Approval Date: July 28, 2006

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 048-761

AUREOMYCIN 90 Granular (Chlortetracycline)

Type A Medicated Article
for Beef and Non-lactating Dairy Cattle

Beef and Non-lactating Dairy Cattle: As an aid in the control of active infection of anaplasmosis caused by *Anaplasma marginale* susceptible to chlortetracycline.

Effect of Supplement

To provide for the use of chlortetracycline in a generic free-choice loose mineral feed containing 6000 grams of chlortetracycline per ton feed and to codify the formula in 21 CFR 558.128.

Sponsored By:

Alpharma Inc.
One Executive Drive
Fort Lee, NJ 07024

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AUREOMYCIN 90 Granular
Type A Medicated Article for Beef and Non-lactating Dairy Cattle

1. GENERAL INFORMATION:

a. File Number:	NADA 048-761
b. Sponsor:	Alpharma Inc. One Executive Drive Fort Lee, NJ 07024 Drug Sponsor Code: 046573
c. Established Name:	Chlortetracycline
d. Proprietary Name:	AUREOMYCIN 90 Granular
e. Dosage Form:	Type A Medicated Article
f. How Supplied:	Chlortetracycline is supplied as a Type A article that is used in the manufacture of a free-choice generic loose mineral feed containing 6000 grams of chlortetracycline per ton of feed.
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	6000 g/ton in the Type C free-choice medicated feed
i. Route of Administration:	Oral, by feed
j. Species/Class:	Beef and non-lactating dairy cattle
k. Recommended Dosage:	0.5 to 2.0 mg chlortetracycline/lb body weight per day in the Type C free-choice medicated feed
l. Pharmacological Category:	Anti-microbial
m. Indications:	Beef and Non-lactating Dairy Cattle: As an aid in the control of active infection of anaplasmosis caused by *Anaplasma marginale*

susceptible to chlortetracycline.

n. Effect of Supplement: To provide for the use of chlortetracycline in a generic free-choice loose mineral feed containing 6000 grams of chlortetracycline per ton feed and to codify the formula in 21 CFR 558.128.

2. EFFECTIVENESS:

a. Dosage Characterization

The supplemental approval for AUREOMYCIN (NADA 048-761) dated April 17, 1996, established the dosage range of 0.5 – 2.0 mg chlortetracycline/lb body weight per day in grazing beef cattle (over 700 lb). This upper feeding limit of 2.0 mg chlortetracycline/lb body weight per day was also later applied to beef and non-lactating dairy cattle as a whole (with no weight restriction) in the subsequent approval under NADA 048-761 dated September 23, 1997, which established a 0-day withdrawal.

b. Substantial Evidence

Four pivotal pasture studies were conducted to determine the rate and variability of chlortetracycline consumption when administered in a free-choice medicated mineral supplement to beef steers and heifers. At each study location cattle were allotted to three pasture replicates (8 to 10 head/group) on the basis of initial body weight. Cattle were given *ad libitum* access to a non-medicated loose mineral supplement during a 14-day pre-study acclimation period and a chlortetracycline-medicated mineral supplement (6000 grams chlortetracycline per ton feed) throughout the 98-day treatment periods.

A. Wrightstown, New Jersey
Study Number: CD-00-02
Investigator:
Ross W. Miller, D.V.M
Alpharma Inc.
Wrightstown, New Jersey

The trial was conducted using growing beef heifers of similar breeding, primarily Angus and Angus crossbreds, that were approximately 12 months of age. The body weights of the cattle, prior to the 2-week acclimation period, were representative of regional production systems and ranged from 716 to 830 pounds. Initial body weight was used to randomize the heifers to three replicates, each consisting of 10 animals contained within one pasture per replicate. Cattle were assigned to native pasture replicates of similar forage quantity and quality. The predominant forage species was orchardgrass, with lesser amounts of timothy, rye, and red clover. Cattle were rotated among pastures every 14 days throughout the study to minimize differences due to pasture conditions. The dose of chlortetracycline tested in

the study was determined by the consumption of medicated mineral. The treatment phase lasted for 98 days.

B. Simpson, Illinois
Study Number: CD-00-03
Investigator:
Frank A. Ireland, M.S.
University of Illinois
Dixon Springs Agricultural Center
Simpson, Illinois

This trial used growing crossbred beef heifers that were approximately 13 to 17 months of age. The body weights of the cattle, prior to the 2-week acclimation period, were representative of regional production systems and ranged from approximately 756 to 898 pounds. Initial body weight was used to randomize the heifers to three replicates, each consisting of 8 animals contained within one pasture per replicate. Cattle were assigned to native pasture replicates of similar forage quantity and quality. The predominant forage species was tall fescue. Cattle were rotated among pastures every 14 days throughout the study to minimize differences due to pasture conditions. The dose of chlortetracycline tested in the study was determined by the consumption of medicated mineral. The treatment phase lasted for 98 days.

C. Huntsville, Texas
Study Number: CC009-0002
Investigator:
C. Pat Bagley, Ph.D.
Sam Houston State University
Huntsville, Texas

The trial used growing beef steers of similar breeding, primarily Brahman and Brahman crossbreds, that were approximately 18 months of age. The body weights of the cattle, prior to the 2-week acclimation period, were representative of regional production systems and ranged from approximately 737 to 973 pounds. Initial body weight was used to randomize the heifers to three replicates, each consisting of 8 animals contained within one pasture per replicate. Cattle were assigned to native pasture replicates of similar forage quantity and quality. The predominant forage species were bermuda and bahia grass. Cattle were rotated among pastures every 14 days throughout the study to minimize differences due to pasture conditions. The dose of chlortetracycline tested in the study was determined by the consumption of medicated mineral. The treatment phase lasted for 98 days.

D. Raleigh, North Carolina
Study Number: CD-00-05
Investigator:
Matthew Poore, Ph.D.
North Carolina State University
Raleigh, North Carolina

The trial used Angus and Angus crossbred beef steers that were approximately 18 months of age. The body weights of the cattle, prior to the 2-week acclimation period, were representative of regional production systems and ranged from approximately 851 to 1014 pounds. Initial body weight was used to randomize the heifers to three replicates, each consisting of 8 animals contained within one pasture per replicate. Cattle were assigned to native pasture replicates of similar forage quantity and quality. The predominant forage species were fescue and bermudagrass with lesser amounts of bluegrass, dallisgrass, orchardgrass, and clover. Cattle were rotated among pastures every 14 days throughout the study to minimize differences due to pasture conditions. The dose of chlortetracycline tested in the study was determined by the consumption of medicated mineral. The treatment phase lasted for 98 days.

Chlortetracycline consumption data for the four studies was analyzed using the Means and General Linear Model (GLM) procedures of SAS. Average daily consumption of chlortetracycline was determined for 14 day periods during the 98 day studies. Results from the statistical analyses of the 14 day periods are listed in Table 1.

Table 1: 14 day periods (mg CTC intake per pound of body weight per day)

Study	N*	Mean	Std. Dev.	Minimum	Maximum
CD-00-02	21	0.962	0.268	0.610	1.454
CD-00-03	21	0.952	0.361	0.383	1.927
CC009-0002	21	0.658	0.335	0.097	1.229
CD-00-05	21	1.081	0.679	0.280	2.734
Combined	84	0.913	0.460	0.097	2.734

*Number of 14-day periods among 3 replicates per study during the 98 day treatment period.

The combined and individual mean chlortetracycline consumption of cattle for the four studies over the 98-day duration of the studies were within the approved levels of 0.5 to 2.0 mg per pound of body weight per day.

3. TARGET ANIMAL SAFETY:

No new target animal safety data are required for the approval of this supplement. The product's target animal safety in beef and non-lactating dairy cattle has been established in the Freedom of Information (FOI) Summary for the new animal drug application for AUREOMYCIN (NADA 048-761) in beef and non-lactating dairy cattle dated February 16, 1996.

4. HUMAN SAFETY:

No new human food safety data are required for the approval of this supplement. The product's human food safety in beef and non-lactating dairy cattle has been established in the Freedom of

Information (FOI) Summary for the new animal drug application for AUREOMYCIN (NADA 048-761) in beef and non-lactating dairy cattle dated September 23, 1997.

5. 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 chlortetracycline when fed to beef and non-lactating dairy cattle at 6000 g chlortetracycline/ton in the Type C free-choice medicated feed to provide 0.5 to 2.0 mg chlortetracycline/lb body weight per day is safe and effective for the claims indicated in section 1 of this FOI Summary.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of the approval. The three years of marketing exclusivity applies only to the use of the product (AUREOMYCIN 90 Granular) when fed to beef and non-lactating dairy cattle at 6000 g chlortetracycline/ton in the Type C free-choice medicated feed to provide 0.5 to 2.0 mg chlortetracycline/lb body weight per day as an aid in the control of active infection of anaplasmosis caused by *Anaplasma marginale* susceptible to chlortetracycline for which this supplement is approved.

Pursuant to 21 CFR 514.106(b)(2), this supplemental NADA approval is regarded as a Category II supplemental change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

The drug is to be fed in Type C medicated feeds in accordance with section 1 of the FOI Summary and the Blue Bird labeling that is attached to this document.

The Center for Veterinary Medicine has concluded that, for this product, adequate directions for use by the layperson have been provided and the product will have over-the-counter (OTC) status. Label directions provide detailed instruction in plain language. The drug product is not a controlled substance. Thus, the drug product is assigned OTC status, and the labeling is adequate for the intended use.

No patent information was submitted by the sponsor with this application.

6. ATTACHMENTS:

Formula for BLUE BIRD AUREO FC Free Choice Mineral Supplement
Type C Cattle Feed Medicated to be Codified in 21 CFR 558.128

Facsimile Labeling is attached as indicated below:

AUREOMYCIN 90 Granular Type A Medicated Article
BLUE BIRD AUREO FC Type C Free-Choice Mineral Supplement

Formula for BLUE BIRD AUREO FC
Free Choice Mineral Supplement
Type C Cattle Feed Medicated
to be Codified in 21 CFR 558.128

Components	IFN	Formula percent	lbs/ton
Dicalcium Phosphate	6-26-335	46.20	924
Salt	6-04-152	15.0	300
Magnesium Oxide	6-02-756	10.67	213.4
Cottonseed Meal	5-01-625	10.00	200
Trace Mineral/Vitamin Premix		3.80	76
Calcium Carbonate	6-01-069	3.50	70
Dried Cane Molasses	4-04-695	3.00	60
Potassium Chloride	6-03-755	2.00	40
Mineral Oil	8-03-123	2.00	40
Iron Oxide	6-02-431	0.50	10
Chlortetracycline Type A medicated article (90 g per pound)		3.33	66.6
Total		100	2000