Date of Approval: September 19, 2002

FREEDOM OF INFORMATION SUMMARY

Supplemental New Animal Drug Application

ANADA 200-189

LINCOMYCIN SOLUBLE Powder
(lincomycin hydrochloride)

"For Revision of the Approved LINCOMYCIN SOLUBLE Powder Labeling: Removing a 6-Day Preslaughter Withdrawal Period in Swine; and Removing a 250-Pound Weight Restriction in Swine."

SPONSORED BY:

ALPHARMA, INC.

1. GENERAL INFORMATION:

a. File Number: **ANADA 200-189**

b. Sponsor: Alpharma Inc.
One Executive Drive
P.O. Box 1399
Fort Lee, NJ 07024
Drug Labeler Code: 046573

c. Established Name: Lincomycin hydrochloride

d. Proprietary Name: LINCOMYCIN SOLUBLE

e. Dosage Form: Soluble Powder

f. How Supplied: 40 g packets and 80 g packets

g. How Dispensed: OTC

h. Amount of Active Ingredients: Each 40 g packet contains lincomycin hydrochloride equivalent to 16 g of lincomycin and each 80 g packet contains lincomycin hydrochloride equivalent to 32 g lincomycin.

i. Route of Administration: Orally in drinking water

j. Species/Class: Swine and broiler chickens

k. Recommended Dosage:

Swine:

Dosage: Administer at a dose rate of 250 mg of lincomycin per gallon of drinking water. In clinical studies, this dose rate provided an average of 3.8 mg of lincomycin per pound of body weight per day.

Treatment period: The drug should be administered for a minimum of 5 consecutive days beyond the disappearance of symptoms (bloody stools) up to a maximum of 10 consecutive days. If water treatment is discontinued prior to this time, a lincomycin treatment program may be continued with lincomycin premix at 100 g lincomycin per ton of complete feed as the sole ration according to label directions.

Administration: One 40 g packet will medicate 64 gallons and one 80 g packet will medicate 128 gallons of drinking water providing 250 mg per gallon. A dose of 3.8 mg lincomycin per pound of body weight may be maintained by medicating the drinking water at a concentration of 250 mg per gallon of drinking water when pigs are consuming

1.5 gallons per 100 pounds of body weight per day. Under these circumstances the concentration of lincomycin required in medicated water may be adjusted to compensate for variations in age and weight of animals, the nature and severity of disease symptoms, environmental temperature and humidity, each of which affects water consumption. For use in automatic water proportioners, prepare the stock solution by dissolving two 40-gram packets, or one 80-gram packet, in 1 gallon of water: then adjust the proportioner to deliver 1 oz of stock solution per gallon of drinking water.

Broiler Chickens:

Dosage: Administer at a dose rate of 64 mg of lincomycin per gallon of drinking water.

Treatment Period: Start medication as soon as the diagnosis of necrotic enteritis is determined. If improvement is not noted within 24 to 48 hours, consult a licensed veterinarian or veterinary diagnostic laboratory to determine diagnosis. The drug should be administered for 7 consecutive days.

Administration: One 40 g packet will medicate 250 gallons and one 80 g packet will medicate 500 gallons of drinking water providing 64 mg/gallon.

l.	Pharmacological Category:	Antimicrobial
m.	Indications:	**Swine:** LINCOMYCIN SOLUBLE is indicated for the treatment of swine dysentery (bloody scours). **Broiler Chickens:** LINCOMYCIN SOLUBLE is indicated for the control of necrotic enteritis caused by *Clostridium perfringens* susceptible to lincomycin.
n.	Pioneer Product:	LINCOMIX® Soluble Powder; lincomycin hydrochloride; NADA 111-636; Pharmacia & Upjohn.
o.	Effects of Supplement:	Removal of the withdrawal period in swine. Removal of the weight restriction in swine.

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily the ANADA Sponsor shows the generic product is bioequivalent to the pioneer, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the Agency may grant a waiver from conducting an *in vivo* bioequivalence study (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guidance, October 2000; see http://www.fda.gov/cvm/guidance/published.htm#documents.)

Based on the formulation characteristics of the generic product, I.D. Russell Company, Laboratories (the original sponsor of this ANADA) was granted a waiver from the requirement for an *in vivo* bioequivalence study for the generic product, LINCOMYCIN SOLUBLE (lincomycin hydrochloride). The generic product is a water-soluble powder administered as an oral solution, contains the same active ingredient in the same concentration and dosage form as the pioneer product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient. The pioneer product, LINCOMIX® Soluble Powder (lincomycin hydrochloride), the subject of Pharmacia & Upjohn NADA 111-636, was approved on January 28, 1983.

The 250-pound weight restriction was removed from the pioneer (NADA 111-636) labeling due to swine feeding practices today resulting in heavier weights being reached in pigs before slaughter. The statement, "The safety of lincomycin has not been demonstrated for pregnant swine or swine intended for breeding," has been added to the label to caution against use in these animals. No exclusivity was granted for this change. A zero-day withdrawal time was approved for the pioneer NADA 111-636 on March 18, 1999 (64 Federal Register, Volume 64, pages 13341 – 13342), with a three-year exclusivity, which subsequently expired. Hence, no new safety or effectiveness data were required for approval of these supplements that provide for removal of the 250-pound weight restriction and a reduction in the preslaughter withdrawal time to zero days.

3. HUMAN SAFETY:

Human Safety Relative to Food Consumption:

- *Tolerances for Residues:*
  The tolerances established for the pioneer product apply to the generic product. The following tolerances are established under 21 CFR 556.360.

  (a) *Acceptable daily intake (ADI).* The ADI for total residues of lincomycin is 25 micrograms per kilogram of body weight per day.

  (b) *Chickens:* A tolerance for residues of lincomycin in chickens is not required.

  (c) *Swine:* Tolerances for lincomycin of 0.6 part per million in liver and 0.1 part per million in muscle are established.

- *Withdrawal Time:*
  When a waiver of the requirement of an *in vivo* bioequivalence study is granted, the withdrawal time is that previously assigned to the pioneer product. A zero withdrawal time is assigned to swine treated with lincomycin hydrochloride soluble powder, under ANADA 200-189.

- *Regulatory Method for Residues:*
  The regulatory analytical method for detection of residues of the drug is a microbiological test using *Sarcina lutea* (ATCC 9341). The analytical method for the determination of lincomycin residues is on file at the Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855.

Human Safety Relative to Possession, Handling and Administration:

The labeling contains adequate caution/warning statements.

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 LINCOMYCIN SOLUBLE (lincomycin hydrochloride soluble powder) when used under the proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile **Generic** Labeling and Currently Approved **Pioneer** Labeling are attached as indicated below:

Facsimile packet and box labeling for generic lincomycin hydrochloride powder – LINCOMYCIN SOLUBLE, water soluble powder: 16 grams lincomycin hydrochloride per 40-gram packet, 32 grams lincomycin hydrochloride per 80-gram packet; 25–40 g packets, 25–80 g packets.

Approved pioneer packet and box labeling for lincomycin soluble powder – LINCOMIX® Soluble Powder: 32 grams lincomycin hydrochloride per 80-gram packet; 24–80 g packets.