United States
Environmental Protection
Agency

Office of
Pesticides and Toxic Substances
Washington DC 20460

Pesticides

540/RS-89-018

EPA

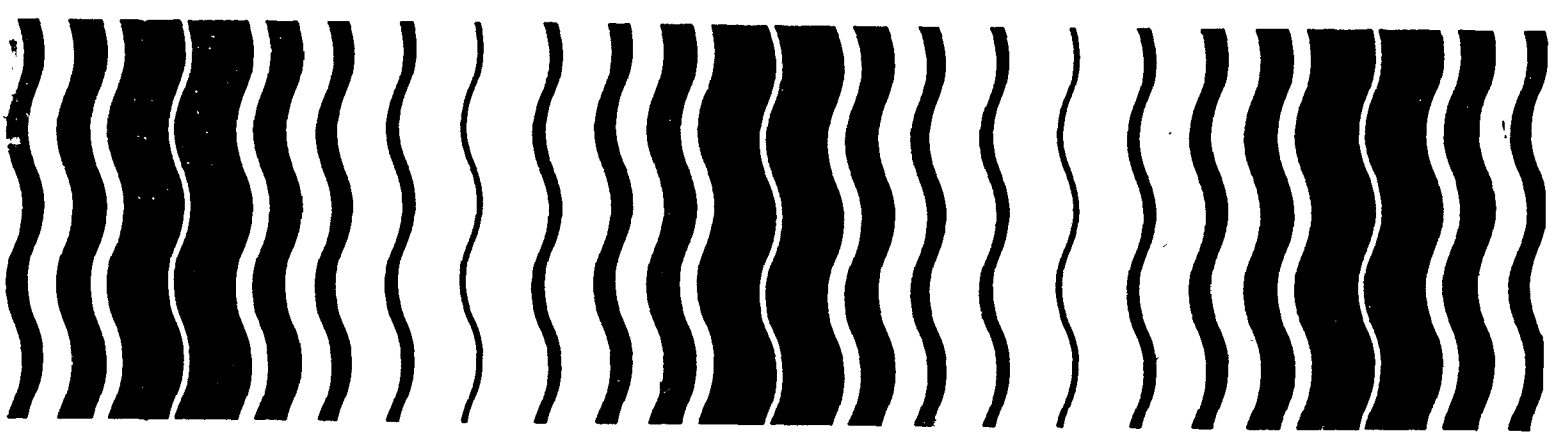
Guidance for the Reregistration of Pesticide Products Containing

OXYTETRACYCLINE

OXYTETRACYCLINE HYDROCHLORID

OXYTETRACYCLINE
CALCIUM COMPLEX

as the Active Ingredient



OMB Control No. 2070-0057
Expires November 1989

GUIDANCE FOR THE REREGISTRATION OF PESTICIDE PRODUCTS

CONTAINING

OXYTETRACYCLINE
[006304]

[CASE NUMBER 0655]

[CAS NUMBER 79-57-2]

OXYTETRACYCLINE HYDROCHLORIDE
[006308]

OXYTETRACYCLINE CALCIUM COMPLEX
[006321]

AS THE ACTIVE INGREDIENTS

DECEMBER 1988

ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF PESTICIDE PROGRAMS

WASHINGTON, D.C. 20460

TABLE OF CONTENTS

APPENDICES

I. DATA APPENDICES

II. LABELING APPENDICES

III. BIBLIOGRAPHY APPENDICES

IV. FORMS APPENDICES

GLOSSARY OF TERMS AND ABBREVIATIONS

ADI	Acceptable Daily Intake. Also known as the Reference Dose or RfD.
a.i.	Active ingredient
ARC	Anticipated Residue Contribution
CAS	Chemical Abstracts Service
CSF	Confidential Statement of Formula
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EP	End Use Product
EPA	U.S. Environmental Protection Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
LC50	Median lethal concentration - a statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water or feed, e.g., mg/l or ppm.
LD50	Median lethal dose - a statistically derived single dose than can be expected to cause death in 50% of the test animals, when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LEL	Lowest Effect Level
MPI	Maximum Permissible Intake
MRID	Master Record Identification (number). EPA's system of recording and tracking studies submitted to the Agency.
MP	Manufacturing Use Product
NPDES	National Pollutant Discharge Elimination System

NOEL	No Observed Effect Level
OPP	Office of Pesticide Programs
OES	Office of Endangered Species, U.S. Fish and Wildlife Service
PADI	Provisional Acceptable Daily Intake
ppm	Parts per million
RfD	Reference Dose
TMRC	Theoretical Maximum Residue Contribution

I. INTRODUCTION

EPA has established the Registration Standards program in order to provide an orderly mechanism by which pesticide products containing the same active ingredient can be reviewed and standards set for compliance with FIFRA. The standards are applicable to reregistration and future applications for registration of products containing the same active ingredient. Each registrant of a product containing an active ingredient subject to this Standard who wishes to continue to sell or distribute that product must bring his product and labeling into compliance with FIFRA, as instructed by this Standard.

The Registration Standards program involves a thorough review of the scientific data base underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether the pesticide meets the "no unreasonable adverse effects" criteria of FIFRA. In its review EPA identifies:

1. Studies that are acceptable to support the data requirements for the currently registered uses of the pesticide.

2. Additional studies necessary to support continued registration. The additional studies may not have been required when the product was initially registered or may be needed to replace studies that are now considered inadequate.

3. Labeling revisions needed to ensure that the product is not misbranded and that the labeling is adequate to protect man and the environment.

The detailed scientific review, which is not contained in this document, but is available upon request,[1] focuses on the pesticide active ingredient. The scientific review primarily discusses the Agency's evaluation of and conclusions from available data in its files pertaining to the pesticide active ingredient. However, during the review of these data the Agency is also looking for potential hazards that may be associated with the end use products that contain the active ingredient. The Agency will apply the provisions of this Registration Standard to end use products if necessary to protect man and the environment.

---

[1]The scientific reviews and Compendium of Acceptable Uses may be obtained from the National Technical Information Service (NTIS), Attn: Order Desk, 5285 Port Royal Road, Springfield, VA 22161. Telephone (703) 487-4650.

EPA's reassessment results in the development of a regulatory position, contained in this Registration Standard, on the pesticide and each of its registered uses. See Section IV - Regulatory Position and Rationale. Based on its regulatory position, the Agency may prescribe a variety of steps to be taken by registrants to maintain their registrations in compliance with FIFRA. These steps may include:

1. Submittal of data in support of product registration;

2. Modification of product labels;

3. Modifications to the manufacturing process of the pesticide to reduce the levels of impurities or contaminants;

4. Restriction of the use of the pesticide to certified applicators or other specially trained individuals;

5. Modification of uses or formulation types; or

6. Specification of packaging limitations.

Failure to comply with these requirements may result in the issuance of a Notice of Intent to Cancel or a Notice of Intent to Suspend (in the case of failure to submit data).

In addition, in cases in which hazards to man or the environment are identified, the Agency may initiate a special review of the pesticide in accordance with 40 CFR Part 154 to examine in depth the risks and benefits of use of the pesticide. If the Agency determines that the risks of the pesticide's use outweigh the benefits of use, the Agency may propose additional regulatory actions, such as cancellation of uses of the pesticide which have been determined to cause unreasonable adverse effects on the environment.

EPA has authority under the Data Call-In (DCI) provisions of FIFRA sec. 3(c)(2)(B) to require that registrants submit data to answer our questions regarding the chemical, toxicological, and environmental characteristics and fate of a pesticide. This Registration Standard lists the data EPA believes are necessary to resolve our concerns about this pesticide. These data are listed in the Tables A, B, and C in Appendix I. Failure to comply with the DCI requirements enumerated in this Registration Standard may result in issuance by EPA of a Notice of Intent to Suspend the affected product registrations.

Registrants are reminded that FIFRA sec. 6(a)(2) requires them to submit factual information concerning possible unreasonable adverse effects of a pesticide at any time that they become aware of such information. Registrants must notify the Agency of any information, including interim or preliminary results of studies, if that information suggests possible adverse effects on man or the environment. This requirement is independent of the specific time requirements imposed by EPA for submittal of completed studies called in by the Agency and continues as long as the products are registered under FIFRA.

II. CHEMICALS COVERED BY THIS STANDARD [2]

A. Description of Chemical

The following chemicals are covered by this Registration Standard:

1. Common Name: Oxytetracycline

Chemical Name: 4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydro-6-methyl-1,11-dioxo-2-naphthacenecarboxamide.

Other Chemical Nomenclature: 2-Naphthacenecarboxamide, 4(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,13,12a-pentahydroxy-6-methyl-1,11-dioxo.

Trade Names: Glomycin, Terrafungine, Riomitsin, Hydroxytetracycline, Berkmycin, Biostat, Impercin, Oxacycline, Oxatets, Oxydon, Oxydumocycline, Oxymycin, Oxypan, Oxytetracid, Ryomycin, Stevacin, Terraject, Terramycin, Tetramel, Tetran, Vendarcin, and Vendracin.

Chemical Class: Antibiotic (produced by the actinomycete Streptomyces rimosus)

Empirical Formula: $C_{22}H_{24}N_2O_9$

Molecular Weight: 460.44

Molecular Structure:

CAS Registry No.: 79-57-2

OPP Shaughnessy Nos.: 006304

Physical/chemical properties: Data gap.

---

[2] Information was obtained from the following sources: The Merck Index, 10th ED., p 6849, Farm Chemicals Handbook'88, p. C218, and the Toxic Substances Control Act Chemical Substances Inventory, p. 1070.

2. Common Name: Calcium oxytetracycline

Chemical Name: [4-(Dimethylamino) 1,4,4a,5,5a,6,11,12a-octahdyro-3,5,6,10,12,12a -hexahydro-6-methyl-1,11- dioxo-2-naphthacenecarboxamide] calcium complex.

Trade Name: Agricultural Terramycin, Mycoshield.

Chemical Class: Antibiotic (produced by the actinomycete Streptomyces rimosus)

Empirical Formula: $C_{22}H_{22}N_2O_9$ Ca

Molecular Weight: 498.52

CAS Registry No.: 7179-50-2

OPP Shaughnessy Nos.: 006321

Physical/chemical properties:

Color: Tan to dark brown

Physical State: Data gap

pH: 7.5-10.5

3. Common Name: Oxytetracycline hydrochloride

Chemical Name: 2-Naphthacenecarboxamide, 4(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro -3,6,10,13,12a-pentahydroxy-6-methyl-1,11-dioxo - monohydrochloride.

Trade Names: Biosolvomycin, Hydrocyclin, Liquamycin, Otetryn, Oxlopar, 5-Hydroxytetracycline Hydrochloride, Terramycin Hydrochloride.

Chemical Class: Antibiotic (produced by the actinomycete Streptomyces rimosus)

Empirical Formula: $C_{22}H_{24}N_2O_9$ HCL
Molecular Weight: 496.9

CAS Registry No.: 2058-46-0

OPP Shaughnessy Nos.: 006308

Physical/chemical properties:

Color: yellow

Physical State:

Odor: Data gap.

Boiling Point: Data gap

Density: Data gap.

Solubility: Soluble in water (1 g/ml), in absolute alcohol (12 mg/ml). Insoluble in ether, petroleum ether and benzene.

Vapor Pressure: Data gap.

pH: 2.0-3.0

B. Regulatory History.

Initial Date of Registration: August 1974

Basic Producer: Pfizer, Inc.

End-Use Registrants: 2

Number of Registrations: The Agency has issued 5 Section 3 registrations and 16 Special Local Need registrations under FIFRA section 24(c).

C. Use Profile:

Type of Pesticide: Plant Fungicide/Bactericide and Algicide.

Pests Controlled: Bacterial and fungal diseases and slime-forming microorganisms.

Registered Uses:

1. Calcium oxytetracycline [17% WP]:
Nectarines, peaches, pears, and creeping Bentgrasses.

2. Oxytetracycline hydrochloride [21.6% soluble concentrate/solid]
-(Tree Trunk Injection) pears, peaches, and ornamental palms)
- Marine antifoulant paint additive.

3. Oxytetracycline hydrochloride [21.6% soluble concentrate/solid]
Formulation Intermediate for Marine antifoulant additive.

Predominant Uses: Pears and peaches (98%).

Minor Uses: Ornamental palms and Bentgrasses.

Annual Usage: 21,350 pounds/ai

Method of Application: Foliar, tree injection, and brush on (marine use).

D. Mode of Activity:

Inhibition of protein synthesis.

III. AGENCY ASSESSMENT

The Agency has reviewed all data in Agency files as of August 1988 supporting the registration of oxytetracycline. Data received by the Agency after this date have not been reviewed for the purposes of this standard. This section discusses the Agency's scientific findings and conclusions based on these data.

A. SUMMARY

1. A review of the oxytetracycline hydrochloride oncogenicity data indicated equivocal evidence of oncogenicity in male and female rats. The Agency concluded that although the findings were termed "equivocal" by the National Toxicology Program, they do not represent positive evidence of carcinogenicity in the rat. A similar study in mice indicated no evidence of oncogenicity.

2. Tolerances for oxytetracycline are limited to peaches (which includes nectarines) and pears, 0.1 ppm and 0.35 ppm respectively. A Reference Dose (RfD) of 1.0 mg/kg/day has been established based on several chronic studies. The Theoretical Maximum Residue Contribution (TMRC) for the U.S. population is 0.000065 mg/kg/day, corresponding to 0.006% of the RfD. A proposed increase in the peach tolerance from 0.1 to 0.35 ppm would result in a TMRC of 0.000118 mg/kg/day. The largest subgroups, nursing and non-nursing infants, represent 0.061% and 0.076% respectively of the current RfD.

3. The potential for development of oxytetracycline resistance due to increase background levels from pesticidal uses to applicators and field workers appears minimal.

4. The Agency is unable to assess the potential for oxytetracycline to contaminate ground water because the environmental fate of oxytetracycline is uncharacterized. However, because of its extensive history of antibiotic use in humans and low exposures, the Agency does not believe that pesticide uses of oxytetracyline use will pose a human hazard via ground water contamination.

5. The Agency is unable to assess the ecological effects of oxytetracycline on terrestrial or aquatic wildlife, because no data are available.

As a result of this Registration Standard review, the Agency has identified missing data required to fully evaluate the environmental and ecological risks associated with the use of oxytetracycline as an fungicide/bactericide and algicide. These data must be developed in order to maintain registrations of existing products or to register any new products containing oxytetracycline.

A summary of these data gaps are given in Section D. Please note that this is only a summary and complete details can be obtained by referring to the data tables in Appendix I

The regulatory position and rationale section of this Registration Standard discusses the Agency's position on each regulatory issue concerning oxytetracycline, and the required labeling sections contains the specific wording specified for each labeling provision.

B. SCIENCE ASSESSMENT

1. Health Effects

a. Adverse Effects from Drug Uses

In humans, oxytetracycline is administered orally and intravenously to treat infectious diseases caused by a wide variety of microorganisms such as rickettsial, mycoplasma pneumoniae, spirochetes, gram-negative bacteria (Bartonella bacilliformis, Pasteurella pestis, Brucella sp.), and gram-positive bacteria (Streptococcus sp., Staphylococcus aureus, Neisseria gonorrhea). The oral dose for adults ranges from 1 to 2 grams per day (orally or intravenously). The usual daily dose for children is 25 to 50 mg/kg.

A variety of adverse effects in humans have been reported from the use of oxytetracycline. The major adverse effects are:

(i). Toxic and Irritative Effects--The antibiotic may cause gastrointestinal irritation. Epigastric burning and distress, abdominal discomfort, nausea, vomiting and diarrhea may occur. Intravenous administration may produce thrombophlebitis. Long-term therapy may produce changes in the peripheral blood. Leukocytosis, atypical lymphocytes, toxic granulation of granulocytes and thrombopenia purpura may occur. A phototoxic reaction may occur, sometimes accompanied by onycholysis and pigmentation of the nails. Liver injury and a delay in blood coagulation may occur. Children under 7 years of age may develop a brown discoloration of the teeth. Treatment of pregnant females may also produce discoloration of the teeth of infants. Oxytetracycline is deposited in the skeleton of fetuses and children which can produce depression of bone growth which is readily reversible when the period of exposure to the drug is short.

(ii). Hypersensitivity--Various skin reactions such as morbilliform rashes, urticaria and generalized dermatitis may occur. Angioedema and anaphylaxis may develop. Other effects which may occur are burning of the eyes, cheilosis, brown or black coating of the tongue, atrophic or hypertrophic glossitis, pruritus ani or vulvae or vaginitis, fever and eosinophilia.

(iii). Other Biological Effects--Administration of oxytetracycline to undernourished adults results in weight loss,increased urinary but not fecal nitrogen excretion, negative nitrogen balance and elevated serum nonprotein nitrogen concentrations. Administration of oxytetracycline, like most antibiotics, may lead to the development of super infections by strains of bacteria or yeasts resistant to the agent.

These effects have been observed from the drug uses of oxytetracycline by oral and intravenous routes of exposure. The pesticide uses have substantially less exposure (virtually no exposure in cases where the pesticide is applied by injection to trees). The exposures are not by the intravenous route and exposure by the oral route is limited to ingestion of fruit from treated trees at levels substantially below those used for drug use. Therefore the Agency does not believe that the adverse effects observed from drug use are of concern from the pesticide uses.

b. Chronic Toxicity

Two 2-year chronic toxicity studies were conducted in rats. In one study, weanling male Osborne-Mendel rats were fed diets containing 0 (180 rats), 100 (100 rats), 1000 (130 rats) and 3000 ppm (100 rats), approximately 0, 5, 50, and 150 mg/kg/body weight/day, oxytetracycline hydrochloride in the diet for a period of 24 months. The NOEL was determined to be 3000 ppm, approximately 150 mg/kg/body weight/day, highest dose tested. In a second study, groups of weanling Sprague Dawley rats (20/sex/group) were fed diets containing 0,100, and 1000 ppm (approximately 0, 5, and 50 mg/kg/day) oxytetracycline hydrochloride in the diet for a period of 24 months. The NOEL for oxytetracycline hydrochloride was 1000 ppm, 50 mg/kg/day, highest dose tested.

Two chronic toxicity studies were conducted in dogs. In the first study each group contained eight male dogs (4 beagles, 4 mongrels). The dogs were fed diets containing 0, 100, 3000, and 10000 ppm, approximately 0, 2.5, 75, and 250 mg/kg/day, oxytetracycline hydrochloride in the diet for a period of 24 months. A yellow discoloration of the long bones and brownish discoloration of the thyroid was observed in all dosed animals at necropsy. The NOEL was determined to be 10000 ppm, approximately 250 mg/kg/day, highest dose tested. In a second study, groups of mongrel dogs/sex were

fed diets containing 0, 5000, and 10000, approximately 0, 125 and 250 mg/kg/day, of oxytetracycline hydrochloride in the diet for a period of 12 months. The NOEL was determined to be 10000 ppm, approximately 250 mg/kg/day, highest dose tested.

These studies were judged to be supplementary because too few animals survived to study termination, and/or too few tissues were examined histologically and/or data were summarized. However, this data requirement is waived based upon availability of both animal and human data from oxytetracycline's drug uses.

c. NCI/NTP Oxytetracycline Oncogenicity Study in the F344N/Rat

In this study, oxytetracycline hydrochloride (purity 98.8%) was administered to groups of F344/N rats fed 0, 25000, and 50000 ppm, approximately 0, 1250 and 2500 mg/kg/day, in the diet for a period of 103 weeks. Fatty metamorphosis of the liver was increased in rats in the 1250 mg/kg group. The National Toxicology Program's Peer Review Committee concluded that ". . . . .there was equivocal evidence[3] of carcinogenicity for male F344/N rats as indicated by increased incidences of pheochromocytomas of the adrenal gland. There was equivocal evidence of carcinogenicity for female F344/N rats as indicated by increased incidences of adenomas of the pituitary gland in the high dose group."

d. NCI/NTP Oxytetracycline Oncogenicity Study in the B6C3F1 Mouse

In this study, oxytetracycline hydrochloride (purity 98.8%) was administered to groups of B6C3F1 mice fed 0, 6300, and 12500 ppm, approximately 0, 945, and 1875 mg/kg/day, in their diet for a period of 103 weeks. Body weights were decreased in mice in the 1875 mg/kg group when compared to controls. The National Toxicology Program's Peer Review Committee concluded that "... there was no evidence of carcinogenicity for male or female B6C3F1 mice fed diets containing 6300 or 12500 ppm of oxytetracycline hydrochloride for 2 years."

---

[3] The NCI/NTP uses five levels of interpretative evaluations in animal carcinogenesis studies; in decreasing order of strength (not potency or mechanism) of the experimental evidence, these are: (i) clear evidence of carcinogenicity (ii) some evidence of carcinogenicity, (iii) equivocal evidence of carcinogenicity, (iv) no evidence of carcinogenicity, and (v) inadequate study of carcinogenicity.

e. Teratogenicity

Thirty-six female Charles River CD (COBS) rats were dosed during days 6 through 15 of gestation with 1200, 1350, and 1500 mg/kg of oxytetracycline hydrochloride. Thirty-seven control dams received corn oil during days 6 through 15 of gestation. There were dose-related decreases in maternal survival and body weight gain, and increases in the incidence of respiratory difficulties and rough coat. In addition, there were significant dose-related decreases in the percent of treated dams found pregnant. There was also a dose-related decrease in fetal body weight. The high incidence of maternal deaths and the fetotoxicity noted in all dose levels tested did not allow for an establishment of a NOEL. The LEL was 1200 mg/kg/day (lowest dose tested).

The significant findings discussed in this study can be attributed to the excessive dose levels used, and the overly stressing of the treated dams.

Groups of 42 female CD-1 mice were dosed during day 6 through 15 of gestation with 0, 1325, 1670, and 2100 mg/kg oxytetracycline hydrochloride. No adverse effects were demonstrated, due probably to the low dose levels used. The NOEL for maternal and developmental toxicity in this study was 2100 mg/kg (highest dose tested)

f. Antibiotic Microbial Resistance

Mature beagles were fed a ground-meal diet containing 0, 2, or 10 ppm, approximately 0, 0.05, or 0.25 mg/kg/day, of oxytetracycline for 44 days. The 10 ppm (0.25 mg/kg/day) diet resulted in a shift from a predominantly drug-susceptible population of enteric lactose-fermenting organisms to a multiple antibiotic-resistant population. A shift to drug-resistance did not occur in the group fed 2 ppm approximately 0.05 /mg/kg/day. NOEL was 0.05 mg/kg/day.

C. TOLERANCE REASSESSMENT

Tolerances have been established for residues of oxytetracycline in two raw agricultural commodities (40 CFR 180.337). Use of oxytetracycline as a drug in food animals is regulated by the FDA according to 21 CFR 520, 522, 524, and 558. The FDA has established tolerances for oxytetracycline in or on meat, fat, meat byproducts, and in uncooked edible tissues of salmonoid fish and catfish (21 CFR 556.500). EPA has evaluated the residue and toxicology data supporting tolerances, and has made the following regulatory determinations:

o Whether the current tolerances and food additive regulations are sufficient to cover the actual residues resulting from use (including uses registered under FIFRA sec. 24(c) and intrastate uses).

o Whether group tolerances can be established in accordance with 40 CFR 180.34(f).

o Whether, in the absence of tolerances, restrictions on use, grazing, or feeding of treated commodities are necessary.

o Whether the tolerances are expressed accurately and in current terminology.

o The current tolerances are sufficient to cover the actual residues resulting from foliar applications only.

o The regulatory determinations resulting from EPA's review are set out in Section IV.A, Regulatory Positions and Rationales.

1. Residue Data

a. Nature of the Residue in Plants

No data are available to evaluate the nature of the residue of oxytetracycline in plants. The Agency has assessed the need for data reflecting the metabolism of oxytetracycline in plants and has concluded that these data are not required because of oxytetracycline drug uses.

b. Nature of the Residue in Animals

No data are available to evaluate the nature of the residue of oxytetracycline in animals. Data on the metabolism of oxytetracycline in food animals are not required, because the exposure of livestock to residues of oxytetracycline is unlikely since there are no registered uses of feed items at the present time.

c. Analytical Methods

The available microbiological assay method for the determination of oxytetracycline residues in or on peaches, nectarines and pears is adequate for data collection and for tolerance enforcement. The Agency will not require any additional analytical methods at this time. The method is similar to Final Action Microbiological Methods I and II in the AOAC Official Methods of Analysis (1984;42.293-42.298).

d. Storage Stability

Available data indicate that oxytetracycline is stable in or on peaches, nectarines, and pears stored at -20 C for up to 90 days.

e. Magnitude of the Residue in Plants

Tolerances for residues in or on plant commodities are adequate.

1. Peaches/Nectarines: The available residue data support the tolerance for foliar application; however, tree injection applications exceed the current established tolerance for peaches.

2. Pears: The available residue data support the established tolerance and are sufficient to assess the adequacy of the label use directions.

2. Toxicology Data

The toxicology data considered in support of the tolerances include:

Study Type	Species	NOEL
Chronic Toxicity	Rat	150 mg/kg/day (HDT)[4]
Chronic Toxicity	Rat	50 mg/kg/day (HDT)
Chronic Toxicity	Dog	250 mg/kg/day (HDT)
Chronic Toxicity	Dog	250 mg/kg/day (HDT)

The Reference Dose (RfD) is based upon a estimated NOEL of 100 mg/kg derived from a comprehensive evaluation of the studies listed. None of the studies listed are of sufficient quality to be used as the critical study in defining the RfD; however, taking all the data together and using a safety factor of 100, the RfD was determined to be 1.0 mg/kg/day.

---

[4] (HDT)-Highest Dose Tested.

The Theoretical Maximum Residue Contribution for the U.S. population was determined to be 0.000065 mg/kg/day, occupying 0.006% of the RfD. The dietary exposure for other subgroups ranged from a low of 0.003% (males 20 years and older) to a high of 0.08% (non-nursing infants less then 1 year of age) of the RfD.

3. Tolerances Issued

Tolerances have been established for residues of oxytetracycline in or on peaches, including nectarines[5], (0.1 ppm) and pears (0.35 ppm) and are expressed in terms of oxytetracycline (40 CFR 180.337). The use of oxytetracycline as a drug in food animals is regulated by the FDA according to 21 CFR 556.500. The FDA has established the following tolerances for residues of oxytetracycline in or on animal commodities: (i) 3 ppm in uncooked kidney and 1 ppm in uncooked muscle, liver, fat and skin of chickens and turkeys;(ii) 0.1 ppm in uncooked edible tissues of swine; (iii) 0.1 ppm in uncooked edible tissues of cattle, beef calves, nonlactating dairy cattle, and dairy calves; and (iv) 0.1 ppm for negligible residues of oxytetracycline in uncooked edible tissues of salmonoid fish and catfish.

Codex MRLs have not been established or proposed for residues of oxytetracycline in or on any food/feed commodity.

---

5 52 Federal Register 33238 defines the crop term "peaches" to include both peaches and nectarines.

D. DATA GAP SUMMARY

The Agency has identified missing data required to fully evaluate the human and environmental risk associated with the use of oxytetracycline. Complete data gaps details may be obtained by referring to the tables in Data Appendices I. (Please refer to the data tables in Appendix I for detailed information regarding these requirements).

ENVIRONMENTAL FATE/EXPOSURE:

Hydrolysis
Photodegradation in water and in soil
Metabolism Studies (lab)
- -Aerobic Soil
- -Anaerobic Soil
- -Anaerobic Aquatic
- -Aerobic Aquatic

Leaching and Adsorption/Desorption
Dissipation Studies (field)
- -Soil
- -Aquatic (Sediment)

FISH & WILDLIFE:

Avian Acute Oral LD50
Avian Dietary LC50
Freshwater Fish LC50 (TGAI)[6]
Freshwater Invertebrate (TGAI)

PRODUCT CHEMISTRY

All product chemistry studies

---

[6] TGAI: Technical grade of the active ingredient

IV. REGULATORY POSITION AND RATIONALE

A. REGULATORY POSITIONS AND RATIONALES

Based on review and evaluation of all available data and other relevant information on oxytetracycline the Agency has made the following determinations:

1. Special Review

Oxytetracycline does not meet the criteria for Special Review.

Rationale: Based on available toxicity data and past use of oxytetracycline as a human drug, the Agency has determined that oxytetracycline does not meet nor does it exceed the criteria specified in 40 CFR 154.7.

2. Restricted Use

Oxytetracycline uses are not being restricted at this time.

Rationale: Section 3(d)(1)(C) of FIFRA provides that some or all uses of a pesticide will be classified for restricted use if the Administrator determines that without such restriction the pesticide "may generally cause unreasonable adverse effects in man or the environment." The Agency has determined that oxytetracycline does not meet any of the risk criteria of 40 CFR 152.170 restricted use classification.

3. New Food Uses

The Agency will continue to grant new uses and new tolerances for oxytetracycline. Existing tolerances for oxytetracycline are adequately supported and will protect the public health.

Rationale: No data gaps exist for plant and animal metabolism, storage stability and residue in the raw agricultural commodities. No data gaps exist in the area of toxicology testing. In addition, the TRMC only occupies 0.006% of the RfD.

4. Adequacy of Current Tolerances

Current tolerances are sufficient to cover the actual residues resulting from foliar applications and tree injection in pears. The Agency will propose that the tolerance level for peaches (including nectarines) be increased from 0.1 ppm to 0.35 ppm.

Rationale: Available data indicate that the established tolerance for peaches would be exceeded as a result of the tree trunk injection uses. An increase of this tolerance by 0.25 ppm would be adequate to cover these uses. The proposed increase, 0.35 ppm, would result in an TRMC of 0.000118 mg/kg/day occupying 0.012% of the RfD.

5. Group Tolerances

The Agency will not propose the establishment of group tolerance for Pome Fruit or Stone Fruit.

Rationale: Group tolerances are not appropriate at the present time because oxytetracycline is currently registered for use in only one member from two of the representative fruit groups (i.e., Pome Fruits: pears and Stone Fruits: peaches).

6. Groundwater Contamination

The Agency is deferring its decision concerning oxytetracycline potential for contaminating groundwater until information on its environmental characteristics and fate have been evaluated. Based on its lack of chronic effects, and use as a human drug, the Agency does not believe that oxytetracycline will pose a hazard to human health via ground water contamination.

Rationale: The Agency is unable to assess the potential for oxytetracycline to contaminate groundwater because the environmental fate of this chemical is uncharacterized. The Agency will assess oxytetracycline potential for groundwater contamination after receipt and review of environmental fate data.

7. Acute and Subchronic Toxicity Testing

The Agency has waived data requirements for acute and subchronic toxicity testing at this time.

Rationale: The Agency believes that there are no toxicological issues pertaining to the use of oxytetracycline as an fungicide on raw agricultural commodities or as an algicide for the prevention of barnacle growth on ship hulls. Although a number of adverse effects have been identified in susceptible humans as an result of its human drug use, these effects are usually seen only after prolonged treatment with oxytetracycline at relatively high dosages.

8. Applicators/Field Workers

The Agency believes that the potential for development of resistant microorganisms in applicators and/or field workers as an result of exposure are negligible.

Rationale: Oxytetracycline is used primarily on pears in the Western growing region, peaches in the Eastern growing region, and on palms, mainly in Florida and Texas. All of the palm applications and some of the pear applications are by injection for which there will be no human exposure. For the remaining applications, approximately 15 percent of peach acreage and 25 to 30 percent of pear acreage (some of which is treated by injection) is treated by foliar spray. Application is made only as needed to prevent disease which is more prevalent in the wet weather. The maximum number of applications are 8 to 10 at 4 to 6 day intervals for pears and 7 day intervals for peaches. Oxytetracycline is applied only when leaves are on the trees. Pears may not be treated after 60 days before harvest and peaches may not be treated after 21 days before harvest. This discontinuous and limited exposure is not likely to produce the constant selective pressure necessary to induce antibiotic resistance in the bacterial flora of the applicators or field workers. In addition, many of the bacterial and rickettsial pathogens that are primarily treated by oxytetracycline would not be infective by dermal or pulmonary routes.

9. Dietary Exposure

Potential for development of oxytetracycline-resistant microorganisms in the diet due to increased background levels from pesticidal uses are minimal.

Rationale: In a previously summarized study, beagle dogs were feed various levels of oxytetracycline in the diet. This study demonstrated that oxytetracycline at 0.05 mg/kg/day did not induce drug resistance to enteric bacteria.

Using this NOEL, 0.05 mg/kg/day, as the RfD (reference dose) and applying it to the proposed tolerance increase in peaches, the Theoretical Maximum Residue Concentration would be 0.000024 mg/kg/day occupying 0.05% of this RfD which allows for a 2,083 margin of exposure[7]. The Agency believes that this margin of exposure will protect against the

---

[7] Maximum amount of exposure producing no measurable adverse effects in animals (or studied humans) divided by the actual amount of human exposure in a population. Previously called the margin of safety.

development of oxytetracycline-resistant microorganisms in the diet due to increase background levels.

10. Priority Review of Data

The Agency will not give priority review to any studies required by this Standard. Data that are flagged under 40 CFR 158.34 for potential adverse effects, or that may be submitted under FIFRA sec. 6(a)(2), however, will receive immediate review upon receipt.

Rationale: Based upon the available data, the Agency has not identified any human health or environmental concerns that would warrant early review of data.

11. Continuation of Current Registrations

While the required data are being developed, currently registered manufacturing-use products (MPs) and end-use products (EPs) containing oxytetracycline may be sold, distributed, formulated and used subject to the terms and conditions specified in this Standard. Registrants must provide or agree to develop and provide additional data, as specified in the Data Appendices in order to maintain existing registrations.

Rationale: Under FIFRA, the Agency does not normally cancel or withhold registration because data are missing or are inadequate [see FIFRA section 3(c)(2)(B) and 3(c)(7)]. Issuance of this Standard provides a mechanism for identifying data needs. These data will be reviewed and evaluated, after which the Agency will determine if additional regulatory actions are necessary.

B. CRITERIA FOR REGISTRATION

To be registered or reregistered under this Standard, products must contain oxytetracycline, bear required labeling, and conform to the product composition, acute toxicity limits, and use pattern requirements listed in this section.

C. ACCEPTABLE RANGES AND LIMITS

1. Product Composition Standard

To be registered or reregistered under this Standard, manufacturing-use products (MPs) must contain this pesticide. Each MP formulation proposed for registration must be fully described with an appropriate certification of limits, stating maximum and minimum amounts of the active ingredient and inert ingredients which are present in products, as well as impurities found at greater than 0.1 percent.

2. Acute Toxicity Limits

The Agency will consider registration of technical grade and manufacturing-use products containing this pesticide provided that the product labeling bears appropriate precautionary statements for the acute toxicity category in which each product is placed.

3. Use Patterns

To be registered under this Standard, manufacturing-use products may be labeled for formulation into end-use products only for the commodities listed in the EPA Compendium of Acceptable Uses (for availability, see page 1). The EPA Compendium lists all registered uses, as well as approved maximum application rates and frequencies.

The use patterns currently registered are as follows:

Terrestrial Food Crop:
Terrestrial Nonfood Crop:
Aquatic Nonfood Crop:

D. LABELING

In order to remain in compliance with FIFRA, products must bear appropriate labeling as specified in 40 CFR 156.10 and this Standard, or must be revised to conform to those specifications. Appendix II contains information on label requirements.

No pesticide product containing this pesticide may be released for shipment by the registrant after December 15, 1989, unless the product bears an amended label which complies with the requirements of this Standard.

No pesticide product containing this pesticide may be distributed or sold after December 15, 1990, unless the product bears an amended label which complies with the requirements of this Standard.

The following specific information must appear on the labeling in order for products to remain in compliance with FIFRA:

1. Ingredients Statement

The ingredient statement for products must list the active ingredient as:

ACTIVE INGREDIENT	
Oxytetracycline Calcium complex	%
or	
Oxytetracycline hydrochloride	%
(20% oxytetracycline)	

2. Use Pattern Statements

All manufacturing-use products must state that they are intended for formulation into end-use products for acceptable use patterns. Labeling must specify sites, which are listed in the EPA Compendium of Acceptable Uses (for availability, see page 1). However, no use may be included on the label where the registrant fails to agree to comply with the data requirements in TABLE A for that use pattern.

V. PRODUCTS SUBJECT TO THIS STANDARD

All products containing one or more of the pesticides identified in Section II.A. are subject to certain requirements for data submittal or changes in composition, labeling or packaging of the product. The applicable requirements depend on whether the product is a manufacturing or end use product and whether the pesticide is the sole active ingredient or one of multiple active ingredients.

Products are subject to this Registration Standard as follows:

A. Manufacturing use products containing this pesticide as the sole active ingredient are subject to:

1. The restrictions (if any) upon use, composition, or packaging listed in Section IV, if they pertain to the manufacturing use product.

2. The data requirements listed in Tables A and B[8]

3. The labeling requirements specified for manufacturing use products in Section IV.

4. Administrative requirements (application forms, Confidential Statement of Formula, data compensation provisions) associated with reregistration.

B. Manufacturing use products containing this pesticide as one of multiple active ingredients are subject to:

1. The data requirements listed in Table A.

2. The labeling requirements specified for manufacturing use products in Section IV.

---

[8]Data requirements are listed in the three Tables in Appendix I of this Registration Standard. The Guide to Tables in that Appendix explains how to read the Tables.

Table A lists generic data requirements applicable to all products containing the pesticide subject to this Registration Standard. Table B lists product-Specific data applicable to manufacturing-use products. The data in Tables A and B need not be submitted by an end-use producer who is eligible for the generic data exemption for that active ingredient.

Table C lists product-specific data applicable to end-use products. The Agency has decided that, in most cases, it will not require the submittal of product-specific data for end-use products at this time. Therefore, most Registration Standards do not contain a Table C.

C. End use products containing this pesticide as the sole active ingredient are subject to:

1. The restrictions (if any) upon use, composition, or packaging listed in Section IV if they pertain to the end use product.

2. If eligible for the generic data exemption[9], the data requirements listed in Table C.

3. If not eligible for the generic data exemption, the data requirements listed in Table A and the data requirements listed in Table C.

4. The labeling requirements specified for end use products in Section IV.

D. End use products containing this pesticide as one of multiple active ingredients are subject to:

1. If not eligible for the generic data exemption, the data requirements listed in Tables A and C.

2. If eligible for the generic data exemption, the data requirements listed in Table C.

3. The labeling requirements specified for end use products in Section IV.

---

[9]If you purchase from another producer and use as the source of your active ingredient only EPA-registered products, you are eligible for the generic data exemption for generic data concerning that active ingredient (Table A) and product-specific data for the registered manufacturing use product you purchase (Table B).

Two circumstances nullify this exemption:

1) If you change sources of active ingredient to an unregistered product, formulate your own active ingredient, or acquire your active ingredient from a firm with ownership in common with yours, you individually lose the exemption and become subject to the data requirements in Table A.

2) If no producer subject to the generic data requirements in Table A agrees to submit the required data, all end-use producers lose the exemption, and become subject to the data requirements in Table A.

VI. REQUIREMENT FOR SUBMISSION OF GENERIC DATA

This portion of the Registration Standard is a notice issued under the authority of FIFRA sec. 3(c)(2)(B). It refers to the data listed in Table A, which are required to be submitted by registrants to maintain in effect the registration of products containing this active ingredient.[10]

A. What are generic data?

Generic data pertain to the properties or effects of a particular active ingredient. Such data are relevant to an evaluation of all products containing that active ingredient regardless of whether the product contains other ingredients (unless the product bears labeling that would make the data requirement inapplicable).

Generic data may also be data on a "typical formulation" of a product. "Typical formulation" testing is often required for ecological effects studies and applies to all products having that formulation type. These are classed as generic data, and are contained in Table A.

B. Who must submit generic data?

All current registrants are responsible for submitting generic data in response to a data request under FIFRA sec. 3(c)(2)(B) (DCI Notice). EPA has decided, however, not to require a registrant who qualifies for the formulator's exemption (FIFRA sec. 3(c)(2)(D) and 40 CFR 152.85) to submit generic data in response to a DCI notice if the registrant who supplies the active ingredient in his product is complying with the data request.

If you are granted a generic data exemption, you rely on the efforts of other persons to provide the Agency with the required data. If the registrants who have committed to generate and submit the required data fail to take appropriate steps to meet the requirements or are no longer in compliance with this data requirements notice, the Agency will consider that both they and you are not in compliance and will normally initiate proceedings to suspend the registrations of both your product(s) and their product(s) unless you commit to submit and submit the required data in the specified timeframe. In such cases, the Agency generally will not grant a time extension for submitting the data.

---

[10]Registrations granted after issuance of this Standard will be conditioned upon submittal or citation of the data listed in this Registration Standard.

If you are not now eligible for a generic data exemption, you may qualify for one if you change your source of supply to a registered source that does not share ownership in common with your firm. If you choose to change sources of supply, the Confidential Statement of Formula must identify the new source(s) and you must submit a Generic Data Exemption Statement.

If you apply for a new registration for products containing this active ingredient after the issuance of this Registration Standard, you will be required to submit or cite generic data relevant to the uses of your product if, at the time the application is submitted, the data have been submitted to the Agency by current registrants. If the required data have not yet been submitted, any new registration will be conditioned upon the new registrant's submittal or citation of the required data not later than the date upon which current registrants of similar products are required to provide such data. See FIFRA sec. 3(c)(7)(A). If you thereafter fail to comply with the condition of that registration to provide data, the registration may be cancelled (FIFRA sec. 6(e)).

C. What generic data must be submitted?

You may determine which generic data you must submit by consulting Table A. That table lists the generic data needed to evaluate current uses of all products containing this active ingredient, the uses for which such data are required, and the dates by which the data must be submitted to the Agency.

D. How to comply with DCI requirements.

Within 90 days of your receipt of this Registration Standard, you must submit to EPA a completed copy of the form entitled "FIFRA Section 3(c)(2)(B) Summary Sheet" (EPA Form 8580-1, enclosed) for each of your products. On that form you must state which of the following six methods you will use to comply with the DCI requirements:

1. You will submit the data yourself.

2. You have entered into an agreement with one or more registrants to jointly develop (or share in the cost of developing) the data, but will not be submitting the data yourself. If you use this method, you must state who will submit the data on which you will rely. You must also provide EPA with documentary evidence that an agreement has been formed which allows you to rely upon the data to be submitted. Such evidence may be: (1) your letter offering to join in an agreement and the other registrant's acceptance of your offer, (2) a written statement by the parties that an agreement exists, or (3) a written statement by the person

who will be submitting the data that you may rely upon its submittal. The Agency will also require adequate assurance that the person whom you state will provide the data is taking appropriate steps to secure it. The agreement to produce the data need not specify all of the terms of the final arrangement between the parties or a mechanism to resolve the terms.

If you and other registrants together are generating or submitting requested data as a task force or consortium, a representative of the group should request a Joint Data Submitter Number, as part of your 90-day response. The request must include the following information:

a. A list of the members of the consortium;
b. The name and address of the designated representative of the consortium, with whom EPA will correspond concerning the data;
c. Identity of the Registration Standard containing the data requirement;
d. A list of the products affected (from all members of the consortium); and
e. Identification of the specific data that the consortium will be generating or submitting.

The Agency will assign a number to the consortium, which should be used on all data submittals by the consortium.

3. <u>You have attempted to enter into an agreement to jointly develop data, but no other registrant has accepted your offer. You request that EPA not suspend your registration for non-compliance with the DCI</u>. EPA has determined that, as a general policy, it will not suspend the registration of a product when the registrant has in good faith sought and continues to seek to enter into a data development/cost sharing program, but the other registrants developing the data have refused to accept its offer. [If your offer is accepted, you may qualify for Option 2 above by entering into an agreement to supply the data.]

In order to qualify for this method, you must:

a. File with EPA a completed "Certification of Attempt to Enter into an Agreement with other Registrants for Develop-ment of Data" (EPA Form 8580-6, enclosed).

b. Provide us with a copy of your offer to the other registrant and proof of the other registrant's receipt of your offer (such as a certified mail receipt). Your offer must, at a minimum, contain the following language or its equivalent:

[Your company name] offers to share in the burden of producing the data required pursuant to FIFRA sec.3(c)(2)(B) in the [name of active ingredient] Registration Standard upon terms to be agreed or failing agreement to be bound by binding arbitration as provided by FIFRA section 3(c)(2)(B)(iii).

The remainder of your offer may not in any way attempt to limit this commitment. If the other registrant to whom your offer is made does not accept your offer, and if the other registrant informs us on a DCI Summary Sheet that he will develop and submit the data required under the DCI, then you may qualify for this option. In order for you to avoid suspension under this method, you may not later withdraw or limit your offer to share in the burden of developing the data.

In addition, the other registrant must fulfill its commitment to develop and submit the data as required by this Notice in a timely manner. If the other registrant fails to develop the data or for some other reason would be subject to suspension, your registration as well as that of the other registrant will normally be subject to initiation of suspension proceedings, unless you commit to submit and submit the required data in the specified timeframe. In such cases, the Agency generally will not grant a time extension for submitting the data.

4. <u>You request a waiver of the data requirement</u>. If you believe that a data requirement does not (or should not) apply to your product or its uses, you must provide EPA with a statement of the reasons why you believe this is so. Your statement must address the specific composition or use factors that lead you to believe that a requirement does not apply. Since the Agency has carefully considered the composition and uses of pesticide products in determining that a data require-ment applies, EPA does not anticipate that many waivers will be granted. A request for waiver does not extend the time-frames for developing required data, and if your waiver request is denied, your registration may be suspended if you fail to submit the data. The Agency will respond in writing to your request for a waiver.

5. <u>You request that EPA amend your registration by deleting the uses for which the data are needed</u>. You are not required to submit data for uses which are no longer on your label.

6. <u>You request voluntary cancellation of the registration of your product(s) for which the data are needed.</u>

E. Registrant Requests Regarding Data Requirements and Agency Responses

All requests for modification of data requirements (inapplicability, waiver), approval of protocols or protocol changes, or time extensions must be submitted in writing. The original requirement remains in effect unless the Agency has notified you in writing that it has agreed to a change in the requirement. While being considered by the Agency, such requests for changes in the requirements do not alter the original requirements or extend the time allowed for meeting the requirement.

F. Test Protocols and Standards

All studies required under this Notice must be conducted in accordance with test standards outlined in the Pesticide Assessment Guidelines, unless other protocol or standards are approved for use by the Agency in writing. All testing must be conducted in accordance with applicable Good Laboratory Practices regulations in 40 CFR Part 160.

The Pesticide Assessment Guidelines, which are referenced in the Data Tables, are available from the National Technical Information Service (NTIS), Attn: Order Desk, 5285 Port Royal Road, Springfield, VA 22161 (tel: 703-487-4650).

Protocols approved by the Organization for Economic Cooperation and Development (OECD) are also acceptable if the OECD-recommended test standards conform to those specified in the Pesticide Data Requirements regulation (Part 158.70). Please note, however, that certain OECD standards (such as test duration, selection of test species, and degradate identification which are environmental fate requirements) are less restrictive than those in the EPA Assessment Guidelines listed above. When using the OECD protocols, they should be be modified as appropriate so that the data generated by the study will satisfy the requirements of Part 158. Normally, the Agency will not extend deadlines for complying with data requirements when the studies were not conducted in accord with acceptable standards. The OECD protocols are available from OECD, 1750 Pennsylvania Avenue, N.W., Washington, D.C. 20006.

G. Procedures for requesting a change in test protocol.

If you will generate the required data and plan to use test procedures which deviate from EPA's Pesticide Assessment Guidelines or the Reports of Expert Groups to the Chemicals Group, Organization for Economic Cooperation and Development (OECD) Chemicals Testing Programme, you must submit for EPA approval the protocols you propose to use.

You should submit your protocols before beginning testing, because the Agency will not ordinarily accept as sufficient studies using unapproved protocols. A request for protocol approval will not extend the timeframe for submittal of the data, nor will extensions generally be given to conduct studies due to submittal of inappropriate protocols. The Agency will respond in writing to your request for protocol approval or change.

H. Procedures for requesting extensions of time.

If you think that you will need more time to generate the data than is allowed by EPA's schedule, you may submit a request for an extension of time.

EPA will view failure to request an extension before the data submittal response deadline as a waiver of any future claim that there was insufficient time to submit the data. While EPA considers your request, you must strive to meet the deadline for submitting the data.

The extension request should state the reasons why you believe that an extension is necessary and the steps you have taken to meet the testing deadline. Time extensions normally will not be granted due to problems with laboratory capacity or adequacy of funding, since the Agency believes that with proper planning these can be overcome. The Agency will respond in writing to any requests for extension of time.

I. Data Format and Reporting Requirements

All data submitted in response to this Notice must comply with EPA requirements regarding the reporting of data, including the manner of reporting, the completeness of results, and the adequacy of any required supporting (or raw) data, including, but not limited to, requirements referenced or included in this Notice or contained in PR Notice 86-5 (issued July 29, 1986). All studies must be submitted in the form of a final report; a preliminary report will not be considered to fulfill the submittal requirement.

J. Existing stocks provision upon suspension or cancellation.

The Agency has determined that if a registration is suspended for failure to respond to a DCI request under FIFRA sec. 3(c)(2)(B), an existing stocks provision for the registrant is not consistent with the Act. Accordingly, the Agency does not anticipate granting permission to sell or distribute existing stocks of suspended product except in rare circumstances. If you believe that your product will be suspended or cancelled and that an existing stocks provision should be granted, you have the burden of clearly demonstrating to EPA that granting such permission would be consistent with the Act. The following

information must be included in any request for an existing stocks provision:

1. Explanation of why an existing stocks provision is necessary, including a statement of the quantity of existing stocks and your estimate of the time required for their sale or distribution; and

2. Demonstration that such a provision would be consistent with the provisions of FIFRA.

VII. REQUIREMENT FOR SUBMISSION OF PRODUCT-SPECIFIC DATA

Under its DCI authority, EPA has determined that certain product-specific data are required to maintain your registrations in effect. Product-specific data are derived from testing using a specific formulated product, and, unlike generic data, generally support only the registration of that product. All such data must be submitted by the dates specified in this Registration Standard.

If you have a manufacturing use product, these data are listed in Table B. If you have an end use product, the data are listed in Table C. As noted earlier, the Agency has decided that it will not routinely require product-specific data for end use products at this time. Therefore, Table C may not be contained in this Registration Standard; if there is no Table C, you are not required to submit the data at this time.

In order to comply with the product specific data requirements, you must follow the same procedures as for generic data. See Section VI.D through J. You should note, however, that product chemistry data are required for every product, and the only acceptable responses are options VI.D.1. (submit data) or VI.D.6.(cancellation of registration).

Failure to comply with the product-specific data requirements for your products will result in suspension of the product's registration.

VIII. REQUIREMENT FOR SUBMITTAL OF REVISED LABELING

FIFRA requires each product to be labeled with accurate, complete and sufficient instructions and precautions, reflecting the Agency's assessment of the data supporting the product and its uses. General labeling requirements are set out in 40 CFR 156.10 (see Appendix II - LABELING and SUMMARY). In addition, labeling language specific to products containing this pesticide is specified in Section IV.D of this Registra-tion Standard. Responses to this Registration Standard must include draft labeling for Agency review.

Labeling must be either typewritten text on 8-1/2 x 11 inch paper or a mockup of the labeling suitable for storage in 8-1/2 x 11 files. Draft labeling must indicate the intended colors of the final label, clear indication of the front panel of the label, and the intended type sizes of the text.

If you fail to submit revised labeling as required, which complies with 40 CFR 156.10 and the specific instructions in Section IV.D., EPA may seek to cancel the registration of your product under FIFRA sec. 6.

IX. INSTRUCTIONS FOR SUBMITTAL

All submittals in response to this Registration Standard must be sent to the following address:

Office of Pesticide Programs
OPP Mailroom (TS-767C)
Environmental Protection Agency
401 M St., SW
Washington, D.C. 20460

Attn: Oxytetracyline Registration Standard

A. Manufacturing Use Products (MUPs) containing the subject pesticide as sole active ingredient.

1. Within 90 days from receipt of this document, you must submit for each product subject to this Registration Standard:

a. Generic Data Exemption Statement (EPA Form 8580-3), if applicable, or the "FIFRA Section 3(c)(2)(B) Summary Sheet" (EPA Form 8580-1), with appropriate attachments.

b. Confidential Statement of Formula (EPA Form 8570-4).

c. Evidence of compliance with data compensation requirements of FIFRA sec. 3(c)(1)(D). Refer to 40 CFR 152.80-152.99.

2. Within 9 months from receipt of this document you must submit:

a. Application for Pesticide Registration (EPA Form 8570-1).

b. Two copies of any required product-specific data (See Table B).

c. Three copies of draft labeling, including the container label and any associated supplemental labeling.

d. Product Specific Data Report (EPA Form 8580-4).

3. Within the times set forth in Table A, you must submit all generic data, unless you are eligible for the generic data exemption. If for any reason any test is delayed or aborted so that the schedule cannot be met, immediately notify the Agency of the problem, the reasons for the problem, and your proposed course of action.

B. Manufacturing Use Products containing the subject pesticide in combination with other active ingredients.

1. Within 90 days from receipt of this document, you must submit:

a. Generic Data Exemption Statement (EPA Form 8580-3), if applicable, or the FIFRA sec. 3(c)(2)(B) Summary Sheet, with appropriate attachments (EPA Form 8580-1).

b. Confidential Statement of Formula (EPA Form 8570-4)

2. Within 9 months of receipt of this document, you must submit:

Three copies of draft labeling, including the container label and any associated supplemental labeling.

3. Within the time frames set forth in Table A, you must submit all generic data, unless you are eligible for the generic data exemption. If for any reason any test is delayed or aborted so that the schedule cannot be met, immediately notify the Agency of the problem, the reasons for the problem, and your proposed course of action.

C. End Use Products containing the subject pesticide as sole active ingredient.

1. Within 90 days from receipt of this document, you must submit:

a. Generic data exemption Statement (EPA Form 8580-3), if applicable, or the FIFRA Section 3(c)(2)(B) Summary Sheet, with appropriate attachments (EPA Form 8580-1).

b. Confidential Statement of Formula (EPA Form 8570-4).

2. Within 9 months from receipt of this document you must submit:

a. Two copies of any product-specific data, if required by Table C.

b. Product Specific Data Report (EPA Form 8580-4), if Table C lists required product-specific data.

c. Three copies of draft labeling, including the container label and any associated supplemental labeling.

3. Within the times set forth in Table A, you must submit all generic data, unless you are eligible for the generic data exemption. If for any reason any test is delayed or aborted so that the schedule cannot be met, immediately notify the Agency of the problem, the reasons for the problem, and your proposed course of action.

D. End Use Products containing the subject active ingredient as one of multiple active ingredients

1. Within 90 days from receipt of this document, you must submit:

a. Generic data exemption Statement (EPA Form 8580-3), if applicable, or the FIFRA Section 3(c)(2)(B) Summary Sheet, with appropriate attachments (EPA Form 8580-1).

b. Confidential Statement of Formula (EPA Form 8570-4).

2. Within 9 months from the receipt of this document, you must submit:

Three copies of draft labeling, including the container label and any associated supplemental labeling.

3. Within the times set forth in Table A, you must submit all generic data, unless you are eligible for the generic data exemption. If for any reason any test is delayed or aborted so that the schedule cannot be met, immediately notify the Agency of the problem, the reasons for the problem, and your proposed course of action.

E. Intrastate Products

Applications for full Federal registration of intrastate products were required to be submitted no later than July 31, 1988. Unless an application for registration was submitted by that date, no product may be released for shipment by the producer after July 31, 1988.

I. DATA APPENDICES

GUIDE TO TABLES

Tables A, B, and C contain listings of data requirements for the pesticides covered by this Registration Standard.

Table A contains generic data requirements that apply to the pesticide in all products, including data requirements for which a "typical formulation" is the test substance.

Table B contains product-specific data requirements that apply only to a manufacturing use product.

Table C contains product-specific data requirements that apply only to an end use product.

The data tables are generally organized according to the following format:

1. Data Requirement (Column 1). The data requirements are listed in the order in which they appear in 40 CFR Part 158. The reference numbers accompanying each test refer to the test protocols set out in the Pesticide Assessment Guidelines, which are available from the National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161.

2. Test Substance (Column 2). This column lists the composition of the test substance required to be used for the test, as follows:

TGAI = Technical grade of the active ingredient
PAI = Pure active ingredient
PAIRA = Pure Active ingredient, radio labeled
TEP = Typical end use formulation
MP = Manufacturing use product
EP = End use product

Any other test substances, such as metabolites, will be specifically named in Column 2 or in footnotes to the table.

3. Use pattern (Column 3). This column indicates the use patterns to which the data requirement applies. Use patterns are the same as those given in 40 CFR Part 158. The following letter designations are used for the given use patterns:

A = Terrestrial, food
B = Terrestrial, non-food
C = Aquatic, food
D = Aquatic, non-food
E = Greenhouse, food
F = Greenhouse, non-food
G = Forestry
H = Domestic outdoor
I = Indoor

Any other designations will be defined in a footnote to the table.

4. Does EPA have data? (Column 4). This column indicates one of three answers:

YES - EPA has data in its files that completely satisfy this data requirement. These data may be cited by other registrants in accordance with data compensation requirements of Part 152, Subpart E.

PARTIALLY - EPA has some data in its files, but such data do not fully satisfy the data requirement. In some cases, the Agency may possess data on one of two required species or may possess data on one test substance but not all. The term may also indicate that the data available to EPA are incomplete. In this case, when the data are clarified, or additional details of the testing submitted by the original data submitter, the data may be determined to be acceptable. If this is the case, a footnote to the table will usually say so.

NO - EPA either possesses no data which are sufficient to fulfill the data requirement, or the data which EPA does possess are flawed scientifically in a manner that cannot be remedied by clarification or additional information.

5. Bibliographic citation (Column 5). If the Agency has acceptable data in its files, this column lists the identifying number of each study. This normally is the Master Record Identification (MRID) number, but may be a GS number if no MRID number has been assigned. Refer to the Bibliography Appendices for a complete citation of the study.

6. Must additional data be submitted? (Column 6). This column indicates whether the data must be submitted to the Agency. If column 3 indicates that the Agency already has data, this column will usually indicate NO. If column e indicates that the Agency has only partial data or no data, this column will usually indicate YES. In some cases, even though the Agency does not have the data, EPA will not require its submission because of the unique characteristics of the chemical; because data on another chemical can be used to fulfill the data requirement; or because the data requirement has been waived or reserved. Any such unusual situations will be explained in a footnote to the table.

7. Timeframe for submission (Column 7). If column t requires that data be submitted, this column indicates when the data are to be submitted, based on the issuance date of the Registration Standard. The timeframes are those established either as a result of a previous Data Call-In letter, or standardized timeframes established by PR Notice 85-5 (August 22, 1985).

8. Footnotes (at the end of each table). Self-explanatory.

Table A
GENERIC DATA REQUIREMENTS FOR OXYTETRACYCLINE

Data Requirement	Composition	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe for Submission
Part 158, Subpart C, Product Chemistry					
Product Identity and Composition					
61-2 - Description of Beginning Materials and Manufacturing Process	TGAI	No[1/]		Yes[2/]	9 Months
61-3 - Discussion of Formation of Impurities	TGAI	No[1/]		Yes[3/]	9 Months
Analysis and Certification of Product Ingredients					
62-1 - Preliminary Analysis of Product Samples	TGAI	No[1/]		Yes[4/]	12 Months
Physical and Chemical Characteristics					
63-2 - Color	TGAI	No[1/]		Yes[5/]	9 Months
63-3 - Physical State	TGAI	No[1/]		Yes[5/]	9 Months
63-4 - Odor	TGAI	No[1/]		Yes[5/]	9 Months
63-5 - Melting Point	TGAI	No[1/]		Yes[5,6/]	9 Months
63-6 - Boiling Point	TGAI	No[1/]		Yes[5,7/]	9 Months
63-7 - Density, Bulk Density or Specific Gravity	TGAI	No[1/]		Yes[5/]	9 Months

Table A
GENERIC DATA REQUIREMENTS FOR OXYTETRACYCLINE

Data Requirement	Composition	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe for Submission
Part 158, Subpart C, Product Chemistry (cont'd)					
Physical and Chemical Characteristics (cont'd)					
63-8 - Solubility	TGAI or PAI	No[1/]		Yes[5/]	9 Months
63-9 - Vapor Pressure	TGAI or PAI	No[1/]		Yes[5/]	9 Months
63-10 - Dissociation Constant	TGAI or PAI	No[1/]		Yes[5/]	9 Months
63-11 - Octanol/Water Partitioning Coefficient	PAI	No[1/]		Yes[5,8/]	9 Months
63-12 - pH	TGAI	No[1/]		Yes[5,9/]	9 Months
63-13 - Stability	TGAI	No[1/]		Yes[5/]	9 Months
Other Requirements:					
64-1 - Submittal of Samples	N/A	N/A	N/A	No	

TABLE A
GENERIC DATA REQUIREMENTS FOR OXYTETRACYCLINE

Part 158, Subpart C, Product Chemistry - Footnotes

1/ Although product chemistry may have been submitted in the past, the Agency has determined that these data must be resubmitted for each pesticide. New data requirements have been introduced and previously submitted data must be updated. Therefore, bibliographic citations for the old data are not applicable.

2/ Complete information must be provided regarding the nature of the process (batch or continuous), the relative amounts of beginning materials and the order in which they are added, the chemical equations for each intended reaction, equipment used to produce each intermediate and the final product, reaction conditions, the duration of each step of the process, purification procedures, and quality control measures. In addition, the name and address of the manufacturer, producer, or supplier of each beginning material must be provided, along with information regarding the properties of each beginning material used to manufacture each product.

3/ A detailed discussion of all impurities that are or may be present at $\geq$0.1%, based on knowledge of the beginning materials, chemical reactions (intended and side) in the manufacturing process, and any contamination during and after production must be submitted.

4/ Five or more representative samples must be analyzed for the amount of active ingredient and each impurity for which a certified limit is required. Complete validation data (accuracy, precision) must be submitted for each analytical method used.

5/ Physicochemical characteristics (color, physical state, odor, melting point, specific gravity, solubility, vapor pressure, dissociation constant, partition coefficient, pH, and stability) as required in 40 CFR 158.190 and more fully described in the Pesticide Assessment Guidelines, Subdivision D, must be submitted.

6/ Data required if the technical chemical is a solid at room temperature.

7/ Data required if the technical product is a liquid at room temperature.

8/ Data required if the technical product is organic or nonpolar.

9/ Data required if the technical substance is dispersible in water.

Table A
Generic Data Requirements for Oxytetracycline

Data Requirement	Composition	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission
§158.240 Residue Chemistry					
171-2 - Chemical Identity[1/]					
171-3 - Directions for Use		(See Index)			
171-4 - Nature of the Residue (Metabolism)					
- Plants	PAIRA	No		No[2/]	
- Livestock	PAIRA	No		No[3/]	
171-4 - Residue Analytical Methods	TGAI	Yes	00058254	No	
171-4 - Storage Stability Data	TEP	Yes	00081151	No	
171-4 - Magnitude of the residue in plants					
Pome Fruits - Pears	TEP	Yes	00039917,00049096 00081266,00162260.	No	
Stone Fruits -Peaches [4/]	TEP	Yes	00064602,00081153 00093605,00135300.	No	
171-4 - Magnitude of the residue in Meat/Milk/Poultry/Eggs		No		No[5/]	

TABLE A
GENERIC DATA REQUIREMENTS FOR Oxytetracycline

§158.240 Residue Chemistry - Footnotes

1/ The same chemical identity data are required as under § 158.740, with emphasis on impurities that could constitute residue problems. Refer to Product Chemistry Data Requirements tables.

2/ Data were not submitted regarding the nature of the residues of oxytetracycline in plants. The Agency has assessed the need for data reflecting the metabolism of oxytetracycline in plants and has concluded that these data are not required.

3/ Data on the metabolism of oxytetracycline in food animals are not needed because the exposure of livestock to residues of oxytetracycline is highly improbable since there are no registered uses on feed items at the present time.

4/ The term peaches is defined to include both peaches and nectarines (40 CFR 180.1(H)).

5/ Presently, there is no potential for livestock consumption of oxytetracycline residues because oxytetracycline is registered for use only on commodities (pears and peaches) that are not used for animal feeds.

Table A
Generic Data Requirements for Calcuim oxytetracycline

Data Requirement	Composition	Use Patterns	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission
Sec. 158.290 Environmental Fate						
Degradation Studies - Lab						
161-1 - Hydrolysis	TGAI or PAIRA	A,B,D	No		Yes	9 Months
Photodegradation						
161-2 - In Water	TGAI or PAIRA	A,B,D	No		Yes	9 Months
161-3 - On Soil	TGAI or PAIRA	A	No		Yes	9 Months
161-4 - In Air	TGAI or PAIRA	A	No		Yes	9 Months
Metabolism Studies - Lab						
162-1 - Aerobic Soil	TGAI or PAIRA	A,B	No		Yes	27 Months
162-2 - Anaerobic Soil	TGAI or PAIRA	A	No		Yes	27 Months
162-3 - Anaerobic Aquatic	TGAI or PAIRA	D	No		Yes	27 Months
162-4 - Aerobic Aquatic	TGAI or PAIRA	D	No		Yes	27 Months

Table A
Generic Data Requirements for Calcuim oxytetracycline (cont'd)

Data Requirement	Composition	Use Patterns	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission[1/]
Sec. 158.290 Environmental Fate (cont'd)						
Mobility Studies						
163-1 - Leaching and Adsorption/Desorption	TGAI or PAIRA	A,B	No		Yes	12 Months
163-2 - Volatility (Lab)	TEP	A	No		Reserved[1/]	
163-3 - Volatility (Field)	TEP	A	No		Reserved[1/]	
Dissipation Studies - Field						
164-1 - Soil	TEP	A,B	No		Yes	27 Months
164-2 - Aquatic (Sediment)	TEP	D	No		Yes	27 Months
164-3 - Forestry	TEP	N/A				
164-4 - Combination and Tank Mixes	TEP	N/A				
164-5 - Soil, Long-Term	TEP	A	No		Reserved[2/]	

Table A
Generic Data Requirements for Calcuim oxytetracycline (cont'd)

Data Requirement	Composition	Use Patterns	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission
Sec. 158.290 Environmental Fate (cont'd)						
Accumulation Studies						
165-1 - Rotational Crops (Confined)	PAIRA	A	No		No[3/]	
165-2 - Rotational Crops (Field)	TEP	A	No		No[3/]	
165-3 - Irrigated Crops	TEP	N/A				
165-4 - In Fish	TGAI or PAIRA	A,D	No		Yes	12 Months
165-5 - In Aquatic Nontarget Organisms	TEP	D	No		Reserved[4/]	

1/ The need for laboratory and field volatility studies will be reassessed upon evaluation of an acceptable vapor pressure study.

2/ May be required pending the receipt and review of data under 162-1 (metabolism:aerobic soil) and 164-1 (dissipation field:soil).

3/ Use sites will not involve rotated crops.

4/ May be required pending receipt and review of data under 165-4 (fish accumulation study).

Table A
Generic Data Requirements for Calcuim oxytetracycline (cont'd)

Data Requirement	Composition	Use Patterns	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission[1/]
Sec. 158.290 Environmental Fate (cont'd)						
Mobility Studies						
163-1 - Leaching and Adsorption/Desorption	TGAI or PAIRA	A,B	No		Yes	12 Months
163-2 - Volatility (Lab)	TEP	A	No		Reserved[1/]	
163-3 - Volatility (Field)	TEP	A	No		Reserved[1/]	
Dissipation Studies - Field						
164-1 - Soil	TEP	A,B	No		Yes	27 Months
164-2 - Aquatic (Sediment)	TEP	D	No		Yes	27 Months
164-3 - Forestry	TEP	N/A				
164-4 - Combination and Tank Mixes	TEP	N/A				
164-5 - Soil, Long-Term	TEP	A	No		Reserved[2/]	

Table A
Generic Data Requirements for Calcuim oxytetracycline

Data Requirement	Composition	Patterns	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe for Submission
Sec. 158.390 Reentry Protection						
132-1 - Foliar Dissipation	TEP	A,B	No		No1/	
132-2 - Soil Dissipation	TEP	A,B	No		No1/	
132-3 - Dermal Exposure	TEP	A,B	No		No1/	
132-4 - Inhalation Exposure	TEP	A,B	No		No1/	
Sec. 158.440 Spray Drift						
201-1 - Droplet Size Spectrum	N/A					
202-1 - Drift Field Evaluation	N/A					

1/Oxytetracycline does not meet the criteria of 40 CFR 158.390 for requiring reentry data (i.e., oxytetracycline has a low mammalian toxicity and there is no epidemiological evidence of adverse effects to humans from its pesticidal uses).

Table A
Generic Data Requirements for Oxytetracycline

Data Requirement	Composition	Use Patterns	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission
§158.340 Toxicology						
81-1 - Acute Oral - Rat	TGAI	A,B	No		No[1/]	
81-2 - Acute Dermal	TGAI	A,B	No		No[1/]	
81-3 - Acute Inhalation	TGAI	A,B	No		No[1/]	
81-4 - Eye Irritation	TGAI	A,B	No		No[1/]	
81-5 - Dermal Irritation	TGAI	A,B	No		No[1/]	
81-6 - Dermal Sensitization	TGAI	A,B	No		No[1/]	
81-7 - Acute Delayed Neurotoxicity	TGAI	A,B	No		No[2/]	
Subchronic Testing						
82-1 - 90-Day Feeding -						
Rodent	TGAI	A,B	No		No[1/]	
Non-rodent	TGAI	A,B	No		No[1/]	

Table A
Generic Data Requirements for Oxytetracycline (cont'd)

Data Requirement	Composition	Use Patterns	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission
§ 158.340 Toxicology						
Subchronic Testing (cont'd)						
82-2 - 21-Day Dermal	TGAI	A,B	No		No[1/]	
82-3 - 90-Day Dermal	TGAI	A,B	No		No[3/]	
82-4 - 90-Day Inhalation	TGAI	A,B	No		No[3/]	
82-5 - 90-Day Neurotoxicity	TGAI	A,B	No		No[2/]	
Chronic Testing						
83-1 - Chronic Testing						
-Rodent	TGAI	A,B	No		No[1/]	
-Nonrodent	TGAI	A,B	No		No[1/]	
83-2 - Oncogenicity						
-Rat	TGAI	A,B	Yes	00159856	No	
-Mouse	TGAI	A,B	Yes	00159856	No	
83-3 -Teratogenicity						
-Rat	TGAI	A,B	Yes	00132391	No	
-Mouse	TGAI	A,B	Yes	00132392	No	

Table A
Generic Data Requirements for Oxytetracycline (cont'd)

Data Requirement	Composition	Use Patterns	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission
§ 158.340 Toxicology						
Chronic Testing (cont'd)						
83-4 - Reproduction	TGAI	A,B	No		No[1/]	
Mutagenicity Testing						
84-2 - Gene Mutation	TGAI	A,B	No		No[1/]	
84-2 - Chromosome Aberration	TGAI	A,B	No		No[1/]	
84-4 - Other Mechanisms of Mutagenicity	TGAI	A,B	No		No[1/]	
Special Testing						
85-1 - General Metabolism	PAI or PAIRA	A,B	No		No[1/]	
_ Antibiotic Resistance	-		Yes	40840101	No	

Table A
Generic Data Requirements for Oxytetracycline (cont'd)

§ 158.340 Toxicology Footnotes

1/ These data requirements are waived based on the availability of human and/ or animal data found in the public literature (Grollman, A. and Grollman, E.F. (1970) Pharmacology and Therapeutics (7th ed.) Lea and Febiger, Philadelphia, PA.; Modern Drug Encyclopedia and Therapeutic Index-A Compendium (1977) New York: Yorke Medical Books, Donnelly Publishing Co.; Physicians Desk Reference (PDR) (1980) Oradell, NJ: Medical Economics Co., pp.1372-1373.; Shulman, J.A. and Sellers, T.F., Jr. (1971) Chemotherapy of Bacterial Infections VII: Other Important Antibiotics. In DiPalma, J.R. (ed) Drill's Pharmacology in Medicine, 4th ed. McGraw-Hill Books Co., Inc., New York, pp. 1729-1754.; Weinstein, L. The Tetracyclines. In Goodman, L., and Gilman, A. (eds). (1970) The Pharmacological Basis of Therapeutics, 4th ed. Macmillan Publishing Co., pp.1240-1244.)

2/ This test is required only for compounds which are organophosphate inhibitors of cholinesterase, or related to such inhibitors or metabolites of such inhibitors. Oxytetracycline is not an organophosphate, therefore a study is not required.

3/ These data are not required due to use pattern.

Table A
Generic Data Requirements for Oxytetracycline

Data Requirement	Composition	Use Pattern	Does EPA Have Data to Satisfy This Requirement? (Yes, No, Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission
§158.490 - Wildlife and Aquatic Organisms						
Avian and Mammalian Testing						
71-1 -Avian Acute Oral Toxicity						
- Upland game bird	TGAI	A,B,D	No		Yes	9 Months
71-2 - Avian Dietary LC_{50}						
- Upland Game Bird	TGAI	A,B,D	No		Yes	9 Months
- Waterfowl	TGAI	A,B,D	No		Yes	9 Months
71-3 - Wild Mammal Toxicity	TGAI	A,B,D	No		No 1/	
71-4 - Avian Reproduction						
- Upland Game Bird	TGAI	A,B,D	No		Reserved 2/	
- Waterfowl	TGAI	A,B,D	No		Reserved 2/	
71-5 - Actual Field Testing for Birds and Mammals	TEP	A,B,D	No		No	

Table A
Generic Data Requirements for Oxytetracycline (cont'd)

Data Requirement	Composition	Use Pattern	Does EPA Have Data to Satisfy This Requirement? (Yes, No, Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission 1/
§158.490 - Wildlife and Aquatic Organisms						
Aquatic Organism Testing						
72-1 - Freshwater Fish LC_{50}						
- Warmwater	TGAI	A,B,D	No		Yes	9 Months
	TEP	A,B,D	No		Reserved 3/	
- Coldwater	TGAI	A,B,D	No		Yes	9 Months
	TEP	A,B,D	No		Reserved 3/	
72-2 - Freshwater Invertebrate LC_{50}	TGAI	A,B,D	No		Yes	9 Months
	TEP	A,B,D	No		Reserved 3/	
72-3 - Estuarine and Marine Organisms LC_{50}						
- Fish	TGAI	A,B,D	No		Reserved 4/	
	TEP	A,B,D	No		Reserved 3/	

Table A
Generic Data Requirements for Oxytetracycline (cont'd)

Data Requirement	Composition	Use Pattern	Does EPA Have Data to Satisfy This Requirement? (Yes, No, Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission 1/
§158.490 - Wildlife and Aquatic Organisms						
72-3 - Estuarine and Marine Organisms LC_{50}						
- Shrimp	TGAI	A,B,D	No		Reserved 4/	
	TEP	A,B,D	No		Reserved 3/	
- Oyster	TGAI	A,B,D	No		Reserved 4/	
	TEP	A,B,D	No		Reserved 3/	
72-4 - Fish Early Life Stage and Invertebrate Life Cycle						
- Freshwater						
- Fish	TGAI	A,B,D	No		Reserved 4/	
- Invertebrates	TGAI	A,B,D	No		Reserved 4/	

Table A
Generic Data Requirements for Oxytetracycline (cont'd)

Data Requirement	Composition	Use Pattern	Does EPA Have Data to Satisfy This Requirement? (Yes, No, Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission 1/
§158.490 - Wildlife and Aquatic Organisms						
72-5 - Fish Life Cycle	TGAI	A,B,D	No		Reserved 1/	
72-6 - Aquatic Organisms Accumulation	TGAI	A,B	No		Reserved 4/	
72-7 - Simulated or Actual Field Testing						
-Aquatic Organisms	TEP	A,B	No		Reserved 4/	

1/ No requirement currently exists.

2/ Reserved pending evaluation of appropriate environmental fate data needed, such as a field and aquatic sediment dissipation study to better define expected residues.

3/ Formulated product testing for acute toxicity to aquatic estuarine and marine organisms is reserved pending the results of testing with the technical grade (TGAI).

4/ Reserved pending evaluation of acute toxicity data on warmwater fish species and freshwater aquatic invertebrates along with appropriate environmental fate information (ie., hydrolysis and photolysis in water). These data are needed to determine if hazardous concentrations of oxytetracycline will reach the aquatic environment when products are used as directed.

Table A
Generic Data Requirements for Oxytetracycline

Data Requirement	Composition	Use Patterns	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission
§158.590 Nontarget Insects						
NONTARGET INSECT TESTING - POLLINATORS						
141-1 - Honey Bee Acute Contact LD50	TGAI	A,B,D	No		Yes	9 Months
141-2 - Honey Bee - Toxicity Residues on Foliage	TEP	A,B,D	No		No[1/]	
141-4 - Honey Bee Subacute Feeding Study	Reserved[2/]					
141-5 - Field Testing for pollinators	TEP	A,B,D	No		No[1/]	
NONTARGET INSECT TESTING - AQUATIC INSECTS						
142-1 - Acute Toxicity to Aquatic Insects	TEP	A,B,D	No		No[3/]	
142-2 - Aquatic Insect Life Cycle Study	TEP	A,B,D	No		No[3/]	
142-3 - Simulated or Actual Field Testing for Aquatic Insects	TEP	A,B,D	No		No[3/]	
NONTARGET INSECT TESTING - PREDATORS AND PARASITES						
143-1 thru 143-3	Reserved[3/]					

Table A
Generic Data Requirements for Oxytetracycline (cont'd)

§158.590 - Nontarget Insects Footnotes

1/ Requirements deferred pending evaluation of data from the acute contact LD50 study.

2/ This requirement is reserved pending development of test methodology.

3/ This requirement is reserved pending Agency decision as to whether the data requirement should be established.

Table B
Product-Specific Data Requirements for Manufacturing-Use Products Containing Oxytetracycline

Data Requirement	Composition[1]	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe for Submission[2]
Part 158, Subpart C, Product Chemistry					
Product Identity and Composition					
61-1 - Product Identity and Disclosure of Ingredients	MP	No[3]		Yes[4]	9 Months
61-2 - Description of Beginning Materials and Manufacturing Process	MP	No[3]		Yes[5]	9 Months
61-3 - Discussion of Formation of Impurities	MP	No[3]		Yes[6]	9 Months
Analysis and Certification of Product Ingredients					
62-1 - Preliminary Analysis of Product Samples	MP	No[3]		Yes[7]	12 Months
62-2 - Certification of Ingredient Limits	MP	No[3]		Yes[8]	12 Months
62-3 - Analytical Methods to Verify Certified Limits	MP	No[3]		Yes[9]	12 Months
Physical and Chemical Characteristics					
63-2 - Color	MP	No[3]		Yes[10]	9 Months
63-3 - Physical State	MP	No[3]		Yes[7]	9 Months

Table B
Product-Specific Data Requirements for Manufacturing-Use Products Containing Oxytetracycline

Data Requirement	Composition	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe for Submission[1/]
Part 158, Subpart C, Product Chemistry (cont'd)					
Physical and Chemical Characteristics (cont'd)					
63-4 - Odor	MP	No[3/]		Yes[7/]	9 Months
63-7 - Density, Bulk Density or Specific Gravity	MP	No[3/]		Yes[7/]	9 Months
63-12 - pH	MP	No[3/]		Yes[7,11/]	9 Months
63-14 - Oxidizing or Reducing Agent	MP	No[3/]		Yes[10,12/]	9 Months
63-15 - Flammability	MP	No[3/]		Yes[10,13/]	9 Months
63-16 - Explodability	MP	No[3/]		Yes[10,14/]	9 Months
63-17 - Storage Stability	MP	No[3/]		Yes[10/]	15 Months
63-18 - Viscosity	MP	No[3/]		Yes[10,15/]	9 Months
63-19 - Miscibility	MP	No[3/]		Yes[10,16/]	9 Months
63-20 - Corrosion Characteristics	MP	No[3/]		Yes[10/]	15 Months
Other Requirements:					
64-1 - Submittal of Samples	N/A	N/A		No	

Table B
Product-Specific Data Requirements for Manufacturing-Use Products Containing Oxytetracycline

Data Requirement	Composition	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe for Submission[1/]
Part 158, Subpart C, Product Chemistry (cont'd)					
Physical and Chemical Characteristics (cont'd)					
63-4 - Odor	MP	No[3/]		Yes[7/]	9 Months
63-7 - Density, Bulk Density or Specific Gravity	MP	No[3/]		Yes[7/]	9 Months
63-12 - pH	MP	No[3/]		Yes[7,11/]	9 Months
63-14 - Oxidizing or Reducing Agent	MP	No[3/]		Yes[10,12/]	9 Months
63-15 - Flammability	MP	No[3/]		Yes[10,13/]	9 Months
63-16 - Explodability	MP	No[3/]		Yes[10,14/]	9 Months
63-17 - Storage Stability	MP	No[3/]		Yes[10/]	15 Months
63-18 - Viscosity	MP	No[3/]		Yes[10,15/]	9 Months
63-19 - Miscibility	MP	No[3/]		Yes[10,16/]	9 Months
63-20 - Corrosion Characteristics	MP	No[3/]		Yes[10/]	15 Months
Other Requirements:					
64-1 - Submittal of Samples	N/A	N/A		No	

TABLE B
PRODUCT-SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING USE PRODUCTS CONTAINING OXYTETRACYCLINE

Part 158, Subpart C, Product Chemistry - Footnotes

1/ Formulation intermediates are also included in the category of manufacturing-use products (MP).

2/ Due dates refer to the number of months following receipt of this Registration Standard, unless otherwise indicated.

3/ Although product chemistry may have been submitted in the past, the Agency has determined that these data must be resubmitted for each pesticide. New data requirements have been introduced and previously submitted data must be updated. Therefore, bibliographic citations for the old data are not applicable.

4/ The chemical name, nominal concentration, Chemical Abstracts (CAS) Registry Number, and purpose of the active ingredient in each intentionally added inert must be provided. For the active ingredients, the following must also be provided: the product, common and trade names; the molecular, structural, and empirical formulas; the molecular weight (weight range; and any experimental or internally assigned code numbers.

5/ Complete information must be provided regarding the nature of the process (batch or continuous), the relative amount of beginning materials and the order in which they are added, the chemical equations for each intended reaction, equipment used to produce each intermediate and the final product, reaction conditions, the duration of each step of the process, purification procedures, and quality control measures. In addition, the name and address of the manufacturer, producer, or supplier of each beginning material must be provided, along with information regarding the properties of each beginning material used to manufacture each product.

6/ A detailed discussion of all impurities that are or may be present at $\geq$0.1%, based on knowledge of the beginning materials, chemical reactions (intended and side) in the manufacturing process, and any contamination during and after production must be submitted.

7/ Five or more representative samples must be analyzed for the amount of active ingredient and each impurity for which a certified limit is required. Complete validation data (accuracy, precision) must be submitted for each analytical method used.

8/ Upper and lower limits for the active ingredients and each intentionally added inert, and upper limits for each impurity present at $\geq$ 0.1% (w/w) and each "toxicologically significant" impurity present at <0.1% (w/w) must be provided and certified. Also, an explanation of how each certified limit was established must be provided (e.g., sample analysis using validated analytical procedures, quantitative estimate based on amounts of ingredients used, etc.). Limits for impurities not associated with the active ingredient need be provided only if they are considered to be of toxicological significance, regardless of the concentration at which they are present. Certification must be submitted on EPA form 857 Rev. 2-85.

TABLE B
PRODUCT-SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING USE PRODUCTS CONTAINING OXYTETRACYCLINE

Part 158, Subpart C, Product Chemistry - Footnotes (cont'd)

9/ Analytical methods must be provided to determine the active ingredient, and each toxicologically significant impurity and intentionally added inert for which certified limits are required. Each method must be accompanied by validation studies indicating its accuracy and precision. These methods must be suitable for enforcement of certified limits.

10/ Physiochemical characteristics (color, physical state, odor, melting point, specific gravity, solubility, vapor pressure, dissociation constant, partition coefficient, pH, and stability) as required in 40 CFR 158.190 and more fully described in the Pesticide Assessment Guidelines, Subdivision D, must be submitted.

11/ Data required if the test substance is dispersible in water.

12/ Data required if the product contains an oxidizing or reducing agents.

13/ Data required if the product contains combustible liquids.

14/ Data required if the product is potentially explosive.

15/ Data required if the product is a liquid.

16/ Data required if the product is a liquid and is be diluted with petroleum solvents.

Table B
Product-Specific Data Requirements for Manufacturing-Use Products Containing Oxytetracycline

Data Requirement	Composition	Use Patterns	Does EPA Have Data to Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?	Timeframe For Data Submission
§ 158.340 Toxicology						
Acute Testing						
81-1 - Acute Oral - Rat	MP[1/]	A,B	No		No[2/]	
81-2 - Acute Dermal	MP	A,B	No		No[2/]	
81-3 - Acute Inhalation - Rat	MP	A,B	No		No[2/]	
81-4 - Eye Irritation - Rabbit	MP	A,B	No		No[2/]	
81-5 - Dermal Irritation -Rabbit	MP	A,B	No		No[2/]	
81-6 - Dermal Sensitization - Guinea Pig	MP	A,B	No		No[2/]	

1/ Formulation intermediates are also included in the category of manufacturing-use products.

2/ These data requirements are waived based on the availability of human and/ or animal data found in the public literature (Grollman, A. and Grollman, E.F. (1970) Pharmacology and Therapeutics (7th ed.) Lea and Febiger, Philadelphia, PA.; Modern Drug Encyclopedia and Therapeutic Index-A Compendium (1977) New York: Yorke Medical Books, Donnelly Publishing Co.; Physicians Desk Reference (PDR) (1980) Oradell, NJ: Medical Economics Co., pp.1372-1373.; Shulman, J.A. and Sellers, T.F., Jr. (1971) Chemotherapy of Bacterial Infections VII: Other Important Antibiotics. In DiPalma, J.R. (ed) Drill's Pharmacology in Medicine, 4th ed. McGraw-Hill Books Co., Inc., New York, pp. 1729-1754.; Weinstein, L. The Tetracyclines. In Goodman, L., and Gilman, A. (eds). (1970) The Pharmacological Basis of Therapeutics, 4th ed. Macmillan Publishing Co., pp.1240-1244.)

II. LABELING APPENDICES

LABEL CONTENTS

40 CFR 156.10 requires that certain specific labeling statements appear at certain locations on the label. This is referred to as format labeling. Specific label items listed below are keyed to the table at the end of this Appendix.

Item 1. PRODUCT NAME - The name, brand or trademark is required to be located on the front panel, preferably centered in the upper part of the panel. The name of a product will not be accepted if it is false or misleading.

Item 2. COMPANY NAME AND ADDRESS - The name and address of the registrant or distributor is required on the label. The name and address should preferably be located at the bottom of the front panel or at the end of the label text.

Item 3. NET CONTENTS - A net contents statement is required on all labels or on the container of the pesticide. The preferred location is the bottom of the front panel immediately above the company name and address, or at the end of the label test. The net contents must be expressed in the largest suitable unit, e.g., "1 pound 10 ounces" rather than "26 ounces." In addition to English units, net contents may be expressed in metric units. [40 CFR 156.10(d)]

Item 4. EPA REGISTRATION NUMBER - The registration number assigned to the pesticide product must appear on the label, preceded by the phrase "EPA Registration No.," or "EPA Reg. No." The registration number must be set in type of a size and style similar to other print on that part of the label on which it appears and must run parallel to it. The registration number and the required identifying phrase must not appear in such a manner as to suggest or imply recommendation or endorsement of the product by the Agency. [40 CFR 156.10(e)]

Item 5. EPA ESTABLISHMENT NUMBER - The EPA establishment number, preceded by the phrase "EPA Est." is the final establishment at which the product was produced, and may appear in any suitable location on the label or immediate container. It must also appear on the wrapper or outside container of the package if the EPA establishment number on the immediate container cannot be clearly read through such wrapper or container. [40 CFR 156.10(f)]

Item 6A. INGREDIENTS STATEMENT - An ingredients statement is required on the front panel. The ingredients statement must contain the name and percentage by weight of each active ingredient and the total percentage by weight of all inert ingredients. The preferred location is immediately below the product name. The ingredients statement must run parallel with, and be clearly distinguished from, other text on the panel. It must not be placed in the body of other text. [40 CFR 156.10(g)]

Item 6B. POUNDS PER GALLON STATEMENT - For liquid agricul- tural formulations, the pounds per gallon of active ingredient must be indicated on the label.

Item 7. FRONT LABEL PRECAUTIONARY STATEMENTS - Front panel precautionary statements must be grouped together, preferably within a block outline. The table below shows the minimum type size requirements for various size labels.

Size of Label on Front Panel in Square Inches	Signal Word Minimum Type Size All Capitals	"Keep Out of Reach of Children" Minimum Type Size
5 and under	6 point	6 point
above 5 to 10	10 point	6 point
above 10 to 15	12 point	8 point
above 15 to 30	14 point	10 point
over 30	18 point	12 point

Item 7A. CHILD HAZARD WARNING STATEMENT - The statement "Keep Out of Reach of Children" must be located on the front panel above the signal word except where contact with children during distribution or use is unlikely. [40 CFR 156.10(h)(1)(ii)]

Item 7B. SIGNAL WORD - The signal word (DANGER, WARNING, or CAUTION) is required on the front panel immediately below the child hazard warning statement. [40CFR 156.10(h)(1)(i)].

Item 7C. SKULL & CROSSBONES AND WORD "POISON" - On products assigned a toxicity Category I on the basis of oral, dermal, or inhalation toxicity, the word "Poison" shall appear on the label in red on a background of distinctly contrasting color and the skull and crossbones shall appear in immediate proximity to the word POISON. [40 CFR 156.10(h)(1)(i)].

Item 7D. STATEMENT OF PRACTICAL TREATMENT - A statement of practical treatment (first aid or other) shall appear on the label of pesticide products in toxicity Categories I, II, and III. [40 CFR 156.10(h)(1)(iii)]

Item 7E. REFERRAL STATEMENT - The statement "see Side (or Back) Panel for Additional Precautionary Statements" is required on the front panel for all products, unless all required precautionary statements appear on the front panel. [40 CFR 156.10(h)(1)(iii)].

Item 8. SIDE/BACK PANEL PRECAUTIONARY LABELING - The precautionary statements listed below must appear together on the label under the heading "PRECAUTIONARY STATEMENTS." The preferred location is at the top of the side or back panel preceding the directions for use, and it is preferred that these statements be surrounded by a block outline. Each of the three hazard warning statements must be headed by the appropriate hazard title. [40 CFR 156.10(h)(2)]

Item 8A. HAZARD TO HUMANS AND DOMESTIC ANIMALS - Where a hazard exists to humans or domestic animals, precautionary statements are required indicating the particular hazard, the route(s) of exposure and the precautions to be taken to avoid accident, injury or damage. [40 CFR 156.10(h)(2)(i)]

Item 8B. ENVIRONMENTAL HAZARD - Where a hazard exists to non-target organisms excluding humans and domestic animals, precautionary statements are required stating the nature of the hazard and the appropriate precautions to avoid potential accident, injury, or damage. [40 CFR 156.10(h)(2)(ii)]

Item 8C. PHYSICAL OR CHEMICAL HAZARD - FLAMMABILITY Precautionary statements relating to flammability of a product are required to appear on the label if it meets the criteria in the PHYS/CHEM Labeling Appendix. The requirement is based on the results of the flashpoint determinations and flame extension tests required to be submitted for all products. These statements are to be located in the side/back panel precautionary statements section, preceded by the heading "Physical/Chemical Hazards." Note that no signal word is used in conjunction with the flammability statements.

Item 9A. RESTRICTED USE CLASSIFICATION - FIFRA sec. 3(d) requires that all pesticide formulations/uses be classified for either general or restricted use. Products classified for restricted use may be limited to use by certified applicators or persons under their direct supervision (or may be subject to other restrictions that may be imposed by regulation).

In the Registration Standard, the Agency has (1) indicated certain formulations/uses are to be restricted (Section IV indicates why the product has been classified for restricted use); or (2) reserved any classification decision until appropriate data are submitted.

The Regulatory Position and Rationale states whether products containing this active ingredient are classified for restricted use. If they are restricted the draft label(s) submitted to the Agency as part of your application must reflect this determination (see below).

If you do not believe that your product should be classified for restricted use, you must submit any information and rationale with your application for reregistration. During the Agency's review of your application, your proposed classification determination will be evaluated in accordance with the provisions of 40 CFR 162.11(c). You will be notified of the Agency's classification decision.

Classification Labeling Requirements

If your product has been classified for restricted use, the following label requirements apply:

1. All uses restricted.

   a. The statement "Restricted Use Pesticide" must appear at the top of the front panel of the label. The statement must be set in type of the same minimum size as required for human hazard signal word (see table in 40 CFR 156.10(h)(1)(iv).

   b. Directly below this statement on the front panel, a summary statement of the terms of restriction must appear (including the reasons for restriction if specified in Section I). If use is restricted to certified applicators, the following statement is required: "For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's Certification."

2. Some but not all uses restricted. If the Regulatory Position and Rationale states that some uses are classified for restricted use, and some are unclassified, several courses of action are available:

   a. You may label the product for Restricted use. If you do so, you may include on the label uses that are unrestricted, but you may not distinguish them on the label as being unrestricted.

b. You may delete all restricted uses from your label and submit draft labeling bearing only unrestricted uses.

c. You may "split" your registration, i.e., register two separate products with identical formulations, one bearing only unrestricted uses, and the other bearing restricted uses. To do so, submit two applications for reregistration, each containing all forms and necessary labels. Both applications should be submitted simultaneously. Note that the products will be assigned separate registration numbers.

Item 9B. MISUSE STATEMENT - All products must bear the misuse statement, "It is a violation of Federal law to use this product in a manner inconsistent with its labeling." This statement appears at the beginning of the directions for use, directly beneath the heading of that section.

Item 10A. REENTRY STATEMENT - If a reentry interval has been established by the Agency, it must be included on the label. Additional worker protection statements may be required in accordance with PR Notice 83-2, March 29, 1983.

Item 10B. STORAGE AND DISPOSAL BLOCK - All labels are required to bear storage and disposal statements. These statements are developed for specific containers, sizes, and chemical content. These instructions must be grouped and appear under the heading "Storage and Disposal" in the directions for use. This heading must be set in the same type sizes as required for the child hazard warning. Refer to Appendix II, STOR, PEST/DIS, and CONT/DIS to determine the storage and disposal instructions appropriate for your products.

Item 10C. DIRECTIONS FOR USE - Directions for use must be stated in terms which can be easily read and understood by the average person likely to sue or to supervise the use of the pesticide. When followed, directions must be adequate to protect the public from fraud and from personal injury and to prevent unreasonable adverse effects on the environment. [40 CFR 156.10]

COLLATERAL LABELING

Bulletins, leaflets, circulars, brochures, data sheets, flyers, or other written or graphic printed matter which is referred to on the label or which is to accompany the product are termed collateral labeling. Such labeling may not bear claims or representations that differ in substance from those accepted in connection with registration of the product. It should be made part of the response to this notice and submitted for review.

SUMMARY-7

LABELING REQUIREMENTS OF THE FIFRA, AS AMENDED

ITEM	LABEL ELEMENT	APPLICABILITY OF REQUIREMENT	PLACEMENT ON LABEL		
			REQUIRED	PREFERRED	
1	Product name	All products	Front panel	Center front panel	
2	Company name and address	All products	None	Bottom front panel or end of label text	If registrant be qualified "Distributed
3	Net contents	All products	None	Bottom front panel or end of label text	May be in met U.S. units.
4	EPA Reg. No.	All products	None	Front panel	Must be in si parallel to o
5	EPA Est. No.	All products	None	Front panel immediately before or following Reg. No.	May appear on the label.
6A	Ingredients statement	All products	Front panel	Immediately following product name	Text must run on the panel.
6B	Pounds/gallon statement	Liquid products where dosage is given as lbs. ai/unit area	Front panel	Directly below the main ingredients statement	
7	Front panel precautionary statements	All products	Front panel		All front pan must be group blocked.
7A	Keep Out of Reach of Children (Child hazard warning)	All products	Front panel	Above signal word	Note type siz
7B	Signal word	All products	Front panel	Immediately below child hazard warning	Note type siz

LABELING REQUIREMENTS OF THE FIFRA, AS AMENDED (cont'

ITEM	LABEL ELEMENT	APPLICABILITY OF REQUIREMENT	PLACEMENT ON LABEL		
			REQUIRED	PREFERRED	
7C	Skull & cross-bones and word POISON (in red)	All products which are Category I based on oral, dermal, or inhalation toxicity	Front panel	Both in close proximity to signal word	
7D	Statement of Practical Treatment or First Aid	All products in Categories I, II, and III	Category I: Front panel unless referral statement is used. Others: Grouped with side panel precautionary statements.	Front panel for all	
7E	Referral statement	All products where precautionary labeling appears on other than front panel	Front panel		
8	Side/back panel precautionary statements	All products	None	Top or side of back panel preceding directions for use	Must be group 8A, 8B, and 8
8A	Hazards to humans and domestic animals	All products in Categories I, II, and III	None	Same as above	Must be prece word.
8B	Environmental hazards	All products	None	Same as above	Environmental caution where

LABELING REQUIREMENTS OF THE FIFRA, AS AMENDED (cont'

ITEM	LABEL ELEMENT	APPLICABILITY OF REQUIREMENT	PLACEMENT ON LABEL REQUIRED	PREFERRED	
8C	Physical or chemical hazards	All pressurized products, others with flash points under 150°F	None	Same as above	Refer to Appe PHYS/CHEM
9A	Restricted block	All restricted products	Top center of front panel	Preferably blocked	Includes a st restriction. PESTICIDE" mu signal word.
9B	Misuse statement	All products	Immediately following heading of directions for use		Required stat "It is a v to use th inconsist
10A	Reentry statement	PR Notice 83-2 or as determined by the Agency	In the directions for use	Immediately after misuse statement	
10B	Storage and disposal block	All products	In the directions for use	Immediately before specific directions for use or at the end of directions for use	Must be set a guishable fro for use. Refer to Appe CONT/DIS, and information a
10C	Directions for use	All products	None	None	May be in met

PHYSICAL-CHEMICAL HAZARDS

Criteria	Required Label Statement
I. Pressurized Containers	
A. Flashpoint at or below 20°F; or if there is a flashback at any valve opening.	Extremely flammable. Contents under pressure. Keep away from fire, sparks, and heated surfaces. Do not puncture or incinerate container. Exposure to temperatures above 130°F may cause bursting.
B. Flashpoint above 20°F and not over 80°F; or if the flame extension is more than 18 inches long at a distance of 6 inches from the valve opening.	Flammable. Contents under pressure. Keep away from heat, sparks, and flame. Do not puncture or incinerate container. Exposure to temperatures above 130°F may cause bursting.
C. ALL OTHER PRESSURIZED CONTAINERS	Contents under pressure. Do not use or store near heat or open flame. Do not puncture or incinerate container. Exposure to temperatures above 130°F may cause bursting.
II. Non-Pressurized Containers	
A. Flashpoint at or below 20°F.	Extremely flammable. Keep away from fire, sparks, and heated surfaces.
B. Flashpoint above 20°F and not over 80°F.	Flammable. keep away from heat and open flame.
C. Flashpoint over 80°F and not over 150°F.	Do not use or store near heat and open flame.
D. Flashpoint above 150°F.	None required.

STORAGE INSTRUCTIONS FOR PESTICIDES

Heading:

All products are required to bear specific label instructions about storage and disposal. Storage and disposal instructions must be grouped together in the directions for use portion of the label under the heading STORAGE AND DISPOSAL. Products intended solely for domestic use need not include the heading "STORAGE AND DISPOSAL."

Storage Instructions:

All product labels are required to have appropriate storage instructions. Specific storage instructions are not prescribed. Each registrant must develop his own storage instructions, considering, when applicable, the following factors:

1. Conditions of storage that might alter the composition or usefulness of the pesticide. Examples could be temperature extremes, excessive moisture or humidity, heat, sunlight, friction, or contaminating substances or media.

2. Physical requirements of storage which might adversely affect the container of the product and its ability to continue to function properly. Requirements might include positioning of the container in storage, storage or damage due to stacking, penetration of moisture, and ability to withstand shock or friction.

3. Specifications for handling the pesticide container, including movement of container within the storage area, proper opening and closing procedures (particularly for opened containers), and measures to minimize exposure while opening or closing container.

4. Instructions on what to do if the container is damaged in any way, or if the pesticide is leaking or has been spilled, and precautions to minimize exposure if damage occurs.

5. General precautions concerning locked storage, storage in original container only, and separation of pesticides during storage to prevent cross-contamination of other pesticides, fertilizer, food, and feed.

6. General storage instructions for household products should emphasize storage in original container and placement in locked storage areas.

PESTICIDE DISPOSAL INSTRUCTIONS

The label of all products, except those intended solely for domestic use, must bear explicit instructions about pesticide disposal. The statements listed below contain the exact wording that must appear on the label of these products:

1. The labels of all products, except domestic use, must contain the statement, "Do not contaminate water, food, or feed by storage or disposal."

2. Except those products intended solely for domestic use, the labels of all products that contain active ingredients that are Acute Hazardous Wastes or are assigned to Toxicity Category I on the basis of oral or dermal toxicity, or Toxicity Category I or II on the basis of acute inhalation toxicity must bear the following pesticide disposal statement:

> "Pesticide wastes are acutely hazardous. Improper disposal of excess pesticide, spray mixture, or rinsate is a violation of Federal Law. If these wastes cannot be disposed of by use according to label instructions, contact your State Pesticide or Environmental Control Agency or the Hazardous Waste representative at the nearest EPA Regional Office for guidance."

3. The labels of all products, except those intended for domestic use, containing active or inert ingredients that are Toxic Hazardous Wastes or meet any of the criteria in 40 CFR 261, Subpart C for a hazardous waste must bear the following pesticide disposal statement:

> "Pesticide wastes are toxic. Improper disposal of excess pesticide, spray mixture, or rinsate is a violation of Federal Law. If these wastes cannot be disposed of by use according to label instructions, contact your State Pesticide or Environmental Control Agency, or the Hazardous Waste representative at the nearest EPA Regional Office for guidance."

4. Labels for all other products, except those intended for domestic use, must bear the following pesticide disposal statement:

> "Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility."

5. Products intended for domestic use only must bear the following disposal statement: "Securely wrap original container in several layers of newspaper and discard in trash."

CONTAINER DISPOSAL INSTRUCTIONS

The label of each product must bear container disposal instructions appropriate to the type of container.

1. Domestic use products must bear one of the following container disposal statements:

Container Type	Statement
Non-aerosol products (bottles, cans, jars)	Do not reuse container (bottle, can, jar). Rinse thoroughly before discarding in trash.
Non-aerosol products (bags)	Do not reuse bag. Discard bag in trash.
Aerosol products	Replace cap and discard containers in trash. Do not incinerate or puncture.

2. All other products must bear container disposal instructions, based on container type, listed below:

Container Type	Statement
Metal containers (non-aerosol)	Triple rinse (or equivalent). Then offer for recycling or reconditioning, or puncture and dispose of in a sanitary landfill, or by other procedures approved by state and local authorities.
Plastic containers	Triple rinse (or equivalent). Then offer for recycling or reconditioning, or puncture and dispose of in a sanitary landfill, or incineration, or, if allowed by state and local authorities, by burning. If burned, stay out of smoke.
Glass containers	Triple rinse (or equivalent). Then dispose of in a sanitary landfill or by other approved state and local procedures.
Fiber drums with liners	Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into application equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by state and local authorities. If drum is contaminated and cannot be reused[1]/, dispose of in the same manner.
Paper and plastic bags	Completely empty bag into application equipment. Then dispose of empty bag in a sanitary landfill or by incineration, or, if allowed by State and local authorities, by burning. If burned, stay out of smoke.
Compressed gas cylinders	Return empty cylinder for reuse (or similar wording).

[1]/ Manufacturer may replace this phrase with one indicating whether and how fiber drum may be reused.

III. BIBLIOGRAPHY APPENDICES

Guide to Use of This Bibliography

1. CONTENT OF BIBLIOGRAPHY. This bibliography contains citations of all studies considered relevant by EPA in arriving at the positions and conclusions stated elsewhere in the Standard. Primary sources for studies in this bibliography have been the body of data submitted to EPA and its predecessor agencies in support of past regulatory decisions. Selections from other sources including the published literature, in those instances where they have been considered, will be included.

2. UNITS OF ENTRY. The unit of entry in this bibliography is called a "study." In the case of published materials, this corresponds closely to an article. In the case of unpublished materials submitted to the Agency, the Agency has sought to identify documents at a level parallel to the published article from within the typically larger volumes in which they were submitted. The resulting "studies" generally have a distinct title (or at least a single subject), can stand alone for purposes of review, and can be described with a conventional bibliographic citation. The Agency has attempted also to unite basic documents and commentaries upon them, treating them as a single study.

3. IDENTIFICATION OF ENTRIES. The entries in this bibliography are sorted numerically by "Master Record Identifier," or MRID, number. This number is unique to the citation, and should be used at any time specific reference is required. It is not related to the six-digit "Accession Number" which has been used to identify volumes of submitted studies; see paragraph 4(d)(4) below for a further explanation. In a few cases, entries added to the bibliography late in the review may be preceded by a nine-character temporary identifier. These entries are listed after all MRID entries. This temporary identifier number is also to be used whenever specific reference is needed.

4. FORM OF ENTRY. In addition to the Master Record Identifier (MRID), each entry consists of a citation containing standard elements followed, in the case of material submitted to EPA, by a description of the earliest known submission. Bibliographic conventions used reflect the standards of the American National Standards Institute (ANSI), expanded to provide for certain special needs.

   a. Author. Whenever the Agency could confidently identify one, the Agency has chosen to show a personal author. When no individual was identified, the Agency has shown an identifiable laboratory or testing facility as author. As a last resort, the Agency has shown the first submitter as author.

b. Document Date. When the date appears as four digits with no question marks, the Agency took it directly from the document. When a four-digit date is followed by a question mark, the bibliographer deduced the date from evidence in the document. When the date appears as (19??), the Agency was unable to determine or estimate the date of the document.

c. Title. In some cases, it has been necessary for Agency bibliographers to create or enhance a document title. Any such editorial insertions are contained between square brackets.

d. Trailing Parentheses. For studies submitted to the Agency in the past, the trailing parentheses include (in addition to any self-explanatory text) the following elements describing the earliest known submission:

(1) Submission Date. The date of the earliest known submission appears immediately following the word "received."

(2) Administrative Number. The next element, immediately following the word "under," is the registration number, experimental use permit number, petition number or other administrative number associated with the earliest known submission.

(3) Submitter. The third element is the submitter, following the phrase "submitted by." When authorship is defaulted to the submitter, this element is omitted.

(4) Volume Identification (Accession Numbers). The final element in the trailing parentheses identifies the EPA accession number of the volume in which the original submission of the study appears. The six-digit accession number follows the symbol "CDL," standing for "Company Data Library." This accession number is in turn followed by an alphabetic suffix which shows the relative position of the study within the volume. For example, within accession number 123456, the first study would be 123456-A; the second, 123456-B; the 26th, 123456-Z; and the 27th, 123456-AA.

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Oxytetracycline Standard

MRID Citation

00039917 California, Department of Food and Agriculture (1972) Residue Results: [Terramycin. (Unpublished study; CDL:093760-D)

00049096 Pfipharmecs (1973) [Residue Study of Terramycin in Pears]. (Compilation; unpublished study received Mar 25, 1974 under unknown admin. no.; CDL:223547-G)

00058254 Pfizer, Incorporated (19??) Microbiological Agar Diffusion Assay for Oxytetracycline in Fruit Extract: Report No. O 12.14. Undated method. (Unpublished study received Apr 1, 1975 under 5E1611; submitted by California, Dept. of Food & Agriculture, Sacramento, Calif.; CDL:095168-G)

00064602 Bly, B. (1980) Letter sent to Eugene Wilson dated Aug 27, 1980 [Residues of terramycin in peaches]. (California, Dept. of Food and Agriculture; unpublished study; CDL:243793-A)

00081151 Wood, R.T. (1977) Letter sent to V.J. Carroll dated Sep 13, 1977: Oxytetracycline stability in fresh peach and pear extracts (QCSA 71886). (Unpublished study received on unknown date under 6E1700; prepared by Biological Control Laboratories, submitted by Interregional Research Project No. 4, New Brunswick, N.J.; CDL:097771-A)

00081153 Carroll, V.J. (1975) Determination of Terramycin (Oxytetracycline) Residues in Peaches. Includes undated standard test procedure no. 0 12.4. (Unpublished study received Oct 31, 1975 under 6E1700; prepared by Pfizer, Inc., submitted by Interregional Research Project No. 4, New Brunswick, N.J.; CDL:097771-G)

00081266 Carroll, V.J. (1974) Determination of Terramycin (Oxytetracycline) Residues in Pears. (California, Dept. of Food & Agriculture; unpublished study; CDL:095187-D)

00093605 Chas. Pfizer & Company (1966) [Determination of Terramycin Residues in Peaches]. (Compilation; unpublished study received Mar 20, 1967 under 7G0584; CDL:090748-D)

00132391 Wolkowski-Tyl, R.; Jones-Price, C.; Ledoux, T.; et al. (1983) Teratologic Evaluation of Oxytetracycline Hydrochloride (CAS 2058-46-0) in CD Rats: RTI Project No. 31U-2077. (Unpublished study received Oct 26, 1983 under 1007-79; prepared by Research Triangle Institute, submitted by Pfipharmecs Div., Pfizer, Inc., New York, NY; CDL:251603-A)

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Oxytetracycline Standard

MRID Citation

00132392 Wolkowski-Tyl, R.; Jones-Price, C,; Ledoux, T.; et al (1982) Teratologic Evaluation of Oxytetracycline Hydrochloride (CAS 2058-46-0) in CD-1 mice: By RTP and NCI for Toxicological Research, Perinatal and Postnatal Evaluation Branch. Jefferson, AK: NCTR. (Contract NO. 222-80-2031 (C); study code no. Mi81-OX; available from NTIS, Springfield, VA 22151; also in unpublished submission received October 26, 1983 under 1007-79; submitted by Pfipharmecs Div., Pfizer, Inc., New York, NY; CDL:251603-F)

00135300 Interregional Research Project No. 4 (1977) The Results of Tests on the Amount of Terramycin Remaining in or on Peaches Including Description of the Analtytical Method Used. (Compilation; unpublished study received Dec 3, 1976 under 7E1894; CDL:097772-A)

00159856 US Public Health Service (1986) Toxicology and Carcinogenesis Studies of Oxytetracycline Hydrochloride (Cas No. 2058-46-0) in F344/N Rats and B6C3F1 Mice: (Feed Studies): Technical Report Series No. 315: :NIH Publication No. 86-2571:: Draft. Unpublished study prepared in cooperation with Physiological Research Laboratories and Midwest Research Institute and others. 194 p.

00162260 Beutel, J. (1980) Letter sent to V. Carroll dated Nov 3, 1980: :Summary of procedure used to secure the Terramycin residue samples from 12 year old Bartlett pear trees in the University of California orchards at Davis, California, during the 1980 season:. Prepared by Univ. of California, Pomology Dept. 11 p.

40840101 Rollins, L.; Gaines, S.; et al. (1975) Animal Model for Determining the No-Effect Level of Antimicrobial Drug on Drug Resistance in the Loctose-Fermenting Enteric Flora. Antimicrobial Agents and Chemotherapy. p. 661-665.

IV. FORMS APPENDICES

EPA Form 8580-1

OMB Approval No. 2070-0057
Expires 11/30/89

FIFRA SECTION 3(C)(2)(B) SUMMARY SHEET	EPA REGISTRATION NO

PRODUCT NAME

APPLICANT'S NAME	DATE GUIDANCE DOCUMENT ISSUED

With respect to the requirement to submit "generic" data imposed by the FIFRA section 3(C)(2)(B) notice contained in the referenced Guidance Document, I am responding in the following manner:

☐ 1. I will submit data in a timely manner to satisfy the following requirements. If the test procedures I will use deviate from (or are not specified in) the Registration Guidelines or the Protocols contained in the Reports of Expert Groups to the Chemicals Group, OECD Chemicals Testing Programme, I enclose the protocols that I will use:

Attach separate page with a list of the data requirements your company agrees to satisfy.

☐ 2. I have entered into an agreement with one or more other registrants under FIFRA section 3(C)(2)(B)(ii) to satisfy the following data requirements. The tests, and any required protocols, will be submitted to EPA by:

NAME OF OTHER REGISTRANT

Attach list of data requirements

☐ 3. I enclose a completed "Certification of Attempt to Enter Into an Agreement with Other Registrants for Development of Data" with respect to the following data requirements:

☐ 4. I request that you amend my registration by deleting the following uses (this option is not available to applicants for new products):

☐ 5. I request voluntary cancellation of the registration of this product. (This option is not available to applicants for new products.)

REGISTRANT'S AUTHORIZED REPRESENTATIVE	SIGNATURE	DATE

EPA Form 8580-6

OMB Approval No. 2070-0057
Expires 11/30/89

CERTIFICATION OF ATTEMPT TO ENTER INTO AN AGREEMENT WITH OTHER REGISTRANTS FOR DEVELOPMENT OF DATA

(To qualify, certify ALL four items)

1. I am duly authorized to represent the following firm(s) who are subject to the requirements of a Notice under FIFRA Section 3(c)(2)(B) contained in a Guidance Document to submit data concerning the active ingredient:

GUIDANCE DOCUMENT DATE

ACTIVE INGREDIENT

NAME OF FIRM	EPA COMPANY NUMBER

(This firm or group of firms is referred to below as "my firm".)

2. My firm is willing to develop and submit the data as required by that Notice, if necessary. However, my firm would prefer to enter into an agreement with one or more other registrants to develop jointly, or to share in the cost of developing, the following required items or data:

3. My firm has offered in writing to enter into such an agreement. Copies of the offers are attached. That offer was irrevocable and included an offer to be bound by an arbitration decision under FIFRA Section 3(c)(2)(B)(iii) if final agreement on all terms could not be reached otherwise. This offer was made to the following firm(s) on the following date(s):

NAME OF FIRM	DATE OF OFFER

However, none of those firm(s) accepted my offer.

4. My firm requests that EPA not suspend the registration(s) of my firm's product(s), if any of the firms named in paragraph (3) above have agreed to submit the data listed in paragraph (2) above in accordance with the Notice. I understand EPA will promptly inform me whether my firm must submit data to avoid suspension of its registration(s) under FIFRA Section 3(c)(2)(B). (This statement does not apply to applicants for new products.) I give EPA permission to disclose this statement upon request.

TYPED NAME	SIGNATURE	DATE

EPA	US Environmental Protection Agency Washington, DC 20460 **Product Specific Data Report**	Registration Standard for:	EPA Registration Number		Form Approved OMB #2070-0057 Expires 11-30-89

Registration Guideline No.	Name of Test	Testing not required for my product listed above *(Check below)*	I am complying with Data Requirements by - Citing MR ID No.	I am complying with Data Requirements by - Submitting Data *(Attached)* *(Check below)*	(For EPA Use Only) Accession numbers assigned
Sec. 158.120 Product Chemistry					
61-1	Identity of ingredients				
61-2	Statement of composition				
61-3	Discussion of formation of ingredients				
62-1	Preliminary analysis				
62-2	Certification of limits				
62-3	Analytical methods for enforcement limits				
63-2	Color				
63-3	Physical state				
63-4	Odor				
63-5	Melting point				
63-6	Boiling point				
63-7	Density, bulk-density, or specific gravity				
63-8	Solubility				
63-9	Vapor pressure				
63-10	Dissociation constant				
63-11	Octanol/water partition coefficient				
63-12	pH				
63-13	Stability				
63-14	Oxidizing/reducing reaction				
63-15	Flammability				
63-16	Explodability				
63-17	Storage stability				
63-18	Viscosity				
63-19	Miscibility				
63-20	Corrosion Characteristics				
63-21	Dielectric breakdown voltage				
Sec. 158.135 Toxicology					
81-1	Acute oral toxicity, rat				
81-2	Acute dermal toxicity, rabbit				
81-3	Acute inhalation toxicity, rat				
81-4	Primary eye irritation, rabbit				
81-5	Primary dermal irritation				
81-6	Dermal sensitization				

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Typed Name and Title	Signature	Date

OMB Approval No. 2070-005
Expiration Date 11/30/89

GENERIC DATA EXEMPTION STATEMENT

EPA Product Registration Number:_____

Registrant's Name and Address: _____

_____

As an authorized representative of the registrant of the product identified above, I certify that:

(1) I have read and am familiar with the terms of the Notice from EPA dated _____ concerning a requirement for submission of "generic" data on the active ingredient _____ named under FIFRA Section 3(c)(2)(B).

(2) My firm requests that EPA not suspend the registration of our product, despite our lack of intent to submit the generic data in question, on the grounds that the product contains the active ingredient solely as the result of the incorporation into the product of another product which contains that active ingredient, which is registered under FIFRA Section 3, and which is purchased by us from another producer.

(3) An accurate Confidental Statement of Formula (CSF) for the above-identified product is attached to this statement. That formula statement indicates, by company name registration number, and product name, the source of the subject active ingredient in my firm's product, or

The CSF dated_____ on file with EPA is complete, current and accurate and contains the information requested on the current CSF Form 8570-4. The registered source(s) of the above named active ingredient in my product(s) is/are _____ and their registration number(s) is/are _____.

My firm will apply for an amendment to the registration prior to changing the source of the active ingredient in our product.

(4) I understand, and agree on behalf of my firm, that if at any time any portion of this Statement is no longer true, or if my firm fails to comply with the undertakings made in this Statement, my firm's product's registration may be suspended under FIFRA Section 3(c)(2)(B).

(5) I further understand that if my firm is granted a generic data exemption for the product, my firm relies on the efforts of other persons to provide the Agency with the required generic data. If the registrant(s) who have committed to generate and submit the required data fail to take appropriate steps to meet requirements or are no longer in compliance with this Notice's data requirements, the Agency will consider that both they and my firm are not in compliance and will normally initiate proceedings to suspend the registrations of my firm's product(s) and their product(s), unless my firm commits to submit and submits the required data in the specified time frame. I understand that, in such cases, the Agency generally will not grant a time extension for submitting the data.

Registrant's authorized representative:_____
(Signature

Dated: _____ _____
(Typed)

EPA Form 8570-27