

Approval Date: OCT - 3 2002

**FREEDOM OF INFORMATION SUMMARY**

**SUPPLEMENTAL NEW ANIMAL DRUG  
APPLICATION**

NADA 141-043

**SYNOVEX® CHOICE (TRENBOLONE ACETATE AND  
ESTRADIOL BENZOATE) IMPLANTS**

**For increased rate of weight gain in steers fed in confinement for  
slaughter.**

**Sponsored by:**

**Fort Dodge Animal Health  
Division of American Home Products Corp.  
800 Fifth Street, NW  
Fort Dodge, IA 50501**

NADA 141-043

FOIS 1

## TABLE OF CONTENTS

<b>1. GENERAL INFORMATION</b>	<b>1</b>
<b>2. EFFECTIVENESS</b>	<b>2</b>
<b>3. TARGET ANIMAL SAFETY</b>	<b>5</b>
<b>4. HUMAN SAFETY</b>	<b>5</b>
<b>Toxicity</b>	<b>5</b>
<b>Acceptable Daily Intake</b>	<b>5</b>
<b>Allowable Incremental Increases</b>	<b>5</b>
<b>Residue Depletion Studies</b>	<b>6</b>
<b>Tolerance</b>	<b>6</b>
<b>Withdrawal Period</b>	<b>6</b>
<b>Regulatory Method</b>	<b>6</b>
<b>5. AGENCY CONCLUSIONS</b>	<b>6</b>
<b>6. ATTACHMENTS</b>	<b>7</b>

## FREEDOM OF INFORMATION SUMMARY

### SYNOVEX<sup>®</sup> Choice (TRENBOLONE ACETATE AND ESTRADIOL BENZOATE) FOR STEERS FED IN CONFINEMENT FOR SLAUGHTER

#### 1. General Information:

- a. File Number: NADA 141-043
- b. Sponsor: Fort Dodge Animal Health  
Division of American Home Products  
800 Fifth Street, NW  
Fort Dodge, Iowa 50501  
  
Drug Labeler Code: 000856
- c. Established Name: Trenbolone Acetate and Estradiol Benzoate
- d. Proprietary Name: SYNOVEX<sup>®</sup> Choice
- e. Dosage Form: Implantation
- f. How Supplied: Implant made up of 4 pellets with each pellet containing 25 mg trenbolone acetate and 3.5 mg estradiol benzoate.
- g. How Dispensed: OTC
- h. Amount of Active Ingredients: 100 mg trenbolone acetate and 14 mg estradiol benzoate
- i. Route of Administration: Subcutaneous implant in the middle of the posterior aspect of the ear
- j. Species/Class: Cattle/Steers fed in confinement for slaughter
- k. Recommended Dosage: One implant containing 100 mg of trenbolone acetate and 14 mg estradiol benzoate. Each implant is made up of four pellets with each pellet containing 25 mg of trenbolone acetate and 3.5 mg estradiol benzoate.
- l. Pharmacological Category: Hormone
- m. Indications: For increased rate of weight gain in steers fed

in confinement for slaughter.

n. Effect of Supplement:

Provides for the administration of a dose of 100 mg trenbolone acetate and 14 mg estradiol benzoate in steers fed in confinement for slaughter for increased weight gain. (Note: The sponsor currently has an approved ear implant containing 28 mg estradiol benzoate and 200 mg trenbolone acetate (Synovex<sup>®</sup> Plus<sup>™</sup>) – see 21 CFR 522.2478)

2. **EFFECTIVENESS**

The supplemental new animal drug application for Synovex<sup>®</sup> Choice contains data from adequate and well-controlled studies demonstrating the effectiveness of the new animal drug for the indications for use and dosage as given in Section 1 above.

**Pivotal Studies:**

Dose Determination

A dose titration study was conducted at three sites using a uniform protocol such that the results could be pooled and summarized. The three sites were in major beef producing areas of the United States using management systems and diets typical of commercial feedlots.

Name and Address of Investigators:

James J. Sheldon, D.V.M., Ph.D.  
Sheldon Agri-business  
Casa Grande, Arizona  
Study Location: El Centro, California

Rodney L. Preston, Ph.D.  
Texas Tech University  
Department of Animal Science  
Lubbock, Texas  
Study Location: New Deal, Texas

Alvin Edwards, D.V.M., Ph.D.  
Kansas State University  
College of Veterinary Medicine

Manhattan, Kansas  
Study Location: Lamar, Colorado

The purpose of this series of studies was to evaluate the dose response for estradiol benzoate (EB) and trenbolone acetate (TBA) on average daily gain of steers fed in confinement for slaughter. The test animals were crossbred animals of Brahman, English and Exotic breeds. For each study, 360 steers were randomized on the basis of weight into 5 blocks of 9 pens with 8 animals per pen, and administered one of the following treatments: 0/0, 0/300, 60/0, 14/100, 28/200, and 42/300 (mg EB/mg TBA). The steers weighed approximately 600 pounds when the studies were initiated. The duration of the studies ranged between 132 and 183 days.

Each steer was administered EB/TBA via subcutaneous implantation of the backside of the mid-ear. The control steers were not implanted. The steers were implanted once at the initiation of each study.

Average daily gain (ADG) data for the steers are summarized in Table 1 for each of these three dose titration studies.

A randomized complete block design was used for all studies and the data were pooled by analysis of variance to determine the significance of the effect of the EB/TBA implant on ADG. There was a significant ( $P < .05$ ) dose effect on ADG with the response plateauing at a dose of 14 mg EB/100 mg TBA. The 14 mg EB/100 mg TBA dose was shown to be significantly ( $P < .05$ ) better than controls, 300 mg TBA alone, and 60 mg EB alone. These data are sufficient to support the claims and dosage specified in Section 1. Because the improvement in ADG by steers treated with 28 mg EB/200 mg TBA was not significantly better than that by steers treated with 14 mg EB/100 mg TBA, the following disclaimer statement has been put on the label for Synovex Plus (28 mg EB/200 mg TBA):

“Synovex Plus is not better for increased average daily gain than Synovex Choice (14 mg EB/100 mg TBA) in steers fed in confinement for slaughter.”

TABLE 1. SUMMARY FROM THREE DOSE TITRATION STUDIES COMPARING THE EFFECT OF VARIOUS LEVELS OF TRENBOLONE ACETATE AND ESTRADIOL BENZOATE ON AVERAGE DAILY GAIN IN FEEDLOT STEERS

EB/TBA (mg)	Location			Pooled Average
	Texas	Colorado	California	
0/0	2.26	3.41	3.10	2.93
0/300	2.53	3.66	2.96	3.06
60/0	2.65	3.66	3.36	3.23
14/100	2.89	3.87	3.38	3.38
28/200	2.82	3.86	3.59	3.43
42/300	2.87	4.08	3.59	3.52

The effects of treatment on yield grade, quality grade, marbling score, and liver abscess incidence were evaluated at slaughter. No effect of treatment was seen in yield grade or the incidence of liver abscesses. Compared to controls, carcasses from steers treated with the 28 mg EB/200 mg TBA and 14 mg EB/100 mg TBA implants exhibited decreased marbling scores (Table 2).

TABLE 2. SUMMARY FROM THREE DOSE TITRATION STUDIES COMPARING THE EFFECT OF VARIOUS LEVELS OF TRENBOLONE ACETATE AND ESTRADIOL BENZOATE ON MARBLING SCORES IN FEEDLOT STEERS

EB/TBA (mg)	LS-means for Marbling Score (standard error = 0.1053)	P-value for one-sided comparison to control
0/0	4.32	-
0/300	4.16	0.1301
60/0	4.01	0.0216
14/100	4.06	0.0391
28/200	3.88	0.0039
42/300	3.87	0.0035

Because of this observed decrease in marbling scores, the following statement is required on the label for the:

- a) 8 pellet, 28 mg EB/200 mg TBA dose (Synovex<sup>®</sup> Plus<sup>™</sup>).

“Studies have demonstrated that the administration of Synovex Plus can result in decreased marbling scores when compared to non-implanted steers.”

- b) 4 pellet, 14 mg EB/100 mg TBA dose (Synovex<sup>®</sup> Choice).

“Studies have demonstrated that the administration of Synovex Choice can result in decreased marbling scores when compared to non-implanted steers.”

### 3. TARGET ANIMAL SAFETY

The supplemental new animal drug application for Synovex<sup>®</sup> Choice references the target animal safety studies summarized in the FOI for NADA 141-043 (61 FR 14482-April 2, 1996, as amended at 61 FR 29479-June 11, 1996). The data from those studies demonstrate the safety of the new animal drug for the indications for use and dosage as given in Sections 1 and 2 above.

### 4. HUMAN SAFETY

- Toxicity:

The toxicity studies summarized in the FOI under NADA 141-043 (61 FR 14482-April 2, 1996, as amended at 61 FR 29479-June 11, 1996) have met the agency's requirement for human food safety for trenbolone acetate.

- Acceptable Daily Intake

The Acceptable Daily Intake (ADI) for total residues of trenbolone is 0.4 ug/kg/day (64 FR 18573).

- Allowable Incremental Increases

Allowable incremental increases of estradiol (E<sub>2</sub>β) have been established by the agency under 21 CFR 556.240. Residues for estradiol and related esters may not exceed the following increments above the concentrations of estradiol naturally present in the untreated animals; in the uncooked edible tissues of heifers, steers,

and calves, 120 parts per trillion (ppt) for muscle, 480 ppt in fat, 360 ppt for kidney, and 240 ppt for liver.

- Residue Depletion Studies

The residue depletion study is summarized in the FOI Summary for NADA 141-043 (61 FR 14482-April 2, 1996, as amended at 61 FR 29479-June 11, 1996).

- Tolerance

A tolerance for total trenbolone residues in uncooked edible tissues of cattle is not needed.

- Withdrawal Time

As summarized in the FOI for NADA 141-043 (61 FR 14482-April 2, 1996, as amended at 61 FR 29479-June 11, 1996) a withdrawal period is not required.

- Regulatory Method

SYNOVEX<sup>®</sup> Choice qualifies for a zero withdrawal and, as such, a regulatory analytical method for residues is not required.

## 5. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrates that an implant containing 100 mg trenbolone acetate and 14 mg estradiol benzoate when administered to steers fed in confinement for slaughter is safe and effective for the claim of increased rate of weight gain.

The Center for Veterinary Medicine has concluded that, for this product, adequate directions for use by the layman have been provided and the product will retain its over-the-counter marketing status.

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 approval. The three years of marketing exclusivity applies only to the use of the product (SYNOVEX<sup>®</sup> Choice); containing 100 mg trenbolone acetate and 14 mg estradiol benzoate for which this supplement is 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.

## 6. ATTACHMENTS

Facsimile labeling for each product are attached as indicated below:

### SYNOVEX® Choice

1. Pouch Panel (front)
2. Pouch Panel (back)
3. Folding Carton
4. Folding Carton (front panel and bottom flap)
5. Folding Carton (back panel)
6. Folding Carton (page 1 fold-out section)
7. Folding Carton (page 2 fold-out section and bottom flap)

### SYNOVEX® Plus

1. Pouch Panel (front)
2. Pouch Panel (back)
3. Folding Carton
4. Folding Carton (front panel and bottom flap)
5. Folding Carton (back panel)
6. Folding Carton (side panel #1)
7. Folding Carton (side panel #2)
8. Folding Carton (page 1 fold-out section)
9. Folding Carton (page 2 fold-out section and bottom flap)



IMPLANTS FOR STEERS FED IN CONFINEMENT FOR SLAUGHTER

# Choice

(trenbolone acetate and estradiol benzoate)

NADA 141-043  
Approved by FDA

NDC 0856-0071-10

Synovex Choice (trenbolone acetate and estradiol benzoate) is a growth promoting implant containing 100 mg of trenbolone acetate and 14 mg of estradiol benzoate. Each implant consists of 4 pellets. Ten implants are provided in each cartridge.

**DIRECTIONS:** Implant complete contents of one cartridge, cell per steer. Approved implantation technique is fully described in the fold-out carton section.

**INDICATIONS FOR USE:** Synovex Choice is recommended for increased rate of weight gain in steers fed in confinement for slaughter.

**NOTE:** Never sacrifice careful, clean technique for speed of implantation.

**NOTE:** Studies have demonstrated that the administration of Synovex Choice can result in decreased marbling scores when compared to non-implanted steers.

**STORAGE:** Store unopened product at room temperature. Avoid excessive heat and humidity. Use product before the expiration date on the label. Once the pouch is opened, unused product may be stored in the end-folded pouch (away from light) for up to six months under refrigerated conditions (2-8 C/36-47 F) or at room temperature (15-30 C/59-86 F) for up to one month.

**DOSAGE:** One implant (four pellets) containing 100 mg of trenbolone acetate and 14 mg of estradiol benzoate is administered to each steer by subcutaneous implantation in the middle one-third of the ear.

Manufactured By A Non-Sterilizing Process

The ten-dose cartridge of Synovex Choice is designed to be used exclusively with a Synovex implanting device.

Keep this and all drugs out of the reach of children.

Restricted Drug (California)—Use Only As Directed

See top of pouch for lot and expiration date

**WARNING:** Implant pellets in ear only. Any other location is a violation of Federal law. Do not attempt salvage of imprinted site for human or animal food.

**FORT DODGE**

Fort Dodge Animal Health  
Fort Dodge, Iowa 50501 USA

FOR ANIMAL USE ONLY  
NOT FOR USE IN HUMANS

01932

6072A

**FORT DODGE**

**NET CONTENTS: One pouch contains ten 10-dose cartridges (100 implants)**

Synovex Choice  
Pouch (back panel) - 100%

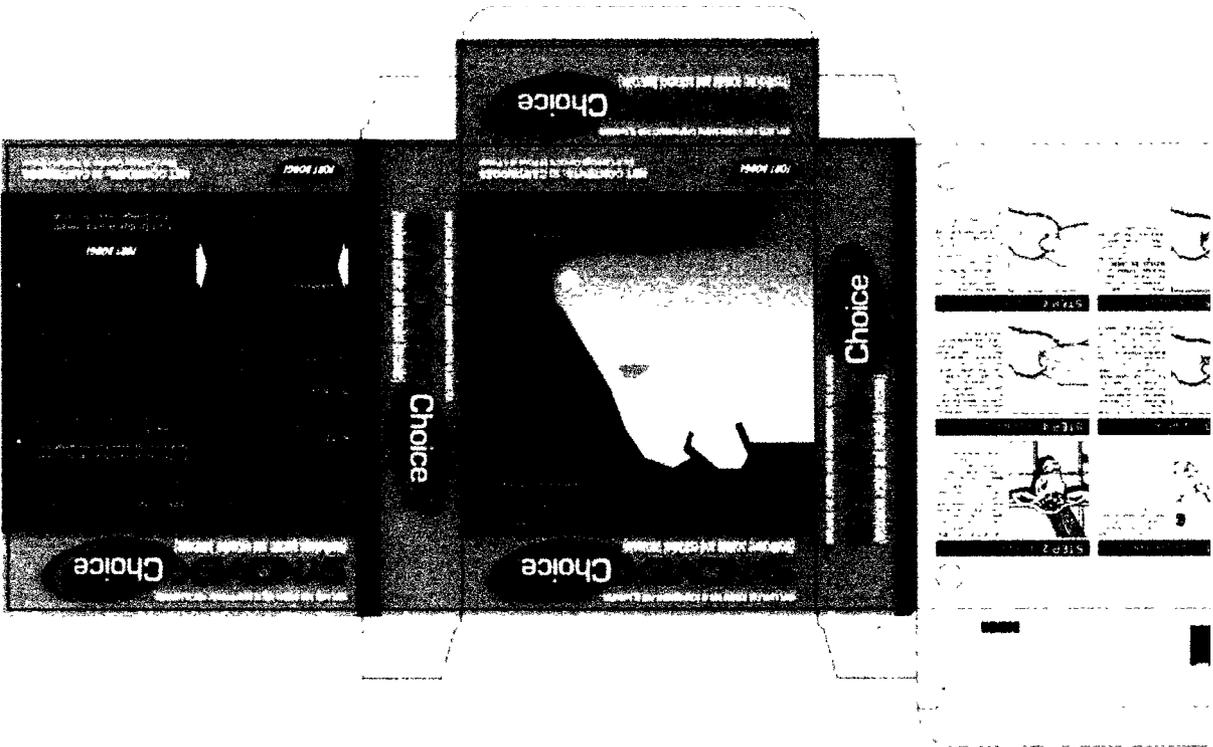
**NET CONTENTS: One pouch contains ten 10-dose cartridges (100 implants)**

**FORT DODGE**

6072A

01932

FOR ANIMAL USE ONLY  
NOT FOR USE IN HUMANS



Slaughter  
NET CONTENTS: One pound  
contains ten 10-dose cartridges  
(100 pellets)  
Manufactured By A  
Non-Sterilizing Process  
Keep this and all drugs out of the  
reach of children  
Restricted Drug (Caution)  
Use Only As Directed

IMPORTANT: Read ALL  
Labels of Carton

**FORT DODGE**

**NET CONTENTS: 10 CARTRIDGES**  
Each Cartridge Contains 10 Rows of 4 Pellets

IMPLANTS FOR STEERS FED IN CONFINEMENT FOR SLAUGHTER

(trenbolone acetate and estradiol benzoate)

**Choice**

IMPLANTS FOR STEERS FED IN CONFINEMENT FOR SLAUGHTER

(trenbolone acetate and estradiol benzoate)

**Choi**

Synovex Choice  
Printed Folding Carton - 84%  
(front panel & bottom flap)

IMPLANTS FOR STEERS FED IN CONFORMANCE FOR SLAUGHTER

# Synovex Choice

(trenbolone acetate and estradiol benzoate)

Synovex Choice (trenbolone acetate and estradiol benzoate) is a growth promoting implant containing 100 mg of trenbolone acetate and 14 mg of estradiol benzoate. Each implant consists of 4 pellets. Ten implants are provided in each cartridge.

**NOTE:** Studies have demonstrated that the administration of Synovex Choice can result in decreased marbling scores when compared to non-implanted steers.

**DOSAGE:** One implant (four pellets), containing 100 mg of trenbolone acetate and 14 mg of estradiol benzoate, is administered to each steer by subcutaneous implantation in the middle one-third of the ear.

The ten-dose cartridge of Synovex Choice is designed to be used exclusively with a Synovex implanting device.

**WARNING:** Implant pellets in ear only. Any other location is a violation of Federal law. Do not attempt salvage of implanted site for human or animal food.

FOR ANIMAL USE ONLY.  
NOT FOR USE IN HUMANS.

**DIRECTIONS:** Implant complete contents of one cartridge cell per steer. Approved implantation technique is fully described in the fold-out carton section.

**NOTE:** Never sacrifice careful, clean technique for speed of implantation.

**STORAGE:** Store unopened product at room temperature. Avoid excessive heat and humidity. Use product before the expiration date on the label.

Once the pouch is opened, unused product may be stored in the end-folded pouch (away from light) for up to six months under refrigerated conditions (2-8 C/36-47 F) or at room temperature (15-30 C/59-86 F) for up to one month.

Open here for implanting directions

**FORT DODGE**

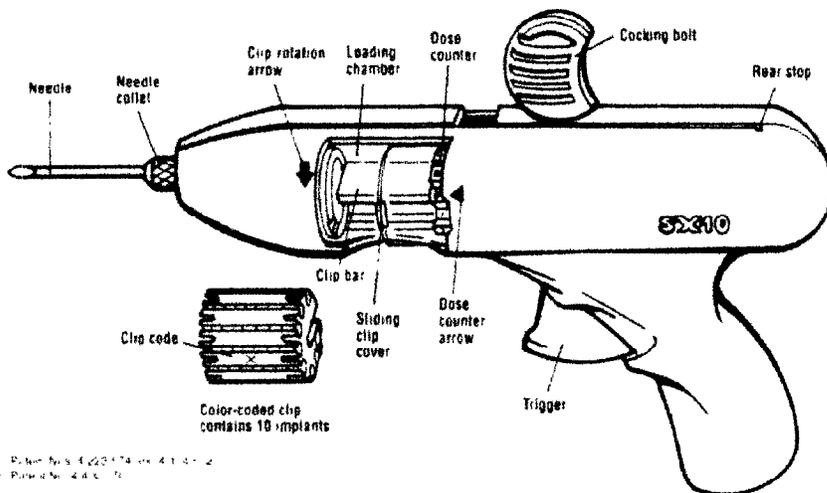
Fort Dodge Animal Health  
Fort Dodge, Iowa 50501 USA

**FORT DODGE**

**NET CONTENTS: 10 CARTRIDGES**  
Each Cartridge Contains 10 Rows of 4 Pellets

Synovex Choice  
Printed Folding Carton - 84%  
(back panel)

# SYNOVEX® SX10® Gun\*



\*1. Pat. No. 4,221,748 or 4,141,412  
 U.S. Pat. No. 4,467,179

## HOW TO IMPLANT SYNOVEX Choice

### PELLETS

#### For Use With Any Synovex Gun.

Study the following instructions carefully, then proceed step by step, until the technique becomes routine. Many head can be implanted per hour by an experienced team, one member of which should be assigned to do nothing but the implantation. Care should be taken to insure the hands of the person administering the implant are clean and only sanitary instruments are used.

## SYNOVEX Choice Implants

Synovex Choice is recommended for steers fed in confinement for slaughter. When properly administered, Synovex Choice implants increase rate of weight gain in steers.

### STORAGE

Store unopened product at room temperature. Avoid excessive heat and humidity.

Use product before the expiration date printed on the label.

Once the pouch is opened, unused product may be stored in the end folded pouch away from light, for up to six months under refrigerated conditions (2-8°C, 36-47°F) or at room

temperature (15-30°C, 59-86°F) for up to one month.

### WARNING

Implant pellets in ear only. Any other location is a violation of Federal law. Do not attempt salvage of implanted site for human or animal food.

Keep this and all drugs out of the reach of children.

Restricted Drug (California) - Use Only as Directed.

Synovex Choice  
 Printed Folding Carton - 84%  
 (Page 1 fold-out section)

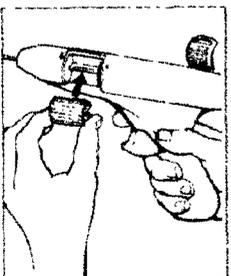
Exp Date

Lot



3984  
01932  
5071A

### STEP 1 Loading The SX10 Gun



Load the SX10 gun following the directions outlined in the instruction manual accompanying each SX10 gun.

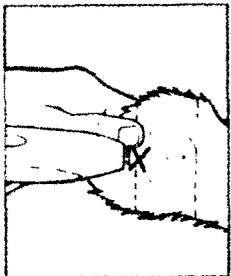
### STEP 2 Restraint



The animal must be confined in a restraint (neck animal squeeze chute or head gate). The implant site on the back of the ear should be prepared by scrubbing with a generous-sized piece of cotton that has been soaked in a germicidal solution.

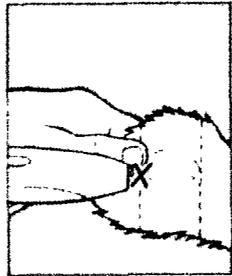
**Note:** If implanting horned cattle, greater safety is provided when the head is controlled by the use of a bull head in case tongs.

### STEP 3 Implant Site



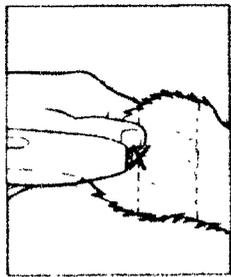
Divide the ear into three imaginary sections as illustrated. The implanted pellets should be deposited in the center one-third of the ear as shown. To accomplish this, the SX10 gun needle should be inserted in the outer one-third of the ear as indicated by the 'X' in the illustration. Implanting too close to the head may cause abnormal sexual behavior. Care should be taken to avoid severing the major arteries of the ear.

### STEP 4 Insert Needle



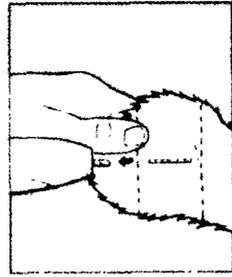
Just before grasping the ear with one hand, release the safety by striking the butt of the gun. Holding the SX10 gun firmly with the other hand, penetrate the skin at the point shown by the 'X'. Thrust the needle under the skin, taking care not to penetrate the cartilage. Ease the SX10 gun forward (toward the base of the ear) until the full needle length is beneath the skin.

### STEP 5 Pellet Implantation



When the needle is completely inserted, activate the instrument by squeezing the trigger completely. Do not withdraw the needle, but allow the automatic needle retractor to release the pellets. This will allow the pellets to be deposited in a straight line in the path of the retracted needle.

### STEP 6 Inspection



Check the implant site if properly administered, the implants should lie in a straight line under the skin. Disinfect the SX10 gun needle in a germicidal solution and recock the instrument by rotating the locking grip left, pull back, rotate right, then push all the way forward. You are now ready to implant the next animal.

(flunixin meglumine and estrogens)

IMPLANTS FOR STEERS, FEED IN COMPARTMENT FOR SILVSTER

# Choice

Synovex Choice  
Printed Folding Carton - 84%  
(Page 2 fold-out section & bottom flap)



IMPLANTS FOR STEERS AND HEIFERS FED IN CONFINEMENT FOR SLAUGHTER

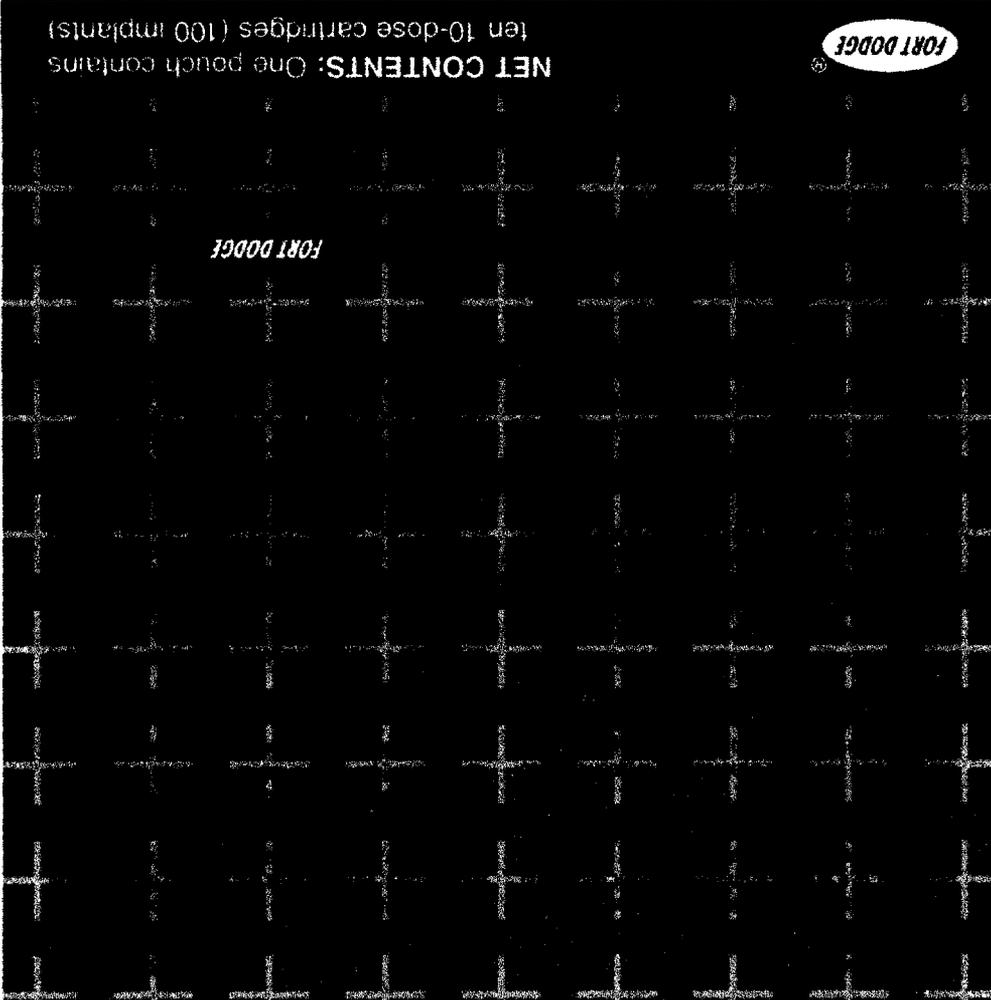
# SYNOVEX<sup>®</sup> PLUS<sup>™</sup>

(trenbolone acetate and estradiol benzoate)

FORT DODGE

FORT DODGE<sup>®</sup>

NET CONTENTS: One pouch contains  
ten 10-dose cartridges (100 implants)



**NET CONTENTS:** One pouch contains ten 10-dose cartridges (100 implants)

**FOR T DODGE**

**SYNOVEX<sup>®</sup> PLUS<sup>™</sup>**  
(trenbolone acetate and estradiol benzoate)  
IMPLANTS FOR STEERS AND HEIFERS FED IN CONFINEMENT FOR SLAUGHTER



### SYNOVEX SX10 Gun\*

**HOW TO IMPLANT SYNOVEX SX10 Implants**

**RELLETS**

**SYNOVEX SX10 Implants**

**NOTE:** The SX10 Gun is designed to deliver a precise dose of Synovex Plus to the site of injury or surgery. The gun is easy to use and requires no special training. The gun is designed to deliver a precise dose of Synovex Plus to the site of injury or surgery.

**STEP 1**

**STEP 2**

**STEP 3**

**STEP 4**

**STEP 5**

**STEP 6**

## SYNOVEX PLUS

FOR THE TREATMENT OF OSTEOARTHRITIS

**SYNOVEX PLUS**

**FOR ANIMAL USE ONLY. NOT FOR USE IN HUMANS.**

**INDICATIONS FOR USE:** Synovex Plus is recommended for treatment of osteoarthritis and associated lameness in horses and in dogs and cats of various breeds. It is also indicated for the treatment of osteoarthritis in dogs and cats.

**NOTE:** Synovex Plus is not to be used for treatment of osteoarthritis in dogs and cats. It is not to be used for treatment of osteoarthritis in horses. It is not to be used for treatment of osteoarthritis in humans.

**CONTRAINDICATIONS:** Do not use in animals with known hypersensitivity to any of the ingredients. Do not use in animals with known hypersensitivity to any of the ingredients.

**CAUTION:** This product is a potent analgesic. It should be used with caution in animals with known hypersensitivity to any of the ingredients.

**WARNING:** Do not use in animals with known hypersensitivity to any of the ingredients.

**IMPORTANT:** Read all directions carefully.

**NET CONTENTS: 100 CAPSULES**

## SYNOVEX PLUS

FOR THE TREATMENT OF OSTEOARTHRITIS

**SYNOVEX PLUS**

**FOR ANIMAL USE ONLY. NOT FOR USE IN HUMANS.**

**INDICATIONS FOR USE:** Synovex Plus is recommended for treatment of osteoarthritis and associated lameness in horses and in dogs and cats of various breeds. It is also indicated for the treatment of osteoarthritis in dogs and cats.

**NOTE:** Synovex Plus is not to be used for treatment of osteoarthritis in dogs and cats. It is not to be used for treatment of osteoarthritis in horses. It is not to be used for treatment of osteoarthritis in humans.

**CONTRAINDICATIONS:** Do not use in animals with known hypersensitivity to any of the ingredients. Do not use in animals with known hypersensitivity to any of the ingredients.

**CAUTION:** This product is a potent analgesic. It should be used with caution in animals with known hypersensitivity to any of the ingredients.

**WARNING:** Do not use in animals with known hypersensitivity to any of the ingredients.

**IMPORTANT:** Read all directions carefully.

**NET CONTENTS: 100 CAPSULES**

Synovex Plus  
Printed Folding Carton - 84%  
(front panel & bottom flap)

IMPLANTS FOR STEERS AND HEIFERS FED IN CONFINEMENT FOR SLAUGHTER

# SYNOVEX<sup>®</sup> PLUS<sup>™</sup>

(trenbolone acetate and estradiol benzoate)

NADA 141-043  
Approved by FDA

NDC 0856-3904-10

**FOR ANIMAL USE ONLY.  
NOT FOR USE IN HUMANS.**

**INDICATIONS FOR USE:**

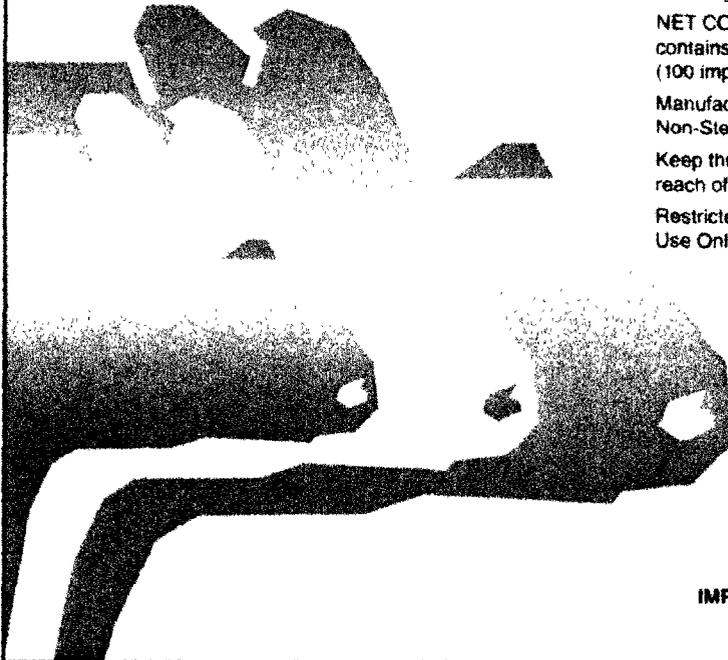
Synovex Plus is recommended for increased rate of weight gain and improved feed efficiency in steers and for increased rate of weight gain in heifers fed in confinement for slaughter.

**NET CONTENTS:** One pouch contains ten 10-dose cartridges (100 implants).

Manufactured By A  
Non-Sterilizing Process

Keep this and all drugs out of the reach of children.

Restricted Drug (California)—  
Use Only As Directed.



**IMPORTANT: Read ALL  
sides of carton**

**FORT DODGE<sup>®</sup>**

**NET CONTENTS: 10 CARTRIDGES**

Each Cartridge Contains 10 Pouches of 8 Pellets

IMPLANTS FOR STEERS AND HEIFERS FED IN CONFINEMENT FOR SLAUGHTER

# SYNOVEX<sup>®</sup> PLUS<sup>™</sup>

(trenbolone acetate and estradiol benzoate)

IMPLANTS FOR STEERS AND HEIFERS FED IN CONFINEMENT FOR SLAUGHTER

IMPLANTS FOR STEERS AND HEIFERS FED IN CONFINEMENT FOR SLAUGHTER

# SYNOVEX<sup>®</sup> PLUS<sup>™</sup>

(trenbolone acetate and estradiol benzoate)

Synovex Plus (trenbolone acetate and estradiol benzoate) is a growth promoting implant containing 200 mg of trenbolone acetate and 28 mg of estradiol benzoate. Each implant consists of 8 pellets. Ten implants are provided in each cartridge.

**NOTE:** Synovex Plus is not better for increased average daily gain than Synovex Choice (100 mg trenbolone acetate/14 mg estradiol benzoate) in steers fed in confinement for slaughter. Studies have demonstrated that the administration of Synovex Plus can result in decreased marbling scores when compared to non-implanted steers and heifers.

**DOSAGE:** One implant (eight pellets), containing 200 mg of trenbolone acetate and 28 mg of estradiol benzoate, is administered to each steer or heifer by subcutaneous implantation in the middle one-third of the ear.

The ten-dose cartridge of Synovex Plus is designed to be used exclusively with a Synovex implanting device.

**WARNING:** Not for dairy or beef replacement heifers. Implant pellets in ear only. Any other location is a violation of Federal law. Do not attempt salvage of implanted site for human or animal food.

FOR ANIMAL USE ONLY  
NOT FOR USE IN HUMANS.

**CAUTION:** Bulling, vaginal and rectal prolapse, udder development, ventral edema and elevated tailheads have occasionally been reported in heifers administered Synovex Plus implants.

**DIRECTIONS:** Implant complete contents of one cartridge cell per steer or heifer. Approved implantation technique is fully described in the fold-out carton section.

**NOTE:** Never sacrifice careful, clean technique for speed of implantation.

**STORAGE:** Store unopened product at room temperature. Avoid excessive heat and humidity. Use product before the expiration date on the label.

Once the pouch is opened, unused product may be stored in the end-folded pouch (away from light) for up to six months under refrigerated conditions (2-8°C/36-47°F) or at room temperature (15-30°C/59-86°F) for up to one month.

**FORT DODGE<sup>®</sup>**

Fort Dodge Animal Health  
Fort Dodge, Iowa 50501 USA

**FORT DODGE<sup>®</sup>**

**NET CONTENTS: 10 CARTRIDGES**  
Each Cartridge Contains 10 Rows of 8 Pellets

▼ Open here for implanting directions ▼

Synovex Plus  
Printed Folding Carton - 84%  
(side panel #1)

12/02  
21/02  
12/02

IMPLANTS FOR STEERS AND HEIFERS FED IN CONFINEMENT

# SYNOVE

(trenbolone acetate and estradiol benzoate)

NADA 141-043  
Approved by FDA



IMPLANTS FOR STEERS AND HEIFERS FED IN CONFINEMENT FOR SLAUGHTER

# SYNOVEX<sup>®</sup> PLUS<sup>™</sup>

(trenbolone acetate and estradiol benzoate)

**FORT DODGE<sup>®</sup>**

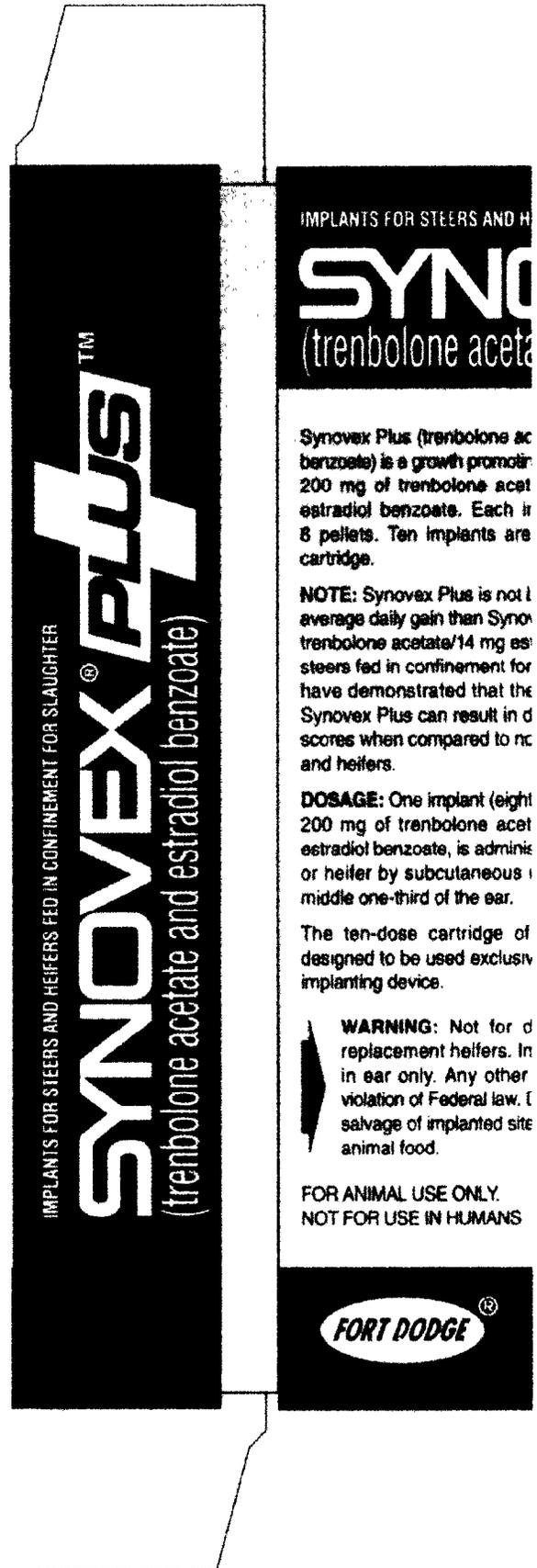
NE

IMPLANTS FOR STEERS AND HEIFERS FED IN CONFINEMENT

# SYNOVE

(trenbolone acetate and estradiol benzoate)

Synovex Plus  
Printed Folding Carton - 84%  
(side panel #2)



IMPLANTS FOR STEERS AND HEIFERS

**SYNOVEX PLUS**  
(trenbolone acetate and estradiol benzoate)

Synovex Plus (trenbolone acetate and estradiol benzoate) is a growth promoter. Each cartridge contains 200 mg of trenbolone acetate and 14 mg of estradiol benzoate. Each cartridge contains 8 pellets. Ten implants are contained in each cartridge.

**NOTE:** Synovex Plus is not intended to produce an average daily gain that is greater than Synovex Plus (trenbolone acetate/14 mg estradiol benzoate) in steers fed in confinement for slaughter. Studies have demonstrated that the Synovex Plus can result in higher carcass scores when compared to control steers and heifers.

**DOSAGE:** One implant (eight pellets containing 200 mg of trenbolone acetate and 14 mg of estradiol benzoate) is administered to a steer or heifer by subcutaneous injection in the middle one-third of the ear.

The ten-dose cartridge is designed to be used exclusively as an implanting device.

**WARNING:** Not for use in replacement heifers. Implant in ear only. Any other use is a violation of Federal law. Do not salvage or implant site for animal food.

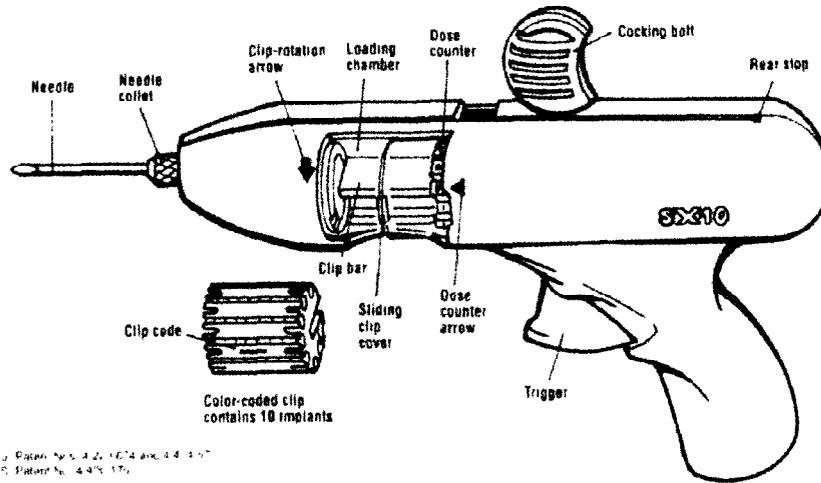
FOR ANIMAL USE ONLY.  
NOT FOR USE IN HUMANS

**FORT DODGE**®

Synovex Plus  
 Printed Folding Carton - 84%  
 (Page 1 fold-out section)



# SYNOVEX® SX10® Gun\*



\* U.S. Patent Nos. 4,211,674 and 4,411,117  
 U.S. Patent No. 4,478,175

## HOW TO IMPLANT



### PELLETS

For Use With Any Synovex Gun.

Study the following instructions carefully, then proceed step by step, until the technique becomes routine. Many head can be implanted per hour by an experienced team, one member of which should be assigned to do nothing but the implantation. Care should be taken to insure the hands of the person administering the implant are clean and only sanitary instruments are used.

## SYNOVEX PLUS™ Implants

Synovex Plus is recommended for steers and heifers fed in confinement for slaughter. When properly administered, Synovex Plus implants increase rate of weight gain and improve feed efficiency in steers and increase rate of weight gain in heifers.

### STORAGE

Store unopened product at room temperature. Avoid excessive heat and humidity.

Use product before the expiration date printed on the label.

Once the pouch is opened, unused product may be stored in the end folded pouch (away from light) for up to six months under refrigerated conditions.

12-16°C (56-61°F) or at room temperature  
 15-30°C (59-86°F), for up to one month

### WARNING

Not for dairy or beef replacement heifers. Implant pellets in ear only. Any other location is a violation of Federal law. Do not attempt salvage of implanted site for human or animal food.

Keep this and all drugs out of the reach of children.

Restricted Drug, California - Use Only as Directed.

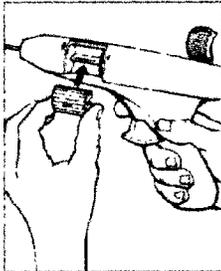




Exp Date

Lot

**STEP 1 Loading The SX10 Gun**



Load the SX10 gun following the directions outlined in the instruction manual accompanying each SX10 gun.

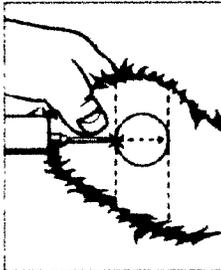
**STEP 2 Restraint**



The animal must be confined in a restraint mechanism squeeze chute or head gate. The implant site on the back of the ear should be prepared by scrubbing with a generous sized piece of cotton that has been soaked in a germicidal solution.

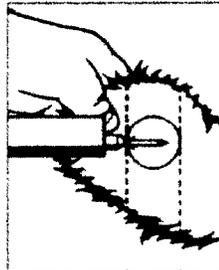
**Note:** If implanting horned cattle, greater safety is provided when the head is controlled by the use of a bull lead (nose tong).

**STEP 3 Implant Site**



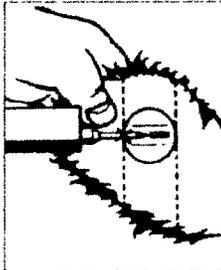
Divide the ear into three imaginary sections as illustrated. The implanted pellets should be deposited in the center one third of the ear as shown. To accomplish this, the SX10 gun needle should be inserted in the outer one third of the ear as indicated by the "X" in the illustration. Implanting too close to the head may cause abnormal sexual behavior. Care should be taken to avoid severing the major arteries of the ear.

**STEP 4 Insert Needle**



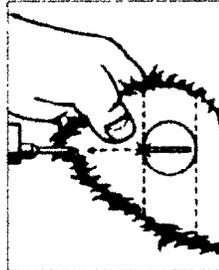
Just before grasping the ear with one hand, release the safety by striking the butt of the gun. Holding the SX10 gun firmly with the other hand, penetrate the skin at the point shown by the "X". Trust the needle under the skin, taking care not to penetrate the cartilage. Ease the SX10 gun forward (toward the base of the ear) until the full needle length is beneath the skin.

**STEP 5 Pellet Implantation**



When the needle is completely inserted, activate the instrument by squeezing the trigger completely. Do not withdraw the needle. But allow the automatic needle retractor to release the pellets. This will allow the pellets to be deposited in a straight line in the path of the retracted needle.

**STEP 6 Inspection**



Check the implant site. If properly administered, the implants should lie in a straight line under the skin.

Disinfect the SX10 gun needle in a germicidal solution and recock the instrument by rotating the cocking grip left, pull back, rotate right, then push the way forward. You are now ready to implant the next animal.

Synovex Choice  
Pouch (front panel) – 100%



**IMPLANTS FOR STEERS FED IN CONFINEMENT FOR SLAUGHTER**

# Choice

(trenbolone acetate and estradiol benzoate)

NADA 141-043  
Approved by FDA

NDC 0850-6071-10

Synovex Choice (trenbolone acetate and estradiol benzoate) is a growth promoting implant containing 100 mg of trenbolone acetate and 14 mg of estradiol benzoate. Each implant consists of 4 pellets. Ten implants are provided in each cartridge.

**INDICATIONS FOR USE:** Synovex Choice is recommended for increased rate of weight gain in steers fed in confinement for slaughter.

**NOTE:** Studies have demonstrated that the administration of Synovex Choice can result in decreased marbling scores when compared to non-implanted steers.

**DOSAGE:** One implant (four pellets) containing 100 mg of trenbolone acetate and 14 mg of estradiol benzoate is administered to each steer by subcutaneous implantation in the middle one-third of the ear.

The ten-dose cartridge of Synovex Choice is designed to be used exclusively with a Synovex implanting device.

**WARNING:** Implant pellets in ear only. Any other location is a violation of Federal law. Do not attempt salvage of implanted site for human or animal food.

FOR ANIMAL USE ONLY  
NOT FOR USE IN HUMANS

**DIRECTIONS:** Implant complete contents of one cartridge cell per steer. Approved implantation technique is fully described in the fold-out carton section.

**NOTE:** Never sacrifice careful, clean technique for speed of implantation.

**STORAGE:** Store unopened product at room temperature. Avoid excessive heat and humidity. Use product before the expiration date on the label. Once the pouch is opened, unused product may be stored in the end-folded pouch (away from light) for up to six months under refrigerated conditions (2-8°C/36-47°F) or at room temperature (15-30°C/59-86°F) for up to one month.

Manufactured By A Non-Sterilizing Process

Keep this and all drugs out of the reach of children.

Restricted Drug (California) – Use Only As Directed.

See top of pouch for lot and expiration date.

**FORT DODGE**

Fort Dodge Animal Health  
Fort Dodge, Iowa 50501 USA

01032

6072A

**FORT DODGE**

**NET CONTENTS: One pouch contains  
ten 10-dose cartridges (100 implants)**

effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

## 6. ATTACHMENTS

Facsimile labeling for each product are attached as indicated below:

### SYNOVEX® Choice

1. Pouch Panel (front)
2. Pouch Panel (back)
3. Folding Carton
4. Folding Carton (front panel and bottom flap)
5. Folding Carton (back panel)
6. Folding Carton (page 1 fold-out section)
7. Folding Carton (page 2 fold-out section and bottom flap)

### SYNOVEX® Plus

1. Pouch Panel (front)
2. Pouch Panel (back)
3. Folding Carton
4. Folding Carton (front panel and bottom flap)
5. Folding Carton (back panel)
6. Folding Carton (side panel #1)
7. Folding Carton (side panel #2)
8. Folding Carton (page 1 fold-out section)
9. Folding Carton (page 2 fold-out section and bottom flap)