Approval Date: March 14, 1996

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 008804

B. Sponsor

Phibro Animal Health
West Chester, PA 19380-6014

C. Proprietary Name

Terramycin-10, 20, 50, 50D, 100, 100D, 100SS, & 200

D. Established Name

Oxytetracycline Type A Medicated Article

E. Dosage Form

Type A Medicated article

F. Dispensing Status

OTC

G. Route of Administration

Oral

H. Dosage and Indication

Animal	Dosage	Indications of Use
Chickens	10-50 g/t	For broiler/fryer chickens: for an increased rate of weight gain and improved feed efficiency. (Use continuously)
Chickens	100-200 g/t	Control of infectious synovitis caused by Mycoplasma synoviae; control of fowl cholera caused by Pasteurella multocida sensitive to oxytetracycline. (Feed continuously for 7 to 14 days)
Chickens	400 g/t	Control of chronic respiratory disease (CRD) and air sac infection caused by Mycoplasma gallisepticum and Escherichia coli susceptible to oxytetracycline. (Feed continuously for 7 to 14 days) WARNING: Zero-day withdrawal period. In low calcium feeds withdraw 3 days before slaughter. Do not administer to chickens producing eggs for human consumption.

Animal	Dosage	Indications of Use
Chickens	500 g/t	Broiler chickens: Reduction of mortality due to air sacculitis (air-sac-infection) caused by Escherichia coli susceptible to oxytetracycline. (Feed for 5 days) WARNING: 24 hours withdrawal period. In low calcium feeds withdraw 3 days before slaughter. Do not administer to chickens producing eggs for human consumption.
Turkeys	10-50 g/t	For growing turkeys: For an increased rate of weight gain and improved feed efficiency. (Use continuously)
Turkeys	200 g/t	Control of infectious synovitis caused by Mycoplasma synoviae susceptible to oxytetracycline. (Feed continuously for 7 to 14 days)
Turkeys	100 g/t	Control of hexamitiasis caused by Hexamita meleagrides susceptible to oxytetracycline. (Feed continuously for 7 to 14 days) Control of complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis) susceptible to oxytetracycline. (Feed continuously for 7 to 14 days) WARNING: At 200 g/ton use level or higher, withdraw 5 days before slaughter. Zero-day withdraw period for lower use levels. Do not administer to turkeys producing eggs for human consumption.
Swine	10-50 g/t	For an increased rate of weight gain and improved feed efficiency. (Use continuously)
Swine	10 mg/lb	Treatment of bacterial enteritis caused by Escherichia coli and Salmonella choleraesuis susceptible to oxytetracycline and control of bacterial pnuemonia caused by Pasteurella multocida susceptible to oxytetracycline. (Feed continuously for 7 to 14 days)
Swine	10 mg/lb	For breeding swine: Leptospirosis (reducing the instances of abortions and shedding of leptospirae) caused by Leptospira pomona susceptible to oxytetracycline. (Feed continuosly for 14 days) WARNING: 5 days withdrawal at 10mg/lb dosage.
Calves, Beef Cattle and Nonlactating Dairy Cattle	0.05-0.1 mg/lb	For calves (up to 250 lbs): For an increased rate of weight gain and improved feed efficiency. (Use continuously)
Calves, Beef Cattle and Nonlactating Dairy Cattle	25 mg/head/day	For calves (250-400 lbs): For an increased rate of weight gain and improved feed efficiency. (Use continuously)
Calves, Beef Cattle and Nonlactating Dairy Cattle	75 mg/head/day	For growing cattle (over 400 lbs): For an increased rate of weight gain, improved feed efficiency and reduction of liver condemnatiøn due to liver abscesses. (Use continuously)
Calves, Beef Cattle and Nonlactating Dairy Cattle	0.5-2.0 g/head/day	For the prevention and treatment of the early stages of the shipping fever complex. (Feed 3-5 days before and after arrival in feedlots.)

Animal	Dosage	Indications of Use
Calves, Beef Cattle and Nonlactating Dairy Cattle	10 mg/lb	For the treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia (shipping fever complex) caused by Pasteurella multocida susceptible to oxytetracycline. (Feed continuously for 7 to 14 days) WARNING: 5 days withdrawal at 10 mg/lb dosage. When used in milk replacers, the treatment claim (10 mg/lb) is limited to bacterial enteritis caused by Escherichia coli only.
Sheep	10-20 g/t	For an increased rate of weight gain and improved feed efficiency. (Use continuously)
Sheep	10 mg/lb	Treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida susceptible to oxytetracycline. (Feed continuously for 7 to 14 days) WARNING: 5 days withdrawal at 10 mg/lb dosage
Honey bees	200 mg/colony	For control of American Foulbrood caused by Bacillus larvae, and European Foulbrood caused by Streptococcus pluton susceptible to oxytetracycline. WARNING: Remove at least 6 weeks prior to main honey flow.
Lobsters	1 g/lb	For control of gaffkemia in lobsters caused by Aerococcus viridans. (Feed for 5 days as the sole ration) WARNING: Withdraw from feed 30 days before harvesting lobsters.
Pacific salmon	250 mg per kilogram of fish per day (11.35 g per 100 lb of fish per day)	For marking of skeletal tissue. (For salmon not over 30 g body weight; administer as sole ration for 4 days in feed) WARNING: Do not liberate fish for at least 7 days following the last administration of medicated feed.
Salmonids	2.5 to 3.75 g per 100 lb of fish per day	Control of ulcer disease caused by Hemophilus piscium furunculosis caused by Aeromonas salmonicida, bacterial hemorrhagic septicemia caused by Aeromonas liquefaciens, and pseudomonas disease. Administer oxytetracycline in mixed ration for 10 days) WARNING: Do not liberate fish or slaughter fish for food for 21 days following the last administration of medicated feed; do not administer when water is below 9 degrees centigrade (48.2 degrees F).
Catfish	2.5 to 3.75g per 100 lb fish per day	Control bacterial hemorrhagic septicemia caused by Aeromonas liquefaciens and pseudomonas disease. (Administer oxytetracycline in mixed ration for 10 days) WARNING: Do not liberate fish or slaughter fish for food for 21 days following the last administration of medicated feed; do not administer when water is below 16 .7 degrees centigrade (62 degrees F).

I. Effect of Supplement

This supplement establishes a zero-day withdrawal period for swine administered oxytetracycline at 10 mg/lb/day for 14 days.

II. EFFECTIVENESS

The drug was the subject of National Academy of Science/National Research Council (NAS/NRC) reports which were published in the FEDERAL REGISTER of May 5, 1970 (FR 70-5446). The Academy evaluated the product as probably effective when used for the control and treatment of specific diseases of livestock and poultry and concluded that use may result in faster gains and improved feed efficiency under appropriate conditions.

The Academy evaluated the subject premix as probably effective when used for the control and treatment of specific diseases of livestock (swine, cattle, sheep,) and poultry (broiler chickens, laying chickens and turkeys),and concluded that the use result in faster gains and improved feed effciency under appropriate conditions.

The Academy concluded that:

1. Labels and package inserts require extensive revision. There is inadequate documentation of claims, excessive claims are made and bold conclusions are reached in the absence of sufficient controlled experimental evidence.
2. Claims for growth promotion or stimulation are not allowed and claims for faster gains and/or feed efficiency should be stated as "may result in faster gains and/or improved feed efficiency under appropriate conditions."
3. Each disease claim should be properly qualified as "appropriate for use in (name of disease) caused by pathogens sensitive to (name of drug)" and if the disease cannot be so qualified the claim must be dropped.
4. The label claims "for prevention of" or, "to prevent" should be replaced with "as an aid in the control of" or, "to aid in the control of."
5. The label claim pertaining to egg production and hatchability should be modified to read, "May aid in maintaining egg production and hatchability, under appropriate conditions, by controlling pathogenic organisms."
6. The labels should carry a warning that treated animals under the conditions that prevail must actually consume sufficient medicated medicated feed, to constitute a therapeutic dose. As a precaution the labels should state what the desired oral dose is in terms of animal weight per day for each species to serve as a guide to effective use of the preparations in feed.
7. The labels should declare the dosage for the treatment of individual animals in terms of the amount of drug which should be given per unit of animal weight.

The Food and Drug Administration concurs with the Academy's findings, interpreting the phrase "...cannot be so qualified..." in paragraph (3) to mean "...is not supported by adequate data..." (See Fed. Reg. vol. 35, NO. 87-Tues, May 5, 1970). FDA then proceeded to review all available data relating to the effectiveness of products subject to NADA 8-804 to determine which label claims were supported by the requisite proof of effectiveness. That review resulted in a letter to the firm dated December 5, 1991, in which the agency stated that it had concluded that such data supported effectiveness for the control and treatment of bacterial diseases susceptible to oxytetracycline hydrochloride in poultry, cattle, swine, sheep, and bees.

Thereafter, the sponsor complied with the evaluation of NAS/NRC and FDA's conclusions by submitting a supplemental application which revised the labeling of its oxytetracycline pre-mix in the following manner:

1. Appropriate oral doses for all the allowable species and claims based on milligrams per pound or grams per ton are on the current labels.
2. Claims pertaining to egg production and hatchablilty have been deleted from the labels.
3. Each disease claim on the label has been properly qualified with the approriate genus and species of bacteria susceptible to oxytetracycline quaternary salts. Disease claims which were not so qualified have been deleted.
4. Claims made for prevention have been revised to read "Control of..." where appropriate.
5. Claims for growth promotion or stimulation have been removed. Allowable claims are for increased rate of weight gain and improved feed effieciency.
6. The manufacturer's label carries the warning statement that treated animals must have the medicated feed adjusted to compensate for variation in age and the weight of animals, the nature and severity of disease signs.

III. TARGET ANIMAL SAFETY

No further safety data are required.

IV. HUMAN FOOD SAFETY

The NAS/NRC evaluation of the drug is concerned only with the effectiveness and safety of the drug for the treated animal. FDA's approval of the supplemental application did not involve reevaluation or reaffirmation of the human food safety data in the parent application.

REGULATORY METHOD FOR RESIDUES

The regulatory analytical method for detection of residues of the drug is a microbiological test using Bacillus cereus var. mycoides (AtCC 11778) suspension. The method is as published by the Food and Drug Administration, "Antibiotic Residues in Milk, Dairy Products an Animal Tissues: Method, Reports, and Protocols, revised October 1968, reprinted December 1974.

V. AGENCY CONCLUSIONS

The DESI finalization supplemental NADA satisfies the requirements of section 512 of the Act and demonstrates that Oxytetracycline Type A Medicated Article (Terramycin) when used under its proposed conditions of use, is safe and effective for the labeled indications. The approval provides for use of Oxytetracycline Type A Medicated article for the control and treatment of specific diseases in swine, cattle, sheep, poultry, lobster, fish and honey bees.

The "probably effective" finding of the NAS/NRC regarding Oxytetracycline hydrochloride which was published in the FEDERAL REGISTER of May 5, 1970, was subsequently reviewed by FDA, resulting in the upgrade to "effective" status with respect to the claims noted in the previous paragraph. The firm submitted revised labeling to conform and, therefore, this supplemental NADA complies with the NAS/NRC evaluation and FDA's conclusions.

Oxytetracycline Type A Medicated Article for use in food-producing animals is currently on the market as an over-the-counter product. When the NADA was reviewed under NAS/NRC/DESI program, it was an over-the-counter product and this marketing status

remains unchanged. Therefore, the Center for Veterinary Medicine has concluded that this product should retain over-the-counter marketing status.

Additionally, this supplemental application is providing for addition of the previous approved claims for lobster, catfish, pacific salmon and salmonids under Pfizer's NADA 38-439,currently codified in the FEDERAL REGISTER, 558.450 on the 50 D and 100 D (dextrose) labels appoved under NADA 8-804.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), these are Category ll changes. The approval of these changes is not expected to have any adverse effect on the safety or effectiveness of this new animal drug and, therefore, did not require a reevaluation of the human food or target animal safety data in the parent application.

Under the Generic Animal Drug and Patent Term Restoration Act of 1988, these approvals do not qualify for an exclusivity period under section 512(c)(2)(F)(iii) of the Federal, Food, Drug, and Cosmetic Act (21 U.S.C. 360b (c)(2)(F)(iii)) because the supplemental applications do not contain reports of new clinical or field investigations (other than bioequivalence or residue studies) and in the case of food producing animals, human food safety studies (other than bioequivalence or residue studies) essential to the approval were conducted or sponsored by Pfizer.

VI. LABELING

Copies of applicable labels may be obtained by writing to the:

Freedom of Information Office
Freedom of Information Staff (HFI-35)
5600 Fishers Lane

Rockville, MD 20855

Or requests may be sent via fax to: (301) 443-1726. If there are problems sending a fax, call (301) 443-2414.

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.