Date of Approval: April 6, 2004

FREEDOM OF INFORMATION SUMMARY

ANADA 200-356

This approval provides for the combined use of two approved Type A Medicated Articles PENNCHLOR, (chlortetracycline calcium complex equivalent to chlortetracycline hydrochloride) DENAGARD (tiamulin hydrogen fumarate), for use in the manufacture of Type B and Type C Medicated Feeds for swine.

Sponsored by:

Pennfield Oil Company
Omaha, Nebraska 68144

I. GENERAL INFORMATION:

a. File Number	ANADA 200-356
b. Sponsor:	Pennfield Oil Co. 14040 Industrial Rd. Omaha, NE 68144 Drug Labeler Code: 053389
c. Established Names**:**	Chlortetracycline calcium complex equivalent to Chlorteracycline HCl Tiamulin hydrogen fumarate
d. Proprietary Names:	PENNCHLOR & DENAGARD
e. Dosage Form**:**	Type A Medicated Articles
f. How Supplied**:**	Chlortetracycline: 50-lb bags Tiamulin hydrogen fumarate: 35-lb bags
g. How Dispensed**:**	OTC
h. Amount of Active Ingredients in Type A Medicated Article:	Chlortetracycline: 50 to 100 g/lb Tiamulin: 10 g/lb
Amount of Active Ingredients in Type B Medicated Article:	Chlortetracycline: 80, 000 g/ton (40 g/lb) Tiamulin: 7,000 g/ton (3.5 g/lb)
i. Route of Administration**:**	These drugs are administered orally by adding the Type A Medicated Articles to complete swine feed (Type B or C medicated feed).
j. Species/Class:	Swine

k. Recommended Dosage in Type C Medicated Feeds:	Chlortetracycline, 400 g/ton to provide 10 mg per pound of body weight daily Tiamulin: 35 g/ton
l. Pharmacological Category:	Antibacterial
m. Indications:	For treatment of swine bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis* and bacterial pneumonia caused by *Pasteurella multocida* susceptible to chlortetracycline, and control of swine dysentery associated with *Brachyspira* (formerly *Serpulina* or *Treponema) hyodysenteriae* susceptible to tiamulin.
n. Pioneer Products:	AUREOMYCIN Chlortetracycline calcium complex equivalent to Chlortetracycline hydrochloride NADA 48-761 Alpharma, Inc. DENAGARD Tiamulin hydrogen fumarate NADA 139-472 Boehringer Ingelheim Vetmedica, Inc. AUREOMYCIN-DENAGARD Chlortetracycline calcium complex equivalent to Chlortetracyline hydrochloride/ Tiamulin hydrogen fumarate NADA 141-011 Boehringer Ingelheim Vetmedica, Inc.
DESI "me-too"	PENNCHLOR Chlortetracycline calcium complex equivalent Chlortetracycline hydrochloride NADA 138-935 Pennfield Oil Company

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

PENNCHLOR and AUREOMYCIN were both found to comply with the results of NAS/NRC/ DESI evaluation for effectiveness as published in the FEDERAL REGISTER (61 FR 35949-35958; July 9, 1996). These products approved under the DESI "me-too"

process were found to be bioequivalent at the codified level 21 CFR § 558.128(e)(3)(iv) of 10 mg/lb of body weight daily for swine.

The Center's fourth generic policy letter dated November 2, 1989, as published in the FEDERAL REGISTER on January 30, 1990 (55 FR 3107), states that the approval of a new generic Type A Medicated Article entitles the sponsor to a waiver from bioequivalence or tissue residue studies for any feed-use combinations approved for the pioneer. Since Alpharma's AUREOMYCIN is considered bioequivalent to Pennfield's PENNCHLOR, Pennfield is entitled to a bioequivalence waiver for the subject combination.

Chlortetracycline (PENNCHLOR-Pennfield) is codified under 21 CFR § 558.128(e)(3). Chlortetracycline (AUREOMYCIN-Alpharma) is codified under 21 CFR § 558.128(e)(3). Tiamulin hydrogen fumarate is codified under 21 CFR § 558.600. The combination of Tiamulin with Chlortetracycline is codified under 21 CFR § 558.600(e)(1)(iii) and the NADA 141-011 was approved on August 20, 1996.

3. HUMAN SAFETY:

· Tolerances for Residues:

The tolerances established for the pioneer product apply to the generic product.

Tolerances for the sums of residues of tetracycline, including chlortetracycline in tissues of swine, are as follows: (a) 2 parts per million (ppm) in muscle; (b) 6 ppm in liver; (c) 12 ppm in fat and kidneys (21 CFR § 556.150). The acceptable daily intake for residues of chlortetracycline is 25 micrograms per kilogram of body weight per day.

Under NADA 141-011, a tolerance for tiamulin of 0.6 part per million was established for 8-*alpha*-hydroxymutilin (marker compound) in liver (target tissue) of swine (21 CFR 556.738).

· Withdrawal Times:
The assigned withdrawal period is the same as the pioneer product.

Based on the limitation in 21 CFR § 558.600(e)(1)(iii), a 2 day withdrawal time is required for the combination of chlortetracycline and tiamulin.

· Regulatory Methods for Residues:

The regulatory analytical method for the determination of residue of chlortetracycline 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, National Center for Antibiotic and Insulin Analysis, FDA, Washington, DC 20204.

An approved regulatory method was used for determining the tiamulin marker residue, 8-*alpha*-hydroxymutilin, in swine liver. This method involves extraction, derivation, and then quantitation by gas chromatography. The limit of quantitation (LOQ) is 50 parts per billion. This method is on file at the Center for Veterinary Medicine, Food and Drug Administration, HFV-199, 7500 Standish Place, Rockville, MD 20855.

4. AGENCY CONCLUSIONS:

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512 (n) of the act and demonstrates that the combination of chlortetracycline and tiamulin hydrogen fumarate when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling and currently approved pioneer labeling are attached below:

Type B and Type C Medicated Feed (Blue Bird) – Generic Labeling for ANADA 200-356

Type B and Type C Medicated Feed (Blue Bird) – Pioneer Labeling for NADA 141-011