

DEC 22 1999

Date of Approval: _____

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 65-480

Chlortetracycline (CTC)

Soluble Powder

Sponsored by:

Pennfield Oil Inc.

NADA 065-480

FOIS-1

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION

NADA Number 65-480

Sponsor: Pennfield Oil Company
Omaha, Nebraska 68144

Generic Name: Chlortetracycline NCl

Trade Name: Chlortetracycline Soluble Powder

Marketing Status: OTC

Effect of the supplement: To revise withdrawal period in swine to zero day.

2. INDICATION FOR USE:

Control and treatment of bacterial enteritis (scours) caused by *Escherichia coli* and bacterial pneumonia associated with *Pasteurella* spp., *Actinobacillus pleuropneumoniae* (*Hemophilus* spp.) and *Klebsiella* spp. For use in swine and calves.

3. A. DOSAGE FORM:

Soluble Powder

B. ROUTE OF ADMINISTRATION:

Oral-For use in drinking water

C. RECOMMENDED DOSAGES:

10 mg per pound body weight in divided doses

4. EFFECTIVENESS:

No further effectiveness data were required.

ANIMAL SAFETY:

No further safety data were required.

6. HUMAN SAFETY

A. TOLERANCE

The FDA has established tolerances for the sum of residues of tetracyclines, including chlortetracycline, oxytetracycline and tetracycline, in tissues of beef cattle, non-lactating dairy cows, calves, swine, sheep, chickens, turkeys and ducks (61 FR 67453, December 23, 1996). The tolerances established for chlortetracycline under 21 CFR 556.150 are as follows: 2 ppm in muscle, 6 ppm in liver, and 12 ppm in kidney and fat.

B. RESIDUE DEPLETION STUDY AND CALCULATION OF A REVISED WITHDRAWAL PERIOD

1. Study number: 403-72-1
2. Study report title: "Report of Chlortetracycline Depletion Studies in the Tissues of Swine Following Oral Administration in the Drinking Water of 10 mg Chlortetracycline per Pound Body Weight for a 45 Day Duration," Project No. 403-72-1, February 8, 1973.
3. Investigators: G. Shipley, DVM,
Director of Clinical Research,
Philips Roxane Clinical Research Farm
Crosby, MO.
4. General Design
 - a. Purpose: This is a tissue residue depletion study for chlortetracycline HCl soluble powder conducted in swine. The study was conducted to comply with Good Laboratory Practices, 21CFR 58. Tissue analyses were conducted by S. Houston, Director of the Analytical Department, Analytical Department, Philips Roxane, Inc., St. Joseph, MO.
 - b. Animals: Nine healthy pigs, weight 38-45 pounds.
 - c. Dosage form: Soluble powder mixed in drinking water to deliver 10 mg chlortetracycline *per* pound body weight.
 - d. Route of administration: Orally.

- e. Doses: Continuously in the drinking water.
- f. Test Duration: 45 days
- g. Pertinent Parameters Measured: Approximately 150 g each of liver, kidney, muscle, fat, and skin.

5. Results

Residue analyses were conducted at the Analytical Department, Philips Roxane, Inc., St. Joseph, MO, using an adapted validated microbiological assay. Tissue residue values are presented in Table 6.1.

Table 6.1 Mean residues (ppm \pm SD) of chlortetracycline in swine tissues following oral administration of chlortetracycline soluble powder at a dose of 10 mg/lb body weight for 45 days.

Withdrawal	Tissue				
	Liver	Kidney	Muscle	Fat	Skin
6 hours	0.52 \pm 0.06	1.22 \pm 0.38	0.37 \pm 0.16	0.63 \pm 0.84	0.39 \pm 0.19
5 days	0.16 \pm 0.04	0.32 \pm 0.09	0.06 \pm 0.03	0.08 \pm 0.06	0.40 \pm 0.06
10 days	0.10 \pm 0.04	0.27 \pm 0.07	0.06	0.20 \pm 0.08	0.08 \pm 0.04

6. Conclusions

A statistical tolerance limit algorithm was used to calculate a withdrawal period with a 99th percentile tolerance limit with 95% confidence. These residue data demonstrate that a zero day preslaughter withdrawal period may be applied to the oral administration of chlortetracycline in swine at a dose of 10 mg/lb BW.

C. REGULATORY ANALYTICAL 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). The method is found in Antibiotic Residues in Milk, Dairy Products, and Animal Tissues: Methods, Reports and Protocols, Revised October 1968, Reprinted December 1974, Nation Center for Antibiotic and Insulin Analysis, FDA, Washington, DC 20204. The level of sensitivity of the assay is 0.04 ppm for chlortetracycline.

7. AGENCY CONCLUSIONS:

This supplemental NADA satisfies the requirements of section 512 of the Act and demonstrates that Chlortetracycline Soluble Powder when used under its proposed conditions of use, is safe and effective for the labeled indications. The supplemental approval provides for the use of this Chlortetracycline Soluble Powder fed to swine with a zero day withdrawal period.

Under the Center's supplemental approval policy [21 CFR 514.106(b)(2)(x)] this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. However, the approval did require a re-evaluation of the human food safety data in the parent application.

8. **Labeling: See Attachment**

Chlortetracycline Soluble Powder
25.6 OZ. PACKET LABELING

TRADENAME

CHLORTETRACYCLINE HCl

SOLUBLE POWDER CONCENTRATE

Antibiotic

For Animal Use In Drinking Water Chlortetracycline Hydrochloride 64 g per pound

This packet contains 102.4 g of chlortetracycline HCl and will make:

- 1,024 gallons (3,876 L) containing 100 mg Pennchlor 64 chlortetracycline HCl per gallon
- 512 gallons (1,938 L) containing 200 mg Pennchlor 64 chlortetracycline HCl per gallon
- 256 gallons (969 L) containing 400 mg Pennchlor 64 chlortetracycline HCl per gallon
- 102.4 gallons (387 L) containing 1,000 mg Pennchlor 64 chlortetracycline HCl per gallon

Net Contents: 25.6 oz (725.7 g)

NADA 65-480

APPROVED BY FDA

Distributed by



14040 Industrial Road Omaha, NE 68144

INDICATIONS AND DIRECTIONS FOR USE

For the control or treatment of the following diseases caused by organisms susceptible to chlortetracycline.

CATTLE

DOSE - 10 mg/lb body weight

Bacterial Pneumonia (Pasteurella spp., Actinobacillus pleuropneumoniae (Hemophilus spp.), Klebsiella spp.), Bacterial Enteritis (Escherichia coli)

One standard teaspoonful of powder contains 500 mg. Administer four such teaspoonfuls in solution to a 2000 lb calf in covered cases. Administer at this rate in the total water consumed over a full 24-hour period, or as a drench in covered cases. Do not administer for more than 5 days.

Distributed by Pennfield Animal Health Omaha, NE 68144

Rev. 11/89



INDICATIONS AND DIRECTIONS FOR USE

For the control or treatment of the following diseases caused by organisms susceptible to chlortetracycline.

SWINE

DOSE - 10 mg/lb body weight

Bacterial Enteritis (Shigella spp.), Bacterial Pneumonia (Pasteurella spp., Actinobacillus pleuropneumoniae (Hemophilus spp.), Klebsiella spp.)

5 packets per 512 gallons. (This will treat 51,200 lb pigs for one day, that is five hundred twelve 100-lb pigs, providing 10 mg/lb body weight). Administer at this rate in the total water consumed over a full 24-hour period. Do not administer for more than 5 days.

CUT HERE

Tradename - Chlortetracycline hydrochloride - 102.4 g per packet (64 g/lb)

WARNING

Use as the sole source of chlortetracycline. Not to be used for more than 5 consecutive days in calves or swine. Zinc withdrawal in swine. Do not administer to calves within 1 day of slaughter.

CAUTION

When used in plastic or stainless steel waterers, or automatic waterers, prepare fresh solutions every 24 hours. When used in galvanized waterers, prepare fresh solutions every 12 hours. When feeding milk or milk replacers, administration one hour before or two hours after feeding is recommended.

General Information on Dosage

Dosages in terms of packets per 512 gallons are based on stated dosages per unit of body weight and average water consumption of the species. Water conditions, ambient temperature, humidity, age, class of livestock and other factors may affect consumption and, therefore, the unit of dosage should be used as a guide to efficacious use in drinking water. Animals must actually consume

INDICATIONS AND DIRECTIONS FOR USE

For the control or treatment of the following diseases caused by organisms susceptible to chlortetracycline.

SHEEP

Bacterial Pneumonia (Pasteurella spp., Actinobacillus pleuropneumoniae (Hemophilus spp.), Klebsiella spp.)

Bacterial Enteritis (Escherichia coli)

DOSE - 10 mg/lb body weight

5 packets per 510 gallons. (This will treat 51,200 lb of pigs for one day, that is five hundred twelve 100-lb pigs, providing 10 mg/lb body weight).

Administer at this rate in the total water consumed over a full 24-hour period. Do not administer for more than 5 days.

INDICATIONS AND DIRECTIONS FOR USE

For the control or treatment of the following diseases caused by organisms susceptible to chlortetracycline.

CATTLE

Bacterial Pneumonia (Pasteurella spp., Actinobacillus pleuropneumoniae (Hemophilus spp.), Klebsiella spp.)

Bacterial Enteritis (Escherichia coli)

DOSE - 10 mg/lb body weight

One standard teaspoonful contains 50 mg. Administer four such teaspoonful in solution to a 200-lb calf in divided doses.

Administer at this rate in the total water consumed over a full 24-hour period, or as a drench in divided doses. Do not administer for more than 5 days.

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Omaha, NE 68144

Rev: 11/99



CUT HERE TO OPEN

TRADENAME

CHLORTETRACYCLINE HCl

SOLUBLE POWDER CONCENTRATE

Antibiotic

For Animal Use In Drinking Water
Chlortetracycline Hydrochloride 64 g per pound

This packet contains 102.4 g of chlortetracycline HCl and will make:

- 1,024 gallons (3,876 L) containing 100 mg Pennchlor 64 chlortetracycline HCl per gallon
- 512 gallons (1,938 L) containing 200 mg Pennchlor 64 chlortetracycline HCl per gallon
- 256 gallons (969 L) containing 400 mg Pennchlor 64 chlortetracycline HCl per gallon
- 102.4 gallons (387 L) containing 1,000 mg Pennchlor 64 chlortetracycline HCl per gallon

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Tradename - Chlortetracycline hydrochloride - 102.4 g per packet (64 g/lb)

WARNING

Use as the sole source of chlortetracycline. Not to be used for more than 5 consecutive days in calves or swine. Zero withdrawal in swine. Do not administer to calves within 1 day of slaughter.

CAUTION

When used in plastic or stainless steel waterers, or automatic waterers, prepare fresh solutions every 24 hours. When used in galvanized waterers, prepare fresh solutions every 12 hours. When feeding milk or milk replacers, administration one hour before or two hours after feedings recommended.

General Information on Dosage

Dosages in terms of packets per 510 gallons are based on stated dosages per unit of body weight and average water consumption of the species. Weather conditions, ambient temperature, humidity, age, class of livestock and other factors may affect consumption and, except where calves are stressed, the unit dosage should be used as a guide to effective use in drinking water. Animals must actually consume

CUT HERE TO OPEN

TRADENAME

CHLORTETRACYCLINE HCl

SOLUBLE POWDER CONCENTRATE

Antibiotic

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Chlortetracycline Hydrochloride 64 g per pound

This packet contains 102.4 g of chlortetracycline HCl and will make:

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INDICATIONS AND DIRECTIONS FOR USE

For the control or treatment of the following diseases caused by organisms susceptible to chlortetracycline.

CALVES

DOSE - 10 mg/lb body wt/day
One standard teaspoonful (200 mg) contains 500 mg. Administer four such teaspoonfuls in solution to 227 g of finished feed.
Administer at this rate in the feed for 5 consecutive days over a full 24-hour period, or as a drench in divided doses. Do not administer for more than 5 days.

- Bacterial Pneumonia (Pasteurella spp., Actinobacillus pleuropneumoniae (Hemophilus spp.), Klebsiella spp.)
- Bacterial Erienteis (Escherichia coli)

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Omaha, NE 68144

Rev. 11/89



INDICATIONS AND DIRECTIONS FOR USE

For the control or treatment of the following diseases caused by organisms susceptible to chlortetracycline.

SWINE

DOSE - 10 mg/lb body wt/day
5 packets per 512 gallons. (This will treat 51,200 lb of pigs for one day; that is five hundred twelve 100-lb pigs, providing 10 mg to body weight.)
Administer at this rate in the total water consumed over a full 24-hour period. Do not administer for more than 5 days.

- Bacterial Erienteis (Scours) (Escherichia coli)
- Bacterial Pneumonia (Pasteurella spp., Actinobacillus pleuropneumoniae (Hemophilus spp.), Klebsiella spp.)

Tradename - Chlortetracycline hydrochloride - 102.4 g per packet (64 g/lb)

CAUTION

When used in plastic or stainless steel waterers, or automatic waterers, prepare fresh solutions every 24 hours. If used in galvanized waterers, prepare fresh solutions every 12 hours. When feeding milk or milk replacers, administration may occur up to two hours after feeding is recommended.

WARNING

Use as the sole source of chlortetracycline. Do not use for more than 5 consecutive days in calves or swine. Zero withdrawal in swine. Do not administer to calves within 1 day of slaughter.

General Information on Dosage

Dosages in terms of packets per 512 gallons are based on stated dosages per unit of body weight and average water consumption of the animals. Weather conditions, ambient temperature, humidity, age, class of livestock and other factors may affect consumption and, except where indicated, withdrawal periods. Do not administer to animals in a state of severe dehydration. Animals must actually consume water in order to receive the antibiotic. Do not administer to animals in a state of severe dehydration.