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EEE BRANCH REVIEW

DATE: IN 1/19/78 OUT 3/14/78 IN _____ OUT _____ IN _____ OUT _____

FISH & WILDLIFE ENVIRONMENTAL CHEMISTRY EFFICACY

FILE OR REG. NO. 239-EUGL

PETITION OR EXP. PERMIT NO. _____

DATE DIV. RECEIVED 1/16/78 and 9/20/76

DATE OF SUBMISSION 1/13/78 and 9/17/76

DATE SUBMISSION ACCEPTED _____

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

DATA ACCESSION NO(S). 232684, 232695

PRODUCT MGR. NO. E. M. Wilson (21)

PRODUCT NAME(S) ORTHO, Funginex, Triforine

COMPANY NAME Chevron Chemical Company, Ortho Division

SUBMISSION PURPOSE Registration for Use on Roses

CHEMICAL & FORMULATION Active Ingredient - Triforine-N,N'-[1,4 piperazinediylbis (2,2,2-trichloroethylidene)]bis (formamide)..... 6.5%

Inert Ingredients.....93.5%

100.0 Pesticide Use

A fungicide to be sprayed by ground applicators on roses to control and prevent black spot, powdery mildew and rust (from proposed label).

100.1 Application Methods/Directions

ORTHO Rose Disease Control contains the active ingredient Triforine, an effective new fungicide which will control and prevent black spot, powdery mildew and rust - the three most important diseases of roses. Used as directed, ORTHO Rose Disease Control will not harm rose flowers or foliage. In addition to roses, powdery mildew on crapemyrtle, phlox and zinnias will also be controlled.

DIRECTIONS

Use ORTHO Rose Disease Control at the rate of 1 Tablespoonful (1/2 fl. oz.) per gallon of water. Spray thoroughly to cover all plant surfaces (both upper and lower leaf surfaces) including new growth. For best results apply with an ORTHO SPRAY-ETTE, ORTHO Lawn & Garden Sprayer or pump-up sprayer. Do not store diluted spray. Use mixture at once. Does not require the addition of wetting agents.

WHEN TO USE

To prevent disease, begin spraying with ORTHO Rose Disease Control when first sign of listed diseases appear in the spring. Apply every 7 to 10 days during the spring and fall. However, if weather conditions that encourage the growth and spread of the disease causing fungi occur during the summer months, it may be necessary to continue spraying throughout the growing season. NOTE: If infection has already occurred on the plants at time of spraying, follow a 7 day application schedule to control the fungus. Then continue on a 7 to 10 day application schedule to prevent re-establishment of the disease. Leaves on which spots have already developed will not clear up, but the unaffected leaves will be protected if a regular spray program is followed.

Combination Spray with Insecticides on Roses - ORTHO Rose Disease Control may be mixed with ISOTOX Insect Spray, or ORTHENE Systemic Insect Spray, or ORTHO Malathion 50 Insect Spray, or ORTHO DIAZINON Insect Spray, or ORTHO Liquid Sevin. Follow directions on each label for insect control. Apply these mixtures only when both an insect(s) and a disease(s) claimed on the labels are present.

100.3 Precautionary Labeling:

ENVIRONMENTAL HAZARD
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.

DIRECTIONS FOR USE
It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

101.0 Chemical and Physical Properties

See previous review by S. Fredericks 3/20/76 and J. Edmundson 4/11/75.

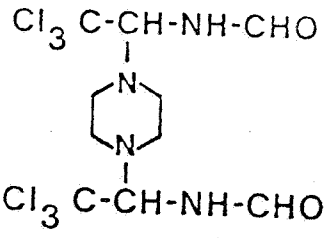
101.1 Chemical Name

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

101.2 Common Name

Funginex, Triforine, CELA W254

101.3 Structural Formula:



Empirical formula: C10H14Cl6N4O2

101.4 Molecular weight:

435

101.5 Physical state, color, odor:

apparently fine-white powder with faint odor (tech.).

101.6 Solubility

Water solubility is approx. 28 ppm at room temperature. Hardly soluble in most common organic and inorganic solvents.

Melting point: approx. 155°C (by decomposition)
Vapour pressure: 2×10^{-7} Torr at 25°C.

102.0 Behavior in the Environment

See J. Edmundson's review of 4/11/75.

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.

102.2 Water: rapid degradation in water (2 days - 1 week).

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).

102.4 Animal: 96% of dose was excreted through urine and feces after 72 hours in the rat.

103.0 Toxicological Properties:

103.1 Acute Toxicity

103.1.1 Mammal: See Toxicological review for 7F1921

Organism	Test	Results
Rat	Acute Oral LC_{50}	> 6000 mg/kg

103.1.2 Bird: See Environmental Safety Review by R. Hitch, 8/23/77, and see attached validation sheet.

Organism	Test	Results
Japanese quail	Acute Oral LD_{50}	Invalid
Bobwhite quail	Dietary LC_{50}	1849 ppm
Mallard duck	Dietary LC_{50}	> 4640 ppm

103.1.3 Fish: See Environmental Safety Review by R. Hitch, 8/23/77.

Organism	Test	Results
Rainbow trout	Acute 96-hr. LC_{50}	> 1000 ppm
Bluegill sunfish	Acute 96-hr. LC_{50}	> 1000 ppm

103.1.4 Aquatic Invertebrates: See Environmental Safety Review by R. Hitch, 8/23/77; also see attached validation sheets.

Organism	Test	Results
Daphnia magna	4-Day TL_{50}	Invalid
Daphnia magna	48-hr. LC_{50}	Invalid

103.2 Dermal Toxicity:

103.2.1 Mammal: See Toxicity review for 7F1921.

Organism	Test	Results
Rat	Dermal LD_{50}	> 10,000 mg/kg

103.4.0 Chronic Toxicity

103.4.1 Mammal

(From the summary of an 81 week carcinogenicity study in mice for triforine (W524) administered in the food; tests performed by Dr. A. Hofmann, Dr. I. Delrich, Dr. N. Sumi, G. Weise, Dr. H. Kollmer, and Dr. I. Weise, Institute for Toxikologie, E. Merck Dormstadt and Aoterlung Expremintelle Pathologic and Toxikologie, C.H. Boehringer Sohn, Ingelheim; dated 9/4/75).

Mice showed no tumorigenic or carcinogenic effects after being subject to Triforine concentrations of 30, 150 and 450 ppm in their food for a period of 81 days. The following mean daily doses (mg/kg body weight) were calculated:

		Week of Study			
		4	26	52	80
Control group	F.	0	0	0	0
	M.				
Group I	F.	6.4	4.5	4.0	3.8
	M.	7.4	5.0	4.0	4.7
Group II	F.	32	23	19	20
	M.	37	26	22	25
Group III	F.	166	112	99	98
	M.	186	130	116	117

Treatment with Triforine (W524) had no influence on behavior, food consumption and body weight development of the mice.

104.0 Hazard Assessment:

This formulation is designed for home and garden use. If label directions are followed and environmental cautions observed, we expect minimal impact on the environment.

FORMULATION: Ortho Rose Disease Control

% a.i.	SC #	CHEMICAL NAME
Technical		N,N'-[1,4-piperazine-diylbis (2,2,2-trichloroethylidene)] bis (formamide)

IA	IB	T	(FW)	EC	R		

Validator: D. J. Urban

Date: 3/14/78

Test Type: Acute Toxicity of Triforme Technical to the Water Flea (Daphnia magna)

Test ID.# ES-H1

CITATION:

Accession No. 232684; Performed by - Gerald A..LeBlanc, EG&G Bionomics, Aquatic Testing Laboratory, 790 Main Street, Wareham, Mass; Dated - December, 1977; Submitted by - Chevron Chemical Company, Ortho Division, 940 Hensley St., Richmond, California, 94804; Submitted on - 1/17/78.

VALIDATION CATEGORY: Invalid

RESULTS:

1) 48-hour LC_{50} = 117.13 (51.24-261.51) ppm

2) "Mortality data derived from the definative test were used to calculate a median lethal concentration (LC_{50}) and its 95% confidence limits utilizing the moving coverage angle method (Harris, 1959)." [1]

3) The nominal test concentrations were 0.78, 6.0, 46, 360, and 2800 ppm.

4) The test temperature was 22 ± 1°C.

5) "At all test concentrations, Triforine technical was visibly present at the test solution surface and bottom. The Triforine also appeared to adhere to daphnids, imparing mobility although not always killing the organism."

VALIDATION CATEGORY RATIONALE:

1) The solubility of Triforine technical in water is only 28 ppm at room temperature. Thus, without solvents, it is virtually impossible to get more than this amount into solution at any applied or nominal concentration. Further, Triforine was visibly present at the surface and bottom of the test chambers, and appeared to adhere to the daphnids;

2) The concentration of toxicant in each treatment was only 13% of the next higher one;

3) the test temperature was higher than the normally recommended test temperature for daphnids - 22 ± 1°C versus 17 ± 1°C.

[1] Harris, E.K. 1959. Confidence Limits for the LD_{50} using the moving average angle method. Biometrics, Vol. 4, #3, pp. 157-164.

CATEGORY REPAIRABILITY/RATIONALE: This study may not be reclassified to core or supplemental status. There is sufficient reason to question whether the nominal concentrations approximate the actual concentrations in the test chambers. The observed increase in mortality with the increase in dose could easily be attributed to the increasing rate of entrapment in the Triforine technical visibly present in the test chambers.

Further, a definative test must meet the following criteria:

"Except for the controls, the concentration of toxicant in each treatment must be at least 60% of the next higher one for basic tests."

The concentration of the toxicant in each treatment was only 13% of the next higher one.

FORMULATION: Ortho Rose Disease Control

% a.i.	SC #	CHEMICAL NAME
(Triforine) Technical		N,N'-[1,4-piperazine-diylbis (2,2,2-trichloroethylidene)]bis (formamide) (W524)

IA	IB	T	(FW)	EC	R		

Validator: D.J. Urban

Date: 3/14/78

Test Type: Avian Acute Oral LD_{50} Japanese quail (Coturnix coturnix, japonica)

Test ID.# ES-C1

CITATION:

Accession No. 232695; Performed by - C. H. Boehringer Sohn, Pharma-Forschung Biologic, Document No. T4; Dated - 9/9/70; Submitted by - Chevron Chemical Company, Ortho Division, Richmond, California, 94804; Submitted on - 3/28/75.

VALIDATION CATEGORY: Invalid

RESULTS:

1) LD_{50} > 6,000 mg/kg body weight.

2) Only a summary was submitted.

3) Three dose levels were tested: 1500, 3000, 6000 mg/kg.

4) Observation period: 14 days.

5) Ten birds per dose level.

VALIDATION CATEGORY RATIONALE: 1) Japanese quail is an unacceptable test species; 2) only a summary was submitted.

CATEGORY REPAIRABILITY/RATIONALE: This study cannot be reclassified to core status. Japanese quail are not indigenous to this country. Further, they may be less sensitive to some chemicals than the preferred test species. Consequently, they are not acceptable test birds. This study may be reclassified to supplemental status if the complete study is submitted to this section for review.

107.0 Conclusions:

107.1 Environmental Fate and Toxicology (Acknowledgement):

Current reviews by Environmental Chemistry and Toxicology were consulted during this review.

107.4 Data Requests:

The following information is required:

a) an avian acute oral LD_{50} for one species of waterfowl (mallard duck, preferably) or one species of upland game bird (bobwhite quail or ring-necked pheasant). The species shall be the same as one of the two species selected for the avian dietary LC_{50}.

b) an acute 48-hour LC_{50} for an aquatic invertebrate (Daphnia sp., preferably).

Current regulations require the above studies to be run with the Technical grade of the active ingredient.

107.5 Data Adequacy:

In reference to the data submitted or referenced to support the proposed registration, the following comments are appropriate:

a) The September 9, 1970 C. H. Boehringer study on Japanese quail is unacceptable, and does not fulfill the requirement for an avian acute oral LD_{50} for one species of waterfowl or one species of upland game bird. Japanese quail is an unacceptable test species. This study cannot be repaired and must be redone.

b) The July 2, 1976, Industrial Bio-Test Laboratory, Inc., study on Daphnia magna does not fulfill the requirement for an acute 48 hours LC_{50} for an aquatic invertebrate. It is inadequate because the study was done on 6.5% active Triforine. This study cannot be repaired. It will have to be conducted again using the technical grade of Triforine.

c) The December 1977 Bionomics Aquatic Testing Laboratory study on Daphnia magna does not fulfill the requirement for an acute 48-hour LC_{50} for an aquatic invertebrate. There is sufficient reason to question whether the nominal concentrations approximate the actual concentrations in the test chambers. Further, this test did not meet the following criteria for a definative basic test: "the concentration of toxicant in each treatment must be at least 60% of the next higher one so that an LC_{50} can be calculated with reasonable accuracy." This study cannot be repaired and must be redone.

The registrant is urged to contact this Section to discuss the problem with the above studies and possible solutions.

Douglas J. Urban Date: March 14, 1978
Environmental Safety Section
EEEB-RD

Note to P.M.

We have identified deficiencies in basic Fish and Wildlife data requirements for new registration. However, we feel that the supporting data are adequate to make a hazard assessment regarding the proposed use of Ortho Rose Disease Control on roses.

We have determined that the proposed use of Ortho Rose Disease Control on roses poses no unreasonable adverse effects to the environment. However, any change in use pattern will require the submission of complete and satisfactory Fish and Wildlife tests.

Doug Urban

Jim Akerman

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