

Approval Date: SEP 3 2003

FREEDOM OF INFORMATION SUMMARY
SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG
APPLICATION

ANADA 200-221

Trenbolone Acetate and Estradiol

COMPONENT TE-IS
Ear Implant

A generic copy of Intervet, Inc.'s REVALOR-IS (NADA 140-897)

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

Sponsored by:

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

ANADA 200-221

FOIS

FREEDOM OF INFORMATION SUMMARY

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

1. GENERAL INFORMATION:

- a. File Number: ANADA 200-221
- 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-IS
- e. Dosage Form: Implantation (ear implant)
- f. How Supplied: As an implant made up of 4 pellets with each pellet containing 20 mg trenbolone acetate and 4 mg estradiol
- g. How Dispensed: OTC
- h. Amount of Active Ingredients: Trenbolone acetate: 80 mg trenbolone acetate activity
Estradiol: 16 mg estradiol activity
- 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 and 16 mg estradiol per animal.
- l. Pharmacological Category: Steroid hormone
- m. Indications: For increased rate of weight gain and improved feed efficiency for steers fed in confinement for slaughter.

- n. Pioneer Product: REVALOR-IS
Trenbolone acetate and estradiol
NADA 140-897
Intervet, Inc.
- o. Effect of Supplement: The supplement provides for the use of a generic copy of Intervet, Inc.'s REVALOR-IS, a 4-pellet ear implant containing 80 mg trenbolone acetate and 16 mg estradiol.

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.

Approval of COMPONENT TE-IS is granted as a supplement to the original ANADA for COMPONENT TE-S. COMPONENT TE-IS is a reduced dose of COMPONENT TE-S with each pellet in COMPONENT TE-IS (total of 4 pellets) containing 20 mg trenbolone acetate (TBA) and 4 mg estradiol in the same formulation as each pellet in COMPONENT TE-S (total of 6 pellets). Likewise, the pioneer product, REVALOR-IS, is a reduced dose of REVALOR S with each pellet in REVALOR-IS (total of 4 pellets) containing 20 mg trenbolone acetate and 4 mg estradiol in the same formulation as each pellet in REVALOR S (total of 6 pellets). COMPONENT TE-S has been shown to be bioequivalent to REVALOR S in an adequate and well controlled blood level bioequivalence study in steers fed in confinement for slaughter, which was previously submitted in support of ANADA 200-221, approved March 20, 1997. Since COMPONENT TE-S has been shown to be bioequivalent to REVALOR S (each composed of six pellets) in feedlot steers, the release (rate and extent) of trenbolone acetate and estradiol from the individual pellets in REVALOR-IS and COMPONENT TE-IS in each animal should be bioequivalent to each other in feedlot steers.

3. HUMAN SAFETY:

- **Allowable Incremental Increases and Acceptable Daily Intake (ADI) of Total Residues:**
The allowable incremental increases established for the pioneer product apply to the generic product. Allowable incremental increases for estradiol in uncooked edible tissues of steers are established under 21 CFR 556.240: 120 ppt for muscle, 240 ppt for liver, 360 ppt for kidney, and 480 ppt for fat.

The Acceptable Daily Intake (ADI) established for the pioneer product applies to the generic product. An ADI for total residues of trenbolone in uncooked edible tissues of cattle is established under 21 CFR 556.739: 0.4 micrograms per kilogram of body weight per day.

- **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. A zero withdrawal is established for implants containing trenbolone acetate and estradiol.

- **Regulatory Method for Residues**

A regulatory method is not required because one was not required for the pioneer product.

4. AGENCY CONCLUSIONS:

This 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 the trenbolone acetate and estradiol (COMPONENT TE-IS), 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:

Box Label (Generic - Steers)
Foil Pouch Label (Generic - Steers)
Package Insert (Generic - Steers)
Box Label (Pioneer - Steers)
Cartridge Label (Pioneer - Steers)
Package Insert (Pioneer - Steers)

**RESTRICTED DRUG – USE ONLY AS DIRECTED (CALIFORNIA) – FOR USE IN ANIMALS ONLY
NOT FOR HUMAN USE – KEEP OUT OF REACH OF CHILDREN**

Storage Conditions: Store in a refrigerator (2°-8°C; 36°-46°F) and protect from sunlight.
Use before the expiration date.

Manufactured by a non-sterilizing process.

COMPONENT[®] TE-IS
BRAND IMPLANTS

**FOR STEERS FED IN
CONFINEMENT FOR SLAUGHTER**

trenbolone acetate 80 mg and
estradiol USP 16 mg



Contents

Dosage

100 IMPLANTS



WARNING: Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 4 pellets (entire contents of one cartridge cell) — in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

Important: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

COMPONENT and COMPONENT One Gun are registered trademarks of Ivy Animal Health, Inc.

Manufactured for VetLife by Ivy Laboratories • Overland Park, KS 66214, USA
VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.

01 09 03 00

COMPONENT[®] TE-IS
trenbolone acetate 80 mg
and estradiol USP 16 mg
FOR STEERS FED IN
CONFINEMENT FOR SLAUGHTER

18.875"

9.5"

3.125"

1/4" Seal Area

COMPONENT[®] TE-IS

BRAND IMPLANTS

trenbolone acetate 80 mg
and estradiol USP 16 mg

FOR STEERS FED IN
CONFINEMENT FOR SLAUGHTER



↑
TEAR HERE

COMPONENT TE-IS contains trenbolone acetate and estradiol for increased rate of weight gain and improved feed efficiency in a slow-release delivery system.

Contains: One Cartridge Belt of 20 implants sealed in a sanitary foil pouch.

Dosage: Administer 1 implant per animal. See package insert for detailed instructions.

Manufactured by a non-sterilizing process.

¹ Patented by Wy Animal Health, Inc., ANADA 200-021. Approved by FDA



One 20-dose Cartridge Belt

18.875"

9.375"

TEAR HERE

WARNING: Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 4 pellets (entire contents of one cartridge cell) — in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

**RESTRICTED DRUG – USE ONLY AS DIRECTED (CALIFORNIA) – FOR USE IN ANIMALS ONLY
NOT FOR HUMAN USE – KEEP OUT OF REACH OF CHILDREN**

Important: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

Storage Conditions: Store in a refrigerator (2°-8°C; 36°-46°F) and protect from sunlight. Use before the expiration date.

COMPONENT is a registered trademark of Ivy Animal Health, Inc.

Manufactured for **VetLife** by Ivy Laboratories • Overland Park, KS 66214, USA
VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.
01 09 02 00

PURCHASE SEAL 20 IMPLANTS



EXP

LOT

GENESIS 1999032
BLACK

COMPONENT[®]
BRAND IMPLANTS



TE-IS

**FOR STEERS FED IN
CONFINEMENT FOR SLAUGHTER**

trenbolone acetate 80 mg and
estradiol USP 16 mg

20-dose Cartridge Belt*

For use with the COMPONENT One Gun***
For Use In Animals Only

Each CARTRIDGE BELT holds 20 doses of COMPONENT[®] TE-IS implants. Each dose of 4 pellets contains a total of 80 mg of trenbolone acetate and 16 mg estradiol. COMPONENT[®] TE-IS implants are recommended for use in steers fed in confinement for slaughter for INCREASED RATE OF WEIGHT GAIN AND IMPROVED FEED EFFICIENCY.

INDICATIONS FOR USE: This product contains trenbolone acetate and estradiol for increased rate of weight gain and improved feed efficiency in a slow-release delivery system.

DOSAGE: Administer 1 implant per animal according to the following instructions.

GENERAL INSTRUCTIONS: Study the instructions which should be followed carefully at all times, avoiding short cuts. Skin infection can be avoided by properly preparing implant site and implanter. During fly season use fly repellent on implant site. One designated team member should always do the implanting. Cleanliness of hands and instruments is important at all times.

WARNING

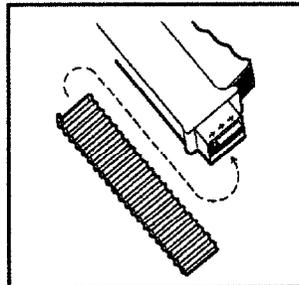
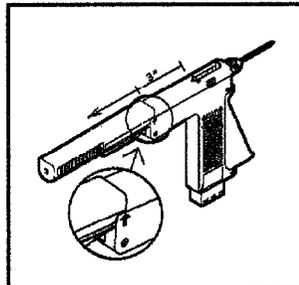
Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 4 pellets (entire contents of one cartridge cell) — in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. **DO NOT** attempt to salvage implantation site for animal feed or human food.

**RESTRICTED DRUG – USE ONLY AS DIRECTED (CALIFORNIA) –
FOR USE IN ANIMALS ONLY – NOT FOR HUMAN USE – KEEP OUT OF
REACH OF CHILDREN**

IMPLANTING INSTRUCTIONS:

Loading the Implanter

Load the Implanter following the instructions supplied with each Implanter.



Restrain the Animal

Speed of implantation as well as safety of handlers is best achieved by restraining animal in a squeeze chute using head restraint. When implanting horned cattle, better control is obtained with additional use of nose tongs.



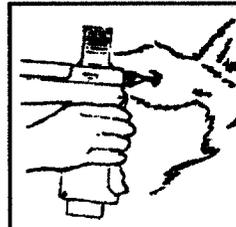
Prepare the Implant Site

Scrub the back side of the ear (implant site) with a piece of clean absorbent cotton which has been soaked with topical germicidal solution. Follow manufacturer's directions on germicide for correct strength and preparation of solution. Avoid getting in animal's eyes.



Where to implant

The full contents of the cartridge should be implanted beneath the skin on the back side of the middle one-third of the ear illustrated in the drawing. The implant must not be closer to the head than the edge of the auricular cartilage ring farthest from the head. The location for insertion of the needle is a point toward the tip of the ear at least a needle length away from the intended deposition site. Avoid injuring the large arteries, veins and cartilage of the ear.



Insert the Needle

With one hand firmly grasp the ear. With the other hand insert needle point through the skin and ease forward on a lateral plane until the entire length of the needle is under the skin.

Implant the Pellets

After inserting the needle fully in the correct implant position squeeze the trigger fully. As the needle is withdrawn from the ear, the controlled-pressure plunger action properly deposits the implant in the needle track. This procedure should prevent breakage or crushing of pellets if otherwise forced into contact with tough fibrous-tissue underlying the skin. The length and total contact area of a single dose are designed to permit absorption of the hormones after implantation to stimulate good weight gain. Broken or crushed pellets may interfere with rates of gain.

Clean the Needle

Clean the implanter needle with alcohol or a properly diluted germicidal solution prior to implanting the next animal.

Storage Conditions

Store in a refrigerator (2°-8°C; 36°-46°F) and protect from sunlight. Use before the expiration date printed on the foil pouch.

ANADA 200-221, Approved by FDA

Manufactured by a non-sterilizing process.

*U.S. Patent No. 4,531,938

**U.S. Patent Nos. 4,762,515 and 5,522,797 – Ivy Animal Health, Inc.

COMPONENT and COMPONENT One Gun are registered trademarks of Ivy Animal Health, Inc.
Manufactured for VetLife by Ivy Laboratories • Overland Park, KS 66214, USA
VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.

INTERVET
 NADA # 140-857, Approved by FDA
 Intervet Inc.
 Millboro, DE 19966
 Made in Australia by
 Intervet GmbH
 Distributed by:
 Intervet (USA) Inc.
 10000 W. Higgins Rd., Suite 100
 Skokie, IL 60077
 Not to be used in animals for subsequent branding or safety
 reasons.
 See enclosed package insert
 for directions.

Expires Date: APR 2004
 Lot Number: 02A017

Revalor-IS

(Iron dextran acetate and dextran)

FOR STEERS FED IN CONFINEMENT FOR SLAUGHTER
Box of 10 x 10 Cartridge Implants

Manufactured by a non-sterilizing process



505016 F8US
010



00021784813006

Revalor-IS

(trenbolone acetate and estradiol)

PACKAGE QUANTITIES:

Box of 10 x 10 implants
Containing 100, 800cc in ten cartridges with 100 implants per cartridge.
Each glass cartridge contains 4 small yellow pellets. Each pellet contains 20 mg of trenbolone acetate and 4 mg estradiol.

STORAGE CONDITIONS:

Store in a refrigerator (2° to 8°C/36°-47°F) and protect from sunlight. Use before the expiration date printed on the box and on the cartridge.

INDICATIONS:

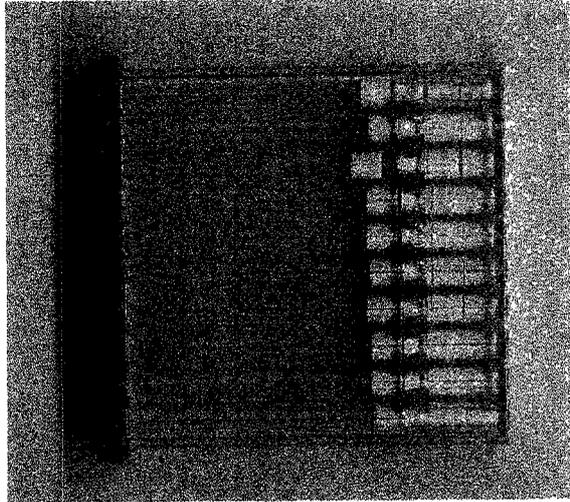
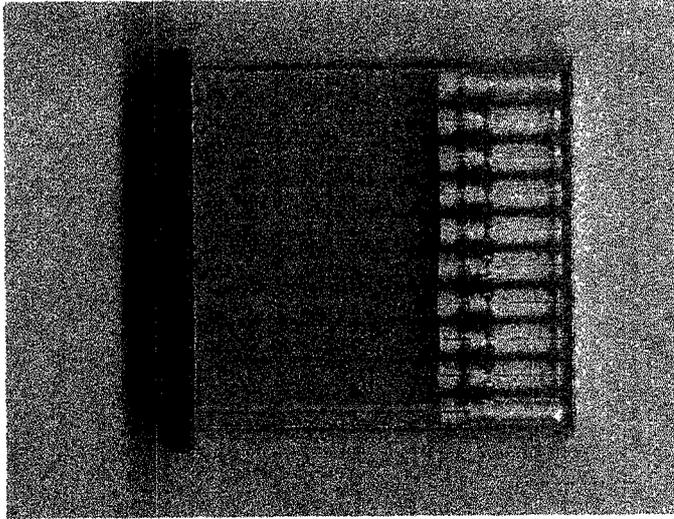
Increases rate of weight gain and improves feed efficiency in a slow-release delivery system.

FOR STEERS FED IN CONFINEMENT FOR SLAUGHTER
Box of 10 x 10 Cartridge Implants

Manufactured by a non-sterilizing process



140x75x75
Pantone Orange 21 Cx
L43
FM 10/26; y=36



Front of Insert

Inside of Insert

Back of Insert



Revalor[®]-IS

(trenbolone acetate and estradiol)

FOR STEERS FED IN CONFINEMENT FOR SLAUGHTER

DESCRIPTION

Revalor[®]-IS (trenbolone acetate and estradiol) is an implant containing 80 mg of trenbolone acetate and 16 mg estradiol. Each implant consists of 4 small yellow pellets. Ten implants are provided in a cartridge.

Manufactured by a non-sterilizing process.

INDICATIONS

Increases rate of weight gain and improves feed efficiency in a slow-release delivery system.

DOSAGE

Dosage Form:

One implant containing 80 mg trenbolone acetate and 16 mg estradiol is administered to each animal. The 4 pellets which make up the dosage of Revalor[®]-IS are contained in one division of the multiple dose cartridge. Ten doses are in each cartridge. The cartridge is designed to be used with a special implant gun.

Route of Administration:

The implant is placed under the skin on the posterior aspect of the ear by means of a special implanter available from Intervet Inc.

508018 GWUS 010



With the animal suitably restrained, the skin on the outer surface of the ear should be cleaned. The implant is then administered by the method shown in the diagram below.

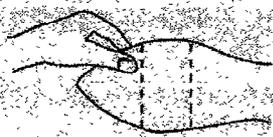


Fig. 1 - Ear of Bovine Ready for Implantation

SITE OF IMPLANTATION

After appropriately restraining the animal to allow access to the ear, cleanse the skin at the implant needle puncture site. It is subcutaneous between the skin and cartilage on the back side of the ear and below the outline of the ear. The implant must not be placed closer to the head than the edge of the cartilage ring furthest from the head. The location of insertion of the needle is a point toward the tip of the ear and at least a needle length away from the intended deposition site. Care should be taken to avoid injuring the major blood vessels or cartilage of the ear.

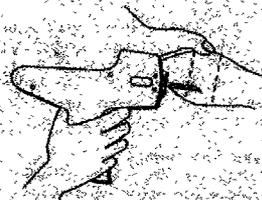
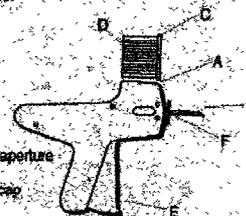


Fig. 2 - Rear View of the Bovine Ear Showing the Site for Insertion of the Implanter Needle.

METHOD OF USE

1. Do not remove the cap of the cartridge containing the implants.
2. Place the cartridge (D) with the capped end to the front into slot at the top of the implanter magazine marked (A) on the diagram.
3. Gently push the cartridge into the slot until it clicks into place.
4. The implanter is then ready for use.
5. Take the ear of the animal firmly with the free hand in the manner shown in Fig. 1. Then insert the needle into the subcutaneous tissue at the point indicated in Fig. 2.
6. After inserting the needle to its full extent, squeeze the trigger (E) gradually. Allow the pellets of the implant to be deposited in a single row.
7. Withdraw the implanter. This will advance the cartridge one groove in the magazine and the next implant is now ready for use.
8. When all the implants have been administered, the cartridge will discharge out the bottom of the magazine and may be replaced by a new one.
9. To change the needle, loosen the needle locking nut labeled (F) in Fig. 3 and replace the needle. Tighten the nut, finger tight and the implanter is ready for use.



- A - Magazine aperture
- B - Needle
- C - Cartridge cap
- D - Cartridge
- E - Trigger
- F - Needle locking nut

Fig. 3 - Diagram of the Implanter and Cartridge

508018 GWUS 010

WARNING

Not to be used in animals intended for subsequent breeding, or in dairy animals. For Animal Treatment Only. Not for Use in Humans. Implant pellets in the ear only. Any other location is in violation of Federal Law. Do not attempt salvage of implanted site for human or animal food.

STORAGE CONDITIONS

Store in a refrigerator (2-8° C, 36-47° F) and protect from sunlight. Use before the expiration date printed on the box and on the cartridge.

PACKAGE QUANTITIES

Box of 10 x 10 cartridge implants.

Made in Austria by
Intervet GmbH

Distributed by
Intervet Inc.
Millsboro, DE 19966

462020-B

Intervet

NADA # 140-897, Approved by FDA