file

122804
SHAUGHNESSY NO.

REVIEW NO.

EEB REVIEW

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TYPE PRODUCT(S): I, D, H, F, N, R, S Miticide/Insecticide

DATA ACCESSION NO(S). 074005

PRODUCT MANAGER NO. G. LaRocca (15)

PRODUCT NAME(S) Abamectin 0.15 EC

COMPANY NAME Merck, Sharp, and Dohme Research Laboratories

SUBMISSION PURPOSE Proposed Experimental Use Permit (EUP) for use on cotton.

SHAUGHNESSY NO.	CHEMICAL & FORMULATION	% A.I.

SECTION 5 EUP REVIEW

Avermectin

100 Experimental Use Label Information

100.1 Pesticide Use

Insecticide/Miticide for use on cotton.

100.2 Formulation Information

Active Ingredient:

Abamectin: Avermectin B_1 [A mixture of avermectins containing $\geq$ 80% Avermectin A_1a, 5-O-demethyl and $\leq$ 20% avermectin A_1a, 5-O-demethyl-25-de-(1-methyl-propyl)-25-(1-methylpropyl)-25-(1-methylethyl)-] 2.0%

Inert Ingredients 98.0%

(1 gallon contains 0.15 pound Abamectin)

100.3 Application Methods, Directions, Rates

Cotton

Aerial and ground treatment permitted on label.

Mid- to Late Season

To evaluate for control of spider mites mid- to late season, apply 8 to 16 fluid ounces per acre depending upon plant size and density of foliage. Apply when mites first appear and repeat as necessary to maintain control. Apply in 5 to 50 gallons of water per acre with ground equipment or in 2 to 15 gallons of water per acre by aircraft.

Early Season (San Joaquin Valley, California)

Evaluate 4 to 8 fluid ounces per acre for early season control of spider mites on cotton in the California San Joaquin Valley. Use ground sprayers only, directing the spray to the cotton plant in 5 to 25 gallons of water per acre.

4 fluid oz contains 0.00469 lb ai.
8 fluid oz contains 0.00938 lb ai.
16 fluid oz contains 0.01875 lb ai.

100.4 Target Organism

Primary Target Pests:

Carmine spider mite (Tetranychus cinnabarinus), Twospotted spider mite (T. urticae), Pacific spider mite (T. pacificus), and Strawberry spider mite (T. turkestani).

Other Target Arthropods:

Cotton Leafperforator (Bucculatrix thurberiella), Plant Bugs (Lygus spp.), Cotton fleahopper (Pseudatomosalis seriatus), Whitefly (Bemisia spp.) and Western flower thrips (Frankliniella occidentalis).

100.5 Precautionary Labeling

ENVIRONMENTAL HAZARDS

This product is toxic to fish and wildlife. Keep out of lakes, ponds, or streams. Do not contaminate water by cleaning of equipment or disposal of wastes.

Do not apply when weather conditions favor drift from target areas.

This product is highly toxic to bees exposed to direct treatment or residues on blooming crops or weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area.

In order to ensure protection of endangered species from exposure to this experimental pesticide, persons authorized to conduct experiments with this product must first consult with State or Federal endangered species authorities responsible for the treatment area.

100.6 Proposed EUP Program

100.6.1 Objectives

Abamectin (MK-936) has exhibited excellent activity on spider mites (twospotted, Carmine, Pacific, and strawberry) when used mid- to late season on cotton at 0.01 to 0.02 lb ai/A.

Due to the sporadic occurrence of spider mites on cotton in all cotton-producing areas outside of California and Arizona, most of the Abamectin data assembled to date are limited to California and Arizona where cotton tests have been conducted in small replicated plots using ground equipment. The objectives of the proposed experimental program are designed to fill data gaps in a number of areas. These areas are:

1. Expand testing into as many geographic areas as possible outside of California and Arizona.

2. Obtain data in all areas using commercial ground sprayers calibrated to deliver 5 to 50 gallons of water per acre.

3. Establish aerial trials and determine the efficacy of Abamectin against spider mites when used in water volumes ranging from 2 to 15 gallons per acre.

4. Determine the optimum range of water volumes for ground and aerial applications.

5. Evaluate early season ground applications of abamectin at 0.005 to 0.01 lb ai/A in the San Joaquin Valley, California.

6. Obtain data on cotton leafperforator, lygus bug, cotton fleahopper, western flower thrips, and whitefly in trials where these pests occur concurrently with spider mites.

100.6.2 Date, Duration

Early season applications for spider mites could occur as early as April 15 to May 1 in the San Joaquin Valley. Late season sprays (up to 20 days before harvest) could be made as late as October 1. Therefore, most of the active program would occur between April and October 1986. The EUP should include the 1-year period April 1, 1986 to April 1, 1987.

100.6.3 Amount Shipped, Geographical Distribution

States, Acreages, and Quantity of Material for Proposed Experimental Use of Abamectin on Cotton in 1986

State	Acreage	Range of Rates to be Evaluated (lb ai/A)	Maximum Number Application	Quantity of Abamectin 0.15 EC Needed (Gallons)
California	2000	0.005-0.02[1]/	3	500
Arizona	750	0.01-0.02	3	187.5
Texas	250	0.01-0.02	3	187.5
New Mexico	100	0.01-0.02	3	25
Tennessee	100	0.01-0.02	3	25
Oklahoma	100	0.01-0.02	3	25
Arkansas	100	0.01-0.02	3	25
Mississippi	200	0.01-0.02	3	50
Louisiana	200	0.01-0.02	3	50
Georgia	200	0.01-0.02	3	50
Alabama	200	0.01-0.02	3	50
South Carolina	100	0.01-0.02	3	25
North Carolina	100	0.01-0.02	3	25
Florida	100	0.01-0.02	3	25
Total	5000 Acres		Total	1250 gallons[2]/ (187.5 lb ai)

[1]/Lower rates (down to 4 fl oz or 0.005 lb ai/A) will be evaluated on early season cotton in the California San Joaquin Valley only. Refer to Section G/3 for details.

[2]/Based on an average of two applications per acre at the maximum rate proposed for evaluation.

101 Hazard Assessment

101.1 Discussion

Under this EUP, Avermectin may be applied to cotton at up to 0.02 lb ai per acre by aerial or ground equipment. A total of 5000 acres in 15 States would be treated a maximum of 3 times.

100.2 Likelihood of Adverse Effects to Nontarget Organisms

The following discussion of toxicity and environmental fate is taken, for the most part, from the October 29, 1985 review on Fire Ant Control.

Summary of Toxicity

Species	Test Material	Results	Category
Bobwhite quail	91%	LD_{50} > 2000 mg/kg	Core
Bobwhite quail	91%	LC_{50} = 3102 ppm	Core
Mallard duck	91%	LC_{50} = 383 ppm	Core
Bluegill	91%	LC_{50} = 9.6 ppb	Core
Rainbow trout	91%	LC_{50} = 3.2 ppb	Core
Daphnia	91%	LC_{50} = 0.34 ppb	Core
Daphnia	MK-936 Tech.	LC_{50} = 0.22 ppb	Core
Daphnia	Avermectin $B_{1}a$	LC_{50} = 0.42 ppb	Core
Daphnia	Polar metabolite*	LC_{50} = 4.2 ppb (binomial) 21.0 ppb moving average)	Core
Daphnia	Moderately polar	6.3 ppb	Core
Daphnia	Nonpolar metabolite	25.4 ppb	Core
Daphnia	Thin film polar metabolite*	76.7 ppb	Core
Daphnia	8α-Hydroxy Avermectin $B_{1}a$**	LC_{50} = 25.5 ppb	Core
Daphnia	91.43%	MATC > 0.03 < 0.09 ppb	Core
Shrimp, mysid		LC_{50} = 0.2 ppb	Core
sheepshead ~~Fathead~~ minnow		LC_{50} = 15 ppb	Core
Oyster embryolarvae	48-hr	LC_{50} = 430 ppb	Core

Avermectin is highly toxic to very highly toxic to mammals (mouse LD_{50} = 13 to 23 mg/kg; rat LD_{50} = 10 to 11 mg/kg; weanling rat LD_{50}= 1.5 mg/kg). It has an effect on reproduction in rats at 0.1 to 0.5 mg/kg day.

The nonpolar metabolite has an LD_{50} of > 48 mg/kg in mice. The polar* metabolite has an LD_{50} of > 5000 mg/kg in mice.

*The polar metabolite is the last one formed and is what the parent becomes after about 27 hours.

**Major soil metabolite of Avermectin $B_{1}a$. This metabolite accounts for up to 20 percent of the total soil residue during the half-life of parent avermectin $B_{1}a$ of 28 to 56 days. Also, the half-life of the metabolite is similar to that of the parent.

Abamectin (MK-936) may persist in the field with a half-life of a month. This was based on a field dissipation study reviewed by EAB (September 5, 1985 review). However, based on another EAB review (August 28, 1985), it is reported that abamectin has a photolytic half-life of 3.5 to 12 hours.

6

Apparently as long as MK-936 is in solution, it photolyzes rapidly. However, as soon as it binds to soil or other organic material it becomes much more persistent.

Based on discussions with Dr. Akiva Abramovitch of EAB and EAB's reviews, abamectin breaks down initially to the Avermectin $B_{1}a$ isomer (p. 6, EAB review, March 28, 1984, EUP on citrus). Evidently, after 27 hours or so, the primary degradate is the polar metabolite (pages 10 to 13 of Merck, Sharpe, and Dohme Research Laboratories document "Response to the Ecological Effects Branch Review" Accession No. 258746).

Avermectin bioaccumulates only slightly (110X maximum) in fish. Dupuration is 95 percent in 14 days.

Aquatic Exposure

It is not possible, without additional environmental fate data, to calculate the levels of exposure to aquatic or estuarine organisms due to runoff.

Based on the assumption that 10 percent of the applied ai could drift to an adjacent body of water, the following levels could occur:

conc. ppb	depth of water
1.5	6 inches
0.24	3 feet
0.12	6 feet

It is not possible to assess the acute hazard to fish, for while the drift estimate is less than the lowest fish LC_{50}, runoff could cause levels which exceed the LC_{50}.

The estimated concentration in 6 inches of water due to drift wil exceed the Daphnia magna LC_{50} of 0.340 ppb. This is likely to cause acute adverse effects to exposed aquatic invertebrate populations in shallow streams and ponds and along the edge of deeper water bodies. Aquatic levels are expected to be even higher when runoff loading is included so acute effects would be even greater.

Chronic effects to fish and aquatic invertebrates are unlikely as Avermectin photolyzes rapidly in water. Furthermore, it is unlikely to bioconcentrate in the food chain as it only bioaccumulates to 110X in bluegill and depurates 95 percent in 14 days. Note that the degradates are less toxic to Daphnia than the parent.

Terrestrial Exposure

The concentration (ppm) on terrestrial food items is:

	Short grass	Long grass	Leafy crops	Forage insects	Seed pods	Fruit
Maximum	4.8	2.2	2.5	1.2	0.3	0.2
Typical	2.5	1.8	0.7	0.7	0.1	0.3

These calculations are based on: Kenaga, E.E. (1973) Factors to be considered in the Evaluation of the Toxicity of Pesticides to Birds in Their Environment. In Environmental Quality and Safety, Global Aspects of Chemistry, Toxicology and Technology as Applied to the Environment, Vol. II. George Thieme Publishers.

This level is much lower than the lowest LC_{50} to birds (Mallard duck, 393 ppm). Avermectin is not expected to have acute effects to birds and since it is expected to degrade within 1 day on plant surfaces it should not have a chronic effect on birds.

The following table shows the concentrations required in mammalian food to cause an acute effect:

Species	Conc. (ppm) Adult	Weanling
Meadow vole (herbivore)	16.4	2.5
Red squirrel (granivore)	141.8	21.3
House mouse (omnivore)	25 0	3.75
Water shrew (insectivore)	4.8	1.5

(LD_{50}=mg/kg x wt grams/consumption per day grams)

Based on these extrapolated values and estimated residue levels, it is possible that occasionally some young mammals may ingest treated food material that is acutely toxic. This acute effect would only occur in the treated field and would not last more than a day as the active ingredient photolyzes on surfaces rapidly. The metabolites are less toxic to mammals than the parent.

Chronic effects are not likely because of the short half-life.

Summary

Aquatic hazard cannot be entirely assessed; however, it is possible that at least aquatic invertebrate populations immediately adjacent to treated area will experience acute adverse effects.

Birds are not expected to experience acute adverse effects; however, it is possible that some young mammals could ingest food that contains acutely toxic residues of Avermectin.

The acute effects to aquatic invertebrates and young mammals would not occur frequently as they are based on worse than typical situations.

Typically there should be no adverse acute effect to aquatic or terrestrial organisms due to the low use rate and short half-life.

Chronic effects are not expected due to the short half-life on surfaces and in water.

101.3 Endangered Species

If Avermectin is applied adjacent to habitat containing endangered mammals, fish, or aquatic invertebrates, it is expected to have an adverse effect on them. There are endangered species associated with cotton agriculture in the following counties.

Arizona:	Graham, Santa Cruz
Texas:	Jeff Davis, Reeves, Pecos, Hays, Burleson, Bastrop
New Mexico:	Chaves, Eddy
Tennessee:	Franklin, Lincoln
Oklahoma:	McCurtain, Le Flore
Arkansas:	Clay, Clark, Cross, Lawrence, St. Francis, Sevier
Mississippi:	Copiah
Alabama:	Butler, Colbert, Conecuh, Covington, Crenshaw, Lauderdale, Marshall, Monroe, Morgan

This is based on the cotton cluster Biological Opinion from OES, USFWS, or personal communication with OES.

If the registrant avoids these counties in the EUP, there will be no effect to endangered species. If Avermectin is experimentally used in these counties, the labeling restriction proposed by the registrant will preclude effects to endangered species.

101.4 Adequacy of Data

The available toxicity data were adequate to perform this hazard assessment. However, there was insufficient environmental fata data. The lack of data did not preclude completion of this EUP hazard assessment, but a

full registration hazard assessment on cotton could not be completed without additional environmental fate data and possibly additional toxicity data.

One study was submitted with this EUP.

Species:	Daphnia magna
Test Type:	48-hour LC_{50}
Test Material:	8 -Hydroxy Avermectin B_{1a} (major soil metabolite)
Results:	LC_{50} = 25.5 ppb
Category:	Core for degradate of Avermectin B_{1a}

101.5 Adequacy of Labeling:

The labeling is adequate.

102 Conclusions

EEB has completed a risk assessment of the proposed EUP to use Abamectin 0.15 EC on cotton. Based on the available data, EEB concludes that the proposed EUP provides for minimal hazards to nontarget nonendangered organisms.

If the registrant avoids the following counties, no adverse effects to endangered species are likely to occur:

Arizona:	Graham, Santa Cruz
Texas:	Jeff Davis, Reeves, Pecos, Hays, Burleson, Bastrop
New Mexico:	Chaves, Eddy
Tennessee:	Franklin, Lincoln
Oklahoma:	McCurtain, Le Flore
Arkansas:	Clay, Clark, Cross, Lawrence, St. Frances, Sevier
Mississippi:	Copiah
Alabama:	Butler, Colbert, Conecuh, Covington, Crenshaw, Lauderdale, Marshall, Monroe, Morgan

If the proposed EUP program includes use of Abamectin 0.15 EC in any of these counties, the registrant's proposed endangered species label statement is required.

The registrant should be notified that while the available data were adequate to perform a cotton EUP hazard assessment, additional data would be needed for full registration of Abamectin 0.15 EC on cotton.

15

Environmental fata data should include:

Soil adsorption constant
Kow (Octanol:water coefficient)
Microbial degradation (half-life)
Hydrolytic Halflife
Molecular weight

Additional data may be required depending on the environmental fata data provided. **Such data may include a fish embryo-larvae test and a shrimp life-cycle study.**

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11

DATA EVALUATION REPORT

1. Chemical: Abamectin

   Sha. No.: 122804

2. Test Material: 8α-Hydroxy Avermectin B_{1a} (Major soil metabolite of Avermectin B_{1a}.)

3. Study/Action Type: 48-Hour LC_{50} with Daphnia magna

4. Study ID: Forbis, A.D.; Georgie, L.; Burgess, D. Acute Toxicity of 8α-Hydroxy Avermectin B_{1a} to Daphnia magna. Analytical Bio-chemistry Laboratories, Study No. 33469, dated August 26, 1985. (Submitted by Merck, Sharp, and Dohme Research Laboratories.) Accession Number 074005

5. Reviewed by: Daniel Rieder, Wildlife Biologist, EEB/HED — Signature: Daniel Rieder — Date: 2/11/86

6. Approved by: Norm Cook, Section Head, Section 2, EEB/HED — Signature: Norman Cook — Date: 2·13·86

7. Conclusions:

   This study is scientifically sound. LC_{50} = 25.5 ppb 95% C.L. = 18 to 32 ppb. This study will fulfill the Guideline requirement for an aquatic invertebrate LC_{50} with a soil degradate of Abamectin.

8. Recommendation: N/A

9. Background:

   This study was submitted to support registration.

10. Discussion of Individual Tests: N/A

11. Methods and Materials:

a. Test Materials: 8 α-hydroxy Avermectin B_{1a}, a soil degradate.

Percent active ingredient: 99+ %

b. Test Organism: Water flea

Species: Daphnia magna
Age/Stage: < 24 hrs
Number per concentration: 20
Source: ABC Laboratory Stock

c. Test Containers: Glass

Size: 250 mL
Organisms per container: 10
Aerated: No
Replicates: 2

d. Test Conditions: Static

Photoperiod: 16 hours per day
Measured concentrations: No
Temperature: 20 °C
Test Solution: Aged wellwater
Controls: Solvent and Untreated
Solvent: Acetone
Protocol References: Committee on Methods for Toxicity Tests With Aquatic Organisms. Methods of Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. (1975) U.S. EPA, Ecol. Res. Serv. 660/3-75009.

American Public Health Association (1980) Standard Methods for the Examination of Water and Wastewater. 15th ed. Washington DC. 1134 p.

e. Statistics:

Reference: Stephan, C.E.; Busch, K.A.; Smith, R.; Burke, J.; and Andrews, R.W. (1978) A Computer Program for Calculating an LC_{50}. U.S. Environmental Protection Agency, Duluth, Minnesota, prepublication manuscript, August 1978.

12. Reported Results:

48-hour LC_{50} = 25.54 ppb 95% C.L. = 18 to 32 ppb.

CONCENTRATION PPB Nominal	MORTALITY 24 hours	48 hours	CONDITIONS DO	pH
Control	0	0	8.3	8.5
Solvent control	0	0		
3.2	0	0	8.0	8.6
5.6	0	0		
10	0	0	8.0	8.6
18	0	0		
32	0	18	7.8	8.6

13. Study Authors' Conclusions:

The 24-hour LC_{50} is greater than 32 ppb. The 48-hour LC_{50} is 25.5 ppb. The 48-hour NOEL is 3.2 ppb. Abnormal effects were observed at 5.6, 10, 18, and 32 ppb.

14. Reviewer Discussion:

a. Methods/Procedure: The test procedure was acceptable.

b. Statistics: The statistical results are compatible with the raw mortality data.

c. Discussion/Results: 8α-hydroxy Avermectin B_1a (a soil degradate of Avermectin) is very highly toxic to aquatic invertebrates.

d. Adequacy: Core

15. Completion of One-liner: One-liner completed.

16. CBI Appendix: N/A

14

122804 Abamectin Degradate Daphnia magna LC50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
32	20	18	90	2.012253E-02
18	20	0	0	9.536742E-05
10	20	0	0	9.536742E-05
5.6	20	0	0	9.536742E-05
3.2	20	0	0	9.536742E-05

THE BINOMIAL TEST SHOWS THAT 18 AND 32 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 25.54447

WHEN THERE ARE LESS THAN TWO CONCENTRATIONS AT WHICH THE PERCENT DEAD IS BETWEEN 0 AND 100, NEITHER THE MOVING AVERAGE NOR THE PROBIT METHOD CAN GIVE ANY STATISTICALLY SOUND RESULTS.

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