

Approval Date: April 18, 2001

**FREEDOM OF INFORMATION SUMMARY**

**ORIGINAL NEW ANIMAL DRUG APPLICATION**

**NADA 141-083**

**Lasalocid (AVATEC<sup>®</sup>) plus Bacitracin zinc (BACIFERM<sup>®</sup>)**

**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 chickens.**

**Sponsored by:**

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

## FREEDOM OF INFORMATION SUMMARY

Combined use of AVATEC<sup>®</sup> and BACIFERM<sup>®</sup> in Broiler Chicken Feeds

### I. GENERAL INFORMATION:

**NADA:** 141-083

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

**Generic Names:** Lasalocid  
Bacitracin zinc

**Trade Names:** AVATEC<sup>®</sup>  
BACIFERM<sup>®</sup>

**Marketing Status:** OTC

### II. INDICATIONS FOR USE:

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 chickens.

### III. DOSAGE:

A. Dosage form: This original NADA provides for the combined use of these two Type A medicated articles, lasalocid as per 21 CFR 558.311, and bacitracin zinc as per 21 CFR 558.78. Lasalocid is supplied as a Type A medicated article containing 90.7 grams lasalocid activity per pound. Bacitracin zinc is supplied as a Type A medicated article in a concentration of 50 grams bacitracin activity per pound.

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

C. Recommended Dosage:

Lasalocid

Lasalocid is added to broiler chicken feed at concentrations from 68 to 113 g/ton for the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

Bacitracin zinc

Bacitracin zinc is added to 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)).

Lasalocid, 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. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* (21 CFR 558.311 (e)(1)(i)). Bacitracin zinc, as provided by Alpharma Inc, has previously been separately approved for use in chicken feed for increased rate of weight gain and improved feed efficiency (21 CFR 558.78 (d)(1)(i)). Effectiveness for both drugs, lasalocid and bacitracin zinc, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Alpharma Inc.'s approved NADAs 96-298 and 46-920, respectively. Because lasalocid and bacitracin zinc both have at least one use that is different from all other animal drugs used in the combination, the NADA must also demonstrate that lasalocid plus bacitracin zinc provide appropriate concurrent use for the intended target population. The use of lasalocid plus bacitracin zinc provides appropriate concurrent use because these drugs are intended to treat different conditions (lasalocid, coccidiosis; bacitracin zinc, growth performance) likely to occur simultaneously with sufficient frequency in broiler chickens. There is no more than one nontopical antibacterial (bacitracin zinc) contained in this combination animal drug intended for use in Type C medicated feed. Lasalocid is not considered to be an antibacterial animal drug for use in broiler chickens for the purposes of

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

**V. ANIMAL SAFETY:**

In accordance with the FFDCFA, 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.

Lasalocid, 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. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* (21 CFR 558.311 (e)(1)(i)). Bacitracin zinc, as provided by Alpharma Inc., has previously been separately approved for use in chicken feed for increased rate of weight gain and improved feed efficiency (21 CFR 558.78 (d)(1)(i)). Target animal safety for both drugs, lasalocid and bacitracin zinc, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Alpharma Inc.'s approved NADAs 96-298 and 46-920, respectively. The Agency has found no substantiated scientific issue relating to the target animal safety of lasalocid or bacitracin zinc 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 FFDCFA, as amended by the Animal Drug Availability Act of 1996, no specific target animal safety studies are required for approval of NADA 141-083.

**VI. HUMAN SAFETY:**

A. Residue Non-Interference Study

Residue data supporting the approved individual uses of bacitracin zinc and lasalocid, each having zero withdrawal times, were submitted in their respective original applications (see Part A, above). The in-life portion of the following study (Study No. CD-98-28) was conducted at Roche Animal Science Research Station (ASRS), Wrightstown, New Jersey, with assays conducted at Analytical Development Corporation, Colorado Springs, Colorado and Analytical Bio-Chemistry (ABC) Laboratories, Columbia, Missouri to establish that each drug in the presence of the other does not exceed its established tolerance at zero withdrawal and that the presence of the drugs in the same chicken tissue did not interfere with the assay of either drug.

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. Skin/fat was analyzed for lasalocid by an established HPLC method. Muscle was analyzed for bacitracin zinc by the official microbiological method.

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 Hours	Lasalocid (ppm)	Bacitracin Zinc (ppm)
0	0.428 ± 0.127	<LOQ of 0.015

Samples of control skin/fat and control muscle were fortified with lasalocid and bacitracin zinc. The data showed that the presence of bacitracin zinc did not interfere with the assay of lasalocid in skin/fat. The presence of lasalocid did not interfere with the assay of bacitracin zinc in the muscle.

Residues for lasalocid and bacitracin zinc were below their respective tolerances at zero withdrawal, the established withdrawal periods for each of the drugs, thereby indicating an absence of interference. The lasalocid data were evaluated using a 99% statistical tolerance with 95% confidence procedure.

#### B. Regulatory Methods

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. The regulatory analytical method for the detection of residues of bacitracin zinc is a microbiological test using *Micrococcus luteus* (ATCC 10240) suspension. The method is published by the Food and Drug Administration, "Antibiotic Residues in Milk, Dairy Products and Animal Tissues: Method, Reports, and Protocols, revised October 1968, reprinted December 1974.

#### **VII. AGENCY CONCLUSION:**

The data submitted in support of this NADA comply with the requirements of § 512 of the FFDCFA and demonstrate that lasalocid (68 to 113 g/ton) plus bacitracin zinc (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.

The data demonstrate that residue for lasalocid and bacitracin zinc were below their respective tolerances at zero withdrawal, the established withdrawal periods for each of the drugs, thereby indicating an absence of interference.

Attached labeling: Type C medicated Feed (Blue Bird)

Net Weight lb (kg) on bag or bulk  
**Lasalocid/Bacitracin zinc 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 increased rate of weight gain and improved feed efficiency in broiler chickens.

**Active Drug Ingredients**

Lasalocid.....68 to 113 g/ton  
Bacitracin zinc.....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<sup>1</sup>, not less than..... %  
Salt<sup>1</sup>, not more than..... %  
Sodium<sup>2</sup>, not less than..... %  
Sodium<sup>2</sup>, not more than..... %

<sup>1</sup>If added.

<sup>2</sup>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