

EEE HATCH REVIEW

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FISH & WILDLIFE ENVIRONMENTAL CHEMISTRY EFFICACY

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TYPE PRODUCT(S): I, D, H, (F,)N, R, S
PRODUCT REG. NO. 22
PRODUCT NAME(S) Ortho Rose Disease Control
COMPANY NAME Ortho-Chevron
SUBMISSION PURPOSE Registration
CHEMICAL & FORMULATION Triforine - N,N'-[1,4-piperazinediyl-bis-(2,2,2-trichloro-ethylidene)]-bis-[formamide]

1.0 Recommendations

1.1 The data is insufficient to assess the hazard in support of registration. The following data will be needed before registration

- 1.1.1 Further clarification of the soil metabolism studies (Reference #1, is needed. Tables 3, 4, 7, 8, 9, 10, and appendices 1, 2, and 3 must be amended to include the actual amount in ppm actually found in each fraction of each sample at each sampling interval in both soil types under aerobic, anaerobic and sterile conditions. The data should be expounded on the basis of percentage of amount initially applied rather than on a relative percentage distribution within a subsample. Some of the bargraphs are misleading in that they imply total accountability of initially applied amount whereas they actually demonstrate relative accountability of recoverable labels at each sampling interval. The laboratory data, including cpm, dpm, background, may also be helpful in the evaluation of this study. This study may not be acceptable for outdoor uses but, this can only be determined after our questions have been answered.**
- 1.1.2 Several questions need to be answered on the leaching study. (Leaching in Cosad Sandy Loam-Ref #10)**
- a. Methylene chloride has not been shown to be a good extracting solvent. Other soil studies use methanol/water. How do we know that all the extractable residues have been removed from the soil for the leaching study of degradation products?**
 - b. In the bound leaching study was the soil extracted first? It appears not, as the results are similar to the organo-soluble leaching study.**
 - c. This study will not be acceptable for any outdoor applications. See enclosure for acceptable leaching study.**
- 1.1.3 A hydrolysis study carried out according to the enclosed protocol. See enclosure (P.M. Enclose page V-33 of second draft guidelines).**

- 1.2 The following data will be needed to assess the hazard of tank mixtures, but it may be obtained after registration.

1.2.1 Tank Mixtures

In addition to the environmental data needed for registration of pesticides the following are also needed to support tank mixtures.

- a. Laboratory study using cold chemicals applied to two soils as recommended in the proposed use. A light and heavy soil will be adequate.
- b. Analysis through two half-lives of each pesticide applied as a mixture and separately. The same soil types are to be used for the comparison of the mixture vs. individually applied chemicals. Sampling depth should be to bottom of container (pot) or 6 inches.

2.0 Introduction

2.1 Ceta Merlk W-524; FMC 28221, Ortho XE 359, Funginex

2.2 Applications for registration of Triforine have been made by other companies. This is the first application for registration from Ortho.

2.3 Roses, Crabapple, Phlox and Zinnias

3.0 Directions For Use

3.1. Mix 0.5 oz./gallon water, spray to cover all plant surfaces.

Begin spraying when foliage appears in spring. Apply every 7-10 days in spring and fall. Apply every 7-10 days in summer if weather conditions encourage growth and spread of fungi.

3.2 Ortho rose disease can be mixed with 150TOX, orthene systemic insect spray, ortho malathion-50, ortho diazinon or ortho liquid sevin.

3.3 Can be mixed with ortho rose and flower food 8-12-4.

4.0 Discussion of Data - Triforine Environmental Impact Report (Feb. 1975)

4.1 Laboratory Soil Metabolism Studies

4.1.1 Soil Degradation of Triforine (Ref #1 FMC Corp)

This was reviewed with data from FMC

Aerobic Metabolism

^{14}C and ^3H labelled triforine were added to both sandyloam and silt loam soils. At 2 and 20 ppm water was added to soil to 70% moisture level, and soils were incubated in biometer flasks at 25-30° C.

Prior to treatment the microbial levels of the soils were evaluated with a respirometer, and they were found to be "microbiologically active."

Labels

Tritium label was on H attached to ring carbons. Carbon labels were on both carbons of the two trichloro ethylene groups.

Anaerobic Metabolism

Samples of Silt loam and sandy loam soil treated at 2 ppm with ^3H -triforine were maintained in flasks for 30 days under aerobic, followed by 30 and 60 day incubations under nitrogen.

Sterile Soil Metabolism

Sandy loam and silt loam soils were sterilized by dry heat, water was added aseptically to 70% moisture. Soil was treated at 2 ppm with ^3H -triforine and incubated 30 days.

Analytical Procedure

Soil was extracted 2X with 90% methanol/water. The extract was partitioned with methylene chloride. The organic and polar phases of the partition were subjected to TLC autoradiography. Solid soil residue was analyzed by combustion.

The nature of bound residues were analyzed by fractionation of the humin, humic acid and fulvic acid fractions.

Radioactive triforine was partitioned between hexane and acetonitrile for the determination of p-value.

Soil Characteristics

	<u>%Sand</u>	<u>%Silt</u>	<u>%Clay</u>	<u>%O.M.</u>	<u>Moisture</u>	<u>C.E.C.</u>	<u>pH</u>
Sandy Loam	75.2	18.0	6.8	3.1	13.0	7.3	6.1
Silt Loam	25.2	51.6	23.2	3.9	22.2	16.8	4.9

Soil metabolism data was presented in a series of tables which have been combined below.

The Fate of Radiolabelled Triforine in Soil

Condition	Aerobic	Aerobic	Aerobic	Aerobic	Sterile	Sterile
Label	³ H	³ H	¹⁴ C	³ H	³ H	³ H
Soil Type	Sandy L	Silt L	Sandy L	Silt L	Sandy L	Silt L
Days	60	60	90	90	30	30
ppm Applied	20	20	20	20	2	22
Compound						

% of Radioactivity Present

Triforine	31.9	11.1	16.9	5.1	29.6	29.5
FMC-29746	0.3	0				
FMC-29745	0.7	0.3	0.9		2.9	2.3
FMC-29748	7.3	4.0	0.5			
FMC-29747			1.3			
Unidentified	16.2	15.0		0.55	1.3	2.1
Non-Extractable	43.7	69.5	34.3	71.0	58.3	54.8
CO ₂ evolved			37.9			
Polar Compounds				23.4	7.9	11.3

Distribution of ³H residues in aerobic soil (2 ppm)

% Distribution

Time (Days)	Sandy Loam			Silt Loam		
	Organic	Polar	Bound	Organic	Polar	Bound
0	90.4	4.6	5.0	87.1	1.7	11.2
7	72.6	5.8	21.7	35.1	11.7	33.8
14	59.3	9.6	31.1	43.9	10.8	45.2
30	44.1	19.4	36.5	35.7	22.1	42.3
60	44.5	13.0	42.6	18.0	17.1	65.0

Results

1. 66 and 89% of bound ^3H was released by HCl and NaOH respectively in fractionation procedure.
2. About 75% of the bound ^{14}C and ^3H was in the fulvic acid, 1.6-15.3% was in the humin and 4.5-16.8% was in the humic acid.
3. Triforine was degraded in sterile soil at 30 days to PNC-29745 and some unidentified polar and organic compounds.
4. P value - Hexane-acetonitrile = 0.001
P value - Benzene-water = 0.50

Comparison of Aerobic, Anerobic and Sterile Studies

	<u>Aerobic</u>	<u>Anerobic</u>	<u>Sterile</u>
Extractable degradation products	Yes	No	Yes
Polar Compounds	No	Yes	Yes
Bound 30 to 40%	Yes	Yes	Yes
Bound over 50%	No	Yes	Yes
Unidentified extractable compounds	Yes	No	Yes

Conclusions

1. Percentages on soil metabolism tables were percent found at that particular time. They should have been percent of radioactivity applied. We must have this information.
2. Bound residues were high and increased with time.
3. Supporting data for radiolabel studies (counting time, possible error, counting efficiency, dpm. etc.) was not included.
4. Sterile soil results show that triforine can be degraded to polar compounds under aseptic conditions.

4.2 Hydrolysis Studies

4.2.1 Stability of Cela W-524 in aqueous solution at room temp. (under diffuse light) (ref #4).

30 ppm aqueous solutions of Triforine were stored in glass bottles for 28 days, at room temperature, either in the dark or under diffuse light (no exposure to UV or direct sunlight).

Triforine was determined at intervals by polarography.

ppm Triforine (parent compound) in Solution

<u>Days</u>	<u>Solutions Kept In Dark</u>	<u>Solutions Exposed To Diffuse Sunlight</u>
0	30.0	30.0
1	26.0	25.9
7	16.5	15.6
14	12.5	9.0
21	5.0	4.8
28	2.5	1.5

Conclusions

1. The half life of Triforine in aqueous solution was a about 8 days, in the dark and under diffuse light.
2. Triforine is hydrolyzed in the dark. No indication given as to what kind and how many hydrolysis products.
3. The pH was not determined and a buffered solution was not used. A hydrolysis study at pH 5.7 and 9 will be needed.

4.2.2 Comparative

4.2.2 Comparative Radio-Thin Layer Chromatographic Investigations of the Decomposition of $^3\text{H}/^{14}\text{C}$ -W-524 (Triforene) in Aqueous Solution (Reference #5).

This was reviewed with data from FMC.

30 ppm of ^{14}C (labelled on both carbons of both trichloroethylene moieties) and ^3H (uniform ring label) were incubated at room temperature in non-buffered aqueous solution in sealed flasks. The pH of aqueous solution was initially 6.2 and rapidly dropped to 3.2. Flasks were exposed to diffused daylight.

Solutions were counted by LSC. $^{14}\text{CO}_2$ was trapped with NaOH.

Aliquots were freeze dried, dissolved in acetone/water, and analyzed by TLC with co-chromatography of parent, and UV and radiometric detection. Spots were scraped and counted.

% of Applied Radioactivity Recovered As Parent Compound

<u>Time (days)</u>	<u>^3H</u>	<u>^{14}C</u>
0	100	100
2	49	53
4	35	28
6	20	20
10	10	11
14	6	11
22	2	4

Results

1. Registrant stated that only minimal quantities of radioactivity were trapped in the NaOH.
2. One TLC run showed 8 degradation products and no parent compound after 22 days.
3. The main degradation product (unidentified) comprised 40-80% of the radioactivity present. It contained both ^3H and ^{14}C labels.
4. After an initial increase in ^3H , the amounts of ^3H and ^{14}C at the origin increased at the same rate and remained at a similar level.
5. 2.5-3% of applied radioactivity was trapped as volatile products.

Conclusions

1. This study was not carried out at pH 5, 7, 9.
2. The parent compound is rapidly hydrolyzed.
3. Registrant stated some degradation took place before the start, and starting material was 95% pure.
4. Triforine was degraded to one major and 8 minor unknown hydrolysis products. Very little $^{14}\text{CO}_2$ or volatile products were evolved.

4.2.3 Decomposition Products of Radioactive Triforine in Aqueous Solution. (Ref #6)

This was reviewed with data from FMC.

30 ppm non-buffered aqueous solutions of ^{14}C (labelled on both carbons of trichloroethylene moiety) and ^3H (uniform ring label) Triforane were incubated at room temperature, in sealed flasks, exposed to diffused daylight for period of 5-6 days and 13 weeks.

Aliquots were freeze dried and the residue was subjected to TLC with co chromatography and identification of spots by a methane flow through counter. Spots were scraped and analyzed by mass spec.

Results

1. Compounds isolated after 6 days were: WOS-2379, WOS-2599, and W-1084.
2. The main degradation product was not identified. It was very unstable and was changed into WOS-2379 possibly by the experimental conditions.
3. After 13 weeks no parent compound was detectable.
4. Main degradation products after 13 weeks were mono and bis glyoxal piperazine, also other piperazine compounds (Structures, but no names or other designations provided) and 3-trichloro, 2-Keto, propionaldehyde were formed.

Conclusions

1. After 13 weeks hydrolysis at pH 3.2, the Triforine had been completely degraded, mainly to mono or bis glyoxal piperazine.
2. Registrant concluded that the compound W-1084, may have been the result of degradation due to experimental conditions.
3. Study was not carried out at pH 5,7 and 9.

4.3 Photodegradation Studies

4.3.1 Studies on the Influence of Light on Degradation of Triforine (Ref #13).

Formulated triforine was applied as a spray to 1 cm thick soil plate to 10 ppm. or mixed with water to 4.0 ppm. Soil and water were irradiated with a xenon lamp (7.5 lux, spectrum similar to sunlight) at 15 cm. for 8 hrs. a day. Soil moisture was maintained.

Analytical method - Samples were heated with sulfuric acid, clearing the tri-chloroethyl group from Triforine or its metabolites, yielding chloral hydrate which was distilled under nitrogen, and assayed by GLC-electron capture.

Soil characteristics: OM-1.4%, pH 7.5, soil particles less than 0.02 mm 31.7%.

% of Applied As Triforine

Total Hours Irradiation	Soil		Water	
	Irradiated	Control	Irradiated	Control
0	96	100	105	105
24	79	96	65	75
48	52	-	50	63
72	16	92	40	55
88	14	90	35	53
120	7	-	30	48

Conclusions:

1. Triforine applied to a soil surface was rapidly photodegraded.
2. Light speeded up the already rapid degradation of Triforine in water.

4.3.2 Investigations into the Decomposition of Triforine on Exposure to Light (Ref #15)

Thin films of Triforine on glass were exposed to 254 nm U.V. light or to natural sunlight (28 days in July). A 5 cm thick soil layer treated with Triforine (1650 ppm?) was exposed to a mercury vapor lamp, with spectral characteristics simulating sunlight. Moisture of the soil was maintained.

Residues were extracted into or taken up in acetone, and analyzed by TLC. Visualization was by spraying with p-benzoquinone or by heating with NaOH.

Quantitation was by GLC assay of TLC spots. Ir. and Mass spec were used for confirmation of the identity of the major photoproduct.

Photolysis On Thin Film By U.V. Light

% of Applied Equivalent to Triferine

<u>Substance</u>	<u>1 Hr.</u>	<u>16 Hrs.</u>	<u>64 Hrs.</u>
Triferine		86	75
W-1088	1.8	2.5	11.9
Unknown	0.5	1.5	5.4
Piperazine	0.1	0.1	2.0
Chloral Hydrate	0.5	10.9	1.5
WOS-2599	0.3	0.1	0.1

TLC analysis of residues resulting from exposure of thin film on glass to sunlight showed a decreased quantity of parent compound and no degradation products. No quantitative results were submitted.

Irradiation of treated soil showed W-1084 to be the major photoproduct. It maximized at 21 days and declined thereafter. No quantitative results were submitted.

Conclusions

1. Photolysis on thin film under U.V. light resulted in loss of one or both of the side chains, resulting in the formation of W-1084, WOS-2599, chloral hydrate and ammonium chloride.

4.2.2 The Decomposition of Triferine in Aqueous Solution by UV Radiation (Ref. #14)

30 ppm aqueous Triferine solutions were exposed to high pressure U.V. for 1 or 5 hours.

Aliquots were concentrated and spotted on TLC, with visualization by fluorescence under U.V. Further identification of TLC spots was by Ir, U.V., Mass Spec and NMR analysis, and co-chromatography.

No quantitative determinations were made.

Results

1. After 1 hr. exposure, TLC showed parent compound, an unknown and a product at the origin.

2. After 5 hrs. exposure only a product at the origin was present. Further analysis showed it to be N-(2,2-dichlorovinyl) Formamide (NOS-2599).

Conclusions

1. Under U.V. light the side chains are cleaved from the piperazine ring to form the compound NOS-2599.
2. Experimenter noted that NOS-2599 was not stable to U.V. and was degraded further.

4.4 Effect on Microorganisms-Influence of Cela-524 on Aerobic Activity in the Soil (Ref. #3)

Technical triforine was added to soil to 4.0 ppm and 20% EC formulation (CA-70203 - Cela Merk) was added to soil to 10 ppm (2 ppm ai). Oxygen consumption was determined by a manometric method.

Oxygen Consumption in Microliters Over 3 hrs. Period

<u>Compound</u>	<u>Day</u>	<u>Treated</u>	<u>Control</u>
Technical	1	92	91
	2	102	102
20-EC Formulation	1	90	89
	2	92	88
	5	104	96

Soil: Sandy loam, 4.2% O.N.

Conclusions:

1. Triforine technical or formulation had no effect on the oxygen consumption of soil microbes in this experiment.
2. The formulated product here is not the same formulation of Triforine as the one being considered for registration in this review.

4.5 Leaching Studies on Cela M-524 (Triforine) in Various Soil Types (Ref. #9)

Formulated triforine was added to 12" leaching columns at 0.2 mg ai/column (close to the maximum dosage rate). Columns were subjected to 7.6" rainfall over 2 days or 1.9" over 5 days.

Water or soil were heated with sulfuric acid, cleaving the tri-chloroethyl group off the parent compound or its metabolites, to form chloral hydrate. Chloral hydrate was isolated by distillation, and assayed by GLC electron capture.

Soil Characteristics

	<u>% Fine Silt And Clay</u>	<u>% O.M.</u>	<u>pH</u>
Loam with Low O.M.	31.7	1.4	7.5
Loam with Medium O.M.	44.8	2.2	7.0
Sand with high O.M.	25.4	5.2	6.8

% of Applied As Triforine

<u>Rainfall</u>	<u>Soil Type</u>	<u>Soil Segment</u>				<u>Leachate</u>
		<u>0-2"</u>	<u>2-4"</u>	<u>4-8"</u>	<u>8-12"</u>	
High Rate	Loam-Lo. O.M.	43.2	38.8	16.8	n	n
	Loam-Med. O.M.	50 50	14	n	n	n
	Sand-Hl. O.M.	84	18	n	n	n
Low Rate	Loam-Lo. O.M.	78	5	n	n	n
	Loam Med. O.M.	67	6	n	n	n
	Sand Hl. O.M.	75	n	n	n	n

n = no detectable residue

Conclusions

1. This study was not carried out according to our protocol. Specifically rainfall should be 20" total, at a flow rate of less than 1" per hour.
2. Recovery is less than 100%. This could be due to rapid hydrolysis of parent compound to products which would not be detectable by the analytical method, or bound residues.
3. Leaching of formulated product did not occur.

4.6 Aged Leaching:

Leaching of ³H-Triforine Residues in Cosad Sandy Loam Soil (Ref. #10) This was reviewed with data from FMC.

A 0.3 x 12" column was packed with sandy loam and saturated. Study was divided into leaching of organo-soluble and bound residues studies. Ten microliters of methylene chloride extract from a 20 ppm 30 day aerobic metabolism study (see previous study) was applied to the column. Extract counted at 334,000 dpm. For the bound residue study, 1 gram (1 x 10⁵ dpm) of Cosad sandy loam bound residues were applied to the top of the columns.

Each column was treated with 0.5" water per day. After 45 days, each column was cut into 24 one half inch segments, and were analyzed by combustion.

Distribution of ³H Triforine Residues

<u>Segment</u>	<u>% Distribution in Column</u>	
	<u>Organo-Soluble</u>	<u>Bound</u>
0-3"	27.2	17.0
3-6"	10.3	4.9
6-9"	8.3	2.6
9-12"	5.1	1.6
Effluent	49.1	47.9
Bound Residue Soil Segment	----	26.0

Soil characteristics: % sand 75.2, % salt 18.0, % clay 6.8,
% O.M. 3.1, moisture 13.0, CEC 7.3, pH 6.1

Conclusions

1. Applicant did not state what amount of Triforine was applied to columns. We must have this.
2. Since no data was given linking dpm to ppm, it was not possible to determine the amount applied.
3. Both applications resulted in 50% of the applied radioactivity being recovered from the leachate water.
4. Environmental uses of Triforine may present serious leaching problems.
5. We have no definite proof of whether soil applied in bound residue study was first extracted with organic solvents.
6. We need to know why a methylene chloride extract was applied to the soil when methylene chloride was not shown to be a good extracting solvent and other soil studies used methanol/water.

4.7 Field Persistence--"Degradation of Cala 524 in Various Soil Types" (Ref. #2)

Bare field plots were treated at 0.5 g ai/m² with CA-70203 formulation. 0-20 cm deep soil core samples were taken at intervals. Soil samples were heated with HCE to cleave chloral hydrate from the Triforine molecule. Chloral hydrate was distilled off, and by

assayed by GLC.

Soil Characteristics

	<u>% Soil Particles(mm)</u>				<u>pH</u>	<u>% OM</u>
	<u><2.0-0.2</u>	<u>0.2-0.02</u>	<u>0.02-0.002</u>	<u><0.002</u>		
Ingelheim Sand	87.4	9.3	0.9	2.3	7.7	0.2
Schwabenheim Loam	1.9	66.5	17.2	14.4	7.5	1.4
Alsenz Loam	13.2	41.9	22.3	22.5	7.0	2.2

Residues as PPM Triforine

<u>Weeks After Treatment</u>	<u>Ingelheim Sand</u>	<u>Schwabenheim Loam</u>	<u>Alsenz Loam</u>
0	2.32	2.15	2.32
1	1.90	1.39	2.24
3	0.62	0.87	0.98
6	0.35	0.44	0.53
9	0.34	0.32	0.20
12	0.23	0.22	0.23
20	0.19	0.22	0.22

Conclusions:

1. Only 10% of the applied Triforine was found in 0-20 cm soil after 12 weeks. First half life was reached in 3 weeks.
2. Registrant notes that extremely dry climatic conditions prevailed during the middle to latter part of this study.

4.8 Plant Metabolism

4.8.1 Transport of Triforine in Barley Plants: Uptake and Metabolism (Ref. 7, Pest. Sci-1973)

Barley plants, planted in peat and sandy soil, were exposed to ¹⁴H (ring) Triforine. Plant shoots and roots and soil were homogenized with methanol. Extract was analyzed qualitatively and quantitatively by TLC. Plants grown in peat were also homogenized with water, and extract was subjected to reverse isotope dilution analysis for piperazine.

Results

Parent compound and 2-4 metabolites were found in the roots, shoots and soil. One of the soil metabolites was not found in plants. The compound N-moneglyoxal piperazine was found in plant roots.

Characterization of Residues in Plants 8 Days Post Treatment

	<u>Sandy Soil</u>	<u>Peat Soil</u>
Parent	43.5	48.4
Metabolites	56.5	41.3
Piperazine	Not Determined	10.3

Conclusions

1. No data was given on the concentration of the metabolites in the soil.
2. Author of paper notes identification of unknown metabolites is in progress.
3. It is not clear to what extent parent was metabolized by plant compared to the amount of metabolites taken up by the plant from soil.

4.8.2 Tests with Triforine in Apple Growing Using $^3\text{H}/^{14}\text{C}$ Triforine (Part of Ref. 8 - dealing with plant metabolism)

Apples on trees were sprayed with $^{14}\text{C}/^3\text{H}$ Triforine. Apples were subjected to surface extraction with methylene chloride followed by acetone and methanol. Apples were homogenized and extracted with acetone and methanol. Extracts were analyzed quantitatively by TLC. Whole apples and peels were assayed by combustion.

Characterization of Residues in Apples

% of Radioactivity Present

Triforine in peels	58.1%
Metabolites in peels	793%
Metabolites in apple (plus small amount of parent)	23.3%
Bound	11.3%

Conclusion:

1. Triforine was metabolized to a certain extent in apples.
2. Metabolites formed were not identified.
3. Metabolites get into the pulp.

4.9 Triforine Residues in Fish - Preliminary Report (Ref #15)

Trout were exposed to 1.0 ppm $^3\text{H}/^{14}\text{C}$ double labelled triforine for 32 days; after which remaining fish were placed in fresh water for 30 days.

Water samples were radioassayed and analyzed for parent compound by TLC.

Fish were eviscerated, beheaded, combusted, and radioassayed.

Residues as PPM Triforine in Fish

Day	
0	0
7	0.28
14	0.20
21	0.12
26	0.26
30	0.18
32	0.17
withdrawal	
1	0.16
14	0.15
30	0.05

Level of total radioactivity in water remained at 1.0 ppm equivalent to triforine.

Level of parent compound in water dropped, while the level of hydrolysis products increased.

Characterization of Residues in Fish tissue

Chloroform extractable	0
Methanol extractable	44
Methanol/water extractable	28
Bound	28

Conclusions:

1. Triforine did not bioaccumulate in edible tissues of fish.
2. Solvent partition characteristics of residues present in fish tissues indicate that these residues are polar metabolites rather than parent compound.
3. We note that this is a preliminary report. We will need the final report when it is complete.

4.10 Animal Metabolism

Excretion and Metabolism of Triforine in the Rat (Ref. #11 interim report)

Male rats were administered Triforine by stomach tube. Triforine was labelled with ^{14}C on trichloroethyl side chain or ^3H on ring. Feces and urine were radioassayed. Urine was extracted, and analyzed by TLC and mass-spec.

Results:

1. 70-78% of applied ^3H was found in urine and 18% was found in feces.
2. 45-55% of applied ^{14}C was found in the urine
3. Most of the applied radioactivity was excreted within 24 hrs.
4. No parent compound was found in urine. W-1084 was the major metabolite in urine.

Conclusions

1. Triforine is metabolized to W-1084 and very rapidly excreted.

Pharmacokinetics of Triforine in Rats. (Ref #12)

Rats were dosed with ^{14}C (labelled on 2 carbons of trichloro-ethyl group) or ^3H (ring labelled) Triforine. Administration was as a tylose suspension or with a glycerol-formal solubilizer.

Results:

1. Almost all of the residue was excreted. The relative amount in urine or feces depended on whether a suspension or solubilized solution was used.
2. Feces contained Triforine plus a small portion of unidentified metabolite. Urine contained W-1084 plus a metabolite.
3. When rats were dosed with W-1084, it was absorbed thru the intestine and excreted unchanged thru the kidneys.

5.0 Summary

- 5.1 [A] Bound residues comprised 43-65% of radioactivity present at 60 days. Persistence could not be determined since residues were expressed as percent present and not applied. Present use is on roses no problems with rotational crops expected.
- 5.2 [B] Aged leaching study resulted in 50% of the applied radioactivity being recovered from the leachate water. Parent leaching study was inadequate, but triforine is very rapidly hydrolyzed, so results of aged leaching study are very relevant here.
- 5.3 [C] Based on the fish study there is very little potential for accumulation in the food chain.
- 5.4 [D]
- 5.5 [E] No indication of a possible need for chronic studies since Triforine is highly unstable in water and this is a minor use pattern.
- 5.6 Brief Summary of all Data
- 5.6.1 Persistence

The results of the soil metabolism study presented in terms of % present rather than percent applied.

5.6.1 cont. Bound residues rapidly build up, comprising 43-65% of radioactivity present at 60 days. Triforine is degraded under aerobic, anaerobic and stable conditions. Route of degradation seems to be chemical rather than microbial.

5.6.2 Hydrolysis

All hydrolysis studies were in unbuffered water, in which PH rapidly fell to PH3. Under these conditions, the parent compound is rapidly hydrolyzed. Very little CO2 or volatiles evolved. At PH 3.2 after 13 weeks it was hydrolyzed to mono and bis glyoxal piperazine. 8 unknowns detected in some studies.

5.6.3 Photostability

Presence of diffuse light rapidly increases the rate of degradation in water. Rapidly photodegraded on soil. Route of photodegradation involves cleavage of two side chains from ring, producing a piperazine ring, chloral hydrate, ammonium chloride and N-(2,2-dichlorovinyl) formamide.

5.6.4 Triforine had no effect on the oxygen consumption of soil microbes.

5.6.5 Subsequent crops

No data submitted

5.6.6 Fish accumulation

Residues in fish (edible) reach only 0.26 and then decreased while water contained 1.0 ppm.

5.6.7 Animal metabolism

Very rapidly excreted in the urine and kidneys.

R. E. May 9/2/75
Ronald E. May. E 8/15/75
Frank J. Schenck 8/11/75
Environmental Chemistry Section
E.E.E.B.

SCIENTIFIC REVIEW LOG

Type of Pesticide: (circle) I R H F D

Product Manager: 22

Reg. No. E.P. No. or Petitioner No.	Type of Review (x)	Type of Registration Action (x)	Rec'd. in Office	Rec'd. in Branch/Section	Reviewer Assignment, Date	Review Initiation, Date	Review Completion, Date	Final Typing, Submitted	Final Typing, Completed
237-806L <i>Triphrine</i>	☐ Efficacy ☐ Fish & Wildlife ☒ Environmental Chem. ☐ Human Safety ☐ Toxicology ☐ Chemistry ☐ Label Chemistry	☒ New--Routine ☐ New--Significant New Use ☐ New--New Chemical ☐ Amend.--Label Revision ☐ Amend.--Added Uses Without Data ☐ Amend.--Added Uses With Data ☐ Resubmission--Without Data ☐ Resubmission--With Data	7/24/75	7/21/75	8/6/75	8/6/75	8/19/75	8/29/75	9/12/75