Approval Date: December 4, 2002

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 107-996

Lasalocid (AVATEC®) plus
Bacitracin methylene disalicylate (BMD®)

1) (68 g/ton Lasalocid and 10 to 50 g/ton Bacitracin Methylene Disalicylate) - For the prevention of coccidiosis caused by *Eimeria tenella, E. necatrix, E. acervulina, E. brunetti, E. mivati* and *E. maxima*, and for increased rate of weight gain and improved feed efficiency in broiler or fryer chickens.

2) (68 to 113 g/ton Lasalocid and 4 to 50 g/ton Bacitracin Methylene Disalicylate) - For the prevention of coccidiosis caused by *Eimeria tenella, E. necatrix, E. acervulina, E. brunetti, E. mivati* and *E. maxima*, and for improved feed efficiency in broiler chickens.

Sponsored by:

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

FREEDOM OF INFORMATION SUMMARY

Combined use of AVATEC® and BMD® in Chicken Feeds
Purpose of supplement: to remove the withdrawal from the product labeling

1. GENERAL INFORMATION

a. File Number:	NADA 107-996
b. Sponsor:	Alpharma Inc. One Executive Drive Fort Lee, New Jersey Drug Labeler Code: 046573
c. Established Name:	Lasalocid Bacitracin methylene disalicylate
d. Proprietary Name:	AVATEC® BMD®
e. Dosage Form:	Type A medicated articles
f. How Supplied:	AVATEC® 50 lb. bags BMD® 50 lb. bags
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	Lasalocid: 3.0, 3.3, 3.8, 4.0, 4.3, 4.4, 5.0, 5.1, 5.5, 5.7, 6.0, 6.3, 6.7, 7.2, 7.5, 8.0, 8.3, 10.0, 12.5, 15, 20, or 50 percent lasalocid activity. Bacitracin methylene disalicylate: 10, 25, 30, 40, 50, 60 or 75 grams of bacitracin activity per pound.
i. Route of Administration:	These drug products are administered orally by adding the Type A medicated articles to complete broiler or fryer chicken feed (Type C medicated feed).
j. Species/Class:	Broiler or fryer chickens
k. Recommended Dosage:	Lasalocid 68 (0.0075 pct) to 113 (0.0125 pct) g/ton for the prevention of coccidiosis caused by *Eimeria tenella, E. necatrix, E. acervulina, E. brunetti, E. mivati,* and *E. maxima.*

	Bacitracin methylene disalicylate 1) 10 to 50 g/ton for increased rate of weight gain and improved feed efficiency for broiler or fryer chickens, and 2) 4 to 50 g/ton for improved feed efficiency for broiler chickens.
l. Pharmacological Category:	Anticoccidial and antibiotic
m. Indications:	1) For the prevention of coccidiosis caused by *Eimeria tenella, E. necatrix, E. acervulina, E. brunetti, E. mivati,* and *E. maxima,* and for increased rate of weight gain and improved feed efficiency in broiler or fryer chickens. 2) For the prevention of coccidiosis caused by *Eimeria necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati,* and *E. maxima,* and for improved feed efficiency in broiler chickens.
n. Effect of Supplement:	The supplemental NADA provides for the removal of the WARNING: "Withdraw three days before slaughter."

2. EFFECTIVENESS:

No re-evaluation of effectiveness was necessary to support this approval.

3. TARGET ANIMAL SAFETY:

No re-evaluation of target animal safety was necessary to support this approval.

4. HUMAN SAFETY:

Toxicity:

Human food safety of this combination product has been established by data in NADAs 96-298 and 46-592 for AVATEC® (lasalocid) and BMD® (bacitracin methylene disalicylate), respectively.

Tolerances for Residue:

In chickens the tolerance for lasalocid (the marker residue) in skin with adhering fat (target tissue) is 1.2 ppm and in liver is 0.4 ppm (21 CFR 556.347). The tolerance for bacitracin methylene disalicylate in the uncooked edible tissues and in eggs of chickens is 0.5 ppm negligible residue (21 CFR 556.70).

Residue Data:

Assay non-interference has been previously demonstrated in the original application and supplement to this NADA. Residue data supporting the approved individual uses of lasalocid and bacitracin methylene disalicylate, each having zero withdrawal times, were submitted in their respective NADAs (see Toxicity, above).

The in-life portion of the following study (Study No. CD-98-28) was conducted at Roche Animal Science Research Station, Wrightstown, NJ, with assays conducted at Analytical Development Corporation, Colorado Springs, CO and Analytical Bio-Chemistry Laboratories, Columbia, MS to establish that each drug in the presence of the other does not exceed its established tolerance at zero withdrawal. Sixty female and 60 male day-old Peterson x Hy-Hubbard broilers were placed in one of the three treatment groups (unmedicated control, 125 ppm lasalocid, or 125 ppm lasalocid + 55 ppm bacitracin zinc) from Day 0 to Day 42 of age. On day 42, 36 female and 36 male birds from the unmedicated control group were sacrificed and skin/fat and breast muscle were collected. On day 43, after a 6-hour withdrawal, 36 female and 36 male broilers from each of the two medicated test groups were sacrificed and skin/fat and breast muscle were harvested. Twelve replicate composites of tissues (each containing similar tissues from 3 female plus 3 male birds) from each treatment were assayed for respective drug residues. Residues for lasalocid and bacitracin were below their respective tolerances at zero day withdrawal, the established withdrawal periods for each of the drugs, thereby indicating an absence of interference.

Mean and Standard Deviation of Lasalocid Residues in Skin/Fat and Mean Bacitracin Residues in Muscle Collected from Chickens Treated with Medicated Feed Containing 125 ppm Lasalocid and 55 ppm Bacitracin Zinc for 6 Weeks		
Withdrawal Time in Days	Lasalocid (ppm)	Bacitracin (ppm)
0	0.428±0.127	<LOQ of 0.015

On the basis of substantial scientific information showing 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 noninterference for 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 radio labeled drug 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 withdrawal period for chickens fed the combination of bacitracin methylene disalicylate (up to 50 g/ton) and lasalocid (68 to 113 g/ton).

Regulatory Methods for Residues:

The method available for measuring lasalocid residues in chicken skin/fat is the regulatory HPLC method, which is described in the FOI summary for NADA 96-298. 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 file at the Center for Veterinary Medicine, HFV-199, Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855.

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 demonstrates that lasalocid when administered at 68 (0.0075 pct) to 113 (0.0125 pct) g/ton plus bacitracin methylene disalicylate at 10 to 50 or 4 to 50 g/ton are safe and effective for the claims indicated in Section 1 of this FOI summary with a zero day withdrawal period.

Pursuant to 21 CFR 514.106 (b)(2), this supplemental 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 Section 1of 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. Historically, the industry is familiar with the handling and mixing of Type A medicated articles into Type B and C medicated feeds. Lasalocid and bacitracin methylene disalicylate are not controlled substances. Thus, labeling is adequate for the intended OTC use.

Lasalocid is under the following U.S. patent numbers:

U.S. Patent Number	Date of Expiration
4594354	June 10, 2003

6. ATTACHMENTS:

Facsimile Labeling is attached as indicated below:
Type C medicated feed (Blue Bird)

Net weight lb (kg) on bag or bulk

Lasalocid/Bacitracin methylene disalicylate Broiler or Fryer Chicken Ration

Type C Medicated Feed

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

ACTIVE DRUG INGREDIENT

Lasalocid……..……. 68 g/ton
Bacitracin methylene disalicylate..…….…….....….10 to 50 g/ton

GUARANTEED ANALYSIS

Crude Protein, not less than……..……_____%
Lysine, not less than…….....……_____%
Methionine, not less than……...……_____%
Crude Fat, not less than……..……...……_____%
Crude Fiber, not more than…….……..……_____%
Calcium, not less than…….....……_____%
Calcium, not more than……..…….....….._____%
Phosphorus, not less than……..……_____%
Salt[1], not less than…….....…._____%
Salt[1], not more than…….....……_____%
Sodium[2], not less than…….....……_____%
Sodium[2], not more than…….....……_____%

[1]If added.
[2]Shall be guaranteed only when total sodium exceeds that furnished by the maximum salt guarantee.

INGREDIENTS

Each ingredient must be named in accordance with the names and definitions adopted by the Association of American Feed Control Officials.

DIRECTIONS FOR USE

Feed continuously as the sole ration.

CAUTION: For broiler or fryer chickens only.

MANUFACTURED BY

BLUE BIRD FEED MILL
Anytown, USA 12345

Net weight lb (kg) on bag or bulk

Lasalocid/Bacitracin methylene disalicylate Broiler Chicken Ration
Type C Medicated Feed

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

ACTIVE DRUG INGREDIENT

Lasalocid……..……. 68 to 113 g/ton
Bacitracin methylene disalicylate..…….…….....…. 4 to 50 g/ton

GUARANTEED ANALYSIS

Crude Protein, not less than……..……_____%
Lysine, not less than…….....……_____%
Methionine, not less than……...……_____%
Crude Fat, not less than……..……...……_____%
Crude Fiber, not more than…….……..……_____%
Calcium, not less than…….....……_____%
Calcium, not more than……..……....….._____%
Phosphorus, not less than……..……_____%
Salt[1], not less than…….....…_____%
Salt[1], not more than…….....……_____%
Sodium[2], not less than…….....……_____%
Sodium[2], not more than…….....……_____%

[1]If added.
[2]Shall be guaranteed only when total sodium exceeds that furnished by the maximum salt guarantee.

INGREDIENTS

Each ingredient must be named in accordance with the names and definitions adopted by the Association of American Feed Control Officials.

DIRECTIONS FOR USE

Feed continuously as the sole ration.

CAUTION: For broiler chickens only.

MANUFACTURED BY
BLUE BIRD FEED MILL
Anytown, USA 12345