

NFA-305

(Dockets Manager
Branch)

Date of Approval Letter:

APR 25 2001

2118 '01 MAY 24 P3:37

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.

NADA 8-622

FOIS 1

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: Southwest Bio-Labs, Inc.
(live phase) 401 N. 17th Street
Las Cruces, NM 88085

Phase two: Colorado Animal Research Enterprises (CARE)
(microbiological analysis) 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 FFDCFA, 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

INDICATIONS AND DIRECTIONS FOR USE
 For the control of the following poultry diseases caused by organisms susceptible to oxytetracycline: Add the following amount to 2 gallons of stock solution when proportioner is set to meter at the rate of 1 ounce per gallon.

CHICKENS Infectious synovitis caused by *Mycoplasma synoviae*
 200-400 mg/gal 5-10
PACKS/2 GALLONS
STOCK SOLUTION

Chronic respiratory disease (CRD) and air sac infection caused by *Mycoplasma gallisepticum* and *Escherichia coli*
 400-800 mg/gal 10-20
10-20

Fowl cholera caused by *Pasteurella multocida*
 200-400 mg/gal 5-10
5-10

Hexamitiasis caused by *Hexamita meleagridis*
 400 mg/gal 10
10

Growing Turkeys—Complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis)
 25 mg/lb body weight daily
 Varies with age & water consumption (1 packet will treat 400 lb of turkeys)

TURKEYS Do not administer to turkeys, cattle or sheep within 5 days of slaughter. Zero-day slaughter withdrawal in swine. Do not administer to chickens or turkeys producing eggs for human consumption. Do not administer this product with milk or milk replacers. Administer 1 hour before or 2 hours after feeding milk or milk replacers.

RECOMMENDED STORAGE: STORE BELOW 25°C (77°F)
FOR ANIMAL USE ONLY
 KEEP OUT OF REACH OF CHILDREN
 Restricted Drug(s) (California), Not For Human Use, Use Only As Directed.
 Refer to package insert for complete directions.

Distilled by
Animal Health
 Kenilworth, NJ 07033
 Div. of Pfizer Inc.
 NY, NY 10017

TO OPEN CUT HERE

Terramycin®
 (oxytetracycline HCl)
 Soluble Powder

A broad-spectrum
antibiotic
 for control and treatment of specific diseases
 in poultry, cattle, swine, sheep, and bees.

This packet contains 10 grams of oxytetracycline HCl

For oral use only

NADA #8-622, Approved by FDA

Net Weight: 6.4 oz (181.4 g)

4163

FOR THE CONTROL AND TREATMENT OF THE FOLLOWING DISEASES CAUSED BY ORGANISMS SUSCEPTIBLE TO OXYTETRACYCLINE:

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

CATTLE, BEEF CATTLE AND NON-LACTATING DAIRY CATTLE
 Bacterial pneumonia (shipping fever complex) caused by *Pasteurella multocida*
 Bacterial enteritis caused by *Escherichia coli*

SHEEP
 Bacterial pneumonia (shipping fever complex) caused by *Pasteurella multocida*
 Bacterial enteritis caused by *Escherichia coli*

HONEY BEES
 For control of American foulbrood caused by *Bacillus larvae*
 The drug is administered in 3 applications of sugar syrup or 3 dustings at 4 to 5-day intervals. The drug should be fed early in the spring or fall and consumed by the bees before main honey flow begins to avoid contamination of production honey.
 Remove at least 6 weeks prior to main honey flow.

CAUTION: Use as sole source of oxytetracycline. Prepare fresh solutions every 24 hours. Special Note: The concentration of drug required in medicated water must be adequate to compensate for variation in the age of the animal, feed consumption rate and the environmental temperature and humidity, each of which affects water consumption.
FOR USE IN DRINKING WATER ONLY, NOT FOR USE IN LIQUID FEED SUPPLEMENTS.

92 01-2358-35-X1
 Made in USA





Animal Health
Eaton, PA 15941, USA
Div. of Pfizer Inc.
NY, NY 10017

Distributed by
Pfizer
Keep Out of Reach of Children
For Animal Use Only
Store Below 25°C (77°F)
Not for Human Use
Restricted Drug (California)—Use Only As Directed

CAUTION: Use as sole source of oxytetracycline. Prepare fresh solutions every 24 hours. Special Note: The concentration of drug required in medicated water must be adequate to compensate for variation in the age of the animal, feed consumption rate, and the environmental temperature and humidity, each of which affects water consumption.
WARNING: Do not administer to turkeys, cattle or sheep within 5 days of slaughter. Zero-day slaughter withdrawal in swine. Do not administer to chickens or turkeys producing eggs for human consumption. Do not administer this product with milk or milk replacers. Administer 1 hour before or 2 hours after feeding milk or milk replacers.
FOR USE IN DRINKING WATER ONLY. NOT FOR USE IN LIQUID FEED SUPPLEMENTS.

62 x 4163
Terramycin®
(oxytetracycline HCl)
Soluble Powder

A broad-spectrum antibiotic for control and treatment of specific diseases in poultry, cattle, swine, sheep, and bees.

Each packet contains 10 grams of oxytetracycline HCl.

For oral use only

Net Contents: 24.8 lb (11.3 kg)
(62 x 6.4 oz unit packages)

NADA 88-622. Approved by FDA



INDICATIONS AND DIRECTIONS FOR USE: Terramycin Soluble Powder is indicated for the treatment of specific diseases caused by organisms susceptible to oxytetracycline. Add the following amount to 2 gal of stock solution when proportioned to treat at the rate of 1 cc/gal.

INDICATIONS	DOSE	PACKS/GAL OF STOCK SOLUTION
CHICKENS Infectious synovitis caused by <i>Mycoplasma synoviae</i> Chronic respiratory disease (CRD) and air sac infection caused by <i>Mycoplasma gallisepticum</i> and <i>Escherichia coli</i> Fowl cholera caused by <i>Pasteurella multocida</i>	200-400 mg/gal 400-800 mg/gal 400-800 mg/gal	5-10 10-20 10-20
TURKEYS Hemorrhagic enteritis caused by <i>Haematis colicarpa</i>	200-400 mg/gal	5-10
INFECTIOUS SYNOVITIS caused by <i>Mycoplasma synoviae</i> For growing turkeys—Complicating bacterial organisms associated with <i>Salmonella</i> (nontyphoid enteritis, colicarpa) or <i>Yersinia</i> Necrotic enteritis at the first clinical signs of disease and continue for 7-14 consecutive days. If improvement is not noted within 24-48 hours, consult a poultry diagnostic laboratory or poultry pathologist to determine diagnosis and determine dosage. For the control and treatment of the following diseases caused by organisms susceptible to oxytetracycline:	400 mg/gal 25 mg/lb of body weight daily	10 Varies with age & water consumed (400 lb of turkey)
SWINE Bacterial enteritis caused by <i>Escherichia coli</i> , <i>Shigella dysenteriae</i> For breeding swine—Leptospirosis (including the incidence of abortion and shedding of leptospira) caused by <i>Leptospira pomona</i>	200 mg/gal	10
CALVES, BEEF CATTLE AND NONLACTATING DAIRY CATTLE Bacterial enteritis caused by <i>Escherichia coli</i> Bacterial pneumonia (shipping fever complex) caused by <i>Pasteurella multocida</i>	200 mg/gal	10
SHEEP Bacterial enteritis caused by <i>Escherichia coli</i> Bacterial pneumonia (shipping fever complex) caused by <i>Pasteurella multocida</i>	200 mg/gal	10
HONEY BEES For control of American foulbrood caused by <i>Bacillus larvae</i>	200 mg/culture	10

The packet will treat 1000 lb. of swine, cattle or sheep at 10 mg/lb.
Administer in the drinking water at a level of 10 mg of oxytetracycline HCl per lb. of body weight daily. Administer up to 14 days.
Administer in the drinking water at a level of 10 mg of oxytetracycline HCl per lb. of body weight daily. Administer up to 14 days.
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Administer in the drinking water at a level of 10 mg of oxytetracycline HCl per lb. of body weight daily. Administer up to 14 days.

Remove at least 8 weeks before main honey flow.

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10 3/4" (W) with 1/2" Tab x 4 1/2" (H)



PMS 116 PMS 485 Black

03-2358-35-X1 Draft #1 2/23/99

INDICATIONS AND DIRECTIONS FOR USE
 For the control of the following poultry diseases caused by organisms susceptible to oxytetracycline: Add 1 tub of soluble powder to the amounts of water listed below to make a stock solution for use in a proportioner set to meter at the rate of 1 ounce per gallon.

	DOSAGE	GAL OF STOCK SOLUTION PER TUB
CHICKENS	200-400 mg/gal	60-30
Infectious synovitis caused by <i>Mycoplasma synoviae</i>	400-800 mg/gal	30-15
Chronic respiratory disease (CRD) and air sac infection caused by <i>Mycoplasma gallisepticum</i> and <i>Escherichia coli</i>	400-800 mg/gal	30-15
Fowl cholera caused by <i>Pasteurella multocida</i>	200-400 mg/gal	60-30
TURKEYS	400 mg/gal	30
Hexamitiasis caused by <i>Hexamita meleagridis</i>	25 mg/lb body weight daily	Varies with age & water consumption (1 tub will treat 61,740 lb of turkeys)
Infectious synovitis caused by <i>Mycoplasma synoviae</i>		
Infactious synovitis—Complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis)		
Growing Turkeys—Complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis)		
Medicate continuously at the first clinical signs of disease and continue for 7-14 consecutive days. If improvement is not noted within 24-48 hours, consult a poultry diagnostic laboratory or poultry pathologist to determine diagnosis and advice on dosage.		
For the control and treatment of the following diseases caused by organisms susceptible to oxytetracycline:		
SWINE	DOSAGE	
Bacterial enteritis caused by <i>Escherichia coli</i> and <i>Salmonella choleraesuis</i>	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per lb of body weight daily. Administer up to 14 days.	
Bacterial pneumonia caused by <i>Pasteurella multocida</i>		
For Breeding Swine: Leptospirosis (reducing the incidence of abortions and shedding of leptospira) caused by <i>Leptospira pomona</i>	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per lb of body weight daily. Administer up to 14 days.	
CALVES, BEEF CATTLE AND NON-LACTATING DAIRY CATTLE		
Bacterial enteritis caused by <i>Escherichia coli</i>	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per lb of body weight daily. Administer up to 14 days.	
Bacterial pneumonia (shipping fever complex) caused by <i>Pasteurella multocida</i>		
SHEEP		
Bacterial enteritis caused by <i>Escherichia coli</i>	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per lb of body weight daily. Administer up to 14 days.	
Bacterial pneumonia (shipping fever complex) caused by <i>Pasteurella multocida</i>		
This tub will treat 154,250 lb of swine, cattle or sheep at 10 mg/lb.		
HONEY BEES	200 mg/colony	
For control of American Foulbrood caused by <i>Bacillus larvae</i>	The drug is administered in 3 applications of sugar syrup or 3 dustings at 4- to 5-day intervals. The drug should be fed early in the spring or fall and consumed by the bees before main honey flow begins to avoid contamination of production honey.	

Remove at least 6 weeks prior to main honey flow.

CAUTION: Use as sole source of oxytetracycline. Prepare fresh solutions every 24 hours.
 Special Note: The concentration of drug required in medicated water must be adequate to compensate for variation in the age of the animal, feed consumption rate, and the environmental temperature and humidity, each of which affects water consumption.

FOR USE IN DRINKING WATER ONLY. NOT FOR USE IN LIQUID FEED SUPPLEMENTS.



Store Below 25°C (77°F)
 For Animal Use Only
 Keep Out of Reach of Children
 Restricted Drug(s) (California)
 Not for Human Use
 Use Only as Directed



Distributed by:
Animal Health
 Exton, PA 19341, USA
 Div. of Pfizer Inc
 NY, NY 10017

992 05-9402-35-X2
 Made in USA

5637

Terramycin-343®

(oxytetracycline HCl)
 Soluble Powder

A broad-spectrum antibiotic

For control and treatment of specific diseases in poultry, cattle, swine, sheep, and bees.

This tub contains 1543.5 grams of oxytetracycline HCl and will make:

7,718 gal (29,215 L) containing
 200 mg of oxytetracycline HCl per gal
 3,859 gal (14,608 L) containing
 400 mg of oxytetracycline HCl per gal
 1,930 gal (7,306 L) containing
 800 mg of oxytetracycline HCl per gal

For oral use only

Net Weight: 4.5 lb (2041.2 g)

NADA #8-622, Approved by FDA



11" (W) x 4 3/4" (H)