Date of Approval: __3/24/99_____

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 138-935

Chlortetracycline (CTC)

Type A Medicated Article

Sponsored by:

Pennfield Oil Company
Omaha, Nebraska 68144

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION

NADA Number	138-935
Sponsor:	Pennfield Oil Company Omaha, Nebraska 68144
Generic Name:	Chlortetracycline Pre-mix
Trade Name:	Pennchlor Type A Medicated Article
Marketing Status:	OTC
Effect of the Supplement:	Changes the withdrawal time from 10 days to one day withdrawal period for cattle

2. INDICATIONS FOR USE: See below

3. A. DOSAGE FORM: Type A Medicated Article

B. ROUTE OF ADMINISTRATION: Oral - For use in Type C medicated feed

C. RECOMMENDED DOSAGES:

Dosage	**Indication for use**
Cattle, beef cattle, And nonlactating dairy Cattle:	
0.1 mg/lb b.w.	Calves (up to 250 lbs.): For an increased rate of weight gain and improved feed efficiency.
25-70 mg/head	Calves(250-400 lbs.): For an increased rate of weight gain and improved feed efficiency
70 mg/head/day	For Growing Cattle(over 400 lbs.): For an increased weight gain and improved feed efficiency and the reduction of liver condemnation due to liver abcesses.

350 mg/head/day	For Beef Cattle: Control of bacterial pneumonia associated with shipping fever complex caused by Pasteurella spp susceptible to chlortetracycline.
350 mg/head/day	For Beef Cattle(under 700 lbs.): Control of active infection of anaplasmosis caused by Anaplasma marginale susceptible to chlortetracycline.
0.5 mg/lb/bw	For Beef Cattle(over 700 lbs.): Control of active infection of anaplasmosis caused by Ananplasma marginale susceptible to chlortetracycline.
10 mg/lb/bw	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.
	Withdrawal period-one day (1-day) for cattle and calves

4. EFFECTIVENESS: No further effectiveness data were required.

5. ANIMAL SAFETY: No further safety data were required.

6. HUMAN FOOD SAFETY:

A. Tolerances for Residues

Recently, the Center for Veterinary Medicine (CVM) revised the tolerances for tetracycline drugs (61 FR 67453). Based on that reevaluation, tolerances for total tetracycline residues in tissues are established as follows:

2 ppm in muscle
6 ppm in liver
12 ppm in kidney
12 ppm in fat

B. Studies to Establish a Withdrawal Time

Title: Chlortetracycline 50 g/ton for dried fermentation solids

Study Number: WARF Institute Number 1092938

Date: October 30, 1972

Study design: Twelve steers were used in the study. The study was begun when animals weighed approximately 500 lbs. and continued for 10 months, by which time the test animals weighed 900-1000 lbs. Calves were assigned to one of three treatment groups. Calves in the treatment groups were fed 175 mg chlortetracycline/head/day as a top dress on a milo-based fattening ration. Three animals served as untreated controls. Animals were slaughtered within 12 hours following the withdrawal of medicated feed, 24 hours after the withdrawal of medicated feed and 48 hours after the withdrawal of medicated feed. At slaughter the following samples were collected: blood plasma (citrate); liver, all; kidneys, both; muscle; fat. Tissue samples were finely ground and assayed for CTC using the official analytical method for residues. Residue values are summarized in Table 1.

Table 1: Mean tissue residue data summary

Withdrawal (hours)	Muscle	Liver	Kidney	Fat
Control	-	-	-	-
12	0.028	0.073	0.078	-
24	-	-	<0.05	-
48	-	-	-	-

C. Calculating the Withdrawal Time

The calves used in the WARF study were not dosed with the maximum codified dose for chlortetracycline. For the withdrawal time analysis, the reported tissue residue values were dose-adjusted to the maximum approved dose for chlortetracycline in cattle (*i.e.*, 175 mg/hd/day for a 1000 lb calf = 0.175 mg/lb *vs.* 10 mg/lb). Using a dose correction factor of 57X, the resulting dose-adjusted residues are 1.6 ppm in muscle (*vs.* a tolerance of 2 ppm), 4.16 ppm in liver (*vs.* a tolerance of 6 ppm), and 4.45 ppm in kidney (*vs.* a tolerance of 12 ppm) at zero withdrawal. The deficiencies associated with the WARF study relative to the current residue depletion study standards preclude the assignment of a zero withdrawal for the use of this

chlortetracycline product in cattle. The mean dose-corrected kidney residue at 24 hours withdrawal is 24% of the codified tolerance (*i.e.*, 2.85 ppm *vs.* a tolerance of 12 ppm) and supports a withdrawal period of 24 hours (1-day) for doses of chlortetracycline in feed up to 10 mg/lb.

D. Regulatory Analytical Methods 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.

7. AGENCY CONCLUSIONS:

This supplemental NADA satisfies the requirements of section 512 of the Act and demonstrates that Pennchlor Type A Medicated Article 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 premix fed to cattle with a one 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 reevaluation of the human food safety data in the parent application. The shorter withdrawal period was based on the revised tolerances for chlotetracycline; 2 ppm in muscle, 6 ppm in liver, 12 ppm in fat and kidney.

8. **Labeling: See Attachment(s)**