Approval Date: August 19, 2003

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPLICATION (ANADA)

ANADA 200-346

COMPONENT® TE-IH (trenbolone acetate and estradiol)

Indications for use: For increased rate of weight gain in heifers fed in confinement for slaughter.

Sponsored by:

Ivy Laboratories,
Division of Ivy Animal Health, Inc.
8857 Bond Street
Overland Park, KS 66214

FREEDOM OF INFORMATION SUMMARY

Component® TE-IH Ear Implant for Heifers Fed in Confinement for Slaughter

1. GENERAL INFORMATION:

a. File Number:	ANADA 200-346
b. Sponsor:	Ivy Laboratories, Division of Ivy Animal Health, Inc. 8857 Bond Street Overland Park, KS 66214 Drug Labeler Code: 021641
c. Established Names:	Trenbolone acetate and estradiol
d. Proprietary Name:	Component® TE-IH
e. Dosage Form:	Implantation (ear implant) as per 21 CFR 522.2477.
f. How Supplied:	As an implant made up of 4 pellets with each pellet containing 20 mg trenbolone acetate and 2 mg estradiol.
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	Trenbolone acetate: 80 mg trenbolone acetate activity. Estradiol: 8 mg estradiol activity.
i. Route of Administration:	Subcutaneous ear implant
j. Species/Class:	Heifers fed in confinement for slaughter
k. Recommended Dosage:	One implant containing 80 mg trenbolone acetate and 8 mg estradiol per animal.
l. Pharmacological Category:	Steroid hormones [a natural occurring estrogen, estradiol and a synthetic testosterone, trenbolone acetate].
m. Indications:	For increased rate of weight gain in heifers fed in confinement for slaughter.
n. Pioneer Product:	Revalor®-IH (trenbolone acetate and estradiol); NADA 140-992; Intervet, Inc.

o. Effect of Supplement: This submission for Component® TE-IH for heifers is a supplement to the original ANADA 200-346 for Component® TE-H. Component® TE-IH is a lower dose of Component® TE-H with each pellet in Component® TE-IH (total of 4 pellets) containing 20 mg trenbolone acetate and 2 mg estradiol in the same formulation as each pellet in Component® TE-H (total of 7 pellets).

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) 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 is required to show 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).

Based on the formulation characteristics of the generic product, Ivy Laboratories, Division of Ivy Animal Health, Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for the generic product Component® TE-IH. The generic product is administered as an implant, contains the same active ingredients 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, Revalor®-IH (trenbolone acetate and estradiol), the subject of Intervet, Inc. (NADA 140-992), was approved on June 19, 2000.

3. HUMAN SAFETY:

- **Tolerances for Residues:**

  The allowable incremental increases established for the pioneer product apply to the generic product. Estradiol is regulated under 21 CFR 556.240. No residues of estradiol, resulting from the use of estradiol or any of the related esters, are permitted in the uncooked edible tissues of heifers, steers, and calves in excess of the following increments above the concentrations of estradiol naturally present in untreated animals: 120 ppt for muscle, 240 ppt for liver, 360 ppt for kidney, and 480 ppt for fat.

  The tolerances established for the pioneer product apply to the generic product. Trenbolone acetate is regulated under 21 CFR 556.739. The Acceptable Daily Intake (ADI) for total residues of trenbolone is 0.4 micrograms per kilogram of body weight per

day. A tolerance for trenbolone residues in uncooked edible tissues of cattle is not needed.

- **Withdrawal Times:**

  When a generic product demonstrates bioequivalence to the pioneer product in a blood level study where the duration of the study exceeds the withdrawal time assigned to the pioneer product, the generic product is assigned the withdrawal time established for the pioneer product. The zero withdrawal is established for implants containing trenbolone acetate and estradiol.

- **Regulatory Method for Residues:**

  A regulatory method is not required.

4. AGENCY CONCLUSIONS:

This supplemental 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 Component® TE-IH (trenbolone acetate and estradiol), when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling (ANADA 200-346) and currently approved pioneer labeling (NADA 140-992) are attached as indicated below:

Box Label (Generic) – 5 foil pouches each containing 1 cartridge belt with 20 cells (100 implants); 1 implant = 1 dose.
Foil Pouch Label (Generic) – 1 cartridge belt with 20 cells (20 implants); 1 implant = 1 dose.
Package Insert (Generic)

Box Label (Pioneer) – box of 10 x 10 cartridge implants (100 doses)
Box Label (Pioneer) – box of 10 x 100 dose packages (1000 doses)
Box Label (Pioneer) – box of 4 x 1000 dose packages (4000 doses)
Cartridge Label (Pioneer) – 1 cartridge with 10 implants (10 doses)
Package Insert (Pioneer)