

FREEDOM OF INFORMATION SUMMARY

AUG 3 1998

Combined use of DECCOX<sup>®</sup> and BMD<sup>®</sup> in Chicken Feeds

I. GENERAL INFORMATION:

**NADA:** 141-102

**Sponsor:** Alpharma Inc.  
One Executive Drive  
Fort Lee, NJ 07024

**Generic Names:** Decoquinat  
Bacitracin methylene disalicylate

**Trade Names:** DECCOX<sup>®</sup>  
BMD<sup>®</sup>

**Marketing Status:** OTC

II. INDICATIONS FOR USE:

For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. mivati*, *E. acervulina*, *E. maxima*, and *E. brunetti*, and for increased rate of weight gain and improved feed efficiency in broiler chickens.

III. DOSAGE:

A. Dosage form: This original NADA provides for the combined use of these two Type A medicated articles, decoquinat as per 21 CFR §558.195, and bacitracin methylene disalicylate as per 21 CFR §558.76. Decoquinat is supplied as a Type A medicated article containing 6 percent decoquinat. Bacitracin methylene disalicylate is supplied as Type A medicated articles in concentrations of 10, 25, 30, 40, 50, 60, or 75 grams bacitracin activity per pound.

B. Route of Administration: Oral, *via* the feed.

C. Recommended Dosage:

Decoquinat

Decoquinat is added to broiler chicken feed at a concentration of 27.2 g/ton for the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. mivati*, *E. acervulina*, *E. maxima*, and *E. brunetti*.

Date of Approval Letter \_\_\_\_\_

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Bacitracin methylene disalicylate

Bacitracin methylene disalicylate is added to broiler chicken feed at concentrations from 4 to 50 g/ton for increased rate of weight gain and improved feed efficiency.

#### IV. EFFECTIVENESS:

In accordance with the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Animal Drug Availability Act 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 demonstrate 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)).

Decoquinatate, as provided by Alpharma Inc., has previously been separately approved for use in broiler chicken feed for the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. mivati*, *E. acervulina*, *E. maxima*, and *E. brunetti* (21 CFR §558.195 (d)). Bacitracin methylene disalicylate, as provided by Alpharma Inc., has previously been separately approved for use in broiler chicken feed for increased rate of weight gain and improved feed efficiency (21 CFR §558.76 (d)(1)(i)). Effectiveness for both drugs, decoquinatate and bacitracin methylene disalicylate, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Alpharma Inc.'s approved NADAs 39-417 and 46-592, respectively.

Because decoquinatate and bacitracin methylene disalicylate both have at least one use that is different from all other animal drugs used in the combination, the NADA must also demonstrate that decoquinatate plus bacitracin methylene disalicylate provide appropriate concurrent use for the intended target population. The use of decoquinatate plus bacitracin methylene disalicylate provides appropriate concurrent use because these drugs are intended to treat different conditions (decoquinatate, coccidiosis; bacitracin methylene disalicylate, growth performance) likely to occur simultaneously with sufficient frequency in broiler chickens. There is no more than one nontopical antibacterial (bacitracin methylene disalicylate) contained in this combination animal drug intended for use in Type C medicated feed. Decoquinatate is not considered to be an antibacterial animal drug for use in broiler

chickens for the purposes of §512(d)(4) of the FFDCa, because decoquinate is approved only for prevention of a protozoal disease in broiler chickens.

**V. ANIMAL SAFETY**

In accordance with the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Animal Drug Availability Act 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 is 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.

Decoquinate, as provided by Alpharma Inc., has previously been separately approved for use in broiler chicken feed for the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. mivati*, *E. acervulina*, *E. maxima*, and *E. brunetti* (21 CFR §558.195 (d)). Bacitracin methylene disalicylate, as provided by Alpharma Inc., has previously been separately approved for use in broiler chicken feed for increased rate of weight gain and improved feed efficiency (21 CFR §558.76 (d)(1)(i)). Target animal safety for each drug, decoquinate and bacitracin methylene disalicylate, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Alpharma Inc.'s approved NADAs 39-417 and 46-592, respectively. The Agency has found no substantiated scientific issue relating to the target animal safety of decoquinate or bacitracin methylene disalicylate when used in combination under this NADA and no scientific issue has been raised by target animal observations submitted as part of the NADA for this combination. Thus, pursuant to FFDCa, as amended by the Animal Drug Availability Act of 1996, no specific target animal safety study(ies) are required for approval of NADA 141-102.

**VI. HUMAN SAFETY:**

In accordance with the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Animal Drug Availability Act 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 of the active ingredients or animal drugs used in the combination at the longest withdrawal 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 drug in the combination.

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Safety for the approved products, decoquinatone and bacitracin methylene disalicylate, has been established by data submitted to NADA 39-417 and 46-592, respectively.

### A. Tolerances:

Tolerances for residues of decoquinatone in uncooked edible tissues of chickens are at 2 ppm in tissues other than skeletal muscle and 1 ppm in skeletal muscle in 21 CFR §556.170.

Tolerances for residues of bacitracin in uncooked edible tissues of chickens are established at 0.5 ppm (0.02 unit/g) in 21 CFR §556.70.

### B. Residue Data:

Cobb broiler chickens were fed medicated feed containing 0.003% decoquinatone, roxarsone at 45 g/ton, penicillin at 50 g/ton as procaine penicillin, and bacitracin at 50 g/ton as zinc bacitracin and were raised in floor pens for 61 days. All tissues of chickens killed at zero withdrawal of medication contained less than the established tolerance for decoquinatone [muscle (range 0.22-0.40 ppm), skin-fat (range 0.88-1.18 ppm), liver (range 0.76-1.04 ppm), and kidney (range 0.92-0.86 ppm)]. There were no positive findings for bacitracin in any of the edible tissues taken at zero withdrawal. This study also provided data to show assay noninterference between bacitracin and decoquinatone.

Substantial scientific information provided by Alpharma Inc. shows that the likelihood of other drugs in combination with bacitracin methylene disalicylate altering the bacitracin residues in tissues of animals is extremely improbable; there are no longer requirements for conducting studies demonstrating tissue residue and analytical method non-interference for Alpharma Inc.'s bacitracin methylene disalicylate where it is included at already approved levels. Such is the case for this combination. Data generated over many years show that residues of bacitracin methylene disalicylate are not detected, whether the drug is used alone or in combination. Studies using radiolabeled drugs confirm that bacitracin is recovered mostly with the feces, with only small amounts of radioactivity associated with the urine.

The available residue chemistry information supports the assignment of a zero day withdrawal period for broiler chickens fed the combination of decoquinatone (27.2 g/ton) and bacitracin methylene disalicylate (4-50 g/ton).

### C. Regulatory Methods for Residues:

A fluorometric method is used to assay tissues for decoquinatone. The method entitled "AOAC Official Method 973.79, Decoquinatone Residues in Animal Tissues, Fluorometric Method" is published in the AOAC Official Methods of Analysis (1995), Chapter 23, p. 4.

A microbiological method is used to assay tissues for bacitracin residues. The method entitled "Modified Microbiological Method for Determination of Bacitracin in Tissues" is on

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display in the Food and Drug Administration's Freedom of Information Publication Room, 5600 Fisher's Lane, Rockville, MD 20857.

### VII. AGENCY CONCLUSION:

The data submitted in support of this NADA comply with the requirements of Section 512 of the FFDCA and demonstrate that decoquinate (27.2 g/ton) plus bacitracin methylene disalicylate (4 to 50 g/ton) are safe and effective for the claims indicated in Section II of this FOI summary.

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 efficacy data in the parent NADAs. The drugs are to be fed in Type C medicated feeds, in accordance with Sections II and III of the FOI Summary and the Blue Bird labeling that is attached to this document.

Residue data show that decoquinate is within the established safe concentrations in edible chicken tissues [muscle (range 0.22-0.40 ppm), skin-fat (range 0.88-1.18 ppm), liver (range 0.76-1.04 ppm), and kidney (0.92-0.86 ppm)]. Bacitracin was undetectable in any of the edible tissues assayed.

Attached labeling: Type C medicated Feed (Blue Bird)

Lot No. \_\_\_\_\_

**NET WEIGHT ON BAG OR BULK**

**BLUE BIRD DECOQUINATE/BMD  
TYPE C BROILER FEED  
MEDICATED**

For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. mivati*, *E. acervulina*, *E. maxima*, and *E. brunetti*, and for increased rate of weight gain and improved feed efficiency in broiler chickens.

**ACTIVE DRUG INGREDIENTS**

Decoquate.....27.2 g/ton  
Bacitracin methylene disalicylate ..... 4 to 50 g/ton

**GUARANTEED ANALYSIS**

Crude Protein, not less than..... %  
Crude Fat, not less than ..... %  
Crude Fiber, not more than ..... %

**INGREDIENTS**

Each ingredient must be specifically named (unless stated as such in the guaranteed analysis listing) in accordance with the names and definitions listed in Title 21 CFR 501.110.

**DIRECTIONS FOR USE**

Feed continuously as the sole ration.

**CAUTION:** Do not feed to laying chickens.

BLUE BIRD FEED MILL  
Any Town, USA 12345