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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MAY 17 1988

MEMORANDUM

SUBJECT: Oxytetracycline Registration Standard

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Attached are the Science Chapter and Generic Data Tables for the Ecological Effects portion of the Oxytetracycline Registration Standard. Data evaluation records will follow at a later date.

cc: J. Heckman, memo only (OD/HED)

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ECOLOGICAL EFFECTS TOPICAL SUMMARY

A. Effects on Birds

Two studies were received under this topic. They were not acceptable for hazard evaluation.

The minimum data required to evaluate the hazard of oxytertacycline to birds are:

1. An avian single dose oral LD_{50} test with the technical grade of the active ingredient utilizing either one species of waterfowl, preferably the mallard duck, or one species of upland game bird, preferably the bobwhite quail; and

2. Two avian dietary LC_{50} tests with the technical grade of the active ingredient utilizing one species of waterfowl, preferably the mallard duck, and one species of upland game bird, preferably the bobwhite quail.

1. Avian Single-Dose Oral LD_{50} - Technical Grade

No avian acute oral studies were submitted. The Guidelines requirement for an avian acute oral study has not been fulfilled.

2. Avian Dietary LC_{50} - Technical

No avian subacute dietary studies were submitted. The Guidelines requirement for avian dietary studies has not been fulfilled.

3. Precautionary Labeling

Due to lack of toxicity data, no pracautionary labeling will be recommended at this time.

B. Effects on Freshwater Fish

One study was received under this topic. It was not suitable for hazard evaluation.

The minimum data required to evaluate the hazard of oxytetracycline to freshwater fish are:

1. Two 96-hour freshwater fish toxicity tests. One test should utilize a coldwater species, preferrably the rainbow trout, and the other should utilize a warmwater species, preferably the bluegill sunfish.

2. When direct exposure of aquatic organisms to a chemical is expected, the formulated product testing is required.

1. Freshwater Fish LC_{50} - Technical

No acute studies were submitted. The Guidlines requirement for acute freshwater fish testing is not fulfilled.

2. Acute Studies - Formulated Products

Acute aquatic toxicity studies on fish with formulated products may be required when the product will be introduced directly into water or when the estimated environmental concentration (EEC) exceeds the LD_{50} of the technical material to fish. Oxytetracycline is registered as a paint additive for aquatic uses. The toxicity of oxytetracycline to fish is not known. Aquatic studies using the formulated product are therefore not required at this time.

3. Precautionary Labeling

Due to lack of toxicity information, no pracautionary labeling will be recommended at this time.

C. Effects on Freshwater Aquatic Invertebrates

No studies were received under this topic.

The minimum data required to assess the hazard of oxytetracycline to freshwater aquatic invertebrates is a 48-hour acute study, using the technical grade of the active ingredient, on first instar Daphnia magna or early instar amphipods, stoneflies, or mayflies.

When there is expected to be direct exposure of aquatic organisms to a chemical, formulated product testing is required. The registered uses of oxytetracycline as an aquatic paint additive fall into this category.

1. Invertebrate Acute LC_{50} - Technical

No studies are available for evaluation of hazard to freshwater aquatic invertebrates from the technical grade of oxytetracycline. The Guidelines requirement for acute toxicity testing of freshwater aquatic invertebrates is not fulfilled.

2. Acute Studies - Formulated Products

Acute aquatic toxicity studies on freshwater invertebrates with formulated products may be required when the product will be introduced directly into water or when the estimated environmental concentration (EEC) exceeds the LD_{50} of the technical material to freshwater invertebrates. Oxytetracycline is registered as a paint additive for aquatic uses. The toxicity of oxytetracycline to aquatic invertebrates is not known. Aquatic studies using the formulated product are therefore not required at this time.

3. Precautionary Labeling

Due to lack of toxicity information, no pracautionary labeling will be recommended at this time.

D. Effects on Estuarine and Marine Organisms

No studies were received under this topic.

Acute toxicity testing with estuatrine and marine organisms is required for a chemical when the TEP is intended for direct application to the marine/estuarine environment or is expected to reach this environment in significant concentrations when the product is used as directed. Oxytetracycline is not expected to enter the estuarine environment in significant concentration as a result of its use as as antimicrobial agent.

1. Technical Material

No studies were submited. There are no guideline requirements for estuarine and marine studies on oxytetracycline at this time.

E. Plant Protection

One study was received under this topic. It was not suitable for hazard evaluation.

Target Area Phytotoxicity data for any site may be required for Special Review and certain public health situations when phytotoxicity is of concern.

All Tier I data on Nontarget Area Phytotoxicity are required for pesticides used in forests and natural grasslands. In addition, all Tier I data are required on the above and for other sites when any of the following conditions are met:

1. Phytotoxicity problems concerning the pesticide arise and open literature data are not available to address the problem.

2. The pesticide may pose problems to endangered or threatened species.

3. Special review has been initiated on the pesticide as a result of phytotoxicity.

There are no plant protection Guidelines requirements for the currently registered uses of oxytetracycline at the present time.

Ecological Effects

The following documents were sent to EEB and received abbreviated reviews. They do not appear in the Topical Summary. The results, however, are cited in the Ecological Effects Profile.

Author(s)	Date	MRID Number
Mraz, Boucher, Callenbach	1956	73375
Scott, Holm, Reynolds	1954	75075
Wellborn, T.L. Jr.	1969	28002
Beutel, J.	1976	108384

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ECOLOGICAL EFFECTS DISCIPLINARY REVIEW

I. ECOLOGICAL EFFECTS PROFILE

A. Technical Product

1. Terrestrial Studies

No data are available to characterize the toxicity of oxytetracycline to birds. Invalid data indicate that oxytetracycline promotes growth of bobwhite quail chicks when they are fed low doses (10 gm/ton of diet) of oxytetracycline (terramycin) for 16 weeks. Similar results were obtained when pheasant chicks were fed 10 mg terramycin/lb. diet.

2. Aquatic Studies

No studies are available to characterize the toxicity of oxytetracycline to aquatic organisms. Unvalidated data indicate that the LC_{50} value for oxytetracycline to striped bass fingerlings is 178 ppm in 96 hr.

3. Plant studies

No studies are available to characterize the toxicity of oxytetracycline to plants. Unvalidated data indicate that oxytetracycline applied to pear trees at 10 times the maximum use rate show no detrimental effects.

4. Toxicity to Estuarine and Marine Organisms

There were no studies of toxicity to estuarine and marine organisms submitted. There is no requirement for this testing on oxytetracycline products at this time when they are used as directed.

B. Formulated Products and Use

Information contained in this section was extracted from 1) "Preliminary Quantitative Usage Analysis of Oxytetracycline," prepared by Yvette S. Hopkins, EAB/BUD, December 22, 1987; 2) Oxytetracycline Draft Index Entry, prepared by SSB/BUD, August 20, 1987; and 3) Qualitative Use Assessment for Oxytetracycline, prepared by E. Neil Pelletier, SSB/BUD, September 14, 1987.

Introduction

Oxytetracycline (OTC) is the common name for the antibiotic known under the trade names of Terramycin® and MycoShield®. OTC is registered as two forms, the hydrochloride or the calcium complex. For residue chemistry purposes EPA uses oxytetracycline as representative of the hydrochloride and the calcium complex. Oxytetracycline is one of a group of broad spectrum antibiotics known as tetracyclines which were developed for control of bacterial diseases in man and animals. It is also used for control of infection in aquarium fish.

Its use for plant disease control was developed by Pfizer, Inc. and uses are limited to application to peach, pear, and palm trees. The hydrichloride form of OTC is used as a direct injection treatment into the tree trunk of peach, pear and various palms. The calcium complex form of OTC is used for foliar application to peach and pear trees. The complex may also be used in Illinois, Indiana and Missouri as a foliar treatment of bent grass to control bacterial wilt through the Special Local Needs (SLN) registration. OTC can also be used as an additive for formulated oil based antifouling paints to extend their activity by suppressing barnacle growth.

Formulations

The OTC hydrochloride is available as 21.6 percent wettable powder or soluble concentrate. The calcium complex form is available as a 17 percent wettable powder. For formulations by use see the EPA Index to Pesticide Chemicals.

Use Sites, Rates and Application

The only domestic basic producer of oxytetracycline is Pfizer, Inc. Chemical Division. OTC is used to treat fire blight and pear decline on pears; bacterial spot and SLN peach X disease; lethal yellowing on Canary Island date palm, coconut palm, date palm and prichardia palm; and bacterial wilt on Toronto creeping bentgrass.

Oxytetracycline is used on pears primarily in the Western growing region (Washington, Oregon and California), peaches in the Eastern production region and on ornamental palms mainly in Florida and Texas. Numerous special local needs registrations exist for OTC.

Oxytetracycline is a minor fungicide. Pears and peaches account for 98% of the total use of oxytetracycline. Each remaining site accounts for no more than one percent of the

total use. Total use of OTS is variable, because repeated spraying may be necessitated by wet weather. On the major crop (pears), approximately 25-30 % of the acreage is treated with OTC, while the percent of peach acreage treated is around 15 %. The annual usage of OTC is summarized in Table 1.

Table 1. Domestic Annual Usage of Oxytetracycline as a Pesticide (1987)[1/]

Site	Pounds Active Ingredient	Percent of Total Use	Treated (Base)[2/] Acres (1000)	Percent of Site Treated	Regional Use
Pears	10,500	48.0	18-22	25-30	West
Peaches	10,500	48.0	15	15	East
Ornamental Palms	250	<2.0	NA[3/]	NA	South
Carpet Bentgrass	100	<1.0	NA	NA	NA
Total	21,350	100	33-37		

1/ Source: C.Cookston, Marketing Manager, Pfizer
2/ Acres represented are an approximation of the number of acres treated, irrespective of the number of applications.
3/ NA - Not Available

Table 2 summarizes the oxytetracycline uses and rates of application as they appear on product labels:

Table 2. Oxytetracycline application and use rates

OTC Calcium Complex:

Site and Disease	Treatment Method	Application No.	Application Intervals	Use Rate a.i./tree
Pears	Foliar spray	8 to 10	4 to 6 days	0.171b[1/]
Peaches	Foliar spray	8 to 9	7 days	0.1251b[2/]

1/ Equivalent to 200 ppm
2/ Equivalent to 150 ppm

Table 2. (cont'd)

OTC Hydrochloride:

Site and Disease	Treatment Method	Application Frequency	Use Rate a.i./tree
Coconut Palm Lethal yellows	Tree trunk Injection	4 month intervals	1.0 to 3.0 g in 0.5 to 16 oz water
Pritchardia palm Lethal yellows	Tree trunk Injection	3 month intervals	1.0 to 3.0 g in 0.5 to 16 oz water
Pears Pear decline	Tree trunk Injection	12 month intervals	0.56 to 0.75g in 192 to 256 oz water

II. RISK ASSESSMENT

No data are available on the toxicity of oxytetracycline to terrestrial or aquatic wildlife. An assessment of the hazards associated with the outdoor use of oxytetracycline as a crop bactericide cannot be completed.

III. ENDANGERED SPECIES CONSIDERATIONS

Due to the lack of nontarget effects data, no endangered/threatened species risk assessments can be made at this time.

IV. PRECAUTIONARY STATEMENTS

A. Manufacturing-Use Products/End Uses Where an Effluent is Likely

Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or public waters unless this product is specifically identified and addressed in an NPDES permit. Do not discharge effluent containing this product to sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Reginal Office of the EPA.

B. End-Use Products

Do not contaminate water when disposing of equipment washwaters.

C. Endangered Species Labeling

There is no endangered species labeling requirement at this time.

V. MAJOR DATA GAPS

Please see Generic Data Requirements Table.

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Generic Data Requirements For Oxytetracycline

Data Requirement	Test Substance 1/	Use Patterns 2/	Does EPA Have Data?	Bibliographic Citation	Must Additional Data Be Submitted?	Timeframe for Submission 3/
§158.145 Wildlife and Aquatic Organisms						
Avian and Mammalian Testing						
71-1 - Avian Acute Oral Toxicity						
- Upland game bird	TGAI	A,B,D	No		Yes	9 mos
71-2 - Avian Subacute Dietary Toxicity						
- Upland game bird	TGAI	A,B,D	No		Yes	9 mos
- Waterfowl	TGAI	A,B,D	No		Yes	9 mos
71-3 - Wild Mammal Toxicity	TGAI	A,B,D	No		No	
71-4 - Avian Reproduction						
- Upland game bird	TGAI	A,B	No		No	
- Waterfowl	TGAI	A,B,D	No		No	
71-5 - Simulated and Actual Field Testing for Mammals and Birds	TEP	A,B,D	No		No	
Aquatic Organisms Testing						
72-1 - Freshwater Fish Toxicity						
- Warmwater	TGAI	A,B,D	No		Yes	9 mos
- Coldwater	TGAI	A,B,D	No		Yes	9 mos

Generic Data Requirements For Oxytetracycline (Cont'd)

Data Requirement	Test Substance 1/	Use Patterns 2/	Does EPA Have Data?	Bibliographic Citation	Must Additional Data Be Submitted?	Timeframe for Submission 3/
§158.145 Wildlife and Aquatic Organisms						
72-2 - Acute Toxicity to Freshwater Invertebrates	TGAI	A,B,D	No		Yes	9 mos
72-3 - Acute Toxicity to Estuarine and Marine Organisms						
- Fish	TGAI	A,B,D	No		No	
- Shrimp	TGAI	A,B,D	No		No	
- Oyster	TGAI	A,B,D	No		No	
72-4 - Fish Early Life Stage and Aquatic Invertebrate Life Cycle						
- Fish	TGAI	A,B,D	No		No	
- Invertebrates	TGAI	A,B,D	No		No	
72-5 - Fish Life Cycle	TGAI	A,B,D	No		No	
72-6 - Aquatic Organism Accumulation	TGAI	A,B,D	No		No	
72-7 - Simulated or Actual Field Testing						
- Aquatic Organisms	TEP	A,B,D	No		No	

Footnotes

1/TGAI = Technical Grade of the Active Ingredient; TEP = Typical End-Use Product.
2/The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Nonfood; C = Aquatic, Food Crop; D = Aquatic, Nonfood; E = Greenhouse, Food Crop; F = Greenhouse, Nonfood; G = Forestry; H = Domestic, Outdoor ; I = Indoor.
3/Due dates refer to the number of months following the registrant's receipt of this Registration Standard, unless otherwise indicated.