

HFA-305

AUG 19 2003

Approval Date: _____

FREEDOM OF INFORMATION SUMMARY
SUPPLEMENTAL ABBREVIATED NEW ANIMAL
DRUG APPLICATION (ANADA)

ANADA 200-346

COMPONENT[®] TE-IH (trenbolone acetate and estradiol)

**Indications for use: For increased rate of weight gain in heifers fed
in confinement for slaughter.**

Sponsored by:

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

ANADA 200-346

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FREEDOM OF INFORMATION SUMMARY

Component[®] TE-IH Ear Implant for Heifers Fed in Confinement for Slaughter

1. GENERAL INFORMATION:

- a. File Number: ANADA 200-346
- 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-IH
- e. Dosage Form: Implantation (ear implant) as per 21 CFR 522.2477.
- f. How Supplied: As an implant made up of 4 pellets with each pellet containing 20 mg trenbolone acetate and 2 mg estradiol.
- g. How Dispensed: OTC
- h. Amount of Active Ingredients: Trenbolone acetate: 80 mg trenbolone acetate activity.
Estradiol: 8 mg estradiol activity.
- i. Route of Administration: Subcutaneous ear implant
- j. Species/Class: Heifers fed in confinement for slaughter
- k. Recommended Dosage: One implant containing 80 mg trenbolone acetate and 8 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 in heifers fed in confinement for slaughter.
- n. Pioneer Product: Revalor[®]-IH (trenbolone acetate and estradiol);
NADA 140-992; Intervet, Inc.

- o. Effect of Supplement: This submission for Component[®] TE-IH for heifers is a supplement to the original ANADA 200-346 for Component[®] TE-H. Component[®] TE-IH is a lower dose of Component[®] TE-H with each pellet in Component[®] TE-IH (total of 4 pellets) containing 20 mg trenbolone acetate and 2 mg estradiol in the same formulation as each pellet in Component[®] TE-H (total of 7 pellets).

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) 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, Division of Ivy Animal Health, Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for the generic product Component[®] TE-IH. 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[®]-IH (trenbolone acetate and estradiol), the subject of Intervet, Inc. (NADA 140-992), was approved on June 19, 2000.

3. HUMAN SAFETY:

- **Tolerances for Residues:**

The allowable incremental increases established for the pioneer product apply to the generic product. Estradiol is regulated under 21 CFR 556.240. No residues of estradiol, resulting from the use of estradiol or any of the related esters, are permitted in the uncooked edible tissues of heifers, steers, and calves in excess of the following increments above the concentrations of estradiol naturally present in untreated animals: 120 ppt for muscle, 240 ppt for liver, 360 ppt for kidney, and 480 ppt for fat.

The tolerances established for the pioneer product apply to the generic product. Trenbolone acetate is regulated under 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. A tolerance for trenbolone residues in uncooked edible tissues of cattle is not needed.

- **Withdrawal Times:**

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.

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-IH (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 (ANADA 200-346) and currently approved pioneer labeling (NADA 140-992) are attached as indicated below:

Box Label (Generic) – 5 foil pouches each containing 1 cartridge belt with 20 cells (100 implants); 1 implant = 1 dose.

Foil Pouch Label (Generic) – 1 cartridge belt with 20 cells (20 implants); 1 implant = 1 dose.

Package Insert (Generic)

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

Box Label (Pioneer) – box of 10 x 100 dose packages (1000 doses)

Box Label (Pioneer) – box of 4 x 1000 dose packages (4000 doses)

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

Package Insert (Pioneer)

**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® T-IH
BRAND IMPLANTS
FOR HEIFERS FED IN
CONFINEMENT FOR SLAUGHTER



COMPONENT T-IH contains trenbolone acetate and estradiol for increased rate of weight gain in a slow-release delivery system.

Contents: 5 foil pouches each containing 1 cartridge belt with 20 cells. Each cartridge cell contains 1 implant dose. Each dose consists of trenbolone acetate 80 mg and estradiol 8 mg.

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

* 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 — 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.

Note: Studies have demonstrated that administration of COMPONENT® T-IH can result in decreased marbling scores when compared to non-implanted heifers.

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 10 03 00

COMPONENT®
BRAND IMPLANTS

T-IH

trenbolone acetate 80 mg
and estradiol USP 8 mg

FOR HEIFERS FED IN
CONFINEMENT FOR SLAUGHTER

3.125"



1/4" Seal Area

9.5"

COMPONENT[®] T -IH

BRAND IMPLANTS

trenbolone acetate 80 mg
and estradiol USP 8 mg

FOR HEIFERS FED IN
CONFINEMENT FOR SLAUGHTER



TEAR HERE

COMPONENT[®] TE-IH contains trenbolone acetate and estradiol for increased rate of weight gain 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.

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



One 20-dose Cartridge Belt

18.875"

9.375"

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**

Note: Studies have demonstrated that administration of COMPONENT® TE-IH can result in decreased marbling scores when compared to non-implanted 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 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 10 02 00

PURCHASE SEAL 20 IMPLANTS



EXP

LOT



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GENESIS 1999#32

TEAR HERE

COMPONENT[®]
BRAND IMPLANTS



TE-IH

**FOR HEIFERS FED IN
CONFINEMENT FOR SLAUGHTER**

trenbolone acetate 80 mg and
estradiol USP 8 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-IH Implants. Each dose of 4 pellets contains a total of 80 mg of trenbolone acetate and 8 mg estradiol. COMPONENT[®] TE-IH Implants are recommended for use in heifers fed in confinement for slaughter for INCREASED RATE OF WEIGHT GAIN.

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

Note: Studies have demonstrated that administration of COMPONENT[®] TE-IH can result in decreased marbling scores when compared to non-implanted 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

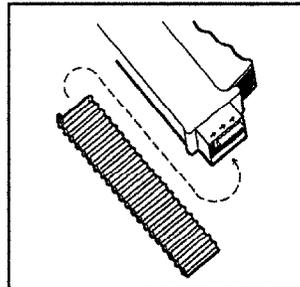
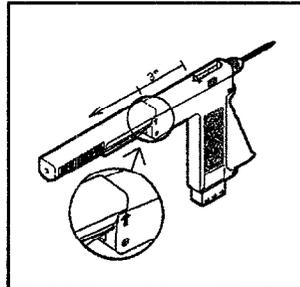
Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 4 pellets (entire contents of one cartridge cell) — in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed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



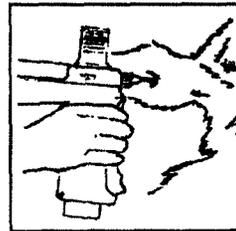
Prepare the Implant Site

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 200-346, 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®-IH

(trenbolone acetate and estradiol)

PACKAGE QUANTITIES:

Box of 10 x 10 implants
Contains 100 doses in ten cartridges with ten implants per cartridge.
Each implant contains 4 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

INDICATIONS:

Increases rate of weight gain in a slow-release delivery system.

NOTE:

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

481300-B

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

Manufactured by a non-sterilizing process



Expiration Date

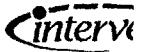
Lot Number:

USE DIRECTIO

See enclosed pack

WARNING:

*Not to be used i
animals. For An
implant pellets in
Federal Law. Do
or animal food.*



NADA # 140-992

Revalor[®]-IH

(trenbolone acetate and estradiol)



50021784814008



FOR HEIFERS FED IN CONFINEMENT FOR SLAUGHTER

NET CONTENTS

Box of 10 x 100 dose packages

Manufactured by a non-sterilizing process

STORAGE CONDITIONS:

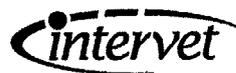
Store in a refrigerator (2-8°C; 36-47°F) and protect from sunlight. Use before the expiration date printed below and on the cartridge.

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.

481430-B

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

LOT
EXP



NADA # 140-992, Approved by FDA

000015

Revalor[®]-IH

(trenbolone acetate and estradiol)



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FOR HEIFERS FED IN CONFINEMENT FOR SLAUGHTER

NET CONTENTS

4 x 1000 dose packages

Manufactured by a non-sterilizing process

STORAGE CONDITIONS:

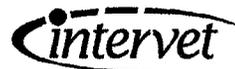
Store in a refrigerator (2-8°C; 36-47°F) and protect from sunlight. Use before the expiration date printed below and on the cartridge.

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.

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509010 ZWUS, 010



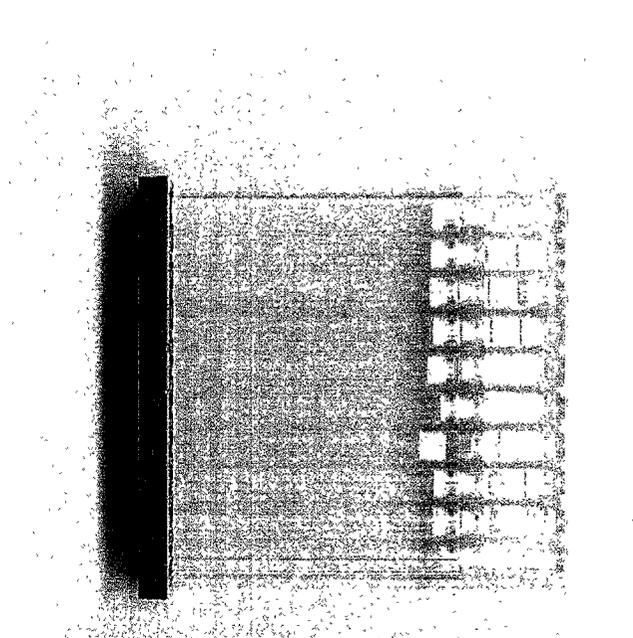
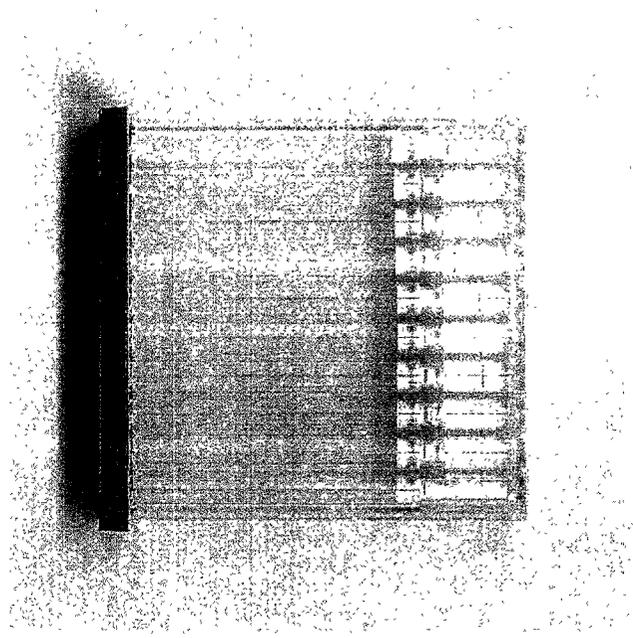
Made in Austria by:
Intervet GesmbH
Distributed by:
Intervet Inc.
Millsboro, DE 19966

LOT
EXP



NADA # 140-992, Approved by FDA

050013



Front of Insert

Inside of Insert

Back of Insert



Revalor®-IH

(trenbolone acetate
and estradiol)

FOR HEIFERS FED IN CONFINEMENT FOR SLAUGHTER

DESCRIPTION

Revalor®-IH is an implant containing 80 mg of trenbolone acetate and 8 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 in a slow-release delivery system.

NOTE

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

DOSAGE

Dosage Form:

One implant containing 80 mg trenbolone acetate and 8 mg estradiol is administered to each animal. The 4 pellets which make up the dosage of Revalor®-IH 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.

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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.

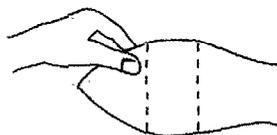


Fig. 1 - Ear of Bovine Ready for Implantation

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.

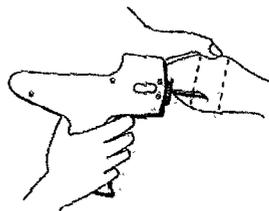
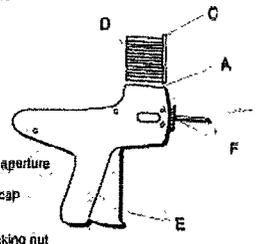


Fig. 2 - Rear View of the Bovine Ear Showing the Site for Insertion of the Implanter Needle.



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

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 GesmbH

Distributed by:
Intervet Inc.
Millsboro, DE 19966

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NADA # 140-992. Approved by FDA

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