107901

(9)

EEE BRANCH REVIEW

DATE: IN 6/13/78 OUT 11/20/78 IN _____ OUT _____ IN _____ OUT _____

FISH & WILDLIFE ENVIRONMENTAL CHEMISTRY EFFICACY

FILE OR REG. NO(S). 21137-4

PETITION OR EXP. PERMIT NO. 7F1921

DATE DIV. RECEIVED 6/8/78

DATE OF SUBMISSION 6/6/78

DATE SUBMISSION ACCEPTED

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

DATA ACCESSION NO(S). 095811

PRODUCT MGR. NO(S). Wilson (21)

PRODUCT NAME(S) Funginex

COMPANY NAME EM Laboratories

SUBMISSION PURPOSE Data review and amendment to add blueberries + peaches

CHEMICAL & FORMULATION Triforine (N,N'-[1,4-piperazinediylbis (2,2,2-trichloroethylidene)] bis [formamide] ... 18.2%

100.1 Pesticidal Use

A fungicide to be applied by ground or air to Highbush blueberries and peaches.

100.2 Formulation Information

An 18.2% EC.

100.3 Application Methods/Directions/Rates

A. Blueberries (Ground and Aerial application)

1. Pacific and Mid Western States
Do not make more than 5 applications from leaf bud break to early petal fall.

a) Apply 24 fl. oz. (0.30 lbs ai/A) for the first four applications - at leaf bud break, 7 to 10 days later, pink bud stage and 7 to 10 days at early bloom.

b) Apply 16 fl. oz. (0.2 lbs ai/A) for the last application - between full bloom and early petal fall.

2. Eastern Seaboard States (for primary infection only)
Do not make more than three applications from leaf bud break to pink bud stage.

a) Apply 24 fl. oz. (0.30 lbs. ai/A at -leaf bud break, 7 to 10 days and pink bud stage.

B. Peach (Ground)

1. For full coverage ground spray only - no more than 3 pre-harvest applications.

a) Apply 12 fl.oz. (0.15 lbs ai/A) to 16 fl. oz. (0.2 lbs ai/A) at 2 or 3 weeks prior to harvest and repeat twice if necessary at 7 to 10 day intervals.

2. California only
For full coverage ground sprays only. Apply two pre-harvest sprays at 12 fl. oz. (0.15 lbs ai/A). Make first application 3 weeks before harvest followed by a second application in 7 to 10 days.

100.4 Target Pests

1. Blueberry - Mummyberry disease (Monilinia Mummyberry)

2. Peach - Brown rot of fruit (Monilinia)

100.5 Precautionary Labeling

Keep out of lakes, ponds and streams. Do not contaminate water by cleaning of equipment or disposal of wastes. Apply this product only as specified on this label.

101.0 Chemical and Physical Properties

101.1 Chemical Name

(N,N' - [1,4 piperazinediylbis (2,2,2 - trichloro-ethylidene)] bis [formamide])

101.2 Common Name

Triforine

101.3 - 103.0 See previous review by D. Urban 3/14/78

Summary of Data Reviewed (R. Engler 4/7/77)

2-year dog feeding study	NEL 100 ppm or 2.5 mg/kg bw/day
2-year rat feeding study	NEL 625 ppm or 31 mg/kg bw/day negative for oncogenicity
18 month mouse feeding study	negative for oncogenicity at 750 ppm or 100 mg/kg bw/day (highest level fed).
3-generation reproduction study (rat)	NEL (reproduction) 2500 ppm, highest feeding level
Metabolism (rat) two studies	Satisfactory to determine major metabolites

104.0 Hazard Assessment

(see previous reviews by R. Hitch 8/23/77 and H. Craven 2/1/77)

104.1.3 Likelihood of Exposure to Non-Target Organisms

Very little acute or subacute hazard to terrestrial wildlife appears 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	Supplementary
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	Supplementary
Bluegill	LC_{50} (Acute 96 hr.) greater than 1000 ppm	Supplementary
Daphnia (6.5% ai)	48 hr. LC_{50} 27ppm	Supplementary
Rat	13 week dietary N.E. level $\geq$ 500 ppm $\geq$ 2500 ppm	2/1/77 EEEB Review
Dog	13 week dietary. No deaths at 30,000 ppm	2/1/77 EEEB Review

Peaches

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.

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 caluculated 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.

Blueberries

There will be much activity on the part of most terrestrial wildlife during this early spring period. Birds will begin their courting, large mammals will be browsing and small mammals will be foraging seeds, dormant insects etc. while nursing their young. However, as stated in the discussion, the toxicity and short half life of triforine suggests little or no acute or subacute hazard. .

An appreciable threat to aquatic wildlife is also unlikely. Secondly the degradation of Funginex in water takes only two to seven days (Review by J. Akerman, 3/28/75). Finally the retention time of this chemical in fish tissue is quite short (see Section 102.4 for a detailed analysis). Firstly, a direct application of 0.3 lb ai. to an acre foot of water would result in 220 ppb in the top 6" of water.

Triforine does not appear to pose an acute or subacute hazard to fish and wildlife, nevertheless an assessment of the potential for reproductive impairment of birds and mammals must also be considered in light of multiple applications during the breeding season. Avian reproduction studies are not available, however the following information suggests little need for requiring these studies to support the use on blueberries:

1. A 3-generation not rat reproduction study yielded a NEL of 2500 ppm.

2. 96% of material is excreted in urine and feces after 72 hours in the rat - unvalidated study

3. A rainbow trout bioaccumulation study showed no accumulation. Exposure to 1 ppm resulted in 0.15 ppm (whole body ?) after a 30 day depuration period - unvalidated study.

4. Half life in plants is 9-10 days - unvalidated study.

5. A single application of 0.3 lb ai results in 75 ppm on short grass immediately after spraying.

6. Total acreage U.S. wide for high bush blueberries is approx. 18,000. The average farm in Atlantic Ct. N.J. contains approx. 50 acres.

104.3 Endangered Species Consideration

No hazard to endangered species is anticipated.

104.4 -
104.5 See conclusions

105.0 Classification
The product should remain unclassified.

106.0 RPAR Criteria
No triggers for fish and wildlife have been pulled.

107.0 Conclusions

107.1 Environmental Fate and Toxicology Acknowledgement
Previous EEB reviews containing toxicology and Environmental Fate information have been examined.

107.2 Classification Labeling
The product should remain unclassified until an acceptable avian acute oral has been submitted.

107.3 Environmental Hazards Labeling
No labeling will be specified until recipt of the acceptable avian acute oral.

107.4 Data Adequacy Conclusions

1. The avian acute oral LD_{50} using Japanese quail is unacceptable to support the registration. Japanese quail are not acceptable test species.

2. Avian reproduction studies will be required for expanded uses with multiple applications. future

3. Data on technical triforine - both with and without solvents - and 6.5% E.C. for daphnia and fish have satisfied the data requirements for aquatic organisms.

107.5 Data Request
The avian acute oral LD_{50} for one species of waterfowl (mallard duck, preferably) or one species of upland game bird (ring-necked pheasant or bobwhite quail).

107.7 Recommendations

Triforine is no more than slightly toxic to aquatic organisms and only slightly toxic to birds and mammals. Although birds and mammals will be exposed the acute, subacute and chronic hazards are not a concern.

Henry T. Craven
Ecological Effects Branch

November 20, 1078

Richard Tucker
Acting Section Head
Ecological Effects Branch

November 20, 1978

Clayton Bushong
Acting Chief
Ecological Effects Branch

12/12/78

107901

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: March 14, 1979

SUBJECT: PP# 7F1921. Triforine in or on blueberries and peaches. Request for Method Trial.

FROM: M. Nelson, Chemist, RCB, HED (TS-769)

TO: Method Evaluation Section, CBIB, BFSD (TS-768)

THRU: Acting Chief, RCB R D Schmitt

EM Laboratories, Inc. is proposing the establishment of tolerances for residues of the fungicide triforine, N,N'-(1,4-piperazinediyl-bis-(2,2,2-trichloroethylidene))-bis-(formamide), in or on blueberries at 0.1 ppm and peaches at 5 ppm.

These will be the first established tolerances for this compound.

You are requested to conduct a trial of the petitioner's method, "Determination of triforine residues" (12/7/76). Two copies of this method are attached, along with representative sample chromatograms and recovery data, and a portion of an RCB review (M. Nelson, 6/12/78) re the methodology which may be of interest.

This proposed enforcement method, as written, utilizes an internal standard, but the try-out should be run without using an internal standard.

Samples of both blueberries and peaches are to be tested. Blueberries are to be fortified at levels of 0, 0.1, and 0.2 ppm with triforine, and peaches are to be fortified at levels of 0, 5, and 10 ppm, also with triforine. Samples are to be run in duplicate and analyzed for triforine residues.

The Pesticides Reference Standards Section (Dr. G. Glasgow) has triforine standards in stock.

The control values reported in the petition were generally ND-0.05 ppm. The limit of detection appears to be $\leq$0.01 ppm, judging from the chromatograms.

We would appreciate it if the report of your method trial results could be submitted to us on or before 6/15/79.

M. Nelson

M. Nelson, Ph.D.

107901

EEE

5/25/79

PP# 7F1921. Triforine in or on blueberries and peaches. Comments on amendment of March 1979.

M. Nelson, Chemist, RCB, HED (TS-769)

P.M. Team 21 (H. Jacoby), HFB, HD (TS-767)

Thru: Acting Chief, RCB

This amendment addresses three (#3, 4, 5) of the seven deficiencies remaining in our (M. Nelson) review of 6/12/78, which see.

Those deficiencies are paraphrased below for convenience, followed by the petitioner's responses, our comments/conclusions thereon, and a general summation of the deficiencies as yet unresolved.

#3. A confirmatory procedure for the residue analysis of triforine.

The petitioner has now supplied the information that two alternate GLC columns of differing polarity (7.5% QF-1 on 80/100 mesh Chromosorb W-AW DMCS; 10% SE-200 on 60/80 mesh Gaschrom Q) have been tested and are available to supplement the column of choice (5% SE-30 on 60-80 mesh Gaschrom Q) for the routine analysis of chloral hydrate formed from triforine.

Comments/Conclusions: This deficiency is considered resolved.

#4. Interference studies for pesticides registered on blueberries and peaches.

Forty-seven pesticides registered in the USA were tested to demonstrate that they did not interfere with the residue analysis of triforine. Some of the chemicals are registered on peaches and blueberries, while others were selected for testing because they are registered on crops which may in the future be added to the label.

Only one of the forty-seven pesticides tested caused interference and that was the insecticide Dylox (aka trichlorofon, not an ANSI name) which, at high concentration (10 ppm), resulted in a GLC peak at the retention time of chloral hydrate which would be equivalent to a residue of 0.[illegible]-0.[illegible] ppm triforine (i.e., approximately the limit of detection). Dylox is not registered (nor has tolerances) on either peaches or blueberries.

Comments/Conclusions: This deficiency is considered resolved.

#5. Frozen storage stability test with triforine.

Samples of blueberries, peaches, apples, and cherries were fortified with 0.1 or 1.0 ppm of triforine and deep-frozen. Samples for analysis have so far been taken at 1 time and at 2 and 4 months thereafter; the study is still on-going and will be conducted for a period of one year.

The data thus far amassed indicates that triforine residues in plant materials under frozen storage conditions remain essentially stable.

Comments/Conclusions: The results of this study which have been made available to-date are reassuring. However, since there still remain other unresolved deficiencies, and since the residue data in the petition was from samples stored up to 35 months (but mostly <1 year), we withhold a conclusion at this time that this deficiency is resolved pending future receipt and evaluation of the stability data reflecting a longer interval of frozen storage.

Conclusions and Recommendations

The following deficiencies still need to be directly addressed/resolved by the petitioner:

1. The formulation still contains inerts which have not yet received clearance/exemption for the proposed uses.

2. Appropriate testing of the formulation for the presence of N-nitroso contaminants is needed.

Additionally, with the next submission, we desire updated data from the on-going frozen storage stability testing.

In the interim (pending receipt/evaluation of the requested up-dated stability data and completion of the on-going FSS), we continue to defer our conclusions re: (a) the appropriateness of the proposed tolerance level for blueberries, and (b) the adequacy of the submitted residue data to support the proposed tolerances on both blueberries and peaches.

Accordingly, for the reasons cited directly above, we recommend that the proposed tolerances for residues of triforine in or on blueberries (0.1 ppm) and peaches (5 ppm) not be established at the present time.

We note that EFB (see R. May, Jr. and S. Creeger reviews of 10/18/77 and 7/13/78) has not recommended favorably for these proposed uses, nor has TOX as yet insofar as we know.

M. Nelson

TS-769:RCB:MJNELSON:sdb:X62610:RM108:WDHR:5/25/79