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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

APR 14 1988

MEMORANDUM

SUBJECT: Oxytetracycline Registration Standard

FROM: Charles L. Trichilo, Ph.D., Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

To: Amy Rispin, Ph.D., Chief
Science Integration Staff
Hazard Evaluation Division (TS-769)

and

L. Rossi
Product Manager Team # 21
Registration Division (TS-767)

Attached are the Product and Residue Chemistry chapters for Oxytetracycline produced by Dynamac Corporation.

The due date for these chapters is May 18, 1988.

This standard includes data available and reviewed up to March 19, 1988.

The Agency has determined that product chemistry data for all technical and manufacturing use products must be resubmitted for each pesticide because new requirements have been introduced and previously submitted data must be updated. Therefore, the Residue Chemistry Branch will no longer evaluate previously submitted product chemistry data to determine their adequacy in meeting the requirements of Subdivision D of the Pesticide Assessment Guidelines. The product Chemistry chapter provides a summary, but not an evaluation, of the available data for the technical grade (1)

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informational purposes only. Attached to the Product Chemistry chapter are comprehensive generic and product specific data requirement tables for the technical grade of the active ingredient and manufacturing-use products, respectively, of oxytetracyciine.

These chapters have undergone secondary review in Residue Chemistry Branch and have been revised to reflect the Branch policies.

The Product Chemistry chapter contains Appendix A. This is to be protected. Only the copies of the chapter in RCB and those sent to L. Rossi, E. Eldredge and Toxicology Branch contain such information.

The Tolerance Assessment Summary (TAS) calculations were not available at the time of issuance of these chapters. When they are completed the information will be forwarded as an addendum to the Residue Chemistry chapter of the oxytetracycline Registration Standard.

Finally, Registration Division please note, Residue Chemistry Branch has completed the data tables for the Residue Chemistry chapter and they are included in this packcage.

If you need additional input please advise

cc: W. Greear/TOX, HED (With CBI Attachment)
L. Rossi/FHB, RD (With CBI Attachment)
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DYNAMAC
CORPORATION

Final Report

Oxytetracycline
Task 1: Product Chemistry Chapter

Contract No. 68-02-4226

April 8, 1988

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
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OXYTETRACYCLINE

PRODUCT CHEMISTRY

TASK 1

INTRODUCTION

FIFRA 3(c)(2)(A) requires the Agency to establish guidelines for registering pesticides in the United States. The Agency, in turn, requires registrants to provide quantitative data on all added ingredients, active and inert, which are equal to or greater than 0.1% of the product by weight.

To establish the composition of products proposed for registration, the Agency requires data and information on the manufacturing and formulation process and a discussion on the formation of manufacturing impurities and other product ingredients, intentional and unintentional. Furthermore, to assure that the composition of the product as marketed will not vary from the composition evaluated at the time of registration, applicants for registration are required to submit a statement certifying upper and lower composition limits for the added ingredients, and upper limits for some unintentional ingredients. Subdivision D of the Pesticide Assessment Guidelines (October 1982) suggests specific precision limits for ingredients based on the variability of the ingredients as a function of the manufacturing process.

The Agency also requires data on the physical and chemical properties of the pesticide active ingredient and its formulations, such as melting and boiling points, ambient vapor pressure, and solubility in various solvents. Corresponding to each of the Topical Discussions listed below are the Guidelines Reference Nos. in "Data Requirements for Pesticide Regulation" (40 CFR 158.120) which explain the minimum data the Agency will need to adequately assess the product chemistry of oxytetracycline (OTC).

	Guidelines Reference No. of 40 CFR 158.120
Product Identity and Composition	61-(1-3)
Analysis and Certification of Product Ingredients	62-(1-3)
Physical and Chemical Characteristics	63-(2-21)

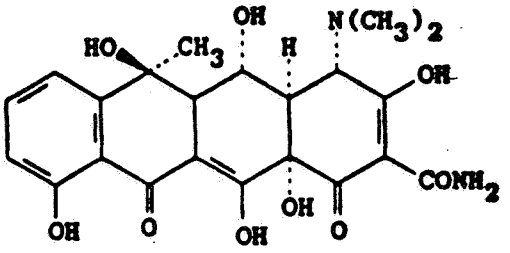
It should be noted that although product chemistry data may have been submitted in the past, the Agency has determined that these data must be resubmitted for each pesticide. New requirements have been introduced, and previously submitted data must be updated. Therefore, available product chemistry data will be summarized in this chapter for the technical grade of the active ingredient only. These data will not be evaluated with regard to

their adequacy in meeting the requirements of 40 CFR Part 158.120, but are presented here for informational purposes only.

PRODUCT IDENTITY AND COMPOSITION

61-1. Product Identity and Disclosure of Ingredients

Oxytetracycline is the chemical name of an antibiotic bactericide/fungicide registered in the U.S. by Pfizer, Inc. The molecular structure is depicted below.



The chemical name for oxytetracycline is 4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. Other common and trade names include: glomycin, terrafungine, riomitsin, hydroxytetracycline, Berkmycin, Biostat, Imperacin, Oxacycline, Oxatets, Oxydon, OxyDumocyclin, Oxymycin, Oxypan, Oxytetracid, Ryomycin, Stevacin, Terraject, Terramycin, Tetramel, Tetran, Vendarcin, and Vendracin.

Other identifying characteristics and codes are:

Empirical Formula:	$C_{22}H_{24}N_2O_9$
Molecular Weight:	460.44
CAS Registry Nos.:	79-57-2 (OTC)
	2058-46-0 (OTC Hydrochloride)
Shaughnessy Nos.:	006304 (OTC)
	006308 (OTC Hydrochloride)
	006321 (Calcium OTC)

The above information was obtained from the following sources: The Merck Index, 10th Ed., p. 6849, Farm Chemicals Handbook '88, p. C218, and Toxic Substances Control Act Chemical Substances Inventory, p. 1070.

61-2. Description of Beginning Materials and Manufacturing Process

The following manufacturing process for oxytetracycline is published in The Merck Index, Merck and Co., Inc., p. 6849:

"Antibiotic substance isolated from the elaboration products of the actinomycete, Streptomyces rimosus, grown on a suitable medium."

Pfipharmecs submitted a description of the production of oxytetracycline. This is discussed in Confidential Appendix A.

If technical oxytetracycline is transported per FIFRA Sec. 3(b)(1) (as amended September 30, 1978 and revised May, 1985), then registration is not required; otherwise, this product must be registered, and data fulfilling the guidelines, including 62-2 and 62-3, must be submitted.

61-3. Discussion of the Formation of Impurities

No data are available on this topic for any technical product.

ANALYSIS AND CERTIFICATION OF PRODUCT INGREDIENTS

62-1. Preliminary Analysis

No data are available on this topic for any technical product.

62-2. Certification of Ingredient Limits

No data are available on this topic for any technical product.

62-3. Analytical Methods to Verify Certified Limits

Phipharmecs (1976; MRID 00109144) submitted a spectrophotometric method for determination of the calcium oxytetracycline complex using Klebsiella pneumoniae (ATCC 10031) as the test organism. Also submitted was a description of an autoturb microbiological method for detection of the calcium oxytetracycline complex. Validation data were not submitted for either method.

PHYSICAL AND CHEMICAL CHARACTERISTICS

Summarized in Table 1 are several reported physical and chemical properties of the unregistered calcium oxytetracycline complex and oxytetracycline hydrochloride used by Pfizer, Inc.

Table 1. Physical and chemical properties of the calcium oxytetracycline complex and oxytetracycline hydrochloride technical.

Guidelines Reference No., 40 CFR 158.120; Name of Property		Description (Product; Reference)
63-2	Color	Tan to dark brown (calcium oxytetracycline); MRID 00109144
63-12	pH	7.5-10.5 (calcium oxytetracycline); MRID 00109144 2.0-3.0 (oxytetracycline hydrochloride); MRID 00039918
63-17	Storage stability	(oxytetracycline hydrochloride) at 37 C for 12 months retained 80.4-97.3% hydration; at 22-25 C, 87.0-99.4% hydration. MRID 00109144

References (used):

00039918 Pfizer, Inc. (1968) Oxytetracycline hydrochloride. (Unpublished study received Jun 6, 1973 under 3E1407; submitted by California, Dept. of Food and Agriculture, Sacramento, Calif.; CDL:093761-C)

00109144 Pfipharmecs (1976) Chemical Study: Myco-shield Brand of Agricultural Terramycin. (Compilation; unpublished study received Sep 3, 1976 under 1007-EX-9; CDL:225537-A)

References (not used):

[The following references do not contain information useful for satisfying product chemistry data requirements for oxytetracycline.]

00039919 California, Department of Food and Agriculture (19??) Terramycin Tree Injection Formula. (Unpublished study; CDL:093761-D)

00049093 Pfipharmecs (19??) Terramycin Tree Injection Formula. (Unpublished study received Mar 25, 1974 under unknown admin. no.; CDL:223547-A)

00057585 California. Department of Food & Agriculture (19??) Chemistry, Processing and Packaging of Agricultural Teramycin. (Unpublished study; CDL:095168-B)

00147249 Regna, P.; Solomons, I. (1950) The chemical and physical properties of terramycin. Annals of New York Academy of Sciences 53(2):229-237.

00164610 Pfipharmecs Div., Pfizer Inc. (1974) Terramycin Tree Injection Formula: [Product Chemistry]. Unpublished compendium. 20 p.

05001575 Palm, E.T.; Young, R.A. (1957) The compatibility of certain organic fungicides and antibiotics in treatment mixtures as indicated by stability and phytotoxicity. Plant Disease Reporter 41(3):151-155.

TABLE A. GENERIC DATA REQUIREMENTS FOR THE TECHNICAL GRADE OF THE ACTIVE INGREDIENT.

Data Requirement	Composition[a]	Does EPA have data to satisfy this requirement?[b]	Bibliographic Citation[b]	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?	Time Frame For Data Submission
158.120 Product Chemistry					
Product Identity and Composition					
61-2 - Description of Beginning Materials and Manufacturing Process	TGAI	No	N/A	Yes[c]	6 months
61-3 - Discussion of Formation of Impurities	TGAI	No	N/A	Yes[d]	6 months
Analysis and Certification of Product Ingredients					
62-1 - Preliminary Analysis of Product Samples	TGAI	No	N/A	Yes[e]	12 months
Physical and Chemical Characteristics					
63-2 - Color	TGAI	No	N/A	Yes[f]	6 months
63-3 - Physical State	TGAI	No	N/A	Yes[f]	6 months
63-4 - Odor	TGAI	No	N/A	Yes[f]	6 months
63-5 - Melting Point	TGAI	No	N/A	Yes[f,g]	6 months
63-6 - Boiling Point	TGAI	No	N/A	Yes[f,h]	6 months
63-7 - Density, Bulk Density or Specific Gravity	TGAI	No	N/A	Yes[f]	6 months
63-8 - Solubility	TGAI or PAI	No	N/A	Yes[f]	6 months
63-9 - Vapor Pressure	TGAI or PAI	No	N/A	Yes[f]	6 months
63-10 - Dissociation Constant	TGAI or PAI	No	N/A	Yes[f]	6 months
63-11 - Octanol/Water Partitioning Coefficient	PAI	No	N/A	Yes[f,i]	6 months
63-12 - pH	TGAI	No	N/A	Yes[f,j]	6 months
63-13 - Stability	TGAI	No	N/A	Yes[f]	6 months
Other Requirements:					
64-1 - Submittal of Samples	N/A	N/A	N/A	No	

(Continued, footnotes follow.)

TABLE A. (Continued).

[a] TGAI = technical grade of the active ingredient. PAI = purified active ingredient.

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

[c] 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 used in the manufacture of each product must be provided, along with information regarding the properties of those materials.

[d] 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.

[e] Five or more representative samples must be analyzed for the amount of active ingredient and each impurity for which certified limits are required. Complete validation data (accuracy and precision) must be submitted for each analytical method used.

[f] Physicochemical characteristics (color, physical state, odor, melting point, boiling point, specific gravity, solubility, vapor pressure, dissociation constant, partition coefficient, pH, and stability) as required in 40 CFR 158.120 and more fully described in the Pesticide Assessment Guidelines, Subdivision D, must be submitted.

[g] Data needed if the technical chemical is a solid at room temperature.

[h] Data required if the technical product is a liquid at room temperature.

[i] Data required if the technical product is organic and nonpolar.

[j] Data required if the test substance is dispersible in water.

TABLE B. PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING-USE PRODUCTS.

Data Requirement	Composition[a]	Does EPA have data to satisfy this requirement?[b]	Bibliographic Citation[b]	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?	Time Frame For Data Submission
158.120 Product Chemistry					
Product Identity and Composition					
61-1. Product Identity and Disclosure of Ingredients	MP	No	N/A	Yes[c]	6 months
61-2 - Description of Beginning Materials and Manufacturing Process	MP	No	N/A	Yes[d]	6 months
61-3 - Discussion of Formation of Impurities	MP	No	N/A	Yes[e]	6 months
Analysis and Certification of Product Ingredients					
62-1 - Preliminary Analysis of Product Samples	MP	No	N/A	Yes[f]	12 months
62-2 - Certification of Ingredient Limits	MP	No	N/A	Yes[g]	12 months
62-3 - Analytical Methods to Verify Certified Limits	MP	No	N/A	Yes[h]	12 months
Physical and Chemical Characteristics					
63-2 - Color	MP	No	N/A	Yes[i]	6 months
63-3 - Physical State	MP	No	N/A	Yes[f]	6 months
63-4 - Odor	MP	No	N/A	Yes[f]	6 months
63-7 - Density, Bulk Density or Specific Gravity	MP	No	N/A	Yes[f]	6 months
63-12 - pH	MP	No	N/A	Yes[f,j]	6 months
62-14 - Oxidizing or Reducing Action	MP	No	N/A	Yes[i,k]	6 months
62-15 - Flammability	MP	No	N/A	Yes[i,l]	6 months
63-16 - Explodability	MP	No	N/A	Yes[i,m]	6 months
63-17 - Storage Stability	MP	No	N/A	Yes[i]	15 months
63-18 - Viscosity	MP	No	N/A	Yes[i,n]	6 months

(Continued, footnotes follow.)

TABLE B. (Continued).

Data Requirement	Composition[a]	Does EPA have data to satisfy this requirement?[b]	Bibliographic Citation[b]	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?	Time Frame For Data Submission
158.120 Product Chemistry (cont.)					
63-19 -Miscibility	MP	No	N/A	Yes[i,o]	6 months
63-20 -Corrosion Characteristics	MP	No	N/A	Yes[i]	15 months
Other Requirements:					
64-1 - Submittal of Samples	N/A	N/A	N/A	No	

[a] Composition: MP = Manufacturing-Use Product.

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

[c] The chemical name, nominal concentration, Chemical Abstracts (CAS) Registry Number, and purpose of the active ingredient and 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 or weight range; and any experimental or internally assigned company code numbers.

[d] 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 used in the manufacture of each product must be provided, along with information regarding the properties of those materials.

[e] 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.

TABLE B. (Continued).

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[f] Five or more representative samples must be analyzed for the amount of active ingredient and each impurity for which certified limits are required. Complete validation data (accuracy and precision) must be submitted for each analytical method used.

[g] Upper and lower limits for the active ingredient and each intentionally added inert, and upper limits for each impurity present at ≥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. Certifications must be submitted on EPA Form 8570 Rev. 2-85.

[h] 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.

[i] Physicochemical characteristics (color, physical state, odor, melting point, boiling point, specific gravity, solubility, vapor pressure, dissociation constant, partition coefficient, pH, and stability) as required in 40 CFR 158.120 and more fully described in the Pesticide Assessment Guidelines, Subdivision D, must be submitted.

[j] Data required if the test substance is dispersible in water.

[k] Data required if the product contains an oxidizing or reducing agents.

[l] Data required if the product contains combustible liquids.

[m] Data required if the product is potentially explosive.

[n] Data required if the product is a liquid.

[o] Data required if the product is a liquid and is to be diluted with petroleum solvents.

DYNAMAC
CORPORATION

Final Report

Oxytetracycline
Task 2: Residue Chemistry Chapter

Contract No. 68-02-4226

April 8, 1988

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
11140 Rockville Pike
Rockville, MD 20852

OXYTETRACYCLINE

RESIDUE CHEMISTRY

Task 2

INTRODUCTION

Oxytetracycline is an antibiotic bactericide/fungicide federally registered for use on peaches and pears. Oxytetracycline formulations registered for use on peach and pear crops include the 17% WP and the 21.6% SC/S. Applications are foliar (WP) or injectable (SC/S). The above formulations contain calcium oxytetracycline or oxytetracycline hydrochloride as the sole active ingredient. Oxytetracycline formulations are also registered for use on ornamentals and in marine antifouling paint. Special Local Need (SLN) registrations are held by California (CA790007), Connecticut (CT840003), Massachusetts (MA800003), Michigan (MI790025), New York (NY790014), Pennsylvania (PA800027), Utah (UT790018) and Washington (WA821138). Tolerances have been established for residues of oxytetracycline in or on peaches and pears (40 CFR 180.337).

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 salmonids and catfish.

NATURE OF THE RESIDUE IN PLANTS

Conclusions:

Data were not submitted regarding the nature of the residue of oxytetracycline in plants. Toxicology Branch has assessed the need for data reflecting the metabolism of oxytetracycline in plants and has concluded that these data are not required. (Oral commumication with A. Kocialski, 4/12/88, TOX memo to follow.)

References (used):

N/A.

Discussion of the data:

N/A.

NATURE OF THE RESIDUE IN ANIMALS

Conclusions:

Data were not submitted regarding the nature of the residue of oxytetracycline in animals. 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.

References (used):

N/A.

Discussion of the data:

N/A.

RESIDUE ANALYTICAL METHODS

Conclusions:

The available microbiological assay method for the determination of oxytetracycline residues in or on peaches and pears is inadequate for data collection and for tolerance enforcement; however, this method is useful for purposes of estimating residues of oxytetracycline. The method is similar to Final Action Microbiological Methods I and II in the AOAC Official Methods of Analysis (1984; 42.293-42.298). This method is nonspecific and insufficiently sensitive for quantitative determination of oxytetracycline because it does not distinguish oxytetracycline from other compounds (other bactericides or natural plant constituents) that may alter the response of the bioassay test organism. The available data indicate that recoveries are generally low and markedly variable (0-45%). The following additional data are required:

- The registrant must submit a method suitable for enforcement, such as an HPLC method, and provide validation data including precision, accuracy, and limits of detection.

- The registrant must submit validation data (precision, accuracy and limits of detection) for the bioassay method used to generate the existing residue chemistry data base. If the requested validation data indicate that the method is not sufficiently sensitive to determine oxytetracycline residues in or on plant commodities at the level of the presently established tolerances, appropriate tolerance levels must be proposed.

Testing of oxytetracycline through multiresidue methods as required in 40 CFR 158.125(b)(15) and published in PAM Vol. I, Appendix II Multiresidue Method Testing is not practical since oxytetracycline is not sufficiently volatile for GLC applications.

References (used):

MRIDs: 00058254.

References (not used):

[The following reference contains duplicate or irrelevant information.]

MRID: 00076808

Discussion of the data:

Pfizer Inc. (19??; MRID 00058254) submitted a bioassay method for determination of oxytetracycline residues in fruit extract. This method is similar to Final Action Microbiological Methods I and II for analysis of oxytetracycline in feeds in the Official Methods of Analysis of the AOAC (1984; 42.293-42.298). The microbiological agar diffusion assay for oxytetracycline in fruit extract method uses Bacillus cereus var. mycoides (ATCC 11778) as the test organism. A spore suspension of B. cereus is added to an agar base layer of Medium #8 and allowed to solidify. After the seed layer hardens, cylinders containing the test samples (which are concentrated by lyophilization and reconstituted with buffer to pH 6.8) and references are placed on the inoculated surface. Samples are incubated for 16-18 hours at 28 C and the diameters of the zones of inhibition are measured. The standard curve is generated using standard stock solutions. Validation data are presented in Table 1.

Table 1. Validation data for the Bacillus cereus cylinder plate bioassay method for determination of oxytetracycline in or on plants.

Commodity	Fortification Range (ppm)	Recovery Range (%)[a]	Reference (MRID)
Peaches	0.8-1.6	91-98 (2)	00081153
	0.5	24-40 (5)	00093605
	0.35	35-42 (5)	00093605
	0.25	0-45 (5)[b]	00093605
	0.10-0.025	0 (15)	00093605
	NR[c]	100-113 (2)	00135300
Pears	0.8[a]	94-120 (6)	00081266
	1.6[a]	32-122 (6)[d]	00081266
	0.5	27- 35 (6)	00039917
	0.35	0- 42 (6)	00039917
	0.25	0 (5)	00039917

[a] The number of samples is given in parentheses.
[b] No detectable oxytetracycline was recovered from two samples.
[c] NR = Not reported.
[d] Average recovery is 93% (n = 6).

The validation data provided with this bioassay method indicate that the method is insufficiently sensitive to detect residues of oxytetracycline in or on peaches and pears at the established tolerances of at 0.1 ppm and 0.35 ppm, respectively. The registrant must submit validation data including precision, accuracy, and limits of detection for peaches and pears.

STORAGE STABILITY DATA

Conclusions:

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

References (used):

MRID: 00081151.

18

References (not used):

[The following MRIDs contain irrelevant or previously cited data.]

MRIDs: 00057584. 00135300. 00161062. 00147208.

Discussion of the data:

Interregional Research Project No. 4 (1977; MRID 00081151) submitted data concerning the stability of oxytetracycline in eight frozen pear and peach samples each stored for 1-90 days at -20 C. Fresh pears and peaches purchased locally were fortified with oxytetracycline at 20 ppm and sampled at 0-90 days using an undescribed microbiological method referenced as S.T.P. O 12.14. Recovery was 99.38% and 102.2% from pears and peaches, respectively, after 90 days of frozen storage.

MAGNITUDE OF THE RESIDUE IN PLANTS

It should be noted that the conclusions stated in this section regarding the adequacy of established tolerances for residues in or on plant commodities may change on receipt of the required analytical method validation data. Residue data presented in the following discussions were obtained using the B. cereus cylinder plate assay method. This method may not be sufficiently sensitive to detect oxytetracycline in or on plant commodities at the present tolerance levels. Tolerances are established at 0.1 ppm (peaches) and 0.35 ppm (pears) at this time.

Application rates are expressed in terms of oxytetracycline base activity (act).

Pome Fruits Group

Conclusions for the Pome Fruits Group:

A crop group tolerance is not appropriate at the present time because oxytetracycline is currently registered for use on only one group member, pears.

Pears

Tolerance:

A tolerance of 0.35 ppm has been established for residues of oxytetracycline in or on pears (40 CFR 180.337).

Use directions and limitations:

The 17% WP formulation of calcium oxytetracycline is federally registered for multiple foliar applications to pears at 0.09-0.17 lb act/A in 50-100 gal water/A. A 60-day PHI has been established through 0.17 lb act/A. A maximum of 10 applications may be made per season at 4- to 6-day intervals. The 17% WP formulation is also registered for use in CA with a 14-day PHI at 0.09-0.17 lb act/A in 50-100 gal water/A [EPA SLN No. CA820086]. Applications may be made 15 times per season at 4- to 6-day intervals. The same formulation is registered for use in WA at 0.09 lb act/A in 3-10 gal water/A using aerial equipment [EPA SLN No. WA820038]. A maximum of 10 applications may be made per season at 4- to 6-day intervals. The 21.6% SC/S formulation of oxytetracycline hydrochloride is registered for a single postharvest injection to pear trees on the West Coast only at 5.68-7.57 g act/tree. The same SC/S is registered for use in CA only as a postharvest injection at 5.68 g act/tree and may be applied twice per season [EPA SLN No. CA780009]. The 21.6% SC/S is registered for injection (infusion application) at 0.05-0.1 g act/tree in CT only [EPA SLN No. CT780003].

Conclusions:

The available data are insufficient to assess the adequacy of the established tolerance for residues of oxytetracycline in or on pears because data do not (i) reflect aerial application with the 17% WP formulation permitted in CA; (ii) injection application with the 21.6% SC/S formulation permitted in CT; and (iii) two injection applications/season with the 21.6% SC/S formulation permitted in CA. The available data do indicate that registered multiple foliar applications with the 17% WP formulation yielded residues of oxytetracycline up to 0.04 ppm. The following additional data are required:

- Data depicting residues of oxytetracycline in or on pears harvested 60 days after the last of 10 foliar applications of the 17% WP at 0.09 lb act/A in 3-10 gal water/A using aerial equipment in WA only [EPA SLN No. WA820038]. Residue data must be obtained using a fully validated analytical method.

- Data depicting residues of oxytetracycline in or on pears harvested at the shortest practical interval after the last of two injections of the 21.6% SC/S at 5.68 g act/tree in CA only [EPA SLN No. CA780009]. Residue data must be obtained using a fully validated analytical method.

- Data depicting residues of oxytetracycline in or on pears harvested at the shortest practical interval following a single injection of the 21.6% SC/S at 0.1 g act/tree made

prior to near bloom formation. Tests must be conducted in CT [EPA SLN No. CT780003]. Residue data must be obtained using a fully validated analytical method.

References (used):

MRIDs: 00039917. 00049096. 00081266. 00162260.

References (not used):

[The following references contain irrelevant or duplicate information.]

MRIDs: 00049095. 00058253. 00088410. 00103387. 00103391. 00116891. 00147208.

Discussion of the data:

University of California, Davis (1980; MRID 00162260) submitted data from a single test conducted in CA concerning residues of oxytetracycline in or on pears sampled 4-60 days after multiple spray applications of the 17% WP calcium OTC formulation at 0.17 lb ai/A (1x the maximum registered use rate). Residues were <0.025(nondetectable)-0.04 ppm in or on 59 samples harvested 4-30 days after the last of 13-17 applications. Residues were nondetectable (<0.025 ppm) in or on 24 pear samples harvested 14 and 60 days after 15 and 9 applications, respectively. Applications were made ca. every 4 days. A single control sample demonstrated no antibiotic activity. Samples were analyzed by the Oxytetracycline Microbiological Assay Plate Method; the implied limit of detection was 0.025 ppm. Samples were stored at 0 C for 23-27 days. Fortification and recovery data were not reported.

Pfipharmecs, Inc. (1973; MRID 00049096) submitted data from three tests conducted in CA concerning residues of oxytetracycline in or on pears harvested 8 days to 11 months after a single injection with the 21.6% SC/S OTC hydrochloride formulation at 50 and 100 ppm (0.5 and 1x the maximum registered use rate). Residues were nondetectable (<0.35 ppm) in or on 65 pear samples harvested 9-11 months after application of the 21.6% SC/S formulation at 100 ppm (1x the maximum registered use rate). In a subsequent test, residues were <0.35 ppm in or on 15 pear samples harvested 8-57 days after treatment with the 21.6% SC/S at 50 and 100 ppm (0.5 and 1x the maximum registered use rate). A single sample harvested 48 days posttreatment bore residues of 0.35 ppm. Six control samples demonstrated no zones of inhibition. Samples were analyzed using an unspecified cylinder plate method with an "approximate" limit of detection of 0.35 ppm. Fortification and recovery data were not submitted. Storage data were not reported.

California Dept. of Food and Agriculture (1974; MRID 00081266) submitted data from two tests conducted in CA concerning residues of oxytetracycline in or on pears harvested 16-69 days after nine spray applications of the 17% WP calcium OTC formulation at 100 ppm (0.5x the maximum registered use rate). Residues were nondetectable (<0.025, <0.05, or <0.1 ppm depending on the test) in or on 26 samples harvested 16-69 days posttreatment. Residues were <0.158 ppm in or on 25 samples harvested 19-63 days after nine applications. Six control samples demonstrated no antibiotic activity. Samples were analyzed using the Oxytetracycline Microbiological Assay Plate Method; the stated limits of detection were 0.025, 0.05 and 0.1 ppm. Recovery was 94-120% and 32-122% from twelve samples fortified with oxytetracycline at 0.8 mcg/mL and 1.6 mcg/mL, respectively. Samples were stored frozen for an unspecified interval prior to analysis.

California Dept. of Food and Agriculture (1972; MRID 00039917) submitted data from six tests conducted in CA concerning residues of oxytetracycline in or on pears. Residues were ca. 0.35 ppm in or on 54 samples harvested at an unspecified interval after one or two injections with the 21.6% SC/S OTC hydrochloride formulation at 50-200 ppm (0.25-1x the maximum registered use rate). Samples were analyzed using the Oxytetracycline Microbiological Assay Plate Method with a stated limit of detection of 0.35 ppm. Residues were ca. 0.35 ppm in or on 18 control samples. Recovery was 0-42% from 17 samples fortified with oxytetracycline at 0.25-0.5 ppm. Samples were stored frozen for an unspecified interval prior to analysis.

The test state of CA(39%) provides adequate geographic representation if CA represents OR(26%), since these states collectively produced 65% of the 1985 U.S. pear crop (Agricultural Statistics, 1986, p. 214). The available data indicate that multiple foliar applications at the maximum registered rate with the 17% WP formulation yielded residues of oxytetracycline at up to 0.04 ppm. However, no data were available data depicting residues that (i) reflect aerial application with the 17% WP formulation permitted in CA; (ii) injection application with the 21.6% SC/S formulation permitted in CT; and (iii) two injection applications/season with the 21.6% SC/S formulation permitted in CA. Additional data are needed.

Stone Fruits Group

Conclusions for the Stone Fruits Group:

A crop group tolerance is not appropriate at the present time because oxytetracycline is currently registered for use on only one group member, peaches.

Peaches

Tolerance:

A tolerance of 0.1 ppm has been established for residues of oxytetracycline in or on peaches (40 CFR 180.337).

Use directions and limitations:

The 17% WP formulation of calcium oxytetracycline is federally registered for multiple foliar applications to peaches after the shuck split stage at 0.31-0.64 lb act/A in 240-500 gal water/A. There is a 21-day PHI in effect through 0.64 lb act/A. A maximum of nine applications may be made per season at 7-day intervals. The 21.6% SC/S formulation of oxytetracycline hydrochloride is registered for postharvest injection at 50-142 mg act/hole in CT, MA, MI, NY, PA, and UT [EPA SLN Nos. CT790007, MA800003, MI790025, NY790014, PA800027 and UT790018]. The same 21.6% SC/S formulation of oxytetracycline hydrochloride is registered for postharvest injection at 1.26-2.52 g act/tree in CA, CT, MA, MI, NY, PA and UT [EPA SLN Nos. CA790178, CT840003, MA800003, MI790025, NY790014, PA800027 and UT790018].

Conclusions:

The available data support the established tolerance and are sufficient to assess the adequacy of the label directions. No additional data are required for this topic.

References (used):

MRIDs: 00064602. 00081153. 00093605. 00135300.

References (not used):

[The following references contain duplicate or irrelevant data.]

MRIDs: 00051538. 00093604. 00109572. 00121730. 00124017.

Discussion of the data:

Interregional Research Project No. 4 (1976; MRID 00135300) submitted data from 11 tests conducted in CT(2), MI(5) and NY(4) concerning residues of oxytetracycline in or on peaches harvested 3-11 months after injection with the 21.6% SC/S at 0.05-3.75 g/tree (0.02-1.5x the maximum registered use rate). In the CT tests, five samples each harvested 3-10 months after injection at 0.75 and 1 g/tree (0.3 and 0.4x the maximum registered use rate) bore residues of <0.025-0.034 ppm. Residues in or on three control samples were <0.025-0.028 ppm. In the MI tests, 20 samples harvested 9-11 months after treatment with pressure, infusion and concentrate injections at 0.05-3.75 g/tree (0.02-

1.5x) bore residues of <0.0125(nondetectable)-0.25 ppm. Residues were <0.0125(nondetectable)-0.054 ppm in or on four control samples. In NY, 12 samples harvested 10 months after injection with oxytetracycline at 0.6-1.2 g/tree (0.24 and 0.48x the maximum registered use rate) bore residues of <0.0125(nondetectable)-0.19 ppm. A single sample harvested 10 months after treatment at 0.8 g/tree (0.32x the maximum registered rate) bore a tolerance-exceeding residue of 0.54 ppm. All samples were analyzed using the Oxytetracycline Microbiological Assay Plate Diffusion Method; the stated limit of detection was 0.0125 ppm. Recovery from two NY samples following an unspecified fortification level was 100-112.5%. Samples were frozen at an unspecified temperature for an unspecified interval prior to analysis.

Pfizer, Inc. (1966; MRID 00093605) submitted data from two tests conducted in MD concerning residues of oxytetracycline in or on peaches harvested at an unspecified interval after treatment with the 17% WP at 66 and 132 ppm (0.44 and 0.88x the maximum registered use rate; volume/tree not specified). Thirty samples each demonstrated no antibiotic activity. When the same concentrations were applied and DMSO [as a surfactant?] was added at two rates, no antibiotic activity was detected. Samples were analyzed using the Oxytetracycline Microbiological Assay Plate Diffusion Method. Recovery was 24-42% from 10 samples fortified with oxytetracycline at 0.35-0.5 ppm and 0-45% from five samples fortified at 0.25 ppm; quantitative recovery could not be attained at concentrations <0.25 ppm. Two control samples demonstrated no antibiotic activity. Samples were frozen at an unspecified temperature for an unspecified length of time prior to analysis.

Interregional Research Project No. 4 (1974; MRID 00081153) submitted data from a single test conducted in NJ concerning residues of oxytetracycline in or on peaches. Residues were <0.125-0.039 ppm in or on 19 samples harvested 21 days after the last of nine applications of the 17% WP at 150 ppm (1x the maximum registered use rate; volume/tree not specified) at 7-day intervals. Samples were analyzed using the Oxytetracycline Microbiological Assay Plate Diffusion Method with a stated limit of detection of 0.0125 ppm. Recovery was 90.6% and 97.5% from two samples fortified with oxytetracycline at 1.6 and 0.8 mcg/mL, respectively. A single control sample demonstrated no antibiotic activity. Samples were stored frozen at an unspecified temperature for an unspecified length of time.

California Dept. of Food and Agriculture (1980; MRID 00064602) submitted data from a single test conducted in CA concerning residues of oxytetracycline in or on peaches harvested at an unspecified interval after injection with the 21.6% SC/S; it was implied in the document that the label directions were followed and treatment was at 1x the maximum registered rate. Residues

were <0.01 ppm (nondetectable) in or on samples from 128 trees. Analytical method, validation data, recoveries and control data were not reported.

Geographic representation was adequate because the test states of CA(68%), NJ(4%), MD(<1%), and CT(<1%) accounted for ca. 70% of 1985 total U.S. peach production (Agricultural Statistics, 1986, p. 212). The available data indicate that registered multiple foliar applications may yield oxytetracycline residues at up to 0.039 ppm and registered injection use of oxytetracycline on peaches may result in residues up to 0.54 ppm.

MAGNITUDE OF THE RESIDUE IN MEAT, MILK, POULTRY AND EGGS

Tolerances:

Use of oxytetracycline as a drug in food animals is regulated by the FDA according to 21 CFR 556.500. The following tolerances for residues of oxytetracycline in or on animal commodities have been established: (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 salmonids and catfish.

There are no established tolerances for residues of oxytetracycline in meat, milk, poultry, and eggs regulated under 40 CFR 180.101, nor are there established or proposed direct animal treatment uses for the bactericide/fungicide oxytetracycline.

Conclusions:

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. Residue data are not required for this topic.

REGULATORY INCIDENTS

USDA Monitoring Data:

USDA monitoring data collected through the National Residue Monitoring Program CY 1973-1986 are available pertaining to oxytetracycline residues in kidney tissue from bulls, calves, cows, ducks, turkeys (young, mature and fry-roast), geese, goats, heifers, horses, chickens (young and mature), rabbits, sheep, steers and swine. The FDA has established the following

administrative tolerances for residues of oxytetracycline in 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 salmonids and catfish (21 CFR 556.500). The summary of oxytetracycline residues are presented in Table 2.

Table 2. Summary of Oxytetracycline residues in kidney tissue from horses, cattle, swine, and ducks collected CY 1973-1986.

Species	Total no. of samples analyzed	Total no. of violative samples	Range of violative samples as % of total
Horses	2,520	1	<1%
Cows	10,706	1	<1%
Calves	19,693	16	<1%
Swine	11,580	1	<1%
Ducks	2,983	1	<1%

Kidney tissue samples from the following animal commodities were nonviolative; total number of samples is indicated in parentheses: bulls (1227), steers (2358), heifers (2107), sheep (3107), goats (1030), young and mature chickens (6894), young, mature and fry-roast turkeys (5791), geese (222) and rabbits (793).

FDA Total Diet Studies and Domestic and Import Surveillance Data:

Information pertaining to oxytetracycline residues in or on food commodities tested through FDA's residue monitoring program were requested by RCB (OPP, EPA) from FDA on Aug. 6, 1987 but have not been received. Upon receipt of the requested data, an addendum to this chapter will be issued incorporating those data.

TOLERANCE REASSESSMENT SUMMARY

It should be noted that the conclusions stated below regarding the adequacy of established tolerances may change on receipt of the required analytical method validation data. Tolerances for residues of oxytetracycline in or on pears and peaches are currently established at 0.35 and 0.1 ppm, respectively, and are expressed in terms of oxytetracycline (40 CFR 180.337); the validation data provided with the bioassay method used to collect residue data indicate that the method may not be sufficiently

sensitive to detect residues of oxytetracycline in or on these commodities at the level of the established tolerances.

The available data are adequate to support the registered use of oxytetracycline on peaches; however pending receipt of the required analytical method validation data, the tolerance for residues in or on peaches may have to be revised.

Additional data are required to support the registered use on pears.

Use of oxytetracycline as a drug in food animals is regulated by the FDA according to 21 CFR 556.500. The following tolerances for residues of oxytetracycline in or on animal commodities have been established: (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 salmonids and catfish.

Codex MRLs have not been established or proposed for residues of oxytetracycline in or on any food/feed commodity; therefore, no questions regarding compatibility between U.S. tolerances and Codex MRLs exist.

The Tolerance Assessment System figures regarding human dietary exposure to oxytetracycline residues will be presented as an addendum to the Residue Chemistry Chapter of the Standard.

MASTER RECORD IDENTIFICATION NUMBERS

The following references were obtained from the master sequence bibliography for oxytetracycline dated 9/30/87.

References (used):

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:226522-A)

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)

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 Analytical Method used. (Compilation; unpublished study received Dec 3, 1976 under 7E1894; CDL:097772-A)

00162260 Beutel, J. (1980) Letter sent to V. Carroll dates Nov 3, 1980: [Summary of procedure used to secure the Terramycin residues 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.

References (not used):

00039918 Pfizer, Incorporated (1968) Oxytetracycline hydrochloride.(Unpublished study received Jun 6, 1973 under 3E1407; submitted by California, Dept. of Food and Agriculture, Sacramento, Calif.; CDL:093761-C)

00039919 California, Department of Food and Agriculture (19??) Terramycin Tree Injection Formula. (Unpublished study; CDL:093761-D)

00049093 Pfipharmecs (19??) Terramycin Tree Injection Formula. (Unpublished study received Mar 25, 1974 under unknown admin. no.; CDL:223547-A)

00049095 Pfipharmecs (1972) Determination of Terramycin Residues in Pears. (Unpublished study received Mar 25, 1974 under unknown admin. no.; CDL:223547-F)

00051538 Mayerhofer, H.J. (1975) Letter sent to Distribution List dated Mar 19, 1975: Termination report QCSA 71729: IDM-HJM-75-42. (Unpublished study received Sep. 8, 1975 under 37787-EX-1; submitted by New York State Agricultural Experiment Station, Highland, N.Y.; CDL:226522-A)

00057585 California. Department of Food & Agriculture (19??) Chemistry, Processing and Packaging of Agricultural Teramycin. (Unpublished study; CDL:095168-B)

00058253 Carroll, V.J. (1974) Determination of Terramycin (Oxytetracycline) Residues in Pears. (Unpublished study received Apr 1, 1975 under 5E1611; prepared by Pfizer, Inc., submitted by California, Dept of Food & Agriculture, Sacramento, Calif.; CDL:095168-F)

00065578 Pfipharmecs (1958) Efficacy of Streptomycin on Peppers, Tomatoes, Pears, Apples, Tobacco and Chrysanthemums. (Compilation; unpublished study, including published data, received May 26, 1954?; Nov 7, 1955?; Nov 13, 1953?; Jan 22, 1954?; Feb 20, 1958 under 1007-6; CDL:229886-A)

00076807 Nyland, G.; Raju, B.C. (1980) Determination of Terramycin Activity in Injected Cherry. (Unpublished study received May 4, 1981 under 1007-79; prepared by Univ. of California--Davis, Dept. of Plant Pathology, submitted by Pfipharmecs, Div. of Pfizer, Inc., New York, N.Y.; CDL:070072-A)

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00082414 Chas. Pfizer & Company, Incorporated (1955?) Residue of Oxytetracycline on Salmon. (Unpublished study received Dec 5, 1956 under PP0111; CDL:092392-AS)

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00088410 Nyland, G. (1973) Letter sent to Charles Strickler dated Dec. 26, 1973: Terramycin residues in pears. (Unpublished study received Jan 11, 1974 under 4E1460; prepared by Univ. of California--Davis, Agricultural Experiment Station, Dept. of Plant Pathology, submitted by California, Dept of Food and Agriculture, Sacramento, Calif.; CDL:093892-A)

00093604 Chas. Pfizer & Company (1967) Oxytetracycline for Control of Bacterial Spot of Peach. (Compilation; unpublished study, including published data, received Mar 20, 1967 under 7G0584; CDL: 092392-A)

00103387 Pfipharmecs (1954) Antibiotic Residue Studies in Various Fruits and Vegetables. (Compilation; unpublished study received May 26, 1954 under 1007-6; CDL:101537-A)

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00108926 Chas. Pfizer & Co., Inc. (1956) Residues of Antibiotics in Chickens. (Compilation; unpublished study received Apr 9, 1956 under PPO111; CDL:090140-S)

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00109144 Pfipharmecs (1976) Chemical Study: Myco-shield Brand of Agricultural Terramycin. (Compilation; unpublished study received Sep 3, 1976 under 1007-EX-9; CDL:225537-A)

00109572 New York State Agricultural Experiment Station (1975) Peach Residue Study QCSA 71729 Results. (Unpublished study received Sep 8, 1975 under 37787-EX-1; CDL:248058-B)

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00116891 California, Dept. of Food and Agriculture (1973) Supportive Data for the Proposed Amendment of the Tolerance Statement on the Use of Terramycin to Control Pear Decline. (Compilation; unpublished study; CDL:092038-A)

00121730 Chas. Pfizer & Co. (1968) Residue Study: Terramycin in Peaches. (Compilation; unpublished study received 1968 under 7GO584; CDL: 092872-B)

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00125058 Pfipharmecs (1956) Efficacy: Oxytetracycline. (Compilation; unpublished study received Jul 31, 1956; Jun 6, 1956; May 10, 1956 under PPOO53; CDL:092334-A)

00125538 Pfipharmecs (1957) Study of the Residue of Oxytetracycline in Salmon. (Compilation; unpublished study received 1957 under PPO111; CDL:092393-A)

00147208 Interregional Research Project No. 4 (1985) Results of Tests on the Amount of Oxytetracycline Base Activity Remaining in Pear Treated up to 14 days before harvest. Unpublished compilation. 44 p.

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00164419 McMahan, J.; Malaspina, A. (1955) Report on Antibiotic Residues in Cooked Poultry: [Oxytetracycline and Chlortetracycline]. Unpublished study prepared by Pfizer, Inc. 11 p.

00164610 Pfipharmecs Div., Pfizer Inc. (1974) Terramycin Tree Injection Formula: [Product Chemistry]. Unpublished compendium. 20 p.

05001575 Palm, E.T.; Young, R.A. (1957) The compatibility of certain organic fungicides and antibiotics in treatment mixtures as indicated by stability and phytotoxicity. Plant Disease Reporter 41(3):151-155.

TABLE A. GENERIC DATA REQUIREMENTS FOR OXYTETRACYCLINE.

Data Requirement	Test substance[1]	Does EPA have data?	Bibliographic citation	Must additional data be submitted?	Time frame for submission[2]
158.125 Residue Chemistry					
171-2. Chemical Identity[3]					
171-3. Directions for use		(See Index)			
171-4. Nature of the residue (Metabolism) - Plants		No	N/A	No[4]	
171-4. Nature of the residue (Metabolism) - Livestock		No	N/A	No[5]	
171-4. Residue analytical methods	TGAI	Partially	00058254.	Yes[6,7]	15 months
171-4. Storage stability		Yes	00081151.	No	
171-4. Magnitude of the residue in plants					
Pome Fruits - Pears	TEP	Partially	00039917. 00049096. 00081266. 00162260.	Yes[8,9,10]	18 months
Stone Fruits - Peaches	TEP	Yes	00064602. 00081153. 00093605. 00135300.	No	

(Continued).

TABLE A. GENERIC DATA REQUIREMENTS FOR OXYTETRACYCLINE.

Data Requirement	Test substance[1]	Does EPA have data?	Bibliographic citation	Must additional data be submitted?	Time frame for submission[3]
171-4. Magnitude of residue in Meat/Milk/Poultry/Eggs		No	N/A	No[11]	

1. Test substance: TGAI = technical grade of the active ingredient; PAI = purified active ingredient; PAIRA = purified active ingredient, radiolabeled; TEP = typical end-use product; EP = end-use product.

2. Data must be submitted within the indicated time frame, based on the date of this Guidance Document.

3. The same chemical identity data are required as under 158.120, with emphasis on impurities that could constitute residue problems. Refer to Product Chemistry Data Requirements tables.

4. Data were not submitted regarding the nature of the residue of oxytetracycline in plants. Toxicology Branch has assessed the need for data reflecting the metabolism of oxytetracycline in plants and has concluded that these data are not required.

5. 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.

6. The registrant must submit a method suitable for enforcement, such as an HPLC method, and provide validation data including precision, accuracy, and limits of detection.

7. The registrant must submit validation data (precision, accuracy and limits of detection) for the bioassay method used to generate the existing residue chemistry data base. If the requested validation data indicate that the method is not sufficiently sensitive to determine oxytetracycline residues in or on plant commodities at the level of the presently established tolerances, appropriate tolerance levels must be proposed.

8. Data depicting residues of oxytetracycline in or on pears harvested 60 days after the last of 10 foliar applications of the 17% WP at 0.09 lb act/A in 3-10 gal water/A using aerial equipment in WA only [EPA SLN No. WA820038]. Residue data must be obtained using a fully validated analytical method.

TABLE A. Footnotes (Continued).

9. Data depicting residues of oxytetracycline in or on pears harvested at the shortest practical interval after the last of two injections of the 21.6% SC/S at 5.68 g act/tree in CA only [EPA SLN No. CA780009]. Residue data must be obtained using a fully validated analytical method.

10. Data depicting residues of oxytetracycline in or on pears harvested at the shortest practical interval following a single injection of the 21.6% SC/S at 0.1 g act/tree made prior to near bloom formation. Tests must be conducted in CT [EPA SLN No. CT780003]. Residue data must be obtained using a fully validated analytical method.

11. 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.