Date of Approval Letter: April 25, 2001

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 008-622

TERRAMYCIN®
(oxytetracycline hydrochloride)
Soluble Powder

and

TERRAMYCIN-343®
(oxytetracycline hydrochloride)
Soluble Powder

"removal of withdrawal period for swine"

Sponsored by:

Pfizer Inc.

I. GENERAL INFORMATION

NADA Numbers:	008-622
Sponsor:	Pfizer, Inc. 235 East 42nd Street New York, New York 10017
Established Names:	oxytetracycline hydrochloride
Proprietary Names:	TERRAMYCIN® Soluble Powder TERRAMYCIN-343® Soluble Powder
Marketing Status:	Over-the-counter (OTC)
Effect of Supplements:	This supplement establishes a zero-day withdrawal period for swine administered oxytetracycline at 10 mg/lb/day for 14 days.

II. INDICATIONS FOR USE

TERRAMYCIN® and TERRAMYCIN-343® Soluble Powder are indicated for a variety of bacterial infections in cattle, sheep, chickens, turkeys, and honeybees associated with organisms susceptible to oxytetracycline.

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*.

SHEEP: Control and treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia (shipping fever complex) caused by *Pasteurella multocida*.

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

CHICKENS: Control of 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*.

TURKEYS: Control of hexamitiasis caused by *Hexamita meleagridis* and infectious synovitis caused by *Mycoplasma synoviae*. Growing turkeys- complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis).

HONEYBEES: Control and treatment of American Foulbrood caused by *Bacillus larvae*.

III. DOSAGE

A. Dosage Form: Water-soluble powder

B. Route of Administration: Oral, via drinking water

C. Recommended Dosage: 10 mg/pound body weight for 14 days (cattle, swine and sheep); 200 mg/colony in 3 applications at 4- to 5-day intervals for honey bees; 200-800 mg/gal for 7-14 days for chickens depending on claim; and 200-400 mg/gal for 7-14 days for turkeys depending on claim; and 25 mg/lb body weight daily for 7-14 days for growing turkeys.

IV. EFFECTIVENESS

No further effectiveness data were required.

V. ANIMAL SAFETY

No further target animal safety data were required.

VI. HUMAN FOOD SAFETY

A. Toxicity Studies: NADA 008-622 was originally approved as safe for use as labeled on May 5, 1970.

B. Safe Concentrations of Total Residues: As documented in the FOI Summary dated May 31, 1996 for NADA 113-232.

C. Tolerance for the marker residue: As documented in the FOI Summary dated May 31, 1996, and codified at 21 CFR 556.500 (61 FR 67453; Dec. 23, 1996) tolerances are established for the sum of residues of the tetracyclines, including chlortetracycline, oxytetracycline, and tetracycline, in tissues of cattle, beef calves, non-lactating dairy cattle, dairy calves, swine, sheep, chickens, turkeys, catfish, lobsters, and salmonids, as follows: 2 parts per million (ppm) in muscle, 6 ppm in liver, and 12 ppm in fat and kidney.

D. Study establishing the withdrawal period in swine

Pfizer Study Number 2522D-60-97-100

1. Purpose: A tissue residue study was conducted to determine the depletion profile of oxytetracycline in uncooked porcine liver, kidney, muscle, and fat at various

withdrawal times following treatment for 14 days with oxytetracycline HCl medicated water at a dose rate of 10 mg OTC HCl/lb BW/day.

2. Investigators: This study was conducted in two phases.

Phase one: (live phase)	Southwest Bio-Labs, Inc. 401 N. 17th Street Las Cruces, NM 88085
Phase two: (microbiological analysis)	Colorado Animal Research Enterprises (CARE) 6200 E. County Rd. 56 Fort Collins, CO 80524

3. Animals: thirty crossbred swine (15 gilts and 15 barrows)

4. Dosage form and dosage: medicated water at a rate to 10 mg OTC HCl/lb BW/day

5. Parameters measured and assay: Oxytetracycline (parent) residues were measured in liver, kidney, muscle, and fat using the regulatory analytical (microbiological) method. LOQ for liver and kidney was 100 ppb; for muscle and fat the LOQ was 75 ppb (microassay).

6. Results of tissue residue study:

Table 6.1. Group oxytetracycline (parent) residues (mean ± SD) in tissues from swine treated with TERRAMYCIN® Soluble Powder in water at a dose rate of 10 mg/lb/day for 14 days as determined by official microbiological assay

Group	Sacrifice Time (hr)	Parent oxytetracycline (ppb)			
		Liver	Kidney	Muscle	Fat
II	10†	370 ±73	1345 ±260	297 ±44	141 ±34
III	24	177 ±53	524 ±134	230 ±55	*
IV	48	302 ±4	692 ±612	189 ±32	*
V	72	200 ±12	339 ±243	172 ±54	*
VI	120	*	198 ±16	*	*
VII	168	*	204 ±49	*	*

†Times below 12 hours support assignment of a zero-day withdrawal period.
*Values were below the limit of quantitation (LOQ).

Tissue residue depletion data support the assignment of a zero withdrawal period for swine.

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

VII. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA satisfy the requirements of Section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that residues of TERRAMYCIN® Soluble Powder and TERRAMYCIN-343® Soluble Powder are safe at a zero-day withdrawal period when these products are administered to swine for 14 days at a level of 10 mg/lb body weight/day.

Tolerances are established in 21 CFR 556.500 for the sum of residues of the tetracyclines, including chlortetracycline, oxytetracycline, and tetracycline, in tissues of cattle, beef calves, non-lactating dairy cattle, dairy calves, swine, sheep, chickens, turkeys, catfish, lobsters, and salmonids, as follows: 2 parts per million (ppm) in muscle, 6 ppm in liver, and 12 ppm in fat and kidney.

There is reasonable certainty that the conditions of use, including directions on labeling can and will be followed in practice. Accordingly, the Agency has concluded that this product shall retain over-the-counter marketing status.

In accordance with 21 CFR 514.106(b)(2)(x) this is a Category II change which did not require reevaluation of safety or effectiveness data in the parent application.

The Agency has carefully considered the potential environmental effects of this action and has concluded that the action is categorically excluded under 21 CFR 25.33(a)(1) from the requirement to prepare an environmental assessment (EA).

Under section 512(c)(2)(F)(iii) of the FFDCA, this approval for food-producing animals does not qualify for marketing exclusivity because the supplemental application does not contain substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food-producing animals, human food safety studies (other than bioequivalence or residue studies) required for the approval and conducted or sponsored by the applicant.

VIII. APPROVED PRODUCT LABELING

A. Facsimile label - Terramycin® Soluble Powder 6.4 oz, 24.8 lb (62 x 6.4 oz unit packages)

B. Facsimile label – Terramycin-343® 4.78 oz, 9.55 oz, and 4.5 lb

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

Freedom of Information Office
FDA/Center for Veterinary Medicine
7500 Standish Place
Rockville, MD 20855