THIS IS PHASE II CHEMICAL REVIEW PACKAGE: FOR Cycloheximide,3-[2-(3,5-dimethyl-2-oxocyclohexyl)-2-hydroxyethyl]-glutarimide.

BRANCH PERFORMING REVIEW: Environmental Chemistry Section.

REVIEWER RESPONSIBLE: Nancy Dodd. Nancy Dodd 8/17/77

DATE COMPLETED: March 8, 1977, May 13, 1977.

APPROVED BY: Ronald E. Ney, Jr., June 17, 1977. R E Ney 8/17/77

BRANCH CHIEF: James G. Touhey DATE: June 21, 1977

PSO: _____ DATE: _____

I. RPAR Candidacy

NA

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Hydrolysis

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
The Upjohn Company	Test lab not available 3/22/72 Report number not available. Acc. #095124	Supplementary	Parent hydrolyzed at pH 8 at 5°, 25°, and 37°C and pH 7 at 25° and 37°C and pH 4.7 at 37°C, Parent was stable at pH 7.1 at 5°C and pH 4.7 at 5° and 25°C. We do not know the degradates.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Aerobic Soil Metabolism

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
The Upjohn Company	Test lab not available 3/22/72 Report #120-9760-30 Acc. #095124	Supplementary	First $T_{1/2}$ parent was 3 days, second $T_{1/2}$ was 8 days by antibiotic assay. We do not know the degradates nor the amount bound.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Effect of Microbes on Pesticides

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
The Upjohn Company	Test lab not available 3/22/72 Report #120-9760-51 Acc. #095124	Supplementary	$T^{1/2}$ in nonsterile soil was 2.25 days. $T^{1/2}$ in sterile soil was 16.8 days.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Effect of Pesticides on Microbes

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
The Upjohn Company	Test lab not available 3/22/72 Report #120-9760-53 Acc. #095124	Supplementary	Cycloheximide does not inhibit populations of bacteria and fungi.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Leaching (Aged)

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
The Upjohn Company	Upjohn 5/24/73 Report #12-9760-92 Acc. #120448	Supplementary	96% of the ^{14}C leached in managed sand. 71% leached in aged sand. 64% of the ^{14}C in leachate in the managed study was parent. Zero parent was found in leachate of the aged study. In the aged study, 20% of the ^{14}C remained in soil.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Leaching (Fast)

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
The Upjohn Company	Upjohn 5/24/73 Report #120-9760-93 Acc. #120448	Supplementary	95.8% of the ^{14}C applied to sand leached.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Leaching

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
None	U.S.D.A. Agricultural Research Center-West, Beltsville Date: 1977 Report #: None Acc. #: None	Supplementary	The bioassay method in combination with soil thin layer chromatography indicated that cycloheximide and cycloheximide oxime are relatively mobile.	None

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)
[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available 3/22/72 Report #120-9760-28 Acc. #095124	Supplementary	No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.	None

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)

[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-29 Acc. #095124	Supplementary	Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.	None

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)
[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-32 Acc. #095124	Supplementary	Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide. INERT INGREDIENT INFORMATION IS NOT INCLUDED	None

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)

[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report # 120-9760-34 Acc. #095124	Supplementary	No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.	None

INERT INGREDIENT INFORMATION IS NOT INCLUDED

1b

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)

[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-35 Acc. #095124	Supplementary	Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.	None

c

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)

[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-46 Acc. #095124	Supplementary	Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide. INERT INGREDIENT INFORMATION IS NOT INCLUDED	None

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)
[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-47 Acc. #095124	Supplementary	Negligible residues were found in soil under the drip line of the tree when the orchard was sprayed with 20 ppm chclohexiмide.	None

INERT INGREDIENT INFORMATION IS NOT INCLUDED

1b

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)

[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-44 Acc. #095124	Supplementary	Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 750 ppm cycloheximide.	None

1b

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)

[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-43 Acc. #095124	Supplementary	Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 500 ppm cycloheximide.	None

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)

[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-33 Acc. #095124	Supplementary	Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 267 ppm cycloheximide. INERT INGREDIENT INFORMATION IS NOT INCLUDED	None

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)

[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-39 Acc. #095124	Supplementary	Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 333 ppm cycloheximide.	None

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)
[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-40 Acc. #095124	Supplementary	Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 333 ppm cycloheximide. INERT INGREDIENT INFORMATION IS NOT INCLUDED	None

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cycloheximide

Inert Ingredient(s)

[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-45 Acc. #095124	Supplementary	Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 500ppm cycloheximide.	None

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Formulation Environmental Chemistry Data Sheet for Review Number Study Type = Field Soil

Active Ingredient(s)
1. Cyclohexamide

Inert Ingredient(s)

[redacted]

Registrant	Test Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-50 Acc. #095124	Supplementary	No residues were found on the 12th day. INERT INGREDIENT INFORMATION IS NOT INCLUDED	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Field Soil

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test lab not available. 3/22/72 Report #120-9760-52 Acc. #095124	Supplementary	Half-life of cycloheximide is 2.1 days.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Fish Accumulation

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	~~Upjohn Co.~~ available. 3/22/72 Report #120-9760-48 Acc. #095125	Supplementary	Concentration of ^{14}C in bluegills ranged from 0.03 to 0.14 ppm during exposure. On the 8th and 9th days of depuration, 0.02 and 0.01 ppm were detected.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Animal Metabolism

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	~~Upjohn~~ not available. 3/22/72 Report #120-9760-14 Acc. #095122	Supplementary	75.68% was eliminated in the urine and 17.96% was eliminated in the feces in 4 days. No parent was eliminated.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Animal Metabolism

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Upjohn not available. 3/22/72 Report #120-9760-17 Acc. #095128	Supplementary	After 4 days of posttreatment 90% of the applied ^{14}C was recovered in excrement. 75-80% of the ^{14}C was excreted in urine. No parent was eliminated.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Animal Metabolism

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Test data not available. 3/22/72 Report #120-9760-49 Acc. #095124	Supplementary	Negligible residues were found in quail 4 and 7 days after treatment with 5 ppm ^{14}C-labeled cycloheximide for 1 month.	None

Pesticide (Technical, Radioisotope) Environmental Chemistry Data Sheet for Review Number

Study Type = Animal Metabolism

Registrant	Testing Lab, Date Report #, Acc. #	Category Status	Test Results	Date Requirement Satisfied
Upjohn Company	Upjohn not available. 3/22/72 Report #120-9760-37 Acc. #095123	Supplementary	Cows excreted 96.5 and 94.4% of the applied doses during an 8 day feeding study. Cows fed 2.0 and 0.7 mg ^{14}C-Cycloheximide secreted 1.30 and 0.376 ppb, respectively, of ^{14}C residues per day in milk.	None

MASTER FILE

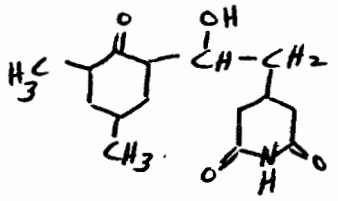
Chemical Name: 3-[2-3,5-dimethyl-2-oxocyclohexyl)-2-hydroxyethyl]-glutarimide.

Common Name: Cycloheximide.

Synonyms: Acti-dione, Naramycin A.

Shaunessey Number: NA (Not applicable).

Chemical Structure:



Pesticide Class: Fungicide, Citrus abscission agent, antibiotic.

Molecular Weight: 281.34

Solubility: 2.1 g/100 ml water at 2°C. Soluble in amyl acetate, chloroform, ether, acetone, methanol, ethanol and other common organic solvents except saturated hydrocarbons.

Vapor Pressure: Not available.

Physical State: Plates.

Color: Colorless.

Specific Gravity: Not available.

Melting Point: 119.5-121°C.

Boiling Point: Not available.

Impurities in Technical Material: Not available.

Degradation/Metabolism Chart

The metabolites and/or degradates by the processes of hydrolysis, photodegradation, aerobic soil metabolism, microbial action, field soil dissipation, fish accumulation, or animal metabolism have not been identified in the environment nor their fate determined. We postulate them to be benzene and pyridine moieties containing phenols and quinones which have been shown to be persistent and possibly available in the environment.

III. Use History/Accident Profile.

NA.

IV. Products/Use Patterns.

A. Terrestrial: Fruit-Nut Crop.

1. Use classification: NA.

2. Labeling

a. Precautionary: NA.

b. Directions for Use and Use Restrictions.

(Directions for use are excerpted from previous reviews. Labels were requested but were not available at time of review.)

Directions for Use on Bearing Cherries:

Use 1 to 1-1/2 ounces of Acti-dione TGF per 100 gals. of water, not to exceed 6 ounces per acre.

Prepare fresh spray mixture each day of spraying.

Do not mix Acti-dione TGF with lime or other alkaline materials. Acti-dione TGF is compatible with most insecticides and fungicides used on cherries.

Apply spray to obtain foliar coverage.

Apply with ground or aerial spray equipment.

Begin applying Acti-dione TGF in second cover sprays when fruit are 5/16 inch in diameter (pea size). Repeat application at 10 to 14 day intervals up to harvest. Apply after harvest as needed.

Do not spray other trees or plants with Acti-dione TGF.

Directions for Use on Oranges (except Valencia):

Oranges (except Valencia) (Florida use only). Apply 1 qt. of acti-aid in 500 gallons of water as a dilute spray to give thorough and uniform coverage of fruit and leaves.

Acti-aid may be used on early and midseason varieties any time after fruit are mature. Do not use after new shoots appear. Do not use on "Valencia" oranges.

Fruit may be harvested 4-7 days after treatment.

For use in Florida only.

Use only on early and midseason orange varieties for processing.

Directions for Use on Citrus:

The extended use is indicated by the name change, TUCO ACTI-AID "Component A" Citrus Abscission Agent for Preharvest Use in Florida on Oranges for Processing Grapefruit, Murcotts, Tangelos, Tangerines, and Temple Oranges."

Directions refer to two types of solution:

1. "Dilute Spray," equivalent to one quart of "Component A" in 500 gallons of water.

2. "Concentrated Spray," equivalent to sprays more concentrated than dilute, including "Aerial Spray" which is equivalent to "Component A" in at least 15 gallons of water.

The following table, copied from the label, summarizes the "Rate" recommendations.

RECOMMENDED APPLICATION RATES OF ACTI-AID IN 500 GAL. OF WATER

CROPS	TIME OF APPLICATION	RECOMMENDED RATE* Component A	Component B
Oranges: Valencia	Jan. 1 thru June 1	1 qt.	0.5 qt.
	June 1 thru Aug. 1	1 qt.	3.0 qt.
Oranges: Early and mid- season	Dec. 1 thru April 1	1 qt.	1.5 qt.
Grapefruit	Oct. 1 thru Feb. 1	0.5 qt.	0.75 qt.
	Feb. 1 thru June 1	0.25 qt.	0.75 qt.
Murcotts	Feb. 1 thru June 1	0.5 qt.	0.75 qt.
Tangelos	Oct. 1 thru Jan. 1	0.5 qt.	0.75 qt.
	Jan. 1 thru Mar. 1	0.25 qt.	0.75 qt.
Tangerines	Oct. 1 thru April 1	1.0 qt.	1.5 qt.
Temple Oranges	Dec. 1 thru Feb. 1	0.5 qt.	0.75 qt.
	Feb. 1 thru May 1	0.25 qt.	0.75 qt.

* See additional label instructions for Valencias.

3. Data Requirements/Gaps

Studies required	Requirement Status
Terrestrial	
Hydrolysis EC-PC-H-1	Data deficiencies.
Photodegradation	No data.

3. Data Requirements/Gaps (continued)

Studies required	Requirement Status
Terrestrial (continued)	
Photodegradation	No data.
Aerobic Soil Metabolism EC-Me-AS-1	Data deficiencies.
Effect of Microbes on Pesticides EC-Me-MEP-1	Data deficiencies.
Effect of Pesticides on Microbes EC-Me-PEM-1	Data deficiencies.
Leaching Leaching (Aged) EC-Mo-L-1	Data deficiencies.
Leaching (Fast) EC-Mo-L-2	Data deficiencies.
Field Soil Dissipation EC-FD-S-1 through EC-FD-S-15	Data deficiencies.
Fish Accumulation EC-AC-F-1	Data deficiencies.

B. Terrestrial: General Noncrop.

1. Use classification: NA
2. Labeling a. Precautionary: NA
2. b. Directions for Use and Use Restrictions:

Use profile was not available at time of review even though requested.

3. Data Requirements/Gaps

Data requirements and gaps are the same for general noncrop use as they are for fruit-nut crop use in this case.

V. Review of Correspondence Files.

NA.

VI. Review of subject file.

The subject files contain reviews dealing with use on bearing cherries, murcotts, citrus, and on turf and ornamentals.

VII. Data Reviews.

A. COVER SHEET

Data Review Number: EC-PC-H-1.

Test Protocol: Hydrolysis.

Chemical Tested: Cycloheximide.

Validation Category Status, Date: Supplementary, 5/24/77.
Reason (if applicable) Useful information.

Repairable, and if so, to what category: No.
If No See evaluation.
If Yes See evaluation.

Repairable to Core Study: No.
If No See evaluation.
If Yes See evaluation.

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP# 2F1252, Vol. 4 of 8, p. R-1667.

Literature Study Number: None

Abstract

Parent was unstable at pH 8 at 5°C, 25°C, and 37°C and pH 7 at 25° and 37°C and pH 4.7 at 37°C. Parent was stable at pH 7.1 at 5°C and pH 4.7 at 5° and 25°C.

B. Data Review.

1. Title of study and review numbers:

Lemin, A. J., 1970. "Chemical Aspects of Cycloheximide." (Outline of Presentation to USDA, PRD on March 24, 1970). Review number EC-PC-H-1.

2. EC title of study:

Hydrolysis.

3. Testing procedure:

Bioactivity was determined after 14 days at pH 8.2, 7.1, 4.7 and 5°, 25°, and 37°C.

4. Results:

% Bioactivity after 14 days

pH	5°C	25°C	37°C
8.2	6	0	0
7.1	58	12	< 1
4.7	85	70	36

5. Conclusions:

Parent was unstable at pH 8 at 5°, 25°, and 37°C and pH 7 at 25° and 37°C and pH 4.7 at 37°C. Parent was stable at pH 7.1 at 5°C and pH 4.7 at 5° and 25°C. We do not know the degradates. The analytical method involves bioactivity rather than a radioisotope.

The hydrolysis study is supplementary. It is not repairable. Since it is not repairable, deficiencies are not listed. A hydrolysis study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-He-AS-1.

Test Protocol: Aerobic Soil Metabolism.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/24/77.
Reason (if applicable) Useful information.

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: The Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP# 2F1252, Vol. 4 of 8, p. R-1211, Report #120-9760-30.

Literature Study Number; None.

Abstract

First $T_{1/2}$--parent was 3 days, second $T_{1/2}$--parent was 8 days by antibiotic assay method.

B. Data Review.

1. Title of study and review numbers:

Retzold, E.N. and D.D. Chapman, "The Stability of Cycloheximide in a Controlled Soil Environment." Review Number EC-Me-AS-1.

2. EC title of study:

Aerobic Soil Metabolism.

3. Testing procedures:

Cycloheximide was added to Florida soil at the rate of 0.2 ppm. Soil characteristics: pH 6.8, temperature 35°C, water content 8%.

4. Results:

Immediately after fortification: 0.185 ppm. First half-life in less than 3 days. Second half-life in less than 8 days. Third half-life in 12 days. Analysis method was antibiotic assay.

5. Conclusions:

Cycloheximide degrades rapidly with a first half-life of 3 days as determined by antibiotic assay.

The aerobic soil metabolism study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. An aerobic soil metabolism study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-Me-MEP-1.

Test Protocol: Effect of Microbes on Pesticides.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: The Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP# 2F1252, Vol. 4 of 8, P. R-1297, Report #120-9760-51.

Literature Study Number: None.

Abstract

$T_{1/2}$ was determined from ^{14}C residues and bioassay activity in sterile and nonsterile soils. Faster degradation occurred in nonsterile soil.

B. Data Review.

1. Title of study and review number:

Petzold, E.N. and D.D. Chapman, "Fate of Cycloheximide when Incorporated into Sterile vs. Nonsterile Soil." Review number EC-Me-MEP-1.

2. EC title of study:

Effect of Microbes on Pesticides.

3. Testing Procedures:

Florida soil was autoclaved at 15 psi overnight. Aliquots of 100 g. of sterile and nonsterile soil were placed in jars. Half-life of cycloheximide in sterile and nonsterile soils was determined from ^{14}C residues and bioassay activity.

4. Results:

Accountability in PPM of C^{14} on Selected Nonsterile Soil Samples

Days of Treatment	Water Extraction No. 1	Water Extraction No. 2	Soil Assay	Total
1	0.111	0.034	0.028	0.173
5	0.024	0.007	0.049	0.080
8	0.004	0.013	0.027	0.044
10	0.007	0.003	0.028	0.038

No. 1 is the first water extraction and No. 2 is the second water extraction.

Half-life[1] in Days of ^{14}C-Residue and Bioassay Activity of Randomly Labeled ^{14}C-Cycloheximide.

Description	Nonsterile Soil	Sterilized Soil
^{14}C on Water Extracts	2.25	16.8
^{14}C on Bioassay Water	2.12	14.0
Bioassay Activity	1.49	9.0

[1] Calculation on fit to model $Y = e^{(A + BX)}$ where Y = ppm observed. X = time on treatment, $T_{.5} = .69315/B$, B = slope, A = intercept.

5. Conclusions: ^{14}C from randomly labeled cycloheximide disappears faster in nonsterile soil, indicating that soil bacteria and fungi transform cycloheximide. Most of the transformed ^{14}C-residue is extractable with water. We do not know the degradates nor the amount bound.

The study on effect of microbes on pesticides is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A study on effect of microbes on pesticides is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-He-PEM-1.

Test Protocol: Effect of Pesticides on Microbes.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable) Microorganisms are not identified.

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP# 2F1252, Vol. 4 of 8, p. R-1275,
Report #120-9760-53.

Literature Study Number: None.

Abstract

Cycloheximide does not inhibit populations of bacteria and fungi.

B. Data review.

1. Title of study and review number:

Petzold, E.N., and A.W. Neff, and R.E. Gosline, "Observation on the Ecology of Microflora in Soil which was Heavily Contaminated with Cycloheximide." Review number EC-Me-PEM-1.

2. EC title of study:

Effect of Pesticides on Microbes.

3. Testing Procedures:

Cycloheximide was applied to sandy soil at the rate of 2 mg/sq. ft. Samples of soil were taken during a 5-day irrigation period and 20 days later.

4. Results:

Cycloheximide does not inhibit populations of bacteria and fungi.

5. Conclusions:

Cycloheximide does not inhibit populations of bacteria and fungi.

The study on effect of pesticides on microbes is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A study on effect of pesticides on microbes is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-Mo-L-1.

Test Protocol: Leaching (Aged).

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable) Bulk density of soil and position of ^{14}C label are not reported.

Repairable, and if so, to what category: Yes, to Core.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: Yes.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 5/24/73.

Accession Number: 120448.

Additional Identifiers: Registration #1023-52, Report #12-9760-92.

Literature Study Number: None.

Abstract

^{14}C residues of cycloheximide leach in sand. Some soil binding occurred during aging. Cycloheximide degrades during aging. None of the ^{14}C in the leachate of the aged study was cycloheximide. 20% of the ^{14}C remained in soil.

B. Data review.

1. Title of study and review numbers:

Staten, F. W., A. M. Thornton, and W. M. Wright, "Soil Leaching Studies on Florida Soil Fortified with ^{14}C Cycloheximide and aged 30 days." Review number EC-Mo-L-1.

2. EC title of study:

Leaching (Aged).

3. Testing procedure:

Water was eluted through aged treated soil at the rate of 0.5 inch/day for 45 days. ^{14}C activity in leachate and soils from aged and nonaged tests were compared.

4. Results:

CONPARISON OF AGED AND NONAGED STUDIES

CYCLOHEXIMIDE ON SOIL

	Nonaged Soil	Aged Study
% ^{14}C radioactivity found in water leach fractions	95.8	70.7
% ^{14}C radioactivity remaining in soil after water leaching	2.6	20.8
% ^{14}C radioactivity in water leach fractions which was cycloheximide by bioassay.	64.45	None Detected

ANALYSIS OF FLORIDA ORANGE GROVE SOIL

% Organic Matter	6.75
% Sand	95.2
% Silt	1.4
% Clay	3.4
pH	7.2
Cation Exchange Capacity (mcg/100 gms)	4.6
% Moisture in Air Dried Soil	2.5

26.9% of the ^{14}C was lost from the soil during 30-day aging. Of the ^{14}C present in the soil after aging, 91.5% was recovered. 20.8% remained in the soil and 70.7% was leached.

SOIL COMBUSTION ANLYSIS, CYCLOHEXIMIDE, 30-DAY AGING

Sample Description	Gms Soil in Total Fraction	Average DPM Found	% of Total DPM
30-day aged soil	100.0	4,579,756	----
0" - 2" leached soil	122.5	517,131	54.3
2" - 4" " "	98.0	147,334	15.5
4" - 6" " "	115.4	115,276	12.1
6" - 8" " "	118.5	71,956	7.6
8" - 10" " "	126.2	39,865	4.2
10" - 12" " "	94.5	34,434	3.6
12" - 14" " "	142.8	25,935	2.7
Totals	917.9 gms	951,931 DPM	100.0%

SOLVENT EXTRACTION OF WATER LEACH FRACTIONS

Sample Description	Average DPM Found 14C Activity	% Extracted from Water into Solvent
*Water samples 8, 9, 10, 11, 12	1,234,681	---
Ethyl acetate extracts combined	1,622	0.13

*After solvent extraction

5. Conclusions:

^{14}C residues of cycloheximide leach in sand. Some soil binding occured during aging. More ^{14}C remained in the soil in the aged study. Cycloheximide is degraded during aging. None of the ^{14}C in the water leach fractions of the aged study was cycloheximide. 20.8% of the ^{14}C remained in the soil and 70.7% leached.

The aged leaching study is supplementary. The study is repairable to core data. Data deficiencies are as follow:

1. Bulk density of the soil is not provided. Leaching may vary in different soils so soil characteristic and bulk density is needed to define results.

2. Position of the ^{14}C label on cycloheximide is not reported. Both rings should be labeled to determine if all residues are recovered and which portion of the molecule leaches.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-Mo-L-2.

Test Protocol: Leaching (Fast).

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 5/24/73.

Accession Number: 120448.

Additional Identifiers: Registration #1023-52. Report #120-9760-93.

Literature Study Number: None.

Abstract

^{14}C equivalents of cycloheximide leach in sand. 95.8% of the applied ^{14}C was found in the water leach fractions.

B. Data Review

1. Title of study and review number:

Staten, F.W., W.H. Wright, and A.M. Thornton, "Soil Leaching Studies on Cycloheximide." Review number EC-Mo-L-2.

2. EC title of study:

Leaching (Fast).

3. Testing procedure:

Florida soil treated with ^{14}C-cycloheximide was eluted with 20 acre-inches of water. ^{14}C in soil and leachate was determined.

4. Results:

SCINTILLATION COUNTING COMBUSTED SOIL SAMPLES
AFTER WATER LEACHING

Sample Description	Average DPM Found	Calcl. mcg. as Cycloheximide
Fortified soil*	7,078,223	---
0" - 2" leached	31,781	5.9
2" - 4" "	30,603	5.6
4" - 6" "	26,131	4.8
6" - 8" "	19,730	3.6
8" - 10" "	14,910	2.7
10" - 12" "	11,228	2.1
12" - 15" "	30,852	5.7
Total in H_2O leached in soil	165,235 DPM	30.4

30.4/1154 x 100 = 2.6% of added material was retained by soil.

Accountability of ^{14}C cycloheximide.

In beaker wash from soil transfer, not on column	3.23%
Retained on soil	2.64%
In 20 water leach fractions	95.84%
	101.7 %

* Before water leaching.

64.5% of the leached ^{14}C was cycloheximide as determined by bioassay and liquid scintillation counting.

5. Conclusions:

^{14}C equivalents of cycloheximide leach in sand. 95.8% of the applied ^{14}C was found in the water leach fractions.

The fast leaching study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A leaching study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-Mo-L-3.

Test Protocol: Leaching.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/26/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: None.

Date Data Submitted: None.

Accession Number: None.

Additional Identifiers: Abstract card 136.

Literature Study Number: None.

Abstract

The bioassay method in combination with soil thin layer chromatography indicated that cycloheximide and cycloheximide oxime are relatively mobile.

B. Data Review.

1. Title of study and review number:

Charles S. Helling, D. Gayle Dennison, and Donald D. Kaufman, "Fungicide Movement in Soils." A.R.S., U.S.D.A., Agricultural Research Center--West, Beltsville, Md. 20705, March 8, 1974. Review number EC-Mo-L-3.

2. EC title of study:

Leaching.

3. Testing procedure:

Bioassay methods in combination with soil thin layer chromatography were used to determine mobility. After plates were leached with pesticide solution, microorganisms were sprayed on the plates and zones of stimulation or inhibition were determined.

4. Results:

Cycloheximide and cycloheximide oxime are relatively mobile compared to other pesticides when tested by this method.

5. Conclusions:

The bioassay method in combination with soil thin layer chromatography indicated that cycloheximide and cycloheximide oxime are relatively mobile.

The leaching study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A leaching study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-1.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP# 2F1252, Vol. 4 of 8, p. R-1533, Report #120-9760-28.

Literature Study Number: None.

Abstract

No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

B. Data Review:

1. Title of study and review numbers:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil (Florida, 1970).

Review number EC-FD-S-1.

2. EC title of study:

Field soil.

3. Testing procedure:

An orchard was sprayed at the rate of 20 ppm cycloheximide and 5.96 gal./tree.

An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of two inches is analyzed.

Soil type: Sandy.
No rainfall between treatment and harvest.

Formulation: Acti-Aid--1 qt. 4.23%.
Cycloheximide + 1.5 qt. Adsee 775 in 500 gal. water.
Treatment dates: April 16, 19, 21, 1970.

4. Results:

Treatment Harvest Interval (Days).	Residue Found in Soil (ppm)
0	< .016*
3	"
5	"

*None detected.

5. Conclusions.

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide and 5.96 gal./tree.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by H.D.

A. COVER SHEET

Data Review Number: EC-FD-S-2.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1538, Report #120-9760-29.

Literature Study Number: None.

Abstract

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

B. Data Review:

1. Title of study and review number:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil (Florida, 1970).

Review number EC-FD-S-2.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 20 ppm cycloheximide and 4.8 gal./tree. An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: Sandy.
No rainfall between treatment and harvest.

Formulation: Acti-Aid (1 qt. 4.23% cycloheximide) + 1.5 qt. Adsee 775 in 500 gal. water.
Treatment date: 5/1/70.
Other pesticides used: Liquid lime sulfur, Ca.

4. Results:

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
0	0.023
6	0.028

5. Conclusions:

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-3.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1542, Report #120-9760-32.

Literature Study Number: None.

Abstract

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

B. Data Review.

1. Title of study and review number:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil (Florida, 1970).

Review number EC-FD-S-3.

2. EC title of study.

Field Soil.

3. Testing Procedure:

An orchard was sprayed at the rate of 20 ppm cycloheximide and spray volume of 1120 gal./A. An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: sandy.
No rainfall.
Formulation: Acti-Aid (1 qt. 4.23% cycloheximide) + 1.5 qt. Adsee 775 in 500 gal. water.
Treatment date: 6/11/70.
Other pesticides used: Copper.

4. Results:

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
Control	<0.012
0	0.033
5	0.056
104	<0.014

5. Conclusions:

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-4.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1546, Report #120-9760-34.

Literature Study Number: None.

Abstract

No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

B. Data Review.

1. Title of study and review numbers:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil. (Florida, 1970). Review number EC-FD-S-4.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 20 ppm cycloheximide and spray volume of 780 gal./A. An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: Sandy.
No rainfall.
Formulation: Acti-Aid (1 qt. 4.23% cycloheximide) + 1.5 qt. Adsee 775 in 500 gal. water.
Treatment date: 6/5/70.

4. Results:

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
Control	<0.012
3	<0.012

5. Conclusions:

No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-5.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1549, Report #120-9760-35.

Literature Study Number: None.

Abstract

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

8. Data Reviews.

1. Title of study and review number:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil. (Florida, 1970). Review number EC-FD-S-5.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 20 ppm cycloheximide and 620 gal./A.

An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: Sandy with some clay.
No rainfall.
Treatment dates: May 13, 1970.
Formulation: Acti-Aid 1.5 qt. 4.23% cycloheximide + 2.25 qt. Adsee 775 in 750 gal. water.

4. Results

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
Control	<0.016
0	<0.016
5	<0.021

5. Conclusions:

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-6.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP# 2F1252, Vol. 4 of 8, p. R-1553,
Report #120-9760-46.

Literature Study Number: None.

Abstract

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

B. Data Reviews.

1. Title of study and review number:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil. (Florida, 1970). Review number EC-FD-S-6.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 20 ppm cycloheximide and spray volume of 820 gal./A.

An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: Sand.
No rainfall.
Treatment date: Dec. 8, 1970.
Formulation: Acti-Aid 1.5 qt. 4.23% cycloheximide + 2.25 qt. Adsee 775 in 750 gal. water.

4. and 5. See below.
The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

4. Results

Treatment-~~Interval~~ Harvest Interval (Days)	Residue Found in Soil (ppm)
Control	< .013
0	< .013
7	.070
38	< .016

5. Conclusions

Negligible residues were found in the top two inches of soil under the drip-line of the tree when the orchard was sprayed with 20ppm cycloheximide.

A. COVER SHEET

Data Review Number: EC-FD-S-7

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1558, Report #120-9760-47.

Literature Study Number: None.

Abstract

Negligible residues were found in soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

B. Data Reviews.

1. Title of study and review numbers:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil. (Florida, 1970). Review number EC-FD-S-7.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 20 ppm cycloheximide and spray volume of 500 gal./A.

Soil type: Sandy.
Climatic conditions between treatment and harvest: Not available.
Formulation: 1 qt. Acti-Aid (4.23% cycloheximide) + 1.5 qt. Adsee 775 in 500 gal. water.
Treatment date: 11/30/70.
Field Sampling Procedure: Depth of soil is not given.

4. Results

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
Control	< .017
0	0.03
7	0.15

5. Conclusions:

Negligible residues were found in soil under the drip line of the tree when the orchard was sprayed with 20 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-8.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1562, Report #120-9760-44.

Literature Study Number: None.

Abstract

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 750 ppm cycloheximide.

B. Data Reviews.

1. Title of study and review number:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil. (Florida, 1970). Review number EC-FD-S-8.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 750 ppm cycloheximide and spray volume of 20 gal./A.

An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: Sand.
No rainfall.
Formulation: 1.5 qt. 4.23% cycloheximide + 2.25 qt. Adsee 775 in 20 gal. water.
Treatment date: December 8, 1970.

4. Results

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
Control	<.013
0	.041
7	.071
38	<.016

5. Conclusions:

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 750 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-9.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1568,
Report #120-9760-43.

Literature Study Number: None.

Abstract

No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 500 ppm cycloheximide.

B. Data Reviews.

1. Title of study and review number:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil. (Florida, 1970). Review number EC-FD-S-9.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 500 ppm cycloheximide and spray volume of 15 gal./A.

An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: Sandy with some clay.
No rainfall.
Formulation: Acti-Aid 0.75 qt. 4.23% cycloheximide + 1.13 qt. Adsee 775 in 15 gal. water.
Treatment date: January 10, 1971.

4. Results:

An orchard was sprayed by aircraft at the rate of 500 ppm cycloheximide and spray volume of 15 gal./A.

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
4	<.016

5. Conclusions:

No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 500 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-10.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1872, Report #120-9760-33.

Literature Study Number: None.

Abstract

No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 267 ppm cycloheximide.

B. Data Reviews.

1. Title of study and review number:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil. (Florida, 1970). Review number EC-FD-S-10.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 267 ppm cycloheximide and 37.5 gal./A.

An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: Sandy.
Rainfall between treatment and harvest: 1.5".
Formulation: Acti-Aid 1 qt. 4.23% cycloheximide + 1.5 qt. Adsee 775 in 37.5 gal. water.
Treatment date: June 25, 1970.

4. Results

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
Control	<0.012
0	<0.012
0	<0.012

5. Conclusions:

No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 267 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-11.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1575, Report #120-9760-39.

Literature Study Number: None.

Abstract

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 333 ppm cycloheximide.

B. Data Reviews:

1. Title of study and review number:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil. (Florida, 1970). Review number EC-FD-S-11.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 333 ppm cycloheximide and spray volume of 70 gal./A.

An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: Sandy with some clay.
No rainfall.
Formulation: Acti-Aid 1 qt. 4.23% cycloheximide + 1.5 qt. Adsee 775 in 30 gal. water.
Treatment date: May 13, 1970.

4. Results:

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
Control	<0.016
0	<0.016
5	<0.021

5. Conclusions:

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 333 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-12.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1579, Report #120-9760-40.

Literature Study Number: None.

Abstract

No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 333 ppm cycloheximide.

B. Data Reviews:

1. Title of study and review number:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil. (Florida, 1970). Review number EC-FD-S-12.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 333 ppm cycloheximide and spray volume of 35 gal./A.

An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: Sandy.
No rainfall.
Formulation: Acti-Aid 1 qt. 4.23% cycloheximide + 1.5 qt. Adsee 775 in 30 gal. water.
Treatment dates: June 5, 1970.

4. Results:

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
Control	<0.012
3	<0.012

5. Conclusions:

No residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 333 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-13.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1584, Report #120-9760-45.

Literature Study Number: None.

Abstract

Negligible residues were found in the top two inches of soil under the drip-line of the tree when the orchard was sprayed with 500 ppm cycloheximide.

B. Data Reviews.

1. Title of study and review number:

Residue Determination for Cycloheximide on Oranges, Leaves, and Soil. (Florida, 1970). Review number EC-FD-S-13.

2. EC title of study:

Field Soil.

3. Testing procedure:

An orchard was sprayed at the rate of 500 ppm cycloheximide and spray volume of 26 gal./A.

An area of one square foot is selected which is directly below the drip edge of the tree. All soil in this area to a depth of 2 inches is analyzed.

Soil type: Sand.
No rainfall.
Formulation: Acti-Aid 1.5 qt. 4.23% cycloheximide + 2.25 qt. Adsee 775 in 30 gal. water.
Treatment date: December 8, 1970.

4. Results

Treatment-Harvest Interval (Days)	Residue Found in Soil (ppm)
Control	<.013
0	.030
7	.040
38	<.016

5. Conclusions.

Negligible residues were found in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 500 ppm cycloheximide.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-14.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/25/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1233, Report #120-9760-50.

Literature Study Number: None.

Abstract

Residues in orchard soil, adjacent soil, and lake water were below the bioassay detection limit on the 12th day.

B. Data Review:

1. Title of study and review number:

Petzold, E. N., and D. D. Chapman. "Cyclohexiimide Residues in a Citrus Orchard and Adjoining Soil and Lake Water After Spraying by Helicopter." Review number EC-FD-S-14.

2. EC title of study:

Field Soil.

3. Testing procedure:

A citrus orchard was sprayed with cyclohexiimide by helicopter. Residues in orchard soil, adjacent soil, and lake water were determined by bioassay.

Application rate: 1 qt. Acti-Aid (4.2% cyclohexiimide) and 1.5 qt. Adsee 775 in 15 gals. water per acre.

4. Results:

Bioassay Results on Samples Taken During Test

ppm Cyclohexiimide After Treating

		0 Day	5th Day	12th Day
Soil from Lake -	0 Ft.	<.016	<.016	<.014
"	100 Ft.	.025	.028	.014
"	200 Ft.	.105	.050	<.014
"	300 Ft.	.029	.057	<.014
Lake Water		<.0016	<.0016	

5. Conclusions:

Residues in soil were below the detection limit on the 12th day.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-FD-S-15.

Test Protocol: Field Soil.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/26/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP #2F1252, Vol. 4 of 8, p. R-1245, Report #120-9760-52.

Literature Study Number: None.

Abstract

Half-life of cycloheximide is 2.1 days when applied to field soil and watered.

B. Data Review.

1. Title of study and review number:

Petzold, E.N., and D. D. Chapman, "Effect of Repeated Applications of Water Upon the Migration and Persistance of Cycloheximide in a Treated Plot of Florida Soil." Review number EC-FD-S-15.

2. EC title of study:

Field Soil.

3. Testing procedure:

Cycloheximide was applied to soil (2 mg/sq. ft.) and irrigated for four days (0.5-0.65 inches/day). Soil samples (0-4", 4-8", 8-12" cores, 2" diameter) were analyzed.

4. Results:

Persistence of less than 10 days was indicated. Half-life of cycloheximide was 2.1 days.

5. Conclusions:

The study indicates a half-life of 2.1 days for cycloheximide applied to field soil and watered.

The field soil study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A field soil study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-Ac-F-1.

Test Protocol: Fish Accumulation.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/27/77.
Reason (if applicable)

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095125.

Additional Identifiers: PP #2F1252, Vol. 8 of 8, Report #120-9760-480.

Literature Study Number: None.

Abstract

Bluegills in a static system did not accumulate residues.

B. Data Review:

1. Title of study and review number:

Petzold, E.N., Chapman, D.D., "Residues of ^{14}C-Cycloheximide in Bluegills from Exposure via Water for a Month" (Revised Report). Review number EC-Ac-F-1.

2. EC title of study:

Fish Accumulation.

3. Testing procedure.

Bluegills weighing 0.4 to 5.2 g were put in declorinated water at 62-64°F aerated at 1.0 l/min. Bluegills were exposed to 0.09 ppm for 10 days and to 0.095 ppm for 20 days in a static system study.

4. Results:

Concentrations of ^{14}C in bluegills ranged from 0.03 ppm to 0.04 ppm during the 30 day exposure period. Undetectable levels were found on 3, 4, 5, 6, and 7 days of depuration. On the 8th and 9th days of depuration, 0.02 and 0.01 ppm were detected.

5. Conclusions:

Water samples were extracted with chloroform. A previous review (8/14/72) indicates that this is not the best procedure as chloroform is not as good a solvent as water.

Results obtained by this procedure indicate that the fungicide is not accumulated in bluegills in a static system.

The fish accumulation study is supplementary. The study is not repairable. Since it is not repairable, deficiencies are not listed. A fish accumulation study is needed.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-0-AM-1.

Test Protocol: Animal Metabolism.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/27/77. This
Reason (if applicable) type data is reviewed by
Chemistry Branch.

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095122.

Additional Identifiers: PP# 2F1252, Vol. 2 of 8, p. R-305,
Report #120-9760-14.

Literature Study Number: None.

Abstract

75.68% of the ^{14}C-labeled cycloheximide applied to rats was eliminated in the urine and 17.96% was eliminated in the feces in 4 days. The ^{14}C recovered did not have antibiotic activity.

B. Data Review.

1. Title of study and review number:

E. N. Petzold and D. D. Chapman, "Excretion of ^{14}C-Labeled Cycloheximide from the Rat after Administration of a Single Oral Dose." Review number EC-0-AM-1.

2. EC title of study:

Animal Metabolism.

3. Testing procedures:

Excretion of ^{14}C-labeled cycloheximide from the rat after administration of a single oral dose was determined.

4. Results:

Table 1. Parts per Billion of ^{14}C-Residue[1] in Rat Tissues after a Four-Day Depletion Period

Rat	#1	#2	#3	#4	#7
Carcass	<1	8	8	26	16
Blood	1	1	2	2	3
Liver	4	<1	4	11	19
Kidney	4	<1	2	11	8

1 After dosing orally with 1-2 mg/kg ^{14}C-Cycloheximide having 7855 DPM/mg.

On the basis of disintegrations per minute, 75.68% of the applied dose was eliminated in the urine and 17.96% was eliminated in the feces in 4 days.

The ^{14}C recovered did not have antibiotic activity. Only 11-33% in the urine could be extracted with chloroform since most was more hydrophilic than cycloheximide.

Only 2.5 to 20.4% in the feces could be extracted since most was adsorbed to the fecal solids.

5. Conclusions:

75.68% of the applied dose was eliminated in the urine and 17.96% was eliminated in the feces in 4 days. The ^{14}C recovered did not have antibiotic activity.

The study is supplementary. It contains useful information.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-0-AM-2.

Test Protocol: Animal Metabolism.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary 5/27/77. This
Reason (if applicable) type data is reviewed by Chemistry Branch.

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095122.

Additional Identifiers: PP# 2F1252, Vol. 2 of 8, p. R-503, Report #120-9760-17.

Literature Study Number: None.

Abstract

After 4 days of posttreatment, 90% of the ^{14}C applied to rats was recovered in excrement. 75-80% of the ^{14}C was excreted in urine. The recovered ^{14}C had no detectable antibiotic activity.

B. Data Review:

1. Title of Study and review number:

E. N. Petzold and D. D. Chapman, "Excretion Rates of ^{14}C-Labeled Residues on Rats Provided with Five Consecutive Daily Doses of Randomly Labeled Cycloheximide."

2. EC title of study:

Animal Metabolism.

3. Testing procedure:

Excretion of ^{14}C residues by rats given 5 consecutive daily doses of cycloheximide was determined.

4. Results:

Table 1. ^{14}C-RESIDUE IN PPB ON TERMINATED RATS

Tissue	92 hr. Posttreatment		
	Rat #16	Rat #18	AVG.
Abdominal Fat[1]	<10	<10	<10
Blood	<10	<10	<10
Brain	<10	<10	<10
Gastrointestinal Tract	<10	<10	<10
Kidney	<10	<10	<10
Liver	<10	<10	<10
Muscle	<10	<10	<10
Remaining Carcass	<10	<10	<10

---

1 Extractable Lipid Activity.

Daily doses were 0.5 mg/kg..

The excreted ^{14}C compounds had hydrophillic properties and no detectable antibiotic activity.

After 4 days of posttreatment, 90% of the applied ^{14}C was recovered in excrement of rats 16 and 18. Seventy-five to 80% of this ^{14}C was excreted in the urine.

5. Conclusions:

After 4 days of posttreatment, 90% of the applied ^{14}C was recovered in excrement. 75-80% of the ^{14}C was excreted in urine. The recovered ^{14}C had no detectable antibiotic activity.

The study is supplementary. It contains useful information.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-0-AM-3.

Test Protocol: Animal Metabolism.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/27/77.
Reason (if applicable) This type data is reviewed by Chemistry Branch.

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095124.

Additional Identifiers: PP# 2F1252, Vol. 4 of 8, p. R-1134, Report #120-9760-49.

Literature Study Number: None.

Abstract

Negligible residues were found in bobwhite quail 4 and 7 days after treatment with 5 ppm ^{14}C-labeled cycloheximide for one month.

B. Data Review:

1. Title of study and review number:

Petzold, E.N., and D.D. Chapman, "Residues of Cycloheximide in Bobwhite Quail," Review number EC-0-AH-3.

2. EC title of study:

Animal Metabolism.

3. Testing Procedure:

Bobwhite quail were fed 5 ppm ^{14}C-labeled cycloheximide for 1 month. ^{14}C residues were determined 4 and 7 days after treatment.

4. Results:

^{14}C Residues Observed in Samples of Quail after Withdrawal of Treatment.

DAYS OFF TEST	TOTAL CARCASS	RESIDUE IN LIVER	TISSUES KIDNEY	(EQUIVALENT PPM)[1] BRAIN	BLOOD
4	0.001	0.0016	0.0008	0.0025	0.0024
7	0.0002	0.0006	0.0017	0.0009	0.0018

1 Values $\leq$ .0014 ppm for blood, .004 ppm for kidney and liver and .005 ppm for carcass are not significant ($P \leq .05$).

5. Conclusions:

Negligible residues were found in quail 4 and 7 days after treatment with 5 ppm ^{14}C-labeled cycloheximide for 1 month.

The study is supplementary. It contains useful information.

Reviewed by N.D.

A. COVER SHEET

Data Review Number: EC-O-AM-4.

Test Protocol: Animal Metabolism.

Chemical Tested: Cycloheximide.

Validation Category Status, date: Supplementary, 5/27/77.
Reason (if applicable) This type data is reviewed by Chemistry Branch.

Repairable, and if so, to what category: No.
If No see evaluation:
If Yes see evaluation:

Repairable to Core Study: No.
If No see evaluation:
If Yes see evaluation:

Registrant: Upjohn Company.

Date Data Submitted: 3/22/72.

Accession Number: 095123.

Additional Identifiers: PP# 2F1252, Vol. 3 of 8, p. R-636, Report #120-9760-37.

Literature Study Number: None.

Abstract

During eight days of treatment, two cows fed 2.0 and 0.7 mg/day excreted 96.5% and 94.4%, respectively, of the ^{14}C applied. The cows secreted 1.30 and 0.376 ppb, respectively, ^{14}C residues per day in milk.

B. Data Review

1. Title of study and review number:

Petzold, E.N., R.E. Gosline, and D.D. Chapman. "The Fate of ^{14}C-Cycloheximide in Lactating Cows." Review number EC-0-AM-4.

2. EC title of study:

Animal Metabolism.

3. Testing Procedure:

Two cows were fed 2.0 and 0.7 mg ^{14}C-cycloheximide/day for 8 days.

4. Results:

During the 8 days, the cows excreted 96.5 and 94.4%, respectively, of the total doses. The cow fed 2 mg/day secreted 1.30 ppb ^{14}C residues in milk per day. Thin layer chromatography indicated 0.17 ppb cycloheximide-like substances present. The cow given 0.7 mg/day secreted 0.376 ppb ^{14}C residues in milk per day. Residues found in cows sacrificed the eighth day are as follow:

Radioisotope Residues in Tissue from Cows Given ^{14}C-Cycloheximide (Equivalent PPB ^{14}C-Cycloheximide).

Tissue	Cow No. 1 2.0 Mg/Day	Cow No. 2 0.7 Mg/Day
Rib Eye Muscle	4.8	0.77
Loin Muscle	3.4	0.59
Round Muscle	4.6	0.72
Heart	5.6	0.57
Liver	9.1	1.64
Kidney	12.0	2.04
Fat, Perirrenal	0.6	0.61
Fat, Viscerol	0.9	-0.66
Bone Marrow	0.9	-0.29
Brain	5.3	0.02
Tongue	3.4	0.61
Pancreas	10.3	0.41
Thymus	3.9	-0.27
Spleen	6.5	0.93
Mammary Glands	6.4	0.37
Bladder	4.7	0.57

5. Conclusions:

During the 8 days, the cows excreted 96.5 and 94.4%, respectively, of the total doses. The cows secreted 1.30 and 0.376 ppb, respectively, ^{14}C residues per day in milk.

The study is supplementary. It contains useful information.

Reviewed by N.D.

C. The following are not considered environmental chemistry:

1. a. A cylinder-Plate Assay for Cycloheximide, E.N. Petzold and D.D. Chapman. Study #120-9760-1, page R-27.

   b. Accession #095121.

   C. Volume #1 of 8 of PP# 2F1252.

   d. Date data submitted 3/22/72.

2. a. A Sensitive Method for Determining Cycloheximide in Oranges, E.N. Petzold and D.C. Chapman. Study #120-9760-3, page R-31.

   b. Accession #095121.

   c. Vol. #1 of 8 of PP# 2F1252.

   d. Date data submitted: 3/22/72.

3. a. Evaluation of a Cylinder-Plate Method for Analysis of Cycloheximide in Oranges. E.N. Petzold, D.D. Chapman and W.M. Wright. Study #120-9760-4, page R-38.

   b. Accession #095121.

   c. Vol. #1 of 8 of PP# 2F1252.

   d. Date data submitted: 3/22/72.

4. a. An Apparatus for Surface Extraction of Oranges. E.N. Petzold and D.D. Chapman. Study #008-9760-2, page R-61.

   b. Accession #095121.

c. Vol. #1 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

5. a. Partitioning of Cycloheximide Between Water and Various Partially Miscible Liquids. E.N. Petzold and D.D. Chapman. Study #120-9760-2, page R-62.

b. Acc. #095121.

c. Vol. #1 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

6. a. Systems for Thin Layer Chromatography of Cycloheximide. E.N. Petzold and D.D. Chapman. (120-9760-12). Study No. 120-9760-12, page R-63.

b. Acc. #095121.

c. Vol. #1 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

7. a. Activity of ^{14}C-Labeled Cycloheximide, Lot 9543-EOH-117. Prepared in a Fermentation Process. E.N. Petzold and D.D. Champan. Study #120-9760-13, page R-64.

b. Acc. #095121.

c. Vol. #1 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

8. a. A Procedure for Trapping ^{14}C-Volatile Fragments from an Orange. In Situ. E.N. Petzold and D.D. Chapman. Study #120-9760-36, page R-94.

b. Acc. #095121.

c. Vol. #1 of 8 of PP# 2F1252.

d. Date data submitted: 3/22/72.

9. a. Evaluation of the Analytical Method for Cycloheximide on Florida Soil. E.N. Petzold and D.D. Chapman. Study #120-9760-26, page R-96.

b. Acc. #095121.

c. Vol. #1 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

10. a. Sampling in the Field for Cycloheximide Assay. E.N. Petzold. Study #120-9760-27, page R-112.

b. Accession #095121.

c. Vol. #1 of 8 of PP# 2F1252.

d. Date data submitted: 3/22/72.

11. a. Ruggedness of the Method for Cycloheximide in Oranges in the Presence of Pesticides. E.N. Petzold and D.D. Chapman. Study No. 120-9760-56, page R-114.

b. Accession #095121.

c. Vol. #1 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

12. a. Stability of Cycloheximide in Oranges. E.N. Petzold and D.D. Chapman. Study #120-9760-5, page R-124.

b. Accession #095122.

c. Vol. #2 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

13. a. The Fate of Cycloheximide on Oranges Stored in a Laboratory ~~Environment~~. E.N. Petzold and D.D. Chapman. Study #120-9760-6, page R-142.

b. Accession #095122.

c. Vol. #2 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

14. a. The Fate of Cycloheximide in the Processing of Oranges. E.N. Petzold and D.D. Chapman. Study #120-9760-10, page R-154.

b. Accession #095122.

c. Vol. #2 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

15. a. Cycloheximide Residue on Hamlin Oranges During a Seven-Day Treatment-Harvest Interval. E.N. Petzold and D.D. Chapman. Study #120-9760-24, page R-207.

b. Accession #095122.

c. Vol. #2 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

16. a. Effects of Relative Humidity and Temperature Upon the Rate of Decline of Surface Extractable Cycloheximide from Orlando Tangelos. E.N. Petzold and D.D. Chapman. Study #120-9760-25, page R-231.

b. Accession #095122.

c. Vol. #2 of 8 of PP #2F1252.

d. Date data submitted: 3/22/72.

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22. a. Residue Determination for Cycloheximide on Oranges (Florida, 1970). Study #120-9760-18, page R-1518.

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24. a. Residue Determination for Cycloheximide on Oranges (Florida, 1970). Study #120-9760-20, page R-1522.

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25. a. Residue Determination for Cycloheximide on Oranges (Florida, 1970). Study #120-9760-21, page R-1526.

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32. a. Residue Determination for Cycloheximide on Oranges (Florida, 1971). Study #120-9760-58, page R-1605.

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d. Date data submitted: 3/22/72.

D. The following investigation is not germane since a mixture of Actidione and Thiram was studied rather than Actidione alone:

a. Meyer, W.A., M.P. Britton, L.E. Gray, and J.B. Sinclair, "Fungicide Effects on Fungal Ecology in Creeping Bentgrass Turf," Vol. 43, March 1971, Issue 3-4, Reg. No. 1023-15.

b. Accession #024388.

c. EPA Registration #1023-15.

d. Effect of Pesticides on Microbes.

e. Date data submitted: 9/21/72.

f. Date previously reviewed: no record.

VIII. Hazard Assessment

A. Crop rotation restriction.

For other uses besides orchard and general noncrop use, rotational crop studies would be needed because metabolites and/or degradates have not been identified in the environment nor their fate determined. We postulate them to be benzene and pyridine moieties containing phenols and quinones which have been shown to be persistent and possibly available in the environment.

B. Disposal Problems.

Persistence of parent compound in soil is short. The metabolites and/or degradates have not been identified in the environment nor their fate determined. We postulate them to be benzene and pyridine moieties containing phenols and quinones which have been shown to be persistent and possibly available in the environment. We do not know what effect the degradates may have.

C. Potential for loss of land resources.

We do not know of any loss of land resources from past use of this chemical. The metabolites and/or degradates

have not been identified in the environment nor their fate determined. We postulate them to be benzenes and pyridine moieties containing phenols and quinones which have been shown to be persistent and possibly available in the environment.

D. Profile of reentry data.

Toxicology branch has indicated the need for reentry data for citrus, cherries, and pears as per attached memo of 6/16/77. Environmental chemistry section does not think that reentry data is needed on each citrus crop (oranges, grapefruit, murcotts, tangelos, tangerines) but only on representative citrus.

E. Profile of residues in the environment.

The following conclusions are made, but it must be noted that the investigations have deficiencies:

1. Metabolism and degradation.

The metabolites and/or degradates have not been identified in the environment nor their fate determined. We postulate them to be benzenes and pyridine moieties containing phenols and quinones which have been shown to be persistent and possibly available in the environment.

2. Hydrolysis.

Bioactivity test at 14 days.

Parent unstable at pH 8 at 5°, 25° and 37°C and pH 7 at 25°C and 37°C and pH 4.7 at 37°C.

Parent stable at pH 7.1 at 5°C and pH 4.7 at 5° and 25°C.

We do not know the degradates.

3. Aerobic soil metabolism.

First $T^{1/2}$ parent 3 days, second $T^{1/2}$ 8 days. Antibiotic assay method. This was not adequate for EC data. We do not know the degradates nor the amount bound.

4. Effects of microbes on the pesticide.

Sterile vs. nonsterile soil ^{14}C study.

Faster degradation or dissipation in nonsterile soil. We do not know the degradates nor the amount bound.

5. Effect of Pesticides on Microbes.

Cycloheximide does not inhibit populations of bacteria and fungi. The microorganisms were not identified.

6. Leaching.

Bioassay of ^{14}C residues.

Rapid study: Parent compound leached and degradates leached.

Aged study: No parent found, degradates leach (70%) and remained in soil. No degradates were analyzed.

A bioassay method in combination with soil thin layer chromatography indicated that cycloheximide and cycloheximide oxime are relatively mobile.

7. Field Soil Study.

Negligible residues were detected in the top two inches of soil under the drip line of the tree when the orchard was sprayed with 20, 267, 333, 500, and 750 ppm cycloheximide.

No residues were found in soil in a citrus orchard, adjoining soil, and lake water 12 days after spraying.

The half-life of cycloheximide is 2.1 days when applied to the field and watered (1/2 inch/day).

8. Fish Accumulation.

^{14}C residues did not accumulate in bluegills during a static system study. During exposure, ^{14}C concentrations ranged from 0.03 to 0.14 ppm.

On the 8th and 9th days of depuration, 0.02 and 0.01 ppm ^{14}C were detected. Water samples were extracted with chloroform. This is not the best procedure as chloroform is not as good a solvent as water.

9. Animal Metabolism.

Of the ^{14}C given rats, 76% was eliminated in the urine and 18% was eliminated in the feces in 4 days. The ^{14}C recovered did not have antibiotic activity and was more hydrophillic than cycloheximide. Cows fed 2.0 and 0.7 mg ^{14}C-labeled cycloheximide per day for 8 days excreted 96.5% and 94.4%, respectively, during the 8 days. The cow fed 2 mg/day secreted 1.30 ppb ^{14}C residues in milk per day. Thin layer chromatography indicated 0.17 ppb cycloheximide-like substances present. The cow given 0.7 mg/day secreted 0.376 ppb ^{14}C residues in milk per day.

IX. Recommendations.

The metabolites and/or degradates have not been identified in the environment nor their fate determined. We postulate them to be benzenes and pyridine moieties containing phenols and quinones which have been shown to be persistent and possibly available in the environment.

Toxicology branch has indicated the need for reentry data for citrus, cherries, and grapes as per attached memo of 6/16/77. Environmental chemistry section does not think that reentry data is needed on each citrus crop (oranges, grapefruit, murcotts, tangelos, tangerines) but only on representative citrus.