

Approval Date: JAN 14 2005

FREEDOM OF INFORMATION SUMMARY
SUPPLEMENTAL ABBREVIATED NEW ANIMAL
DRUG APPLICATION

ANADA 200-346

COMPONENT TE-200
(trenbolone acetate and estradiol)

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

Sponsored by:

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

FREEDOM OF INFORMATION SUMMARY

1. 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. Established Names: Trenbolone acetate and estradiol
- d. Proprietary Name: COMPONENT TE-200
- e. Dosage Form: Implantation (ear implant)
- f. How Supplied: As an implant made up of 10 pellets with each pellet containing 20 mg trenbolone acetate and 2 mg estradiol. One cartridge belt holds 20 implants.
- g. How Dispensed: OTC
- h. Amount of Active Ingredients: Trenbolone acetate: 200mg trenbolone acetate activity.
Estradiol: 20 mg estradiol activity.
- i. Route of Administration: Subcutaneous ear implant
- j. Species/Class: Steers and heifers fed in confinement for slaughter
- k. Recommended Dosage: One implant containing 200 mg trenbolone acetate and 20 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 and improved feed efficiency in steers and heifers fed in confinement for slaughter.

- n. Pioneer Product: REVALOR-200; trenbolone acetate and estradiol; NADA 140-992; Intervet, Inc.
- o. Effect of Supplement: This supplement provides for the addition of heifers to the label of Ivy Laboratories' approved product COMPONENT TE-200 (trenbolone acetate and estradiol). The indications are for increased rate of weight gain and improved feed efficiency in steers and heifers fed in confinement for slaughter.

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.

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, Div. of Ivy Animal Health, Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for the generic product COMPONENT TE-200. 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-200 (trenbolone acetate and estradiol), the subject of Intervet, Inc. (NADA 140-992), was approved for use in heifers on December 6, 2001.

3. HUMAN SAFETY:

- **Tolerances for Residues:**

The tolerance established for the pioneer product applies to the generic product. A tolerance for total trenbolone residues in uncooked edible tissues of cattle is not needed (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 (21 CFR 556.739).

Estradiol is regulated under 21 CFR 556.240 on the basis of allowable incremental increases. The allowable incremental increases established for the pioneer product apply to the generic product. No residues of estradiol, resulting from the use of

estradiol or any of the related esters, are permitted in the uncooked edible tissues of heifer, steers, and calves in excess of the following increments above the concentrations of estradiol naturally present in untreated animals: 120 ppt for muscle, 480 ppt for fat, 360 ppt for kidney, and 240 ppt for liver.

- **Withdrawal Times:**

Because a waiver of the *in vivo* bioequivalence study was granted, the withdrawal times are those previously assigned to the pioneer product.

The withdrawal time is zero days.

- **Regulatory Method for Residues:**

A regulatory method is not required because the generic product is assigned a zero withdrawal.

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-200 (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 and currently approved pioneer labeling are attached as follows:

Generic Labeling for ANADA 200-346:

COMPONENT TE-200

Box Label – box of 5 cartridge belts of 20 implants each (100 doses)

Foil Pouch (Front)

Foil Pouch (Back)

Cartridge Label – 1 cartridge with 20 implants (20 doses)

Package Insert (Front)

Package Insert (Back)

Pioneer Labeling for NADA 140-992:

REVALOR-200

Box Label – box of 10 x 10 cartridge implants (100 doses) (2 sides)

Box Label – box of 10 x 100 cartridge implants (1000 doses)

Box Label – box of 4 x 1000 cartridge implants (4000 doses)

Cartridge Label – 1 cartridge with 10 implants (10 doses)

Package Insert

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

COMPONENT[®] TE-200

BRAND IMPLANTS FOR STEERS AND HEIFERS
fed in confinement for slaughter

trenbolone acetate 200 mg and
estradiol USP 20 mg



COMPONENT TE-200 contains trenbolone acetate and estradiol for increased rate of weight gain and improved feed efficiency in a slow-release delivery system.

Contents: 5 foil pouches each containing 1 cartridge cell* with 20 pellets. Each cartridge cell contains 1 implant dose. Each dose consists of trenbolone acetate 200 mg and estradiol 20 mg.

Dosage: Administer 1 implant per animal. See package insert for detailed instructions. Do not use in veal calves.

* Patented by Ivy Animal Health, Inc. ANADA 200-346, Approved by FDA

100 IMPLANTS



WARNING: Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 10 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.

A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

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

NOTE: Component TE-200 is not better for increased average daily gain or improved feed efficiency than Component TE-H (140 mg trenbolone acetate/14 mg estradiol) in heifers fed in confinement for slaughter. Studies have demonstrated that the administration of Component TE-200 can result in decreased marbling scores when compared to non-implanted steers and heifers.

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

Manufactured by a non-sterilizing process.

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 14 03 01

Use With Gray
Component
One Gun Only



trenbolone acetate 200 mg
and estradiol USP 20 mg
fed in confinement for slaughter

COMPONENT[®] TE-200

9.5"

3.125"

1/4" Seal Area

COMPONENT[®] TE-200
 BRAND IMPLANTS
FOR STEERS AND HEIFERS
 fed in confinement for slaughter

trenbolone acetate 200 mg
 and estradiol USP 20 mg



TEAR HERE

COMPONENT TE-200 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. Do not use in veal calves.

Manufactured by a non-sterilizing process.
 * Patented by Ivy Animal Health, Inc. ANADA 200-346. Approved by FDA

One 20-Dose Cartridge Belt



9.375"

WARNING: Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 10 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.

A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

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

Note: Component TE-200 is not better for increased average daily gain or improved feed efficiency than Component TE-H (140 mg trenbolone acetate/14 mg estradiol) in heifers fed in confinement for slaughter. Studies have demonstrated that the administration of Component TE-200 can result in decreased marbling scores when compared to non-implanted steers and heifers.

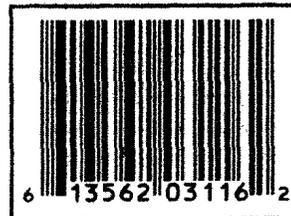
Important: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

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

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

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VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.
01 14 02 01

PURCHASE SEAL 20 IMPLANTS



EXP

LOT

TEAR HERE

GENESIS 1999032

COMPONENT TE-300
LOT XXXXX EXP XXX XX

COMPONENT[®]
BRAND IMPLANTS

VetLife

TE-200

FOR STEERS AND HEIFERS

fed in confinement for slaughter

trenbolone acetate 200 mg and
estradiol USP 20 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-200 Implants. Each dose of 10 pellets contains a total of 200 mg of trenbolone acetate and 20 mg estradiol. COMPONENT[®] TE-200 Implants are recommended for use in steers and heifers 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. Do not use in veal calves. Effectiveness and animal safety in veal calves have not been established.

NOTE: COMPONENT[®] TE-200 is not better for increased average daily gain or improved feed efficiency than COMPONENT[®] TE-H (140 mg trenbolone acetate/ 14 mg estradiol) in heifers fed in confinement for slaughter. Studies have demonstrated that the administration of COMPONENT[®] TE-200 can result in decreased marbling scores when compared to non-implanted steers and heifers.

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 — 10 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.

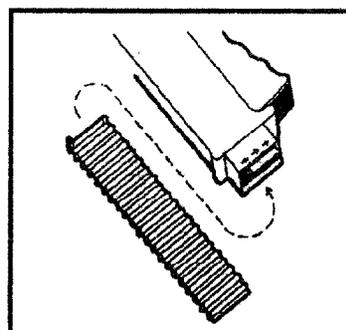
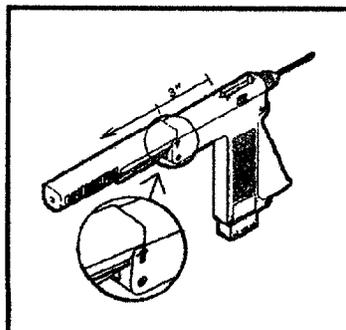
A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

**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

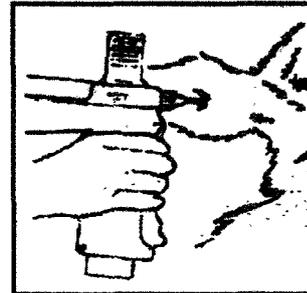
Speed of implantation as well as safety of handlers is best achieved by restraining animal in a squeeze chute using head restraint. When implanting horned cattle, better control is obtained with additional use of nose tongs.

**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 disinfectant in animal's eyes.

**Where to Implant**

The full contents of one cartridge cell 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 are 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 200-346, 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.

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



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Revalor[®]-200

(trenbolone acetate and estradiol)

PACKAGE QUANTITIES:

Box of 10 x 10 implants

Contains 100 doses in ten cartridges with ten implants per cartridge, each dose contains 10 small yellow pellets. Each pellet contains 20 mg of trenbolone acetate and 2 mg estradiol.

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.

USES:

This product is a slow-release anabolic agent containing trenbolone acetate and estradiol which increases rate of weight gain and improves feed efficiency in steers and heifers fed in confinement for slaughter.

NOTE:

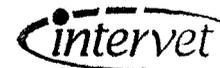
Revalor[®]-200 is not better for increased average daily gain or improved feed efficiency than Revalor[®]-H (140 mg trenbolone acetate/14 mg estradiol) in heifers fed in confinement for slaughter.

Studies have demonstrated that the administration of Revalor[®]-200 can result in decreased marbling scores when compared to non-implanted steers and heifers.

**FOR STEERS AND HEIFERS FED
IN CONFINEMENT FOR SLAUGHTER**

Box of 10 x 10 Cartridge Implants

Manufactured by a non-sterilizing process





Revalor[®]-200

(trenbolone acetate and estradiol)

**FOR STEERS AND HEIFERS FED
IN CONFINEMENT FOR SLAUGHTER**

Box of 10 x 10 Cartridge Implants

Manufactured by a non-sterilizing process



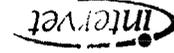
LOT
EXP

USE DIRECTIONS:

See enclosed package insert.

WARNING:

Not to be used in animals 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.



NADA # 140-092, Approved by FDA

Made in Austria by:
Intervet GesmbH
Distributed by:
Intervet Inc.
Millsboro, DE 19966

482000-C

Revalor[®]-200

(trenbolone acetate and estradiol)



50021784820009

**FOR STEERS AND HEIFERS FED IN
CONFINEMENT FOR SLAUGHTER
NET CONTENTS**

Box of 10 x 100 dose packages

Manufactured by a non-sterilizing process

STORAGE CONDITIONS:

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

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.

482030-C

508998 CWUS, 011



Made in Austria by:
Intervet GesmbH

Distributed by:
Intervet Inc.
Millsboro, DE 19966

LOT

EXP



NADA # 140-992, Approved by FDA

Revalor[®]-200

(trenbolone acetate and estradiol)



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**FOR STEERS AND HEIFERS FED IN
CONFINEMENT FOR SLAUGHTER**

NET CONTENTS

4 x 1000 dose packages

Manufactured by a non-sterilizing process

STORAGE CONDITIONS:

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

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.

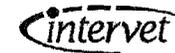
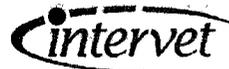
Made in Austria by
Intervet GesmbH

Distributed by:
Intervet Inc.
Millsboro, DE 19966

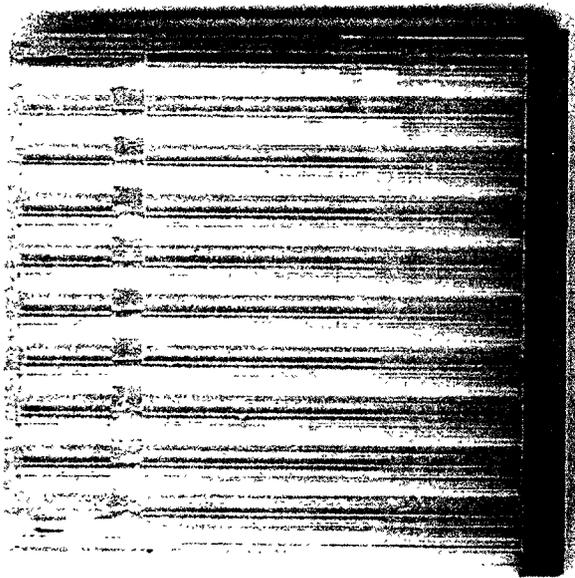
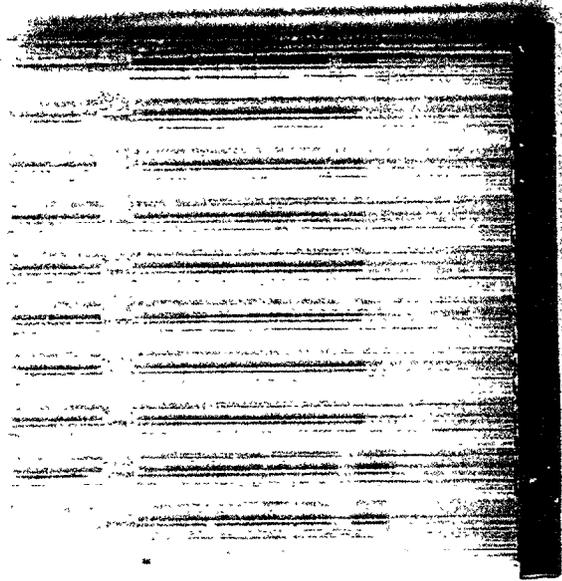
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EXP

782000-C

508999 ZWUS, 011



NADA # 140-992, Approved by FD



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 cartridge.

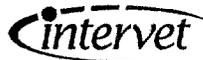
PACKAGE QUANTITIES

Box of 10 x 10 cartridge implants

Made in Austria by
Intervet GesmbH

Distributed by:
Intervet Inc.
Millsboro, DE 19966

482200-A



NADA # 140-992. Approved by FDA

509000 GWUS 011



Revalor®-200

(trenbolone acetate
and estradiol)

FOR STEERS AND HEIFERS FED IN CONFINEMENT FOR SLAUGHTER

DESCRIPTION

Revalor®-200 (trenbolone acetate, CAS Registry Number 10161-34-9, and estradiol, CAS Registry Number 50-28-2) is an implant containing 200 mg of trenbolone acetate and 20 mg estradiol. Each implant consists of 10 small yellow pellets. Ten implants are provided in a cartridge.

Manufactured by a non-sterilizing process

INDICATIONS FOR USE

This product contains trenbolone acetate and estradiol in a slow-release delivery system which increases rate of weight gain and improves feed efficiency in steers and heifers fed in confinement for slaughter.

NOTE

Revalor®-200 is not better for increased average daily gain or improved feed efficiency than Revalor®-H (140 mg trenbolone acetate/14 mg estradiol) in heifers fed in confinement for slaughter.

Studies have demonstrated that the administration of Revalor®-200 can result in decreased marbling scores when compared to non-implanted steers and heifers

DOSAGE

Dosage Form:

One implant containing 200 mg trenbolone acetate and 20 mg estradiol is administered to each animal. The 10 pellets which make up the dosage of Revalor®-200 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.

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

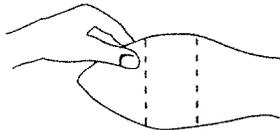


Fig 1 - Ear of Bovine Ready for Implantation

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 midline of the ear. The implant must not be placed closer to the head than the edge of the cartilage ring farthest 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.

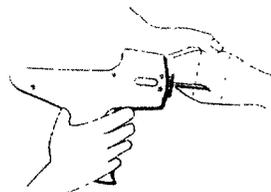


Fig 2 - Rear View of the Bovine Ear Showing the Site



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 fall out of 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

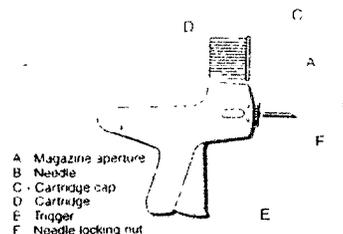


Fig 3 - Diagram of the Implanter and Cartridge