Approval Date:_____

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-109

Lasalocid (AVATEC®) plus Bacitracin Zinc (BACIFERM®)

For the prevention of coccidiosis caused by *Eimeria meleagrimitis*, *E. gallopavonis*, and *E. adenoeides*, and for increased rate of weight gain and improved feed efficiency in growing turkeys.

Sponsored by:

Roche Vitamins Inc.
45 Waterview Blvd.
Parsipanny, NJ 07054

FREEDOM OF INFORMATION SUMMARY

Combined use of AVATEC® and BACIFERM® in Turkey Feeds

I. GENERAL INFORMATION:

NADA: 141-109

Sponsor: Roche Vitamins Inc.
45 Waterview Boulevard
Parsippany, NJ 07054-1298

Generic Names: Lasalocid
Bacitracin zinc

Trade Names: AVATEC®
BACIFERM®

Marketing Status: OTC

II. INDICATIONS FOR USE:

For the prevention of coccidiosis caused by *Eimeria meleagrimitis*, *E. gallopavonis*, and *E. adenoeides*, and for increased rate of weight gain and improved feed efficiency in growing turkeys.

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 concentrations of 50 grams bacitracin activity per pound.

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

C. Recommended Dosage:

Lasalocid	Lasalocid is added to growing turkey feed at concentrations from 68 to 113 g/ton for the prevention of coccidiosis caused by *Eimeria meleagrimitis*, *E. gallopavonis*, and *E. adenoeides.*

Bacitracin zinc	Bacitracin zinc is added to growing turkey 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 Roche Vitamins Inc., has previously been separately approved for use in growing turkey feed for the prevention of coccidiosis caused by *Eimeria meleagrimitis*, *E. gallopavonis*, and *E. adenoeides* (21 CFR §558.311 (e)(1)(xiv)). Bacitracin zinc, as provided by Roche Vitamins Inc., has previously been separately approved for use in growing turkey 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 Roche Vitamins 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 growing turkeys. 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 growing turkeys for the purposes of §512(d)(4) of the FFDCA, because lasalocid is approved only for prevention of a protozoal disease in growing turkeys.

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.

Lasalocid, as provided by Roche Vitamins Inc., has previously been separately approved for use in growing turkey feed for the prevention of coccidiosis caused by *Eimeria meleagrimitis*, *E. gallopavonis*, and *E. adenoeides* (21 CFR §558.311 (e)(1)(xiv)). Bacitracin zinc, as provided by Roche Vitamins Inc., has previously been separately approved for use in growing turkey 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 Roche Vitamins 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 FFDCA, as amended by the Animal Drug Availability Act of 1996, no specific target animal safety study(ies) are required for approval of NADA 141-109.

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 human 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.

A. Toxicity Studies

Safety of this combination product has been established by data in NADA 96-298 for lasalocid and NADA 46-920 for bacitracin zinc.

As part of the approval of this combination product, the human food safety information on the individual components was updated. An Acceptable Daily Intake (ADI) of 0.01 mg/kg/day for lasalocid is established.

B. Tolerances

The tolerance of 0.5 ppm (0.02 unit per gram), negligible residue for bacitracin zinc in turkeys has been codified previously under 21 CFR 556.70.

C. 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-97-11) was conducted at Roche Animal Science Research Station (ASRS), Wrightstown, New Jersey, with assays conducted at Animal Science Research, Analytical/Metabolic Laboratory, Fairlawn, New Jersey 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 turkey tissue did not interfere with the assay of either drug.

Twenty Nicholas poults (10 males, 10 females) were assigned to one of four treatment groups: unmedicated feed, 125 ppm lasalocid, 55 ppm bacitracin zinc, or 125 ppm lasalocid and 55 ppm bacitracin zinc. The treatment period was from Day 0 to Day 105 of age. On Day 105, after a 6-hour withdrawal period, five birds of each sex were slaughtered from each treatment group. Liver was analyzed for lasalocid by an established HPLC method. Muscle was analyzed for bacitracin zinc by the official microbiological method.

Mean Lasalocid Residues in Liver and Mean Bacitracin Residues in Muscle Collected from Turkeys Treated with Medicated Feed Containing 125 ppm Lasalocid and 55 ppm Bacitracin Zinc for 15 Weeks

Withdrawal Time in Hours	Lasalocid (ppb)	Bacitracin Zinc (ppm)
0	37.3 $\pm$ 30.4	< LOQ of 0.015

Samples of control liver 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 the liver. 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.

D. Regulatory Methods

The method available for measuring lasalocid residues down to 5 ppb in turkey liver is the regulatory HPLC method for lasalocid in chicken skin/fat and in cattle liver which is described in the FOI summary for NADA 96-298. The regulatory analytical method for detection of residues of the bacitracin zinc is a microbiological test using *Sarcina subflava* (ATCC 7468) or *Micrococcus subflavus* (ATCC 10240). The method is found in Antibiotic Residues in Milk, Dairy Products an Animal Tissues: Method, Reports, and Protocols, Revised October 1968, Reprinted December 1974, National Center for Antibiotic and Insulin Analysis, FDA, Washington, DC, 20204.

VII. AGENCY CONCLUSION:

The data submitted in support of this NADA comply with the requirements of Section 512 of the FFDCA 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 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.

Attached labeling: Type C medicated Feed (Blue Bird)