Date of Approval: February 2, 1999

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 065-470

BMD® SOLUBLE

(soluble bacitracin methylene disalicylate)

"...as an aid in the prevention and control of necrotic enteritis in replacement chickens caused by *Clostridium perfringens* susceptible to bacitracin methylene disalicylate."

Sponsored by:

Alpharma Inc.

I. GENERAL INFORMATION

NADA Number: 065-470

Sponsor: Alpharma Inc.
One Executive Drive
Fort Lee, New Jersey 07024

Established Name: soluble bacitracin methylene disalicylate

Proprietary Name: BMD® SOLUBLE

Marketing Status: OTC

Supplement Effect: This supplement provides for the addition of a class, replacement chickens, to be added to the previously approved product, BMD® SOLUBLE.

II. INDICATIONS FOR USE

Replacement chickens: as an aid in the prevention and control of necrotic enteritis caused by *Clostridium perfringens* susceptible to bacitracin methylene disalicylate.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION AND RECOMMENDED DOSAGE

A. Dosage Form

BMD® SOLUBLE is available in foil packets weighing 4.1 oz (116.2 g). Each packet of soluble powder contains 51.2 g bacitracin activity from bacitracin methylene disalicylate equivalent to 200 g bacitracin activity per pound or to 18,520 units bacitracin (master standard) per gram.

B. Route of Administration

BMD® SOLUBLE is administered orally in the drinking water.

C. Recommended Dosage

As an aid in the prevention of necrotic enteritis: BMD® SOLUBLE should be added to clean drinking water at a concentration of 100 mg/gallon.

As an aid in the control of necrotic enteritis: BMD® SOLUBLE should be added to clean drinking water at a concentration of 200 to 400 mg/gallon for 5 to 7 days or as long as clinical signs persist, and then the concentration should be reduced to prevention level (100 mg/gallon).

The medicated water should be provided continuously as the sole source of drinking water. Fresh solution should be prepared daily.

IV. EFFECTIVENESS

It has been established in NADA 46-592 and NADA 65-470 that *x* grams of bacitracin methylene disalicylate/ton of feed is approximately equivalent to *2x* mg bacitracin methylene disalicylate/gallon of water (e.g., 400 mg/gal is equivalent to approximately 200 g of feed grade BMD/ton of feed). Because the effectiveness of bacitracin methylene disalicylate as an aid in the prevention (50 g/ton) and control (100 to 200 g/ton) of necrotic enteritis in replacement chickens has previously been established under NADA 46-592, and also because 100, 200, and 400 mg BMD/gallon of water have been determined to be equivalent to 50, 100, and 200 g BMD per ton of feed, additional effectiveness studies were not required for this supplemental application.

V. ANIMAL SAFETY

The safety of administering up to 4000 g/ton of BMD in the feed (approximately equivalent to 8000 mg BMD/gallon of water) of broiler chickens for up to eight weeks has previously been demonstrated under NADA 46-592. Similarly, the safety of administering up to 1000 g/ton of BMD in the feed of laying hens for five months has also previously been demonstrated under NADA 46-592. For additional information, refer to NADA 46-592 FOI Summaries for the supplemental approvals of bacitracin methylene disalicylate for use in laying chickens for increased egg production and improved feed efficiency for egg production, and for use in broiler chickens as an aid in the prevention and control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin.

Based on the margin of safety previously documented in the safety studies summarized for use of this drug in broiler chickens and laying hens, additional safety studies were not required for this supplemental application.

VI. HUMAN SAFETY

The human food safety of this product has been previously established under this NADA. For additional information refer to the FOI Summaries for the supplemental approvals for use of bacitracin methylene disalicylate in broiler chickens as an aid for the prevention and control of necrotic enteritis caused by *Clostridium perfringens* susceptible to bacitracin methylene disalicylate.

Other information can be found in the FOI Summaries for the supplemental approvals under NADA 46-592 for use of BMD in chickens for increased egg production and improved feed efficiency for egg production, for use in broiler and replacement chickens as an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin, and for use in broiler chickens as an aid in the control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin.

Tolerance and Residue Depletion: The tolerance for residues of bacitracin in the edible uncooked tissues of chickens, turkeys, and quail has been established as 0.5 ppm (0.02 unit per gram), negligible residue (21 CFR 556.70).

FOI Summaries under NADA 46-592 highlight two relevant studies. In the first, chickens were fed 1000 g BMD/ton of feed for eight weeks with no detection of residues in target tissue at zero withdrawal, while in the second, laying hens were fed 1000 g/ton for five months with no detection of residues either in tissues or in egg yolk and egg whites. These two studies were determined to be sufficient to support a zero withdrawal period for replacement (breeder and layer) chickens that would be treated with BMD at levels up to 200 g/ton. In view of the fact that 100, 200, and 400 mg BMD/gallon have been determined to be equivalent to 50, 100, and 200 g BMD per ton of feed as an aid for the prevention and control of necrotic enteritis in broilers, the two studies are also adequate to support the assignment of a zero withdrawal period for replacement (breeder and layer) chickens that will be treated with BMD via the soluble powder.

Regulatory Method for Residues: A microbiological assay method is used to assay tissues for bacitracin residues. The method, entitled "Modified Microbiological Method for Determination of Bacitracin in Tissues," is on file at the Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855.

VII. AGENCY CONCLUSIONS

The data submitted in support of this NADA supplement 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 bacitracin methylene disalicylate soluble powder, when administered in the drinking water of replacement chickens at a concentration of 100 mg/gallon (for prevention) or 200 to 400 mg/gallon (for control), is safe and effective as an aid in the prevention and control of necrotic enteritis caused by *Clostridium perfringens* susceptible to bacitracin methylene disalicylate.

Proper use by lay persons can be expected because the directions are clearly written and there is reasonable certainty that the conditions of use, including mixing directions on the label, can and will be followed by the producer. The agency has concluded that this product can be approved for over-the-counter use.

The agency has determined under 21 CFR 25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug and, therefore, did not require a reevaluation of the human food or target animal safety data in the parent application.

VIII. APPROVED LABELING

A copy of the draft facsimile labeling is attached to this document.

BMD® Soluble Foil Packet Label