Approval Date: January 29, 2007

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-448

HEIFERMAX 500 (melengestrol acetate) plus OPTAFLEXX (ractopamine hydrochloride), and RUMENSIN (monensin sodium)

Type A Medicated Articles

Indication for use: 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:

Ivy Laboratories
Div. of Ivy Animal Health, Inc.

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

a. File Number:	ANADA 200-448
b. Sponsor:	Ivy Laboratories Div. of Ivy Animal Health, Inc. 8857 Bond Street Overland Park, KS 66214 Drug Labeler Code: 021641
c. Established Name:	Melengestrol acetate, ractopamine hydrochloride, and monensin sodium
d. Proprietary Name:	HEIFERMAX 500, OPTAFLEXX, and RUMENSIN
e. Dosage Form:	Type A medicated articles for use in combination for the manufacture of three-way dry and liquid Type B or Type C medicated feeds
f. How Supplied:	Melengestrol acetate – 40 lb container (liquid) Ractopamine – 25 lb bag Monensin – 50 lb bag
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	HEIFERMAX 500: 500 mg of melengestrol acetate activity per pound of premix OPTAFLEXX: 45.4 grams of ractopamine hydrochloride activity per pound of premix RUMENSIN: 20, 30, 40, 60, 80, or 90.7 grams of monensin sodium activity per pound of premix
i. Route of Administration:	Orally in feed
j. Species/Class:	Beef cattle; heifers fed in confinement for slaughter

k. Recommended Dosage:	Add 0.5 to 2.0 pounds per head per day of medicated feed containing 0.125 to 1.0 mg of melengestrol acetate per pound to provide 0.25 to 0.5 mg melengestrol acetate per head per day to a Type C medicated feed containing 9.8 to 24.6 g/ton ractopamine hydrochloride to provide 90 to 430 mg ractopamine per head per day, and 10 to 30 g/ton monensin sodium to provide 0.14 to 0.42 mg monensin/lb body weight/day up to 360 mg depending on the severity of the coccidiosis challenge.
l. Pharmacological Category:	Hormone, beta adrenergic agonist, and anticoccidial.
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. Generic Products:	HEIFERMAX 500 Liquid Premix; melengestrol acetate; ANADA 200-343; Ivy Laboratories, Div. of Ivy Animal Health, Inc. HEIFERMAX 500, OPTAFLEXX, and RUMENSIN; melengestrol acetate, ractopamine hydrochloride, and monensin sodium; ANADA 200-448; Ivy Laboratories, Div. of Ivy Animal Health., Inc.
o. Pioneer Products:	MGA 500; melengestrol acetate; NADA 039-402; Pharmacia & Upjohn Co., a Division of Pfizer, Inc. 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 500, OPTAFLEXX, and RUMENSIN; melengestrol acetate, ractopamine hydrochloride, and monensin sodium, NADA 141-234; Elanco Animal Health, A Division of Eli Lilly & Co.

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). 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.

Ordinarily, the ANADA sponsor shows that the generic product is bioequivalent to the pioneer, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an in vivo bioequivalence study. (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

This approval is for the use of HEIFERMAX 500 (melengestrol acetate) in combination with OPTAFLEXX (ractopamine hydrochloride), and RUMENSIN (monensin sodium) for the manufacture of three-way combination Type C medicated feeds. This combination product is a generic copy of MGA 500 (melengestrol acetate) plus OPTAFLEXX and RUMENSIN sponsored by Elanco Animal Health, A Division of Eli Lilly & Co.

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 pioneer 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). Melengestrol acetate is codified under 21 CFR 558.342. Ractopamine is codified under 21 CFR 558.500. Monensin is codified under 21 CFR 558.355. The combination of melengestrol acetate, ractopamine hydrochloride, and monensin sodium is codified under 21 CFR 558.500(e)(2).

3. HUMAN SAFETY:

- **Tolerances for Residues:**
  The tolerance established for the pioneer product applies to the generic product. A tolerance of 25 parts per billion (ppb) is established for residues of the parent compound, melengestrol acetate, in fat of cattle under 21 CFR 556.380.

Tolerances of 0.09 parts per million (ppm) in liver (the target tissue) and 0.03 ppm in the muscle of cattle are established for ractopamine hydrochloride under 21 CFR 556.570. The Acceptable Daily Intake for total residues of ractopamine hydrochloride is 1.25 micrograms per kilogram of body weight per day. A tolerance of 0.05 ppm is established for negligible residues of monensin sodium in the edible tissues of cattle under 21 CFR 556.420.

- **Withdrawal Times:**
  Because a waiver of the *in vivo* bioequivalence study was granted, the withdrawal times are those previously assigned to the pioneer product.

  A withdrawal time is not required for the use of this generic three-way drug combination.

- **Regulatory Method for Residues:**
  Practical regulatory methods for analysis of tissue residues of melengestrol acetate, ractopamine hydrochloride and monensin sodium may be found in the *Food Additives Analytical Manual* on display in FDA's Freedom of Information Public Room (Parklawn Building, Room 12A30).

4. AGENCY CONCLUSIONS:

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that the combination of HEIFERMAX 500, OPTAFLEXX, and RUMENSIN when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling is attached as follows:

Generic Labeling for ANADA 200-448:
Blue Bird labeling (Type C):
Heifer Supplement
Liquid Supplement
Ractopamine hydrochloride and monensin sodium