Date of Approval Letter: March 15, 2002

FREEDOM OF INFORMATION SUMMARY

NEW ANIMAL DRUG APPLICATION

NADA 141-185

Combination of Deccox® AND Aureomycin® in Cattle Feed
(decoquinate and chlortetracycline)

"Calves, beef and non-lactating dairy cows. For the prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii*; for the treatment of bacterial enteritis caused by *Escherichia coli* and for bacterial pneumonia caused by *Pasteurella multocida* susceptible to chlortetracycline"

Sponsored by:

Alpharma, Inc.

I. GENERAL INFORMATION

NADA Number:	141-185
Sponsor:	Alpharma, Inc. One Executive Drive Fort Lee, New Jersey 07024
Established Names	decoquinate chlortetracycline
Proprietary Names:	Deccox® Aureomycin®
Marketing Status:	Over-The-Counter (OTC)

II. INDICATIONS FOR USE

Calves, beef and non-lactating dairy cattle. For the prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii*; for the treatment of bacterial enteritis caused by *Escherichia coli* and for bacterial pneumonia caused by *Pasteurella multocida* organisms susceptible to chlortetracycline.

III. DOSAGE

A. *Dosage Form:* Type A Medicated Articles to be mixed with cattle feed to produce a Type C medicated feed for use as the sole ration.

B. *Route of Administration:* Oral, in feed

C. *Recommended Dose:*

Deccox®:	13.6 to 27.2 g/ton (22.7 mg/100 lb body weight/day)
Aureomycin®:	500 to 1000 g/ton (10 mg/lb body weight/day)

The resultant feed containing both drugs is then fed as the only feed for the durations as specified in 21 CFR 558.195(d) and 21 CFR 558.128(d)(1)(xii), but not for more than 5 days which is the recommended duration for chlortetracycline.

IV. EFFECTIVENESS

In accordance with the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Animal Drug Availability Act (ADAA) of 1996, if the active ingredients or animal drugs intended for use in combination in animal feed have previously been separately approved for the particular uses and conditions of use for which they are intended for use in combination, FDA will not refuse to approve an NADA for the combination on effectiveness grounds unless the Agency finds that the NADA fails to demonstrate that 1) there is substantial evidence to indicate that any active ingredient or animal drug intended

only for the same use as another active ingredient or animal drug in the combination makes a contribution to the labeled effectiveness, 2) each of the active ingredients or animal drugs intended for at least one use that is different from all other active ingredients or animal drugs used in the combination provides appropriate concurrent use for the intended target population, or 3) where the combination contains more than one nontopical antibacterial active ingredient or animal drug, there is substantial evidence that each of the nontopical antibacterial active ingredients or animal drugs makes a contribution to the labeled effectiveness (21 USC 512(d)(4)(D)).

Decoquinate (Deccox®) at 13.6 to 27.2 g/ton, as provided by Alpharma Inc., has previously been separately approved for use in cattle feed for the prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii*, and is codified in 21 CFR 558.195(d). Chlortetracycline (Aureomycin®) at 500 to 1000 g/ton, as provided by Alpharma Inc., has previously been separately approved for use in cattle feed for the treatment of bacterial enteritis caused by *Escherichia coli*, and for the treatment of bacterial pneumonia caused by *Pasteurella multocida* organisms susceptible to chlortetracycline, and is codified in 21 CFR 558.128(d)(1)(xii). Effectiveness for each drug, decoquinate and chlortetracycline, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in the approved NADAs 039-417 and 048-761, respectively. Because decoquinate and chlortetracycline each have at least one use that is different from all other animal drugs used in the combination, the NADA must also demonstrate that decoquinate plus chlortetracycline provide appropriate concurrent use for the intended target population. The use of decoquinate plus chlortetracycline provides appropriate concurrent use because these drugs are intended to treat different conditions (decoquinate, coccidiosis; chlortetracycline, bacterial enteritis and pneumonia) likely to occur simultaneously with sufficient frequency in calves, beef, and non-lactating dairy cattle. There is no more than one nontopical antibacterial (chlortetracycline) contained in this combination animal drug intended for use in Type C medicated feed. Decoquinate is not considered to be an antibacterial animal drug for use in cattle for the purposes of 512(d)(4) of the FFDCA, as amended by the ADAA of 1996, because decoquinate is approved for the prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii* in calves, beef and non-lactating dairy cattle. Thus, pursuant to FFDCA, as amended by the ADAA of 1996, no new effectiveness studies are required for the approval of NADA 141-185.

V. ANIMAL SAFETY

In accordance with the FFDCA, as amended by the ADAA of 1996, if the active ingredients or animal drugs intended for use in combination have previously been separately approved for the particular uses and conditions of use for which they are intended for use in combination, FDA will not refuse to approve an NADA for the combination on target animal safety grounds unless there is a substantiated scientific issue specific to an active ingredient or animal drug used in the combination or a scientific issue raised by target animal observations contained in studies submitted to the NADA for the combination and FDA finds that the application fails to establish that such combination active ingredient or animal drug is safe for the target animal.

Target animal safety for each drug, decoquinate and chlortetracycline, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Alpharma's approved NADAs 039-417 and 048-761, respectively. The Agency has found no substantiated scientific issue relating to the target animal safety of decoquinate or chlortetracycline when used in combination in this NADA and no scientific issue has been raised by target animal observations submitted as part of this NADA for this combination. Thus, pursuant to FFDCA, as amended by the ADAA of 1996, no new target animal safety study(ies) is(are) required for the approval of NADA 141-185.

VI. HUMAN SAFETY

In accordance with the FFDCA, as amended by the ADAA of 1996, if the active ingredients or animal drugs intended for use in combination have previously been separately approved for the particular uses and conditions of use for which they are intended for use in combination, FDA will not refuse to approve an NADA for the combination on target animal safety grounds unless one or more active ingredients or animal drugs used in the combination at the longest withdrawal time for the respective active ingredients or animal drugs in the combination exceeds the established tolerance, or one or more active ingredients or animal drugs in the combination interferes with the method of analysis for another active ingredient or animal drug in the combination.

A. *Toxicity Studies:* Safety of this combination product has been established by data in NADA 039-417 for decoquinate and NADA 048-761 for chlortetracycline as Aureomycin®.

B. *Tolerances:* Tolerances for decoquinate in cattle have been codified previously under 21CFR 556.170: 2 ppm in tissues other than skeletal muscle and 1 ppm in skeletal muscle. Tolerances for chlortetracycline in cattle have been codified previously under 21 CFR 556.150: 2 ppm in muscle, 6 ppm in liver, and 12 ppm in fat and kidney.

C. *Residue Non-Interference Study:* The combination use of 13.6 to 27.2 g/ton decoquinate and 500 to 1000 g/ton (equivalent to 10 mg/lb BW daily) chlortetracycline (as ChlorMax™) is already approved under NADA 141-147. The present application would permit an alternate source of chlortetracycline (as Aureomycin®). Through the DESI process Aureomycin® and ChlorMax™ were determined to be equivalent at the 10 mg/lb BW dosage in cattle. In view of this equivalence, FDA can rely on the residue data from NADA 141-147 to support the approval of the combination use of 13.6 to 27.2 g/ton decoquinate and 500 to 1000 g/ton chlortetracycline (as Aureomycin®).

Residue data supporting the individual uses of decoquinate and chlortetracycline as Aureomycin®, having zero withdrawal were submitted in their original applications (see Part A above). A tissue residue depletion study conducted at Southwest Bio-Labs, Las Cruces, New Mexico (Study No. RAC002-98CH53xx) using crossbred cattle and described in the Freedom of Information Summary for original NADA 141-147 (approved September 29, 2000) demonstrates that residues for decoquinate and

chlortetracycline as Aureomycin® were below their respective tolerance at twelve hours withdrawal, thereby confirming the established zero hour withdrawal period for chlortetracycline, as well as indicating an absence of interference.

D. *Regulatory Methods:* The regulatory method for the determination of decoquinate in tissues uses a fluorometric assay procedure and is found in *Official Methods of Analysis of AOAC International,* 16th edition. The regulatory method for detection of chlortetracycline residues is a microbiological test using *Bacillus cereus* var. *mycoides* (ATCC 11778) as the test organism (Antibiotic Residues in Milk, Dairy Products, and Animal Tissues: Methods Reports, and Protocols, Food and Drug Administration, Washington, D.C., 1968). These methods are on file at the Center for Veterinary Medicine, Food and Drug Administration (HFV-199), 7500 Standish Place, Rockville. Maryland 20855.

VII. AGENCY CONCLUSIONS

The information submitted in support of this NADA and in the referenced files satisfies the requirements of Section 512(d)(4) of the FFDCA and 21 CFR 514 of the implementing regulations. The data demonstrate that the combination Type C medicated feed is safe and effective in calves, beef and nonlactating dairy cattle for the uses approved in the application.

For decoquinate, a tolerance of 2 ppm in tissues other than skeletal muscle and 1 ppm in skeletal muscle in cattle has been codified previously under 21 CFR 556.170. For chlortetracycline, a tolerance of 2 ppm in muscle, 6 ppm in liver, and 12 ppm in fat and kidney in cattle has been codified previously under 21 CFR 556.150.

There is reasonable certainty that the conditions of use, including directions on labeling, can and will be followed by cattle producers. Accordingly, the agency has concluded that this product should retain over-the-counter marketing status.

Pursuant to 21 CFR 514.106(b)(2)(vi), this combination NADA approval is regarded as a Category II supplemental change which did not require a reevaluation of safety and effectiveness data in the parent NADAs.

The Agency has carefully considered the potential environmental effects of this action and has concluded that the action qualifies for a categorical exclusion from the requirement of preparing an environmental assessment in accordance with 21 CFR 25.33(a)(2).

VIII. APPROVED LABELING (attached)

Copies of specimen (Blue Bird) Type B and Type C medicated feed labels are attached to this FOI summary.

A. Bluebird DCX + AUREO Type B Cattle Feed Medicated
B. Bluebird DCX + AUREO Type C Cattle Feed Medicated