Approval Date: March 20, 1997

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

ANADA 200-221

B. Sponsor

Ivy Laboratories, Inc.
8857 Bond Street
Overland Park, KS 66214

C. Proprietary Name

Component™ TE-S

D. Established Name

trenbolone acetate and estradiol

E. Dosage Form

Implantation

F. Dosage Regimen

120 mg trenbolone acetate and 24 mg estradiol per implant

G. Route of Administration

Subcutaneous ear implant; one implant containing 120 mg trenbolone acetate and 24 mg estradiol per animal

H. Indication

For increased rate of weight gain and improved feed efficiency in feedlot steers.

II. EFFECTIVENESS AND TARGET ANIMAL SAFETY

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act, (53 FR 50460, December 15, 1988, First GADPTRA Policy Letter) 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 data and drug effectiveness data are not required for approval of an ANADA. An ANADA relies on the target animal safety and drug effectiveness data in the pioneer's new animal drug application.

The abbreviated new animal drug application contains data from an adequate and well-controlled investigation demonstrating bioequivalence of COMPONENT™ TE-S to the parent drug, Revalor®-S. The bioequivalence study was conducted by Tony Janes, CAVL, Inc. & CRC, 9602 South Washington, Amarillo, TX 79118. The purpose of the study was to demonstrate bioequivalence of COMPONENT™ TE-S to Revalor®-S through comparison of

blood serum trenbolone-17ß and estradiol-17ß in steers implanted with COMPONENT™ TE-S and Revalor®-S.

Eight-four steers were used as test animals in a 91-day study. There were 14 animals per pen with 7 animals from each treatment represented. Steers weighed between 763 and 873 lbs. when the study was initiated. COMPONENT™ TE-S and Revalor®-S were administered subcutaneously in the middle third of the ear with the respective implanting devices.

Blood samples were collected from Day 2 through Day 91 at regular predetermined intervals to monitor serum levels of trenbolone-17ß and estradiol-17ß by radioimmunoassay.

Natural log of area under the curve (LAUC) and natural log of maximum concentration (LCmax) of trenbolone-17ß and estradiol-17ß profiles were evaluated as pivotal bioequivalence parameters. Time to maximum concentration (Tmax) was evaluated as an ancillary parameter. For LAUC and LCmax, a randomized complete block analysis was performed with pen representing the block effect and treatment the fixed effect. The percents to which the 90% confidence intervals lie within the least squares means of the reference formulation (Revalor®-S) were computed as outlined in the FDA/CVM Bioequivalence Guideline (4/12/90).

The analysis of pivotal parameters, LAUC and LCmax indicate blood-level bioequivalence of COMPONENT™ TE-S to Revalor®-S. Tables 1 & 2 below summarize the LAUC and LCmax results for trenbolone-17ß and estradiol-17ß, respectively. Tmax was analyzed nonparametrically to determine medical significance.

Table 1. Differences Between Treatments for LAUC and LCmax of Trenbolone-17ß Concentration

Analysis Variable	LS Mean Component TE-S	LS Mean Revalor-S	Difference	Lower 90% CI	Upper 90% CI	Component TE-S % of Revalor-S
LAUC	9.8326	9.8011	0.0315	-0.1262	0.1891	88.14 to 120.82
LCMAX	6.6436	6.6790	-0.0354	-0.2287	0.1580	79.56 to 117.12

Table 2. Differences Between Treatments for LAUC and LCmax of Estradiol-17ß Concentration

Analysis Variable	LS Mean Component TE-S	LS Mean Revalor-S	Difference	Lower 90% CI	Upper 90% CI	Component TE-S % of Revalor-S
LAUC	8.6419	8.6619	-0.0200	-0.1908	0.1510	82.63 to 116.30
LCMAX	5.3084	5.2389	-0.0695	-0.1345	0.2735	87.42 to 131.46

III. HUMAN FOOD SAFETY

New human food safety data (other than tissue residue data) are not required for approval of an ANADA. An ANADA relies on the human food safety data in the pioneer's new animal drug application.

Allowable Incremental Increases and Safe Concentrations of Residues
The allowable incremental increases and safe concentrations established for the pioneer product apply to the generic product. Allowable incremental increases for estradiol in uncooked edible tissues of cattle are established under 21 CFR 556.240: 120 ppt in muscle, 240 ppt in liver, 360 ppt in kidney, and 480 ppt in fat. The safe concentrations for total trenbolone residue in uncooked edible tissues of cattle are established under 21 CFR 556.739: 50 ppb in muscle, 100 ppb in liver, 150 ppb in kidney, and 200 ppb in fat.

Withdrawal Time
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 because the generic product is assigned a zero withdrawal.

IV. AGENCY CONCLUSIONS

The data submitted in support of this ANADA comply with the requirements of section 512 of the Act and demonstrate that Component™ TE-S is safe and effective for the indications stated on the product labeling.

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.