cleaning of equipment or dispose of wastes."

IV Data Requirements

Additional information on phytotoxicity testing is required, see Table A. These data may be submitted as part of a conditional registration.

Table A  
Isoxaben Generic Data Requirements

Data Requirement	Composition 1/ Pattern 2/	Use	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIRFA Section 3(c)(2)(B)?
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\$158.145 Wildlife and Aquatic Organisms

AVIAN AND MAMMALIAN TESTING

71-1 - Avian Oral LD50	TGAI	A, B	yes	250793	No
71-2 - Avian Dietary LC50					
a. Upland Game Bird	TGAI	A, B	yes	250793	No
b. Waterfowl	TGAI	A, B	yes	250793	No
71-3 - Wild Mammal Toxicity	TGAI	A, B	no		No 3/
71-4 - Avian Reproduction	TGAI	A, B	yes	073292	No
71-5 - Simulated and Actual Field Testing - Mammals and Birds	TEP	A, B	no		No. 4/

Table A  
Isoxaben Generic Data Requirements (continued)

Data Requirement	Composition1/ Pattern2/ Use	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?
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§158.145 Wildlife and Aquatic Organisms (cont'd)

AQUATIC ORGANISM TESTING

72-1 - Freshwater Fish LC50

- a. Warmwater TGAI A,B yes 250793 no
- b. Coldwater TGAI A,B yes 250793 no

72-2 - Acute LC50 Freshwater TGAI A,B yes 250793 no  
Invertebrates

72-3 - Acute LC50 Estuarine TGAI no no  
and Marine Organisms

72-4 - Fish Early Life Stage TGAI A,B yes 252915 no  
and Aquatic Invert.  
Life Cycle

Table A  
Isoxaben Generic Data Requirements (continued)

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Data Requirement	Composition <sup>1</sup> / Pattern <sup>2</sup> / Use	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?
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\$158.145 Wildlife and Aquatic Organisms (cont'd)

AQUATIC ORGANISM TESTING

72-5 - Fish Life Cycle	TGAI	A,B	no	No 4/
72-6 - Aquatic Organisms Accumulation	TGAI	A,B	no	no 6/
72-7 - Simulated or Actual Field Testing Aquatic Organisms	TEP	A,B	no	no 4/

Table A  
Isoxaben Generic Data Requirements (continued)

Data Requirement	Composition 1/ Use Pattern 2/	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?
<u>\$158.150 Plant Protection</u>				
121-1 - TARGET AREA PHYTOTOXICITY	TEP A,B	no		no 3/
<u>NONTARGET AREA PHYTOTOXICITY</u>				
<u>TIER I</u>				
122-1 - Seed Germination/ Seedling Emergence	TGAI A,B	no		yes 7/
122-1 - Vegetative Vigor	TGAI A,B	no		yes 8/
122-2 - Aquatic Plant Growth	TGAI A,B	no	250793	no 4/
<u>TIER II</u>				
123-1 - Seed Germination/ Seedling Emergence	TGAI A,B	no		yes 7/
123-1 - Vegetative Vigor	TGAI A,B	no		reserved 5/
123-2 - Aquatic Plant Growth	TGAI A,B	no		no 4/

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Table A  
Isoxaben Generic Data Requirements (continued)

Data Requirement	Composition <sup>1</sup> / Pattern <sup>2</sup> / Use	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?
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\$158.150 Plant Protection (cont'd)

TIER III

124-1 - Terrestrial Field	TEP A,B	no		no 4/
124-2 - Aquatic Field	TEP A,B	no		no 4/

- 1/ Composition: TGAI = Technical Grade of the Active Ingredient; PAI = Pure 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/ Not currently a requirement.
- 4/ Lower tier data indicate test is not required.
- 5/ Reserved pending results of lower tier testing.
- 6/ The study submitted to EAB provides adequate information on bioaccumulation of isoxaben. 7/ Tier I information on the numbers of seeds planted and number that germinated for each species tested in each test level in the seedling emergence test (Saunders et al. 1987, 40531301) that the seed germination requirement could be fulfilled with this study.
- 8/ Vegetative vigor data are still required. However, if the registrant provides additional information on the screening study that was mentioned on page 10 of Saunders et al, 1987, 40531301, that this study could fulfill the requirement for vegetative vigor testing. The additional data required include the species tested, test material or formulation, age of plants and response. If this additional information is sufficient to allow EBB to assess hazard to nontarget plants and conclude safety, not additional testing is required.

file

DATA EVALUATION REPORT

1. Chemical: Isoxaben (sha. no. 125851)
2. Test Material: Technical Grade, 95.5% ai
3. Study Type: Mollusc 48-Hour Embryo Larvae Study
4. Study Identification: Dionne, Emily. 1987. Acute Toxicity of Isoxaben to Embryo-Larval Stages of the Quahog Clam (Mercenaria mercenaria). Unpublished study prepared by Springborn Life Sciences, Inc. submitted by Lilly Research Laboratories. Study No: 1982.0787.6100.514. Accession No: 405313-02.
5. Review By: Daniel Rieder, Wildlife Biologist Daniel Rieder 5-24-88  
Ecological Effects Branch  
Hazard Evaluation Division
6. Approved By: Norman J. Cook, Head, Section 2 Norman J. Cook 5-24-88  
Ecological Effects Branch  
Hazard Evaluation Division
7. Conclusion: This study has been reviewed and found to be scientifically sound. It fulfills the guideline requirement for a mollusc 48-hour embryo larvae study and is adequate to assess hazard to oysters provided the concentrations in estuaries are not expected to exceed 0.96 ppm. The EC50 is assumed to be greater than 0.96 ppm (measured concentration) since there was 40% reduction at that test level. That concentration was the only test level and represents the maximum solubility attained with a nominal concentration of 100 ppm. This study indicates that isoxaben is no more than highly toxic to oysters. No additional acute testing with bivalves is required at this time.
8. Recommendations: N/A
9. Background: This study was submitted to support section 3 registration.
10. Discussion of Individual Studies: N/A

11. Materials and Methods:

Technical isoxaben (95.5% ai) was tested against embryo-larvae of the quahog (*Mercenaria mercenaria*). The nominal test concentration was 100 ppm, however, the solubility of isoxaben precluded measured levels of greater than 0.96 ppm. There were 4 replicates in the control and 3 replicates in the test level.

Test solution was natural seawater filtered through a 5 um porosity polypropylene core filter. No solvent was used in this study, however, in other estuarine and aquatic studies, solvents were used to enhance solubility but to no avail. Nine hundred ml of test solution were added to three 1 L glass beakers. Each test vessel was inoculated with 28,000 embryos within 2.5 hours of fertilization. Test temperature was maintained at 19-20 degrees Celsius, photoperiod was 16 hours of light per day.

The analytical method for isoxaben consisted of measuring the test material directly by high-performance liquid chromatography.

After 48 hours the larvae were collected with a 37 um mesh sieve and preserved with 1 ml of neutralized formalin. The number of normally developed 48-hour larvae was determined from each replicate.

Statistics involved calculating the percent reduction of normal larvae by subtracting the mean number of normal 48-hour embryos from the number of normal embryos in the controls and dividing that by the mean number of normal embryos in the controls and multiplying the result by 100.

12. Reported Results:

The following shows the reported results.

Concentration ppm	Number Normally Developed Larvae		Mean	Percent Reduction		
	Nominal	Measured Repl.			Per Repl.	
Control	ND	A	23,600	24,400		
	ND	B	28,000			
	0.04 <sup>1</sup>	C	20,800			
	0.02 <sup>1</sup>	D	25,200			
	<u>0-hr</u>	<u>48-hr</u>				
100	0.89	1.01	A	13,600	14,533	40.4%
	<sup>2</sup>	1.05	B	19,200		
	0.86	1.05	C	10,800		

<sup>1</sup> Detection Limit = 0.02 mg/L.

<sup>2</sup> Sample bottle broken during shipment.

13. Study Author's Conclusions:

The 48-hour EC50 for clam embryos and larvae exposed to isoxaben was empirically estimated to be  $> 0.96$  mg/L, the mean measured concentration during this exposure.

14. Reviewer's Discussion:

A. Test Procedure: The test procedure was acceptable.

B. Statistical Analysis: None were performed beyond determining the percent reduction.

C. Discussion of Results: The results suggest that isoxaben is no more than moderately toxic to clams.

D. Category of Study: Supplemental. This study would be adequate to assess hazard to bivalves provided the EEC does not exceed approximately 1 ppm.

15. Completion of One-Liner: Completed

16. CBI Attachments: N/A

DATA EVALUATION REPORT

1. Chemical: Isoxaben / 125851
2. Test Material: Technical, 95.5%
3. Study Type: 96-hour LC50 with Grass shrimp
4. Study Identification: Grothe, D.W. and R.R. Mohr, 1987  
Acute Toxicity of Isoxaben to the grass shrimp Palaemonetes pugio  
in a Static Test System.  
Laboratory: Lilly Research Laboratories  
Study No/Date: CO1387/October 14, 1987  
Study Submitted to EPA by Eli Lilly  
Accession No: 405313-03
5. Review By: Daniel Rieder, Wildlife Biologist Daniel Rieder 5-24-88  
Ecological Effects Branch  
Hazard Evaluation Division
6. Approved By: Norman J. Cook, Head, Section 2 Norman J. Cook 5-24-88  
Ecological Effects Branch  
Hazard Evaluation Division
7. Conclusion: This study has been reviewed and found to be scientifically sound. It fulfills the requirement for an acute study and is adequate to assess hazards to estuarine shrimp provided that estimated concentrations do not exceed 1 mg/L. Based on the results, it is assumed that the LC50 of isoxaben to shrimp is greater than 1 mg/L and that it is no more than highly toxic to these organisms. No additional acute testing is required for estuarine shrimp at this time.
8. Recommendations: N/A
9. Background: This study was submitted to support section 3 registration.
10. Discussion of Individual Studies: N/A

11. Materials and Methods:

Test Material: Isoxaben 95.5% ai  
Test Organism: Grass shrimp  
Source: SP Engineering                      No/Level: 10/Replicate  
Replicates: 1 for water and acetone control, 3 for trt. level.  
Length:  $20.9 \pm 1.8$  mm      Weight:  $0.08 \pm 0.02$  g  
Acclimation: 35 days  
Organisms per container: 10      Loading: 0.21 g/L

Test Containers: glass aquaria, 10 liter  
containing 4 liters test solution.  
Aeration: Yes (measured test concentrations)  
Test Concentrations: one at 100 mg/L nominal  
Test Conditions: Static                      Photoperiod: 16 hrs/day  
Temperature:  $22 \pm 2$  C  
Test Solution: Reconstituted sea water; 15 o/oo  
Controls: Untreated and Solvent (Acetone)

12. Reported Results: 96-hour LC50 > 1 ppm Measured concentration

No mortality or adverse physiological or behavioral effects were observed in any container, controls or treatments.

13. Study Author's Conclusions: Under the conditions of this study, isoxaben was not acutely toxic to shrimp at 100 ppm nominal concentration.

14. Reviewer's Discussion:

A. Test Procedure: The test procedure was acceptable. Test concentrations were measured.

B. Statistical Analysis: None required.

C. Discussion of Results: The results show that isoxaben is no more than highly toxic to shrimp.

D. Category of Study: Supplemental

15. Completion of One-Liner: Completed

16. CBI Attachments: N/A

DATA EVALUATION REPORT

1. Chemical: Isoxaben / 125851
2. Test Material: Technical, 95.5%
3. Study Type: Fish 96-hour LC50 with Sheepshead Minnow
4. Study Identification: Gries, Christian, . 1987  
Acute Toxicity of Isoxaben to the Sheepshead Minnow (Cyprinodon variegatus) in a Static Test System.  
Laboratory: Lilly Research Laboratories  
Study No/Date: F01587/October 14, 1987  
Study Submitted to EPA by Eli Lilly  
Accession No: 405313-04
5. Review By: Daniel Rieder, Wildlife Biologist Daniel Rieder 5-24-88  
Ecological Effects Branch  
Hazard Evaluation Division
6. Approved By: Norman J. Cook, Head, Section 2 Norman J. Cook 5-24-88  
Ecological Effects Branch  
Hazard Evaluation Division
7. Conclusion: This study has been reviewed and found to be scientifically sound. It fulfills the requirement for an estuarine fish acute study and is adequate to assess hazards to estuarine fish provided that estimated concentrations do not exceed 0.87 mg/L. Based on the results, it is assumed that the LC50 of isoxaben to estuarine fish is greater than 0.87 mg/L and that it is no more than highly toxic to estuarine fish. No additional acute testing is required for estuarine fish at this time.
8. Recommendations: N/A
9. Background: This study was submitted to support section 3 registration.
10. Discussion of Individual Studies: N/A

11. Materials and Methods:

Test Material: Isoxaben 95.5% ai  
 Test Organism: Sheepshead minnow  
 Source: SP Engineering No/Level: 10/Replicate  
 Replicates: 1 for water and acetone control, 3 for trt. level.  
 Length: mean=35.7 mm ± 2.1 mm Weight: mean=0.85 g  
 Acclimation: 35 days, 48 hrs without food  
 Organisms per container: 10 Loading: 0.34 g/L

Test Containers: glass aquaria, 57 liter  
 containing 25 liters test solution.  
 Aeration: Yes (measured test concentrations)  
 Test Concentrations: one at 100 mg/L nominal  
 Test Conditions: Static Photoperiod: 16 hrs/day  
 Temperature: 21.8 ± 0.6 C Test Solution: Reconstituted sea  
 Controls: Untreated and Solvent water; 150/00  
 (Acetone)

12. Reported Results: 96-hour LC50>0.87 ppm

CONCENTRATION (PPM)			MORTALITY	CONDITIONS
NOMINAL	MEASURED PPM			
	0-HR, 48-H, 96-H		96-HOUR	See attached table
control	ND	ND ND	0	
sol. cont.	ND	ND ND	0	
100	0.98, 0.80, 0.79		0	
100	1.02, 0.82, 0.78		0	
100	0.99, 0.85, 0.90		0	

No adverse physiological or behavioral effects were observed in any container.

13. Study Author's Conclusions: Under the conditions of this study, isoxaben was no more than highly toxic to estuarine fish.

14. Reviewer's Discussion:

A. Test Procedure: The test procedure was acceptable. Test concentrations were measured.

B. Statistical Analysis: None required.

C. Discussion of Results: The results show that isoxaben is no more than highly toxic to fish.

D. Category of Study: Supplemental

15. Completion of One-Liner: Completed

16. CBI Attachments: N/A