Date of Approval: February 28, 2006

FREEDOM OF INFORMATION SUMMARY

Supplemental New Animal Drug Application

NADA 138-935

PENNCHLOR Type A Medicated Article
(chlortetracycline)

To provide for a change in the withdrawal time for cattle from one day to zero days.

Sponsored by:

Pennfield Oil Co.

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1. GENERAL INFORMATION:

a.	File Number:	NADA 138-935
b.	Sponsor:	Pennfield Oil Company 14040 Industrial Rd. Omaha, NE 68144 Drug Labeler Code: 048164
c.	Established Name:	Chlortetracycline
d.	Proprietary Name:	PENNCHLOR Type A Medicated Article
e.	Dosage form:	Type A medicated article
f.	How Supplied:	50 pound bag
g.	How Dispensed:	OTC
h.	Amount of Active Ingredients:	50, 90, and 100 g/pound
i.	Route of Administration:	Oral – Mixed in feed
j.	Species/Class:	Cattle, swine, sheep, chickens, and turkeys
k.	Recommended Dosage:	Cattle – 25 to 350 mg/head/day (0.1, 0.5, and 10 mg/lb body weight [BW]/day) Swine – 10 to 400 grams/ton (10 mg/lb BW/day) Sheep – 20 to 50 grams/ton (80 mg/head/day) Chickens – 10 to 500 grams/ton

Turkeys – 10 to 500 grams/ton (25 mg/lb BW/day)

l. Pharmacological Category: Antimicrobial

m. Indications: Cattle:

Calves, beef cattle, and nonlactating dairy cattle.

For Calves (up to 250 lbs) – For an increased rate of weight gain and improved feed efficiency.

For Calves (250-400 lbs) – For an increased rate of weight gain and improved feed efficiency.

For Growing Cattle (over 400 lbs.) - For an increased rate of weight gain, improved feed efficiency and reduction of liver condemnation due to liver abscesses.

For Beef Cattle – For the control of bacterial pneumonia associated with shipping fever complex caused by Pasteurella spp. susceptible to chlortetracycline.

For Beef Cattle (under 700 lbs.) – Control of active infection of anaplasmosis caused by Anaplasma marginale susceptible to chlortetracycline.

For Beef Cattle (over 700 lbs.) – Control of active infection of anaplasmosis caused by Anaplasma marginale susceptible to chlortetracycline.

For Calves, Beef, and Nonlactating Dairy Cattle – For treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida susceptible to chlortetracycline. (Treat for not more than 5 days)

Sheep:

For Growing Sheep – For an increased rate of weight gain and improved feed efficiency.

For Breeding Sheep - Reducing the incidence of (vibrionic) abortion caused by Campylobacter fetus infection susceptible to chlortetracycline.

Swine:

For Growing Swine – For an increased rate of weight gain and improved feed efficiency.

For Swine - Reducing the incidence of cervical lymphadenitis (jowl abscesses) caused by Group E Streptococci susceptible to chlortetracycline.

For Breeding Swine - Control of leptospirosis (reducing the instances of abortions and shedding of leptospirae) caused by Leptospira pomona susceptible to chlortetracycline. (Feed continuously for 14 days)

For Swine - Treatment of bacterial enteritis caused by Escherichia coli and Salmonella cholerasuis and bacterial pneumonia caused by Pasteurella multocida susceptible to chlortetracycline. (Feed for not more than 14 days)

Chickens:

For Broiler/fryer chickens: For an increased rate of weight gain and improved feed efficiency.

For Chickens - Control of infectious synovitis caused by Mycoplasma synoviae susceptible to chlortetracycline. (Feed continuously for 7-14 days)

For Chickens - Control of chronic respiratory disease (CRD) and air sac infection caused by Mycoplasma gallisepticum and Escherichia coli susceptible to chlortetracycline. (Feed continuously for 7-14 days)

For Chickens - Reduction of mortality due to Escherichia coli infections susceptible to chlortetracycline. (Feed for 5 days)

Turkeys:

For Turkeys: Growing Turkeys – For an increased rate of weight gain and improved feed efficiency.

For Turkeys - Control of infectious synovitis caused by Mycoplasma synoviae susceptible to chlortetracycline. (Feed continuously for 7-14 days)

For Turkeys - Control of hexamitiasis caused by Hexamita meleagrides susceptible to chlortetracycline. (Feed continuously 7-14 days)

For Turkeys: Turkey poults not over 4 weeks of age: Reduction of mortality due to paratyphoid caused by Salmonella typhimurium susceptible to chlortetracycline.

For Turkeys - Control of complicating bacterial organisms associated with bluecomb (transmissible

		enteritis, coronaviral enteritis) susceptible to chlortetracycline. (Feed continuously for 7-14 days)
n.	Effect of Supplement:	To change the withdrawal time for cattle for PENNCHLOR Type A Medicated Article from one day to zero days.

2. EFFECTIVENESS:

No new effectiveness data were required for the approval of this supplement. The product's effectiveness was established in the original Freedom of Information (FOI) Summary dated February 16, 1996.

3. TARGET ANIMAL SAFETY:

No new target animal safety data were required for the approval of this supplement. The product's target animal safety was established in the original FOI Summary dated February 16, 1996.

4. HUMAN FOOD SAFETY:

a. Toxicology:

An Acceptable Daily Intake (ADI) of 25 µg/kg bodyweight/day has been established previously for total residues of tetracyclines including chlortetracycline, oxytetracycline, and tetracycline under 21 CFR 556.150. The ADI is apportioned as 40% to tissues and 60% to milk.

An assessment was presented on the effects of chlortetracycline residues present in edible tissues of cattle on human intestinal flora. It was concluded that the amount of active chlortetracycline residues reaching the human colon following a zero-day withdrawal period for cattle probably will not have any adverse effect on human intestinal flora.

b. Residue Chemistry:

1. Summary of Residue Chemistry Studies

Tissue Residue Depletion Study of Chlortetracycline from Edible Tissues of Cattle Dosed with Pennchlor Type A Medicated Article at a Rate Equivalent to 10 mg of Chlortetracycline Hydrochloride Activity per Pound of Body Weight for 5 Days . Study No. C-0205. October 2002.

Study Director: Dan C. Ronning

Testing Facility: Colorado Animal Research Enterprises, Fort Collins, Colorado

The study was conducted in accordance with Good Laboratory Practices (GLPs as described in 21 CFR 58).

Commercial crossbred cattle derived from Angus and Hereford breeds were used. The animals were approximately 7 months old and ranged from 514 to 678

pounds body weight. The test group consisted of 6 steers and 6 heifers. The control group consisted of 1 steer and 1 heifer. The cattle were acclimated for 22 days prior to dosing. The test cattle were fed 11 mg chlortetracycline HCl activity/pound body weight/day for 5 days. Control animals received unmedicated basal feed. On study day 1, the control cattle were slaughtered by mechanical stunning and exsanguination. The test cattle were slaughtered after 5 days of treatment by electrocution and exsanguination. Residues of chlortetracycline in kidneys of each animal were measured using the regulatory method.

Chlortetracycline Levels in Kidney from Cattle Fed 11 mg chlortetracycline HCl activity/pound bodyweight/day for 5 days (n=1).		
Gender	Chlortetracycline Levels in ppm	Mean (standard deviation)
heifer	6.088	7.330 (2.988)
heifer	4.324	
heifer	10.678	
heifer	10.420	
heifer	3.898	
heifer	8.570	
steer	11.774	7.004 (3.096)
steer	8.162	
steer	4.431	
steer	6.713	
steer	2.979	
steer	7.965	Overall Mean 7.167 (2.906)

Pilot Tissue Residue Depletion Study of Chlortetracycline from Edible Tissues of Cattle Dosed with Pennchlor Type A Medicated Article at a Rate Equivalent to 10 mg of Chlortetracycline Hydrochloride Activity Per Pound of Body Weight for 5 Days. Study No. C-0305

Study Director: Dan C. Ronning

Testing Facility: Colorado Animal Research Enterprises, Fort Collins, Colorado

The study was not conducted in accordance with Good Laboratory Practices (GLPs as described in 21 CFR 58).

Four steers and four heifers (approximately one year old, body weight ranging from 728 to 878 pounds) were used as test animals. No control cattle were used. The cattle were fed 10.5 mg chlortetracycline HCl activity/lb body weight/day for 5 days. The cattle were slaughtered by electrocution and exsanguination after 5 days of treatment. Kidney samples were analyzed for chlortetracycline residues with the regulatory method.

2. Target Tissue and Marker Residue Assignment

Although a target tissue is not designated for chlortetracycline, residues deplete most slowly from kidney. Therefore, kidney was used to monitor the depletion of chlortetracycline in cattle in this study. Microbiologically active residues (parent drug plus metabolites) are measured with the method noted below.

3. Tolerance Assignment

Tolerances for chlortetracycline in edible tissue of cattle are established as 2 ppm in muscle, 6 ppm in liver, and 12 ppm in fat and kidney (21 CFR 556.150).

4. Withdrawal Times

A zero-day withdrawal time is supported by data in Study No. C-0205 and C-0305. Individual and mean chlortetracycline residue concentrations in kidney were below the 12 ppm tolerance.

c. Microbial Food Safety

A characterization of the potential microbial food safety hazard(s) attributable to the proposed change to a zero-day withdrawal time for the approved use of chlortetracycline in cattle was assessed. The Agency has determined that the proposed change from a one-day withdrawal time to a zero-day withdrawal time for the approved use of chlortetracycline in cattle does not, at this time, change the microbial food safety of this approved use of chlortetracycline.

d. Analytical Methods for Residues

1. Determinative Method

The regulatory method for detection of chlortetracycline residues is a cylinder-plate microbiological test.

2. Availability of Method

The validated regulatory method for detection of residues of chlortetracycline is available from the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

5. USER SAFETY:

Human warnings are provided on the product labeling as follows:

NOT FOR HUMAN USE

6. AGENCY CONCLUSIONS:

The data submitted in support of this 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 PENNCHLOR Type A Medicated Article, when used under its proposed conditions of use, is safe and effective for the labeled indications.

The Agency has concluded that this product may retain over-the-counter marketing status because adequate directions for use have been written for the layperson and the conditions of use prescribed on the label are likely to be followed in practice.

In accordance with 21 CFR 514.106(b)(2)(x), this is a Category II change. The safety and effectiveness data in the parent application did not need to be reevaluated. However, the approval did require a reevaluation of the human food safety data in the present application. The shorter withdrawal period was based on new data provided to the Agency.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval for food-producing animals does not qualify for marketing exclusivity because the application does not contain substantial evidence of the effectiveness of the drugs 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 of the application and conducted or sponsored by the applicant.

No patents were submitted with this application.

6. ATTACHMENTS:

Facsimile labeling is attached as indicated below:

a. PENNCHLOR 50 (chlortetracycline)Type A Medicated Article (Pennfield label)
b. PENNCHLOR 50 G (chlortetracycline)Type A Medicated Article (Pennfield label)
c. PENNCHLOR 50 (chlortetracycline)Type A Medicated Article (Durvet label)
d. PENNCHLOR 50 G (chlortetracycline)Type A Medicated Article (Durvet label)
e. PENNCHLOR 90 G (chlortetracycline)Type A Medicated Article (Pennfield label)
f. PENNCHLOR 100 Hi-Flo (chlortetracycline)Type A Medicated Article (Pennfield label)
g. PENNCHLOR 100 G (chlortetracycline)Type A Medicated Article (Pennfield label)