Date of Approval: April 27, 2006

FREEDOM OF INFORMATION (FOI) SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-424

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

Type A Medicated Articles

Indication for use: For suppression of estrus (heat), increased rate of weight gain, improved feed efficiency, increased leanness, prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*, and reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces* (*Corynebacterium*) *pyogenes* in heifers being 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 200-424
b. Sponsor:	Ivy Laboratories, Div. of Ivy Animal Health, Inc. 8857 Bond Street Overland Park, KS 66214 Drug Labeler Code: 021641
c. Established Names:	Melengestrol acetate, ractopamine hydrochloride, monensin sodium, and tylosin phosphate
d. Proprietary Names:	HEIFERMAX 500, OPTAFLEXX, RUMENSIN, and TYLAN
e. Dosage Form:	Type A medicated articles for use in combination for the manufacture of four-way Type C medicated feeds
f. How Supplied:	HEIFERMAX 500 – liquid premix OPTAFLEXX – dry premix RUMENSIN – dry granulated premix TYLAN – dry premix
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	HEIFERMAX 500: 500 mg of melengestrol acetate activity per pound of premix OPTAFLEXX: 45 g ractopamine hydrochloride per pound of premix RUMENSIN: 20, 30, 45, 60, 80, or 90.7 g of monensin sodium activity per pound of premix TYLAN: 10, 40 or 100 g of tylosin phosphate activity per pound of premix
i. Route of Administration:	Orally in feed
j. Species/Class:	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 per head per day to a Type C medicated feed containing 9.8 to 24.6 g/ton ractopamine hydrochloride, 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, and 8 to 10 g/ton tylosin phosphate.
l. Pharmacological Category:	Steroid hormone, beta adrenergic agonist, anticoccidial, and antimicrobial
m. Indications:	For suppression of estrus (heat), increased rate of weight gain, improved feed efficiency, increased leanness, the prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*, and reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces (Corynebacterium) pyogenes* in heifers being fed in confinement for slaughter for the last 28 to 42 days on feed.
n. Generic Product:	HEIFERMAX 500 plus OPTAFLEXX, RUMENSIN, and TYLAN; melengestrol acetate, ractopamine hydrochloride, monensin sodium and tylosin phosphate; ANADA 200-424; Ivy Laboratories, Div. of Ivy Animal Health, Inc.
o. Pioneer Product/Listed Product:	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. TYLAN; tylosin phosphate; NADA 012-491; Elanco Animal Health, A Division of Eli Lilly & Co.

OPTAFLEXX, RUMENSIN, TYLAN, and MGA 500; ractopamine hydrochloride, monensin sodium, tylosin phosphate, and melengestrol acetate; NADA 141-233; Elanco Animal Health, A Division of Eli Lilly & Co.

2. TARGET ANIMAL SAFETY AND 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 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 Guidance, revised October 9, 2002).

This approval is for the use of HEIFERMAX 500 (melengestrol acetate) in combination with OPTAFLEXX (ractopamine hydrochloride), RUMENSIN (monensin sodium), and TYLAN (tylosin phosphate) for the manufacture of four-way combination Type C medicated feeds. This combination product is a generic copy of MGA 500 (melengestrol acetate) plus OPTAFLEXX, RUMENSIN, and TYLAN, 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. Tylosin is codified under 21 CFR 558.625. The combination of melengestrol acetate ractopamine, monensin, and tylosin is codified under 21 CFR 558.500(e)(2).

3. HUMAN SAFETY:

- **Tolerances for Residues:**
  The tolerances established for the pioneer product apply to the generic product. A tolerance of 25 ppb is established for residues of the parent compound, melengestrol acetate, in fat of cattle as codified under 21 CFR 556.380.

The tolerance of 0.03 part per million in muscle and 0.09 part per million in liver is established for residues of ractopamine hydrochloride in cattle as codified under 21 CFR 556.570.

A tolerance of 0.05 ppm is established for negligible residues of monensin in the edible tissues of cattle as codified under 21 CFR 556.420.

A tolerance of 0.2 ppm is established for negligible residues of tylosin in uncooked fat, muscle, liver, and kidney in cattle as codified under 21 CFR 556.740.

- **Withdrawal Times:**
  The withdrawal times for the generic product are those previously assigned to the pioneer product.

  No withdrawal times are assigned.

- **Regulatory Method for Residues**
  Withdrawal times are not assigned for any of the drug ingredients in this combination product. Therefore, regulatory methods for residues are not available.

4. AGENCY CONCLUSIONS:

This ANADA filed 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 medicated feed use combination product HEIFERMAX 500 plus OPTAFLEXX, RUMENSIN, and TYLAN, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling is attached as indicated below:

Generic Labeling for ANADA 200-424:
Blue Bird labeling for Type C medicated feeds – liquid and dry melengestrol acetate; ractopamine, monensin, and tylosin