Date of Approval: December 3, 2004

FREEDOM OF INFORMATION (FOI) SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-343

HEIFERMAX 500
(melengestrol acetate)
Liquid Premix

Type A Medicated Article

For Increased Rate of Weight Gain, Improved Feed Efficiency and Suppression of Estrus in Heifers

Sponsored by:
Ivy Laboratories,
Division of Ivy Animal Health, Inc.

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

a. File Number:	ANADA 200-343
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
d. Proprietary Name:	HEIFERMAX 500 Liquid Premix
e. Dosage Form:	Type A Medicated Article
f. How Supplied:	40 pound (18 kg) (4.627 gal [17.5 L]) containers
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	500 mg melengestrol acetate per pound
i. Route of Administration:	Oral
j. Species/Class:	Cattle/Heifers
k. Recommended Dosage:	**Heifers Fed in Confinement for Slaughter**: HEIFERMAX 500 Liquid Premix should be thoroughly mixed in liquid Type C medicated feed which must be fed at 0.5 to 2.0 pounds per head daily to provide 0.25 to 0.5 mg of melengestrol acetate per head per day. Average daily intakes approximating the middle of this range provide the most optimal and economical improvements in rate of weight gain and feed utilization. Constant daily intakes of 0.35 to 0.50 mg per head per day give a high degree of estrus suppression. Levels of 0.25 to 0.35 mg provided a lower but still effective degree of estrus suppression. Withdrawal periods of three to five days or more should be avoided to prevent the possibility that the heifers may come into estrus (heat) at loading time.

Heifers Intended for Breeding:
HEIFERMAX 500 Liquid Premix should be thoroughly mixed in the supplement to provide 0.50 mg of melengestrol acetate per head per day.

Do not exceed 24 days of feeding of melengestrol acetate to heifers intended for breeding. A reduced conception rate can be expected if heifers are bred at estruses observed within 1 to 12 days after withdrawal of melengestrol acetate, whereas heifers bred at subsequent observed estruses are expected to have normal conception rates.

l. Pharmacological Category: Hormone

m. Indications: Heifers Fed in Confinement for Slaughter: For increased rate of weight gain, improved feed efficiency and suppression of estrus (Heat). Heifers Intended for Breeding: For suppression of estrus (Heat).

n. Pioneer Product: MGA 500; melengestrol acetate; NADA 039-402; Pharmacia & Upjohn 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 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).

Based on the formulation characteristics of the generic product, Ivy Laboratories, Div. of Ivy Animal Health, Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for HEIFERMAX 500 (melengestrol acetate) Liquid Premix. The generic product is marketed as a Type A Medicated Article, contains the same active ingredient in the same concentration and dosage form as the pioneer product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient. The pioneer product MGA 500

(melengestrol acetate), the subject of Pharmacia & Upjohn Co. NADA 039-402, was approved on May 22, 1968.

3. HUMAN SAFETY:

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

- **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 melengestrol acetate in heifers.

- **Regulatory Method for Residues:**
  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.
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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 HEIFERMAX 500 Liquid Premix, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling and currently approved pioneer labeling are attached as indicated below:

<u>Generic Labeling for ANADA 200-343:</u>
HEIFERMAX 500 (melengestrol acetate) Liquid Premix
1 – Type A Medicated Article container label (front and back); 1 – Type C Medicated Feed blue bird label

<u>Pioneer Labeling for NADA 039-402:</u>
MGA 500 (melengestrol acetate) Liquid Premix
1 – Type A Medicated Article container label (onsert); 1 – Type C Medicated Feed blue bird label