FREEDOM OF INFORMATION SUMMARY
FOR
SYNOVEX® Plus™ (Estradiol Benzoate and Trenbolone Acetate)

1. GENERAL INFORMATION

NADA Number: 141-043

Sponsor: Fort Dodge Animal Health
Div. of American Home Products Corp.
800 Fifth St. NW.
Fort Dodge, IA 50501

Generic Name: Trenbolone Acetate and Estradiol Benzoate

Trade Name: Synovex® Plus

Marketing Status: Over-the-counter (OTC)

Effect of Supplement: This supplement provides for the implantation of Synovex® Plus in steers fed in confinement for slaughter for increased rate of weight gain.

2. INDICATIONS FOR USE

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.

3. DOSAGE FORM(S), ROUTE OF ADMINISTRATION, AND RECOMMENDED DOSAGE

The dosage form is implantation. The route of administration is subcutaneous implantation on the posterior aspect of the middle one-third of the ear by means of an implant gun. The recommended dosage is one implant containing 200 mg trenbolone acetate (TBA) and 28 mg estradiol benzoate (EB). The implant consists of eight pellets with each pellet containing 25 mg TBA and 3.5 mg EB. Each implant is contained in one division of a ten dose cartridge. The cartridge is designed to be used with a Synovex implanting device.

4. EFFECTIVENESS

The effectiveness requirement for this supplemental new animal drug application for Synovex Plus in steers, with the indications for use and dosage as given in Sections 2 and 3 above, is met by utilizing the existing database in NADA 141-043 and conducting the additional adequate and well-controlled studies included in this supplemental application.

Pivotal Studies:

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, AZ
Study Location: El Centro, CA

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

Alvin Edwards, D.V.M., Ph.D.
Kansas State University
College of Veterinary Medicine
Manhattan, KS
Study Location: Lamar, CO

The purpose of the studies was to evaluate the dose response for TBA and EB on average daily gain (ADG) of steers fed in confinement for slaughter. The test animals were cross-bred 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 to 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 the study.

ADG data for the steers are summarized in Table 1 for each of the three dose titration studies.

A randomized compete 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 28 mg EB/200 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 as provided in Sections 2 and 3.

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

	Location			
EB/TBA (mg)	Texas	Colorado	California	Pooled Average
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. A decrease in marbling scores was observed. No effect of treatment was seen in yield grade or the incidences of liver abscesses. Because of the observed decrease in marbling scores, the following statement is required on the label: Studies have demonstrated that the administration of Synovex Plus can result in decreased marbling scores when compared to non-implanted steers.

5. TARGET ANIMAL SAFETY

Target animal safety is established by data in the parent application. Therefore, no further studies were required.

6. HUMAN SAFETY

Human safety is established by data in the parent application. Therefore, no further studies were required.

7. AGENCY CONCLUSIONS

Adequate data demonstrates the safe and effective use of Synovex® Plus for increased rate of weight gain when administered to steers fed in confinement for slaughter.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change providing for the implantation of Synovex® Plus in steers fed in confinement for slaughter. 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.

8. LABELING

Three (3) pages of labeling are attached as follows:

1. Implant folding carton label
2. Implant fold-out labels of outer folding carton
3. Foil pouch label