

Approval Date: _____

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-129

Lasalocid (AVATEC[®]) plus Bambermycins (FLAVOMYCIN[®])

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:

**Hoechst Roussel Vet
30 Independence Blvd.
P.O. Box 4915
Warren, New Jersey 07059**

FREEDOM OF INFORMATION SUMMARY

Combined use of AVATEC[®] and FLAVOMYCIN[®] in Broiler Chicken Feeds

I. GENERAL INFORMATION

NADA: 141-129

Sponsor: Hoechst Roussel Vet
30 Independence Blvd.
P.O. Box 4915
Warren, NJ 07059

Generic Names: Lasalocid
Bambermycins

Trade Names: AVATEC[®]
FLAVOMYCIN[®]

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 NADA provides for the combined use of these two Type A medicated articles: lasalocid as per 21 CFR 558.311, and bambermycins as per 21 CFR 558.95. Lasalocid is supplied as a Type A medicated article in a concentration of 90.7 grams lasalocid activity per pound. Bambermycins is supplied as a Type A medicated article in concentrations of 2, 4 or 10 grams bambermycins 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*.

Bambermycins

Bambermycins is added to broiler feed at concentrations from 1 to 2 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 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)). Bambermycins, as provided by Hoechst Roussel Vet, has previously been separately approved for use in broiler chicken feed for increased rate of weight gain and improved feed efficiency (21 CFR 558.95 (d)(1)(i)). Effectiveness for each drug, lasalocid and bambermycins, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Roche Vitamins Inc.'s approved NADA 96-298, to which Hoechst Roussel Vet has a right of reference, and in Hoechst Roussel Vet's approved NADA 44-759, respectively. Because lasalocid and bambermycins each 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 bambermycins provide appropriate concurrent use for the intended target population. The use of lasalocid plus bambermycins provides appropriate concurrent use because these drugs are intended to treat different conditions (lasalocid, coccidiosis; bambermycins, performance) likely to occur simultaneously with sufficient frequency in broiler chickens. There is no more than one nontopical antibacterial (bambermycins) 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 FFDCA, because lasalocid 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 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 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)). Bambermycins, as provided by Hoechst Roussel Vet, has previously been separately approved for use in broiler chicken feed for increased rate of weight gain and improved feed efficiency (21 CFR 558.95 (d)(1)(i)). Target animal safety for each drug, lasalocid and bambermycins, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Roche Vitamins Inc.'s approved NADA 96-298, to which Hoechst Roussel Vet has a right of reference, and in Hoechst Roussel Vet's approved NADA 44-759, respectively. The Agency has found no substantiated scientific issue relating to the target animal safety of lasalocid or bambermycins 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) is (are) required for approval of NADA 141-129.

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. Tolerances

A tolerance for lasalocid in chicken tissues has been established at 1.2 ppm in skin/fat (21 CFR 556.347). In accordance with 21 CFR 556.1(a)(4), a tolerance is not required for the use of bambermycins in broiler chicken feed.

B. Tissue Residue and Assay Noninterference Data

The following work was conducted by Hoffman-LaRoche. At least 64 birds were continuously fed a combination medicated feed containing 113 g/ton lasalocid, 3 g/ton bambermycins and 45.4 g/ton roxarsone. Samples of muscle, liver and skin/fat were collected from eight birds sacrificed at zero withdrawal. All tissues were analyzed for bambermycins with a microbiological assay having sensitivity of about 25 ppb. Only skin/fat samples were analyzed for lasalocid with a thin-layer bioautographic method having a sensitivity of about 10 ppb. No residues of bambermycins were detected in any tissue samples. Lasalocid residues averaged 0.27 ppm, with a range of 0.19 to 0.44 ppm.

The noninterference of bambermycins and lasalocid in each other's tissue residue assay was established in a tissue residue study conducted by Roche Vitamins, Inc.'s NADA 112-687. The available residue chemistry information supports the assignment of a zero withdrawal period for broiler chickens fed the combination of lasalocid (68 to 113 g/ton) and bambermycins (1 to 2 g/ton).

C. Regulatory Methods for Residues

A regulatory method for bambermycins in tissues of broiler chickens is not required because bambermycins is regulated with no requirement of either a withdrawal period or a tolerance.

A thin-layer bioautographic method is available for measuring lasalocid in tissues of broiler chickens.

VII. AGENCY CONCLUSIONS

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 bambermycins (1 to 2 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 Section II and III of the FOI Summary and the Blue Bird labeling that is attached to this document.

The available residue chemistry information supports the assignment of a zero withdrawal period for broiler chickens fed the combination of lasalocid (68 to 113 g/ton) and bambarmycins (1 to 2 g/ton).

Attached labeling: Type C medicated feed (Blue Bird).