107901

(5)

EEE BRANCH REVIEW

DATE: IN 2/25/77 OUT 8/23/77 IN ____ OUT ____ IN ____ OUT ____

FISH & WILDLIFE ENVIRONMENTAL CHEMISTRY EFFICACY

FILE OR REG. NO. 21137-4

PETITION OR EXP. PERMIT NO. 7F1921

DATE DIV. RECEIVED Feb. 8, 1977

DATE OF SUBMISSION Feb. 8, 1977

DATE SUBMISSION ACCEPTED Mar. 17, 1977 (Date of Filing, Mar. 21, 1977)

TYPE PRODUCTS(S): I, D, H, F, N, R, S Fungicide

DATA ACCESSION NO(S).

PRODUCT MGR. NO. 21137

PRODUCT NAME(S) Funginex

COMPANY NAME E. M. Laboratories

SUBMISSION PURPOSE Petition: Registration for amended use on peaches and blueberries

CHEMICAL & FORMULATION Triforine - 20% active

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100.0 Pesticidal Use - A fungicide to be sprayed by aerial or ground applicators on blueberries and peaches (from proposed label).

100.1 Application Methods/Directions/Rates (quote from proposed label)

Highbush Blueberry
Mummyberry Disease (Monilinia vaccinii-corymbosae)

Apply 24 fl. oz. of Funginex per acre in 20-50 gallons of water for aerial application.

Do not apply as a dilute spray. Do not mix with wetting agents, spreader-stickers or other adjuvants.

Make first application at leaf bud break and repeat in 7 to 10 days. Make third application at pink bud stage and repeat in 7 to 10 days at 25% to 50% bloom. Reduce the rate to 16 fl. oz./acre and apply last spray between full bloom and early petal fall.

Do not make more than five applications from leaf bud break to early petal fall.

Peach
Brownrot (Monilinia fructicola) (Monilinia laxa)

For ground application only. Apply 3 preharvest sprays of 12 to 16 fl. oz., per 100 gallons of water, or 36 to 48 fl. oz., per acre, at 7 to 10 day intervals. Make the first application 2 to 3 weeks before harvest and the last application just prior to harvest.

Since spray requirements may vary due to different climatic and other conditions, follow official local or state recommendations where applicable.

In California Only:

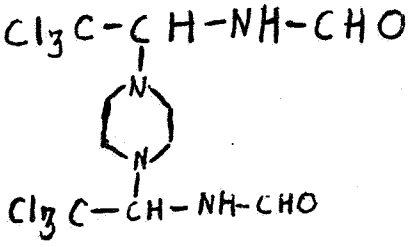
Apply 2 preharvest sprays of 12 fl. oz., per 100 gallons of water or 48 fl. oz., per acre. Make the first application 3 weeks before harvest, followed by a second application 7 to 10 days later.

Do not mix Funginex with wetting agents, spreader-stickers, or other adjuvants.

Do not let spray mixture stand in tank overnight.

Do not use this material if it cannot be applied according to the use schedule on the label.

101.3 Structural formula (from Environmental Safety data abstract of 3/28/75 registration submission)



101.4 Molecular Weight - 435 (from Mar. 20, 1976, EEEB Rev.)

101.5 Physical State, Color, Odor - fine white powder with faint odor (tech). (from Mar. 20, 1976, EEEB Rev.)

101.6 Solubility - In H_2O is 28 ppm at room temperature. (from Mar. 20, 1976, EEEB Rev.) Solubility in other liquids was not submitted.

102.1 Soil - 1/2 life ~ 2 weeks (slower in dry seasons) degradation is probably chemical rather than biological. Parent compound may not leach; but metabolites appear to be fairly mobile in soil. (Quote from 3/20/76 EEEB review)

102.2 Water - Rapid degradation in water (2 days - 1 week). (Quote from 3/20/76 EEEB review)

102.3 Plant - Uptake by roots and transported to aerial portions of plant with half-life of 9-10 days (study done with 3 week old barley plants after a soil drench). (Quote from 3/20/76 EEEB review)

102.4 Animal - 96% of dose was excreted through urine and feces after 72 hours in the rat. (Quote from 3/20/76 EEEB review)

102.4 Data Review Number: ES-VII-GG-1

Test: Bioaccumulation in Fish

Species: Rainbow trout (Salmo gairdneri)

Results: Triforine and its degradates were not differentially accumulated in fish tissues. While living in water treated with 1 ppm Triforine, the fish tissues contained 0.13 to 0.26 ppm of Triforine and its degradation products. Thirty days after the exposure, the concentration had decreased to 0.05 ppm.

Chemical: Triforine (N,N-[1,4-piperazinediylbis(2,2,2-trichloroethylidene)]bis[formamide])

Title: 3H/14C - Triforine Residues in Fish

Study Date: January, 1975

Researcher: Dr. M. Wotshokowsky, E. Merck

Registrant: E. M. Laboratories

Validation Category: This study has not been validated by environmental chemistry.

Abstract: Triforine labeled with carbon and hydrogen isotopes was proportionally added to test water containing rainbow trout to a level of 1 ppm. After 32 days, the fish tissues contained 0.16 ppm or less of triforine and its degradation products. After exposure was terminated for 30 days, the concentration of residues had diminished to 0.05 ppm.

103.1.2 Data Review Number: ES-VII C-1

Test: Avian Acute Oral LD_{50}

Species: "Quail" - the species name is not given

Japanese quail D.J.D. 2/14/78

Results: The LD_{50} is greater than 6000 parts per million. No confidence limits are given.

Chemical: Triforine

Title: Acute Toxicological Investigation

Study Date: September 9, 1970

Researcher: H. Boehringer Sohn

Registrant: E. M. Laboratories, Inc.

Validation Category: Invalid

Category Repairability: Repairable to a core study with submittal of the following: species of quail

Abstract: This is a brief outline of an acute LD_{50} study of Triforine against an unspecified species of quail.

103.1.3 Data Review Number: (ES)-(VII) G-1

Test: Acute 96 hour LC_{50} (Coldwater fish)

Species: Rainbow trout (Salmo guirdneri)

Results: The LC_{50} was greater than 1000 parts per million.

Chemical: Triforine

Title: Acute Toxicity of Triforine to Bluegill (Lepomis macrochirus) and rainbow trout (Salmo gairdneri)

Study Date: March, 1973

Researcher: Dr. Kenneth J. Macek, Bionomics Inc.

Registrant: E. M. Laboratories

Validation Category: ~~Core~~ RKI+ Supplementary

Abstract: The LC_{50} of Triforine for rainbow trout was determined to be more than 1000 parts per million as no deaths occurred within a 96-hour period at this level.

103.1.3 Data Review Number: (ES)-(VII) F-1

Test: Acute, Static, Fish LC_{50} (Warmwater)

Species: Bluegill (Lepomis macrochirus)

Results: The LC_{50} was greater than 1000 parts per million.

Chemical: Triforine

Title: Acute Toxicity of Triforine to Bluebill (Lepomis macrochirus) and Rainbow Trout (Salmo gairdneri)

Study Date: March, 1973

Researcher: Dr. Kenneth J. Macek, Bionomics, Inc.

Registrant: E. M. Laboratories

Validation Category: ~~Core~~ Supplementary

Abstract: The LC_{50} of Triforine was determined to be greater than 1000 parts per million as no deaths occurred at this level during a 96-hour period.

103.1.4 Data Review Number: (ES)-VII-H-1

Test: Aquatic Invertebrate Acute LC_{50}

Species: Daphnia magna

Results: The LC_{50} or "TL_{50}" for Daphnia magna exposed to Triforine was determined to be 27 ppm with confidence limits of 21 to 35 ppm.

Chemical: Triforine

Title: Four-day Static Aquatic Toxicity Studies with Triforine 6.5% EC in Daphnia magna

Study Date: July 2, 1976

Researcher: Keplinger, M. L. et. al. Industrial Biotest Laboratories

Registrant: E. M. Laboratories

Validation Category: Supplementary RKH

Category Repairability: This test was not done on the technical grade.

Abstract: The LC_{50} for Triforine on Daphnia magna was determined. A positive control using DDT was also made.

Not a Standard Test

Data Review Number: (ES)-VII-GG-1

Test: Dietary Toxicity for bees and toxicity tests on guppies. Neither has a definite protocol.

Species: Not specified

Results: The effects of an unspecified chemical (code name WF-57), presumed by this reviewer to be Triforine(R), appear to be confounded with dimethyl-formamide, n-butanol, cyclohexanone, and N-methylpryrrolidone in the dietary bee study. Guppies were exposed to 50 ppm Triforine without effect.

Chemical: Only the code numbers are specified

Title: Concerning the Toxic Effects of WS24 and Solvents in Fish and Bees

Study Date: Not specified

Researcher: Dr. Geisthardt of H. Boehringer Sohn

Registrant: E. M. Laboratory

Validation Category: Invalid

Category Repairability: No. The technical grade was not used. The toxicity of the four chemicals tested concurrently on guppies is not known. Guppies are not acceptable test species.

Abstract: Observations were made on the reactions of guppies and bees after their exposure to a combination of chemicals.

103.2 Date Review Number: ES-VII-D-1

Test Avian subacute dietary LC_{50} (Upland game bird)

Species: Bobwhite quail

Results: The avian subacute LC_{50} was calculated to be 1849 ppm with 95% confidence limits of 1142 to 2994 ppm.

Chemical: Triforine

Title: Eight-Day Dietary LC_{50}-Bobwhite Quail-Triforine Final Report

Study Date: June 11, 1973

Researcher: Hazleton Laboratories, Inc. F. E. Renn and R. Fink

Registrant: E. M. Laboratories

Validation Category: Core

Abstract: An 8-day dietary subacute LC_{50} was run on Triforine for the bobwhite quail. Both positive (dieldrin) and negative controls were run.

103.2 Data Review Number: ES-VII-E-1

Test: Avian subacute dietary LC_{50} (Wild waterfowl)

Species: Mallard Duck

Results: The LC_{50} was calculated to be greater than 4640 ppm.

Chemical: Triforine

Title: Eight-day Dietary LC_{50} - Mallard Ducks - Triforine. Final Report

Study Date: June 11, 1973

Researcher: R. Fink and Frederick E. Reno

Registrant: E. M. Laboratories, Inc.

Validation Category: Core

Abstract: A dietary subacute test was run on Triforine against mallard ducks. Both positive (Dieldrin) and negative controls were run concurrently. No toxic effects were observed after dosing the bird diet at 4640 ppm for five days.

104.1.1 Adequacy of Toxicity Data

The following toxicity studies have been accepted for meeting the core requirements for a pesticide fish and wildlife hazard evaluation:

1. The June 11, 1973, Hazleton Laboratory study on Bobwhite quail fulfills the requirement for a subacute dietary LC_{50} on an upland game bird.

2. The June 11, 1973, Hazleton Laboratory study on mallard ducks meets the requirement for a subacute dietary LC_{50} on an upland game bird.

3. The March, 1973, ~~Bionomics~~ Inc. study on rainbow trout satisfies the requirement for an acute LC_{50} for a cold-water fish.

4. The March, 1973, Bionomics Inc. study on bluegill sunfish satisfies the requirement for an acute LC_{50} for a warm-water fish.

104.1.2 Additional Data Required

Two required studies are deficient in the manner discussed below:

1. The species name of the "quail" used in the September 9, 1970, C. H. Boehringer Sohn experiment must be submitted. If this species was the bobwhite quail, then the test will be accepted. If some other species was used, then this acute avian LD_{50} will have to be repeated.

2. The Industrial Biotest Laboratory study on Daphnia magna is inadequate in that it was run on 6.5% active Triforine. This test will have to be conducted again using technical grade Funginex to meet the requirement for an acute 48 hr., LC_{50} for an aquatic invertebrate.

Another study which is not currently required and is not likely to be required was submitted. This is Dr. Geisthardt's study on bees and guppies. No more information will be requested in regard to this experiment because several toxins were tested concurrently on the same organisms.

104.1.3 Likelihood of Exposure to Non-Target Organisms

Very little hazard to terrestrial wildlife sppears to be posed by the Funginex use proposed in this application. The LD and LC_{50}'s submitted are extremely high:

Species	LC or LD_{50}	Study Status
Quail	LD_{50} Greater than 6000 mg/kg	Repairable
Bobwhite quail	8 day dietary LC_{50} 1849 ppm	Core
Mallard	8 day dietary LC_{50} greater than 4640 ppm	Core
Rainbow trout	LC_{50} (Acute 96 hr.) greater than 1000 ppm	Core
Bluegill	LC_{50} (Acute 96 hr.) greater than 1000 ppm	Core
Rat	13 week dietary N.E. level $\geq$500 ppm $\geq$2500 ppm	1/26/77 EEEB Review
Dog	13 week dietary. No deaths at 30,000 ppm	1/26/77 EEEB Review

The residue levels calculated from the proposed maximum application rate would be fairly low. If a peach grower made three applications of Funginex within two weeks the maximum residue accumulation in the soil to the depth of 0.1 inches will be 29.7 ppm (computations are shown below in the discussion appendices).

In order to determine the maximum residue levels occurring on plants and the animals which eat them, degradation of Funginex was assumed to be by photolysis only. The photolytic degradation rate to 75 per cent of the original within 64 hours (see ultraviolet light study submitted to Environmental Chemistry) was used in this analysis. It was estimated that the maximum residue accumulation would range from 9 ppm on peaches to 310 ppm on short range grass. This would result in a .792 mg/kg and a 27.280 mg/kg calculated

accumulation in bobwhites foraging in peach orchards and short range grass, respectively. The Funginex LD_{50} on quail is over 6000 mg/kg so little or no acute harm from this application rate is expected.

An appreciable threat to aquatic wildlife is also unlikely. The degradation of Funginex in water takes only two to seven days (Review by J. Akerman, 3/28/75). Furthermore, the retention time of this chemical in fish tissue is quite short (see Section 102.4 for a detailed analysis).

Appendix to Discussion

Computations for Concentration in Soil

1/2 life in soil = 14 days (Review by J. Akerman, 3/28/75) assuming the highest application rate of three applications of 48 fl. oz. (20% a.i.) with at least seven days between each spraying.

Number of Applications

	1*	7 days	2*	7 days	3*	
Proportion of applications remaining undegraded in the soil	1.00		0.75 1.00		0 0.75 1.00 2.25	active applications remain undegraded

The number of ounces, of active ingredients per application = % active X application weight (in ounces) = 20% X 48 fl. oz. = 9.6 fl. ounces of active ingredients.

*Application number

Appendix to Discussion

The number of ounces of active ingredient per acre = number of applications remaining undegraded = 2.25 total applications X 9.6 ounces of active ingredient = 21.6 oz. or 1.35 lbs./acre maximum accumulation of active ingredient.

From the nomograph, an application rate of 1.5 lbs. per acre will result in a residue within the top 0.1 inch of the soil of 33 ppm, therefore:

$$\frac{\text{residue resulting from a 1.35 lb. application}}{33} = \frac{1.35}{1.5} =$$

a residue of 29.7 ppm in the upper 1/10" of soil can be interpolated from a 1.35 pound per acre application.

Appendix to Discussion

Calculation of the maximum residue accumulation on peaches and short range grass and the possible accumulation in an animal (bobwhite quail)

Assumption #1 - 12 hours of light per day

Assumption #2 - 25% photolytic degradation in 64 hrs.

	1	64 hrs.	2	148 hrs.	3
Proportion of application remaining undegraded on plant surface	1.00	0.75	0.68 1.00	0.51 0.75	0.47 0.68 1.00 2.15 applications remaining on plants

Number of ounces of active ingredients per application X number of applications = total ounces of active ingredients on the plants =

9.6 x 2.15 = 20.64 ounces a.i. = 1.29 lbs.

From the tables this would result in a residue of 210 ppm on short range grass and a 9 ppm residue on peaches.

Appendix to Discussion

Calculation of Funginex exposure to quail foraging on short range grass and peach tree insects.

$$\frac{\text{food eaten per day}}{\text{weight of animal}} \times \text{pesticide residue(ppm)} = \frac{\text{Mg pesticide}}{\text{Kg.of Bird}}$$

$$\text{peach exposure} = 0.088 \times 9 \text{ ppm} = \frac{0.792 \text{ mg}}{\text{Kg. bird weight}}$$

$$\text{short range grass exposure} = 0.088 \times 310 \text{ ppm} =$$

$$27.28 \text{ mg/kg}$$

105.0 Conclusions

Additional data required to support the registration are:

1. The species name of the quail used in the 9/9/70, H. Boehringer Sohn Avian Acute Oral LD_{50}.

2. Submission of an aquatic invertebrate acute LC_{50} on the technical grade of Funginex (preferably with Daphnia magna). The July 2, 1976, test by Industrial Biotest is not adequate as it was run on a 6.5% active ingredient formulation.

The subacute dietary studies on bobwhite quail and mallard ducks and the acute fish studies have been reviewed and are acceptable in support of the registration.

RKH

Robert K. Hitch
Fish and Wildlife Section
EEE Branch, August 23, 1977