Approval Date: February 13, 2004

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-221

Trenbolone Acetate and Estradiol, and Tylosin Tartrate (COMPONENT TE-IS WITH TYLAN)

For increased rate of weight gain and improved feed efficiency for steers fed in confinement for slaughter.

Supplemental approval to provide for the addition of a tylosin tartrate pellet as a local antibacterial to COMPONENT TE-IS

Sponsored by:

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

FREEDOM OF INFORMATION SUMMARY

COMPONENT TE-IS with TYLAN Ear Implant for Steers Fed in Confinement for Slaughter

1. GENERAL INFORMATION:

a. File Number:	ANADA 200-221
b. Sponsor:	Ivy Laboratories Div. of Ivy Animal Health, Inc. 8857 Bond Street Overland Park, KS 66214 Drug Labeler Code: 021641
c. Established Names:	Trenbolone acetate and estradiol, and tylosin tartrate
d. Propriety Names:	COMPONENT TE-IS with TYLAN
e. Dosage Form:	Implantation (ear implant) as per 21 CFR 522.2477.
f. How Supplied:	Each box contains 5 foil pouches each containing 1 cartridge belt with 20 cells. Each cartridge cell contains 1 implant dose. Each implant dose consists of 4 pellets each containing 20 mg trenbolone acetate and 4 mg estradiol and 1 pellet containing 29 mg tylosin tartrate.
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	Trenbolone acetate: 80 mg trenbolone acetate. Estradiol: 16 mg estradiol. Tylosin tartrate: 29 mg tylosin tartrate.
i. Route of Administration:	Subcutaneous ear implant
j. Species/Class:	Steers fed in confinement for slaughter
k. Recommended Dosage:	One implant containing 80 mg trenbolone acetate, 16 mg estradiol, and 29 mg tylosin tartrate per animal.
l. Pharmacological Category:	Steroid hormone and antibacterial

m. Indications:	For increased rate of weight gain and improved feed efficiency for steers fed in confinement for slaughter.
n. Effect of Supplement:	This supplement provides for the addition of a tylosin tartrate pellet as a local antibacterial to COMPONENT TE-IS.

2. DRUG EFFECTIVENESS:

a. Substantial Evidence:

The effectiveness requirement for this supplemental new animal drug application, with the indication for use and dosage as given in Section 1 above, is met by utilizing the information contained in the Freedom of Information (FOI) Summary for the abbreviated new animal drug application for COMPONENT TE-S (ANADA 200-221) which was approved March 20, 1997, and contains adequate data from a well-controlled study included in this supplemental application. COMPONENT TE-IS was approved as a supplement to ANADA 200-221 on September 3, 2003. It is the same formulation as COMPONENT TE-S differing only in the number of pellets (4 versus 6). The following effectiveness study conducted with COMPONENT TE-S is therefore applicable to COMPONENT TE-IS:

Title of Study: Induction of Implant Site Abcesses in Steers and the Effect of Addition of a Tylosin Tartrate Pellet
Study Number: Ivy A0776

A study was conducted by William Barton, CAVL, Inc, Amarillo, TX to evaluate the effectiveness of COMPONENT TE-S with TYLAN (120 mg trenbolone acetate and 24 mg estradiol (6 pellets), and 29 mg tylosin tartrate (1 pellet)) to lower the incidence of ear abscess formation. An implant site abscess induction model was developed to reliably create a high abscess rate in test animals. This model was used to test the ability of a tylosin tartrate pellet to reduce implant site abscess incidence in animals expected to develop an ear abscess. In the study, 46 beef steers were subjected to the abscess-inducing culture at the same time they were implanted with either COMPONENT TE-S with a TYLAN pellet or COMPONENT TE-S alone. Implant sites were observed at regular intervals up to 35 days following implantation. Abscess rate at each time point was significantly lower ($P<0.0001$) in animals treated with COMPONENT TE-S with a TYLAN pellet compared to animals treated with COMPONENT TE-S alone, with the maximum incidence of abscesses of 5% and 100%, respectively.

3. TARGET ANIMAL SAFETY:

Target animal safety of COMPONENT TE-IS is established by data in the FOI Summary for the parent application (ANADA 200-221) approved March 20, 1997. The data provided in the effectiveness study described above were sufficient to conclude that the use of the tylosin tartrate pellet was safe for use in cattle. No further studies were required.

4. HUMAN SAFETY:

Human safety is established for COMPONENT TE-IS by data in the FOI Summary in the parent application (ANADA 200-221) which was approved March 20, 1997. No further residue studies were required for use of the tylosin tartrate pellet.

A. Microbial Food Safety

The Agency evaluated the microbial food safety for COMPONENT TE-IS ear implants containing 80 mg trenbolone acetate, 16 mg estradiol, and 29 mg of tylosin. The sponsor submitted a microbial food safety "hazard identification" for review. This "hazard identification" information addressed drug-specific characteristics, information on bacterial resistance, and data gaps and emerging science relative to antimicrobial resistance and the use of tylosin in cattle. Upon review of this information, the Agency concluded that use of this product in cattle does not contribute significantly to the emergence or selection of macrolide resistant bacteria of public health concern.

5. 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 trenbolone acetate and estradiol, and tylosin tartrate (COMPONENT TE-IS with TYLAN), when used under its proposed conditions of use, is safe and effective for its labeled indications.

The Center for Veterinary Medicine has concluded that, for this product, adequate directions for use by the layperson have been provided and the product will have over-the-counter (OTC) status. Label directions are accompanied by pictorial diagrams and detailed instruction in plain language. The drug is not a controlled substance. Thus, the product is assigned OTC status, and the labeling is adequate for the intended use.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this supplemental approval qualifies for THREE years of marketing exclusivity beginning on the date of the approval, the basis for which is Ivy Study #A0776, described in Section 2 above. The three years of marketing exclusivity applies only to the addition of the tylosin tartrate pellet as a local antibacterial for which this supplement was approved.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

COMPONENT TE-IS with TYLAN is under the following U.S. patent number:

U.S. Patent Number	Date of Expiration
5,874,098	May 28, 2017

6. ATTACHMENTS:

Facsimile Generic Labeling is attached as indicated below:

COMPONENT TE-IS with TYLAN Box Label
COMPONENT TE-IS with TYLAN 20 Dose Foil Pouch Label (Front)
COMPONENT TE-IS with TYLAN 20 Dose Foil Pouch Label (Back)
COMPONENT TE-IS with TYLAN Package Insert (Front)
COMPONENT TE-IS with TYLAN Package Insert (Back)