Approval Date: July 9, 2000

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 008-622

B. Sponsor

Pfizer Inc.
Lee's Summit, MO 64081

C. Proprietary Name

Terramycin Soluble Powder

D. Established Name

oxytetracycline soluble powder

E. Dosage Form

Soluble Powder

F. Dispensing Status

OTC

G. Dosage Regimen

10mg/pound body weight (cattle, swine, and sheep), various concentrations in water for poultry, and in food for honey bees.

H. Route of Administration

Oral

I. Indication

Calves, Beef Cattle and Non-Lactating Dairy
Control and treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia (shipping fever complex) caused by Pasteurella multocida susceptible to oxytetracycline.

Sheep
Control and treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida susceptible to oxytetracycline.

Swine
Control and treatment of bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesis* bacterial pneumonia caused by *Pasteurella multocida* susceptible to oxytetracycline. For Breeding Swine: Leptospirosis (reducing the incidence of abortions and shedding of leptospira) caused by *Leptospira pomona*.

Chickens
Infectious synovitis caused by *Mycoplasma synoviae*, chronic respiratory disease (CRD) and air sac infection caused by *Mycoplasma gallisepticum* and *Escherichia coli*, and fowl cholera caused by *Pasteurella multocida* susceptible to oxytetracycline.

Turkeys
Control of hexamitiasis caused by *Hexamita meleagridis* susceptible to oxytetracycline, control of infectious synovitis caused by *Mycoplasma synoviae* susceptible to oxytetracycline. Growing turkeys-control of complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis) susceptible to oxytetracycline.

Honey Bees
Control and treatment of American and European Foulbrood caused by Bacillus larvae

J. Effect of Supplement

One supplemental application is a Category II change to bring the drug product into compliance with the National Academy of Science/National Research Council Drug Efficacy Study Implementation (NAS/NRC/DESI) recommendations. The other supplemental application is a Category II change providing for a tolerance of O.1 ppm in uncooked edible tissues in sheep.

II. EFFECTIVENESS

NADA 008-622 was originally approved as safe for use as labeled on September 17, 1952. The drug was the subject of National Academy of Sciences/National Research Council (NAS/NRC) reports which were published in the FEDERAL REGISTER of May 5, 1970 (FR 70-5446). The Academy evaluated Terramycin Animal Formula Soluble Powder as effective for use in the treatment of hexamitiasis. They 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 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 water, or 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 drinking water or 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 008-622 to determine which label claims were supported by the requisite proof of effectiveness. That review resulted in a letter to the firm dated February 19, 1982, 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 HCl soluble powder in the following manner:

1. The appropriate oral dose of 10 mg per pound body weight daily in each species (swine, cattle, and sheep) has been incorporated in the labeling.
2. Claims for growth promotion or feed efficiency are not included.
3. Each disease claim on the label has been properly qualified with the appropriate genus and species name susceptible to oxytetracycline hydrochloride. 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 egg production and hatchability are not included.
6. The manufacturer's label carries the warning statement that treated animals must have the medicated water adjusted to compensate for variation in age and the weight of the animal, the nature and severity of disease signs, and environmental temperature and humidity, each of which affects water consumption.
7. The labels carries the appropriate dosage for the treatment of individual animals in terms of the amount of drug which should be given per unit of animal weight.

III. TARGET ANIMAL SAFETY

NADA 008-622 was originally approved as safe on September 17, 1952. 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 re-evaluation or reaffirmation of the human food safety data in the parent application. The firm submitted a separate supplement requesting a tolerance of 0.1 ppm for uncooked edible tissues in sheep be codified.

WITHDRAWAL TIMES:
Turkeys, swine, cattle and sheep: 5 days
Honey Bees-Remove at least 6 weeks prior to main honey flow.

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 Soluble Powder (Terramycin) when used under its proposed conditions of use, is safe and effective for the labeled indications. The approval provides for use of Oxytetracycline Soluble Powder for the control and treatment of specific diseases in swine, cattle, sheep, poultry 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 Soluble Powder 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, the supplemental application providing for addition of the tolerance of 0.1 ppm in uncooked edible tissues in sheep is acceptable and approved.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), these are Category II changes. The approval of this 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 re-evaluation 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 and conducted or sponsored by the applicant were required.

VI. Attachments

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

Food and Drug Administration
Freedom of Information Staff (HFI-35)
5600 Fishers Lane
Rockville, MD 20857

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.