Date of Approval: January 26, 2007

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

ANADA 200-346

COMPONENT TE-200 with TYLAN

Trenbolone Acetate and Estradiol with Tylosin
Hormone Ear Implant
Steers and Heifers Fed in Confinement for Slaughter

This supplement provides for the addition of a 29 mg tylosin tartrate pellet as a local antibacterial to COMPONENT TE-200 for use in steers and heifers fed in confinement for slaughter.

Sponsored by:

Ivy Laboratories

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I. GENERAL INFORMATION:

A. File Number:	ANADA 200-346
B. Sponsor:	Ivy Laboratories Div. of Ivy Animal Health, Inc. 8857 Bond Street Overland Park, KS 66214 Drug Labeler Code: 021641
C. Proprietary Name:	COMPONENT TE-200 with TYLAN
D. Established Name(s):	Trenbolone Acetate and Estradiol with Tylosin
E. Pharmacological Category:	Steroid hormone, antibacterial
F. Dosage Form:	Implantation (ear implant) as per 21 CFR 522.2477
G. Amount of Active Ingredient(s):	200 mg trenbolone acetate activity 20 mg estradiol activity 29 mg tylosin tartrate activity
H. How Supplied:	Each box contains 5 foil pouches each containing 1 cartridge belt with 20 cells. Each cartridge cell contains 1 implant dose. Each dose consists of 10 pellets each containing 20 mg of trenbolone acetate (200 mg) and 2 mg estradiol (20 mg) with 1 pellet of tylosin tartrate (29 mg) as a local antibacterial.
I. How Dispensed:	OTC
J. Dosage:	One implant containing 200 mg trenbolone acetate and 20 mg estradiol with 29 mg tylosin tartrate.
K. Route of Administration:	Subcutaneous implantation on the posterior aspect of the middle one-third of the ear by means of an implant gun.
L. Species/Class(es):	Steers and heifers fed in confinement for slaughter
M. Indication(s):	For increased rate of weight gain and improved feed efficiency for steers and heifers fed in

confinement for slaughter.

N. Effect of Supplement: This supplement provides for the addition of a 29 mg tylosin tartrate pellet as a local antibacterial to COMPONENT TE-200 for use in steers and heifers fed in confinement for slaughter.

II. EFFECTIVENESS:

A. Dosage Characterization:

This supplemental approval does not change the previously approved dosage. The FOI Summaries for the original approval of ANADA 200-346 dated September 27, 2002, and supplemental approval dated April 21, 2003, contains dosage characterization information for steers and heifers fed in confinement for slaughter.

B. Substantial Evidence:

1. Tylosin Tartrate Pellet Efficacy/Induction Study Number: Ivy A1076

A study was conducted by William Barton, CAVL, Inc, Amarillo, TX to evaluate the effectiveness of COMPONENT TE-H with TYLAN (140 mg trenbolone acetate and 14 mg estradiol (7 pellets), and 29 mg tylosin tartrate (1 pellet)) to lower the incidence of ear abscess formation. This study was previously accepted for approval of COMPONENT TE-H with a tylosin tartrate pellet (see FOI Summary dated April 18, 2003), and now has been determined to be an appropriate model for COMPONENT TE-200, since COMPONENT TE-200 and COMPONENT TE-H are the same formulation and differ only in the number of pellets (10 versus 7). 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, 40 beef heifers were subjected to the abscess-inducing culture at the same time they were implanted with either COMPONENT TE-H with a TYLAN pellet or COMPONENT TE-H 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-H with a TYLAN pellet compared to animals treated with COMPONENT TE-H alone, with the maximum incidence of abscesses of 5% and 100%, respectively.

III. TARGET ANIMAL SAFETY:

CVM did not require target animal safety studies for this supplemental approval. The FOI Summary for the original approval of ANADA 200-346 dated September 27, 2002,

contains a summary of target animal safety studies for steers and heifers fed in confinement for slaughter.

IV. HUMAN FOOD SAFETY:

A. Toxicology:

CVM did not require toxicology studies for this supplemental approval.

B. Residue Chemistry:

CVM did not require residue chemistry studies for this supplemental approval.

C. Microbial Food Safety:

The Agency evaluated available microbial food safety information for COMPONENT TE-200 ear implants containing 200 mg trenbolone acetate, 20 mg estradiol, and 29 mg of tylosin tartrate for use in cattle fed in confinement for slaughter, for increased rate of weight gain and improved feed efficiency. The sponsor submitted a microbial food safety *hazard characterization* for review. This *hazard characterization* addressed drug-specific characteristics, information on bacterial resistance, data gaps and emerging science relative to antimicrobial resistance and the use of tylosin tartrate in cattle. Upon review of this information, the Agency concluded that the supplemental use of 29 mg tylosin tartrate in ear implants for cattle fed in confinement for slaughter does not contribute significantly to the emergence or selection of macrolide resistant bacteria of public health concern.

D. Analytical Method for Residues:

The analytical method for detection of residues of tylosin is on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855. A regulatory method was not required for either trenbolone acetate or estradiol.

V. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to COMPONENT TE-200 with TYLAN:

"FOR USE IN ANIMALS ONLY – NOT FOR HUMAN USE – KEEP OUT OF REACH OF CHILDREN."

The material safety data sheet for COMPONENT TE-200 with TYLAN indicates there are no special measures for exposure control or personal protection so long as the product is handled according to directions stipulated on product labeling.

VI. AGENCY CONCLUSIONS:

The data submitted in support of this ANADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514. The data demonstrate that COMPONENT TE-200 with TYLAN, when used according to the label, is safe and effective for increased rate of weight gain and improved feed efficiency for steers and heifers fed in confinement for slaughter. Additionally, data demonstrate that residues in food products derived from steers and heifers fed in confinement for slaughter treated with COMPONENT TE-200 with TYLAN will not represent a public health concern when the product is used according to the label.

A. Marketing Status:

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.

B. Exclusivity:

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of the approval. 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.

C. Supplemental Applications:

This supplemental ANADA did not require a reevaluation of the safety or effectiveness data in the original ANADA (21 CFR §514.106(b)(2)).

D. Patent Information:

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

VII. ATTACHMENTS:

Facsimile Labeling:
COMPONENT TE-200 with TYLAN Carton Label
COMPONENT TE-200 with TYLAN Pouch Label
COMPONENT TE-200 with TYLAN Package Insert