Date of Approval: June 2, 2014

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-560

ACTOGAIN 45 plus RUMENSIN plus MGA

ractopamine hydrochloride plus monensin USP plus melengestrol acetate

Type A Medicated Articles for Use in the Manufacture of Type C Medicated Feeds

Heifers Fed in Confinement for Slaughter

For increased rate of weight gain, improved feed efficiency, increased carcass leanness, prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*, and suppression of estrus (heat) in heifers fed in confinement for slaughter for the last 28 to 42 days on feed.

Sponsored by:

Zoetis Inc.

Table of Contents

I. GENERAL INFORMATION:

A. File Number

ANADA 200-560

B. Sponsor

Zoetis Inc.
333 Portage St.
Kalamazoo, MI 49007

Drug Labeler Code: 054771

C. Proprietary Name

ACTOGAIN 45 plus RUMENSIN plus MGA

D. Established Name

ractopamine hydrochloride plus monensin USP plus melengestrol acetate

E. Pharmacological Category

Ractopamine hydrochloride – beta-adrenergic agonist
Monensin USP – ionophore/anticoccidial
Melengestrol acetate – steroid hormone

F. Dosage Form

Type A medicated articles for use in the manufacture of Type C medicated feeds (dry and liquid)

G. Amount of Active Ingredient in Currently Marketed Products*

Ractopamine hydrochloride – 45.4 g/lb
Monensin USP – 90.7 g/lb
Melengestrol acetate – 200 and 500 g/lb

*The sponsors of these individual currently marketed Type A medicated articles may have approvals for other strengths of these products that are for use in the same species and class, for the same indications, and at the same dosages, but are not currently marketing those strengths of these Type A medicated articles. Such strengths, when legally marketed, are also approved for use in the manufacture of the Type C medicated feed that is the subject of this approval.

H. How Supplied

ACTOGAIN (ractopamine hydrochloride) 45 – 25 lb (11.34 kg) bag
RUMENSIN (monensin USP) – 25 kg (55.12 lb) bag
MGA (melengestrol acetate) – 50 lb (22.6 kg) bag (dry), 40 lb (18 kg) container (liquid)

I. Dispensing Status

OTC

J. Dosage Regimen

Ractopamine and Monensin Plus:

Ractopamine is fed continuously as the sole ration at a concentration of 9.8 to 24.6 g of ractopamine hydrochloride per ton of complete feed to provide 90 to 430 mg/hd/day ractopamine/head/day.

Monensin is added to the ration at a concentrations of 10 to 40 g of monensin USP per ton of complete feed at a rate of 0.14 to 0.42 mg monensin/lb body weight per day, depending on the severity of the coccidiosis challenge, up to 480 mg/hd/day of monensin for the last 28 to 42 days on feed.

Melengestrol acetate supplements (liquid and dry):

Must be top dressed or mixed with a complete ration containing ractopamine (9.8 to 24.6 g/ton) and monensin (10 to 40 g/ton). Feed at the rate of 0.5 to 2.0 pounds per head per day to provide 0.25 to 0.5 mg melengestrol acetate per head per day. Feed melengestrol acetate in this combination for the final 28 to 42 days on feed.

K. Route of Administration

Oral, in feed

L. Species/Class

Heifers fed in confinement for slaughter

M. Indications

For increased rate of weight gain, improved feed efficiency, increased carcass leanness, prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*, and suppression of estrus (heat) in heifers fed in confinement for slaughter for the last 28 to 42 days on feed.

N. Approved Original Generic Type A Medicated Article

ACTOGAIN 45; ractopamine hydrochloride; ANADA 200-548; Zoetis Inc.

O. Reference Listed New Animal Drug

OPTAFLEXX plus RUMENSIN plus MGA; ractopamine hydrochloride plus monensin USP plus melengestrol acetate; NADA 141-234; Elanco Animal Health, A Division of Eli Lilly & Co.

The individual Type A medicated articles approved for use in the manufacture of combination medicated feeds are:

OPTAFLEXX; ractopamine hydrochloride; NADA 141-221; Elanco Animal Health, A Division of Eli Lilly & Co.

RUMENSIN; monensin sodium; NADA 095-735; Elanco Animal Health, A Division of Eli Lilly & Co.

MGA 100 PREMIX, MGA 200 PREMIX and MGA 500 LIQUID PREMIX; melengestrol acetate; NADA 039-402; Zoetis Inc

II. BIOEQUIVALENCE:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act of 1988, an abbreviated new animal drug application (ANADA) may be submitted for a generic version of an approved new animal drug (reference listed new animal drug). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

According to CVM's fourth policy letter issued on November 2, 1989, with regard to the implementation of GADPTRA, after the approval of an ANADA for a generic Type A medicated article, the generic sponsor is entitled to approval for all the feed-mixed combinations for which the RLNAD is approved. Bioequivalence and tissue residue studies are not required for the approval of the generic feed use combinations (Type B or C medicated feeds). Ractopamine hydrochloride is codified under 21 CFR 558.500, monensin USP is codified under 21 CFR 558.355, and melengestrol acetate is codified under 21 CFR 558.342. The combination of ractopamine hydrochloride, monensin USP, and melengestrol acetate is codified under 21 CFR 558.500(e)(2)(viii).

III. EFFECTIVENESS:

CVM did not require effectiveness studies for this approval.

IV. TARGET ANIMAL SAFETY:

CVM did not require target animal safety studies for this approval.

V. HUMAN FOOD SAFETY:

The following are assigned to this product for cattle:

A. Tolerances for Residues:

The tolerances established for the feed use RLNAD apply to the generic feed use combination new animal drug product.

The tolerance for ractopamine hydrochloride (the marker residue) is 0.09 parts per million (ppm) in the liver (the target tissue), and 0.03 ppm in the muscle, under 21 CFR 556.570(b)(1). The acceptable daily intake ADI for total residues of ractopamine hydrochloride is 1.25 micrograms per kilogram of body weight per day.

The tolerance for monensin is 0.1 ppm in the liver, and 0.05 ppm in the muscle, kidney, and fat, under 21 CFR 556.420(b)(1). The ADI for total residues of monensin is 12.5 micrograms per kilogram of body weight per day.

The tolerance for residues of melengestrol acetate in fat is 25 parts per billion, under 21 CFR 556.380.

B. Withdrawal Periods:

Because a waiver from the requirement to demonstrate bioequivalence was granted for the Type A medicated article, ACTOGAIN 45, the withdrawal periods for the combination Type C medicated feeds are those previously assigned to the RLNAD product.

When used together, ractopamine hydrochloride, monensin USP, and melengestrol acetate are approved with a zero-day withdrawal period.

C. Regulatory Method for Residues:

The determination of residues of ractopamine in the liver and muscle of cattle, swine and turkeys is by High Performance Liquid Chromatography (HPLC). The confirmation of residues of ractopamine in the liver and muscle of cattle, swine and turkeys is by Liquid Chromatography/Electrospray Ionization Triple Tandem Quadrupole Mass Spectrometry (LC/ESI-MS-MS). The validated regulatory methods for determination and confirmation of residues of ractopamine are available from CVM, FDA, 7500 Standish Place, Rockville, MD 20855.

The regulatory analytical method for monensin is the method developed by Eli Lilly & Co., Box 708, Greenfield, IN 46140 (Method 5801654, "Determination of Monensin in Tissues and Eggs") on file at the Center for Veterinary Medicine, Food and Drug Administration, HFV-199, 7500 Standish Place, Rockville, Maryland 20855.

The analytical method for the determination of melengestrol acetate in tissues uses a gas chromatographic assay procedure. This method is found in Official Methods of Analysis of AOAC International, 16th edition.

VI. USER SAFETY:

CVM did not require user safety studies for this approval.

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to ractopamine hydrochloride:

WARNING
The active ingredient, ractopamine hydrochloride, is a beta-adrenergic agonist. Individuals with cardiovascular disease should exercise special caution to avoid exposure. Not for use in humans. Keep out of the reach of children. The ractopamine hydrochloride formulation (Type A Medicated Article) poses a low dust potential under usual conditions of handling and mixing. When mixing and handling ractopamine hydrochloride, use protective clothing, impervious gloves, protective eye wear, and a NIOSH-approved dust mask. Operators should wash thoroughly with soap and water after handling. If accidental eye contact occurs, immediately rinse

eyes thoroughly with water. If irritation persists, seek medical attention. The material safety data sheet contains more detailed occupational safety information.

VII. AGENCY CONCLUSIONS:

This information submitted in support of this ANADA satisfies the requirements of section 512(n) of the Federal Food, Drug, and Cosmetic Act and demonstrates that ACTOGAIN 45 plus RUMENSIN plus MGA, when used according to the label, is safe and effective.