

Date of Approval: April 24, 2017

FREEDOM OF INFORMATION SUMMARY
SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-269

Revalor[®]-XH

Trenbolone acetate and estradiol extended-release implant

Extended-release implant

Beef heifers fed in confinement for slaughter

This supplement provides for addition of a new implant with the following indication: For increased rate of weight gain and improved feed efficiency for up to 200 days after implantation in beef heifers fed in confinement for slaughter.

Sponsored by:

Intervet, Inc.

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I. GENERAL INFORMATION

A. File Number

NADA 141-269

B. Sponsor

Intervet, Inc.
2 Giralda Farms
Madison, NJ 07940

Drug Labeler Code: 000061

C. Proprietary Name

Revalor[®]-XH

D. Established Name

Trenbolone acetate and estradiol extended-release implant

E. Pharmacological Category

Steroid hormone

F. Dosage Form

Extended-release implant

G. Amount of Active Ingredient

One dose (implant) contains 200 mg of trenbolone acetate and 20 mg estradiol in 6 coated and 4 uncoated pellets, each containing 20 mg trenbolone acetate and 2 mg estradiol.

H. How Supplied

Ten doses (implants) are provided in a cartridge and each box contains 10 cartridges (100 implants)

I. Dispensing Status

OTC

J. Dosage Regimen

One dose (implant) containing 200 mg trenbolone acetate and 20 mg estradiol is administered to each animal. The implant is placed under the skin on the posterior aspect of the ear by means of an implanting tool.

K. Route of Administration

Subcutaneous implantation on the posterior aspect of the ear by means of an implanting tool. The implanting tool is available from Intervet, Inc.

L. Species/Class

Beef heifers fed in confinement for slaughter

M. Indication

For increased rate of weight gain and improved feed efficiency for up to 200 days after implantation in beef heifers fed in confinement for slaughter.

N. Effect of Supplement

This supplement provides for addition of a new implant with the following indication: For increased rate of weight gain and improved feed efficiency for up to 200 days after implantation in beef heifers fed in confinement for slaughter.

II. EFFECTIVENESS

A. Dosage Characterization

Multi-site dose titration and field effectiveness studies were conducted in beef heifers for the approval of Revalor[®]-H and Revalor[®]-IH (NADA 140-992), and were previously accepted by the Agency as evidence of the effectiveness of this dose (200 mg trenbolone acetate and 20 mg estradiol) for increased rate of weight gain and improved feed efficiency for beef heifers fed in confinement for slaughter. The effectiveness studies summarized in the Freedom of Information (FOI) Summary for NADA 140-992 (approved December 13, 1994) justify the doses of trenbolone acetate and estradiol in the initial and slow-release components of the extended-release formulation.

B. Substantial Evidence

1. Type of Study: Multi-center dose confirmation and field effectiveness study
 - a. Title: "Multi-Center Field Dose Confirmation Study for Clinical Efficacy and Safety of two Long-Acting Trenbolone Acetate and Estradiol Extended-Release Implants (Revalor[®]-XH and Revalor[®]-200 C) on the Performance and Carcass Characteristics of Feedlot Heifers".
 - b. Study Dates: The study was initiated on February 7, 2013 and was finalized on June 11, 2014.
 - c. Study locations: The study was conducted at four study sites at three locations (one each in Idaho and Texas, two in Nebraska). Site selection covered a broad range of management and environmental conditions, representative of the U.S. feedlot industry. Locations are listed in Table II.1.

Table II.1. Study identifier and study locations

Site	Location
A	Canyon, TX
B	Parma, ID
C	Oakland, NE
D	Oakland, NE

d. Study design:

- 1) Objective: To demonstrate that Revalor[®]-XH increases average daily gain (ADG) and improves feed efficiency (FE) for up to 200 days after implantation in beef heifers fed in confinement for slaughter.
- 2) Study Animals: A total of 1223 heifers, representative of breeds or breed-types typically seen in U.S. feedlots, weighing on average 645 pounds, were enrolled in three treatment groups: control, Revalor[®]-XH, or another implant. In each of the four sites, 288 or 360 heifers were enrolled and randomly assigned to one of the treatment groups (n=96 or 120 per group; 8 or 10 heifers per pen).
- 3) Experimental Design: The study utilized a randomized complete block design. Animals were blocked based on initial body weight and randomly assigned to one of the treatment groups.
- 4) Treatment Groups: There were three treatment groups: Control (sham), Revalor[®]-XH, and another implant. Only results from the Revalor[®]-XH and control treatment groups are reported.
- 5) Drug Administration: Implants were placed subcutaneously in the middle third of the back of the ear in treated animals. Control animals were sham implanted (implant needle inserted in the ear, but no implant was inserted) using a technique identical to that of the implanted cattle. Personnel who collected study data (other than data related to test article administration and accountability) were masked to treatments.
- 6) Measurements and Observations: Individual body weights were collected for all animals on days -2, 0, 70, and 140 after implantation, and a final weight was collected just prior to shipment for slaughter. Final dates varied from site to site, from 182 to 203 days after implantation, according to when animals reached market weight. These data were used to calculate ADG. Feed consumption (feed issued minus feed weighback) was recorded to allow for calculation of FE. All animals within a study site were weighed prior to shipment for slaughter when the study animals were judged to have reached market condition.

No animals were excluded from the overall analyses of ADG and FE. Data from animals that were removed from study or that died prior to study conclusion were used in the analyses by using the body or carcass weight measured at the time of removal or death. Carcass data was not included for animals that were removed from the study prior to its completion.

To evaluate implant safety, individual ear evaluations to detect ear abscesses, other ear abnormalities, and the presence of an implant were conducted on days 35 and 70. In addition, all animals were observed daily during the study for abnormalities. Illnesses, injuries, and treatments were documented and evaluated.

- e. **Statistical Methods:** The effectiveness variables, ADG and FE from day 0 to final measurement and the carcass variables (calculated yield grade, quality grade number, hot carcass weight, dressing percentage, and marbling score number) were analyzed using mixed linear models. Pen was the experimental unit and treatment was included as a fixed effect in the model. Random effects included were site, site by treatment interaction, and block within site. Each implant treatment group was compared to the negative (sham) control.
- f. **Results:** Both ADG and FE were significantly improved for Revalor[®]-XH treated animals compared to the negative control ($P < 0.05$) for the overall (Day 0 to final) study period (Table II.2).

Table II.2. Analysis of ADG and FE during the overall study

Variable	Control	Revalor[®]-XH	Standard Error
ADG, day 0 to final	2.70	3.15*	0.1012
FE, day 0 to final	7.58	6.90*	0.4204

*versus control, $P < 0.05$

The main effect of treatment was statistically significant for calculated yield grade, hot carcass weight, dressing percent, and marbling score (Table II.3). Heifers treated with Revalor[®]-XH had significant improvements in calculated yield grade, hot carcass weight, and dressing percentage. Quality grade number was unaffected by treatment; however, Revalor[®]-XH treated heifers produced carcasses with significantly lower marbling scores compared to the control group, although still within the "Choice" grade.

Table II.3. Analysis of carcass data

Variable	Control	Revalor [®] -XH	Standard Error
Calculated yield grade	2.63	2.55*	0.2045
Quality grade number‡	2.07	2.10	0.0399
Hot carcass weight	702.41	761.34*	25.9795
Dressing percent	59.89	60.46*	0.6877
Marbling score‡‡	509.83	490.11*	11.7839

*versus control, P <0.05

‡ Quality grade: Prime = 1; Choice = 2; and Select = 3

‡‡ Marbling score: 300 to 399 = Select; 400 to 699 = Choice; 700+ = Prime

- g. Adverse Events: No adverse reactions attributable to the drug were reported in this study. Animal removals and adverse events were for common feedlot ailments and the frequency of occurrence was not related to use of the drug. No bulling or other undesirable behaviors were observed in any of the study cattle. For ear abscesses, the main effect of treatment was not significantly different from controls on either evaluation day.

A total of 83 (control, n=44; Revalor[®]-XH, n=39) adverse events were reported across all study sites. The predominant observations were for respiratory tract disorders (control, n=18; Revalor[®]-XH, n=13) and musculoskeletal disorders (control, n=17; Revalor[®]-XH, n=10). Death was a low-frequency event, occurring in only 1/408 (0.25%) and 7/408 (1.72%) of control and Revalor[®]-XH treated animals, respectively. Twenty-one heifers died or were removed from the study (9 control and 12 Revalor[®]-XH; Table II.4).

Table II.4. Animal removals by treatment and study site

Site	Control	Revalor [®] -XH
A	1	4
B	1	1
C	4	1
D	3	6
TOTAL	9	12

- h. Conclusions: This study demonstrated that Revalor[®]-XH (trenbolone acetate and estradiol extended-release implant) is safe and effective for increased rate of weight gain and improved feed efficiency for up to 200 days after implantation in beef heifers fed in confinement for slaughter.

2. Type of Study: Implant Payout Study

- a. Study Dates: This study was conducted between December 1, 2004 and June 23, 2004.
- b. Study Location: De Soto, KS
- c. Study Design:
- 1) Objective: To evaluate the implant payout profiles of trenbolone acetate (TBA) and estradiol (E2 β) in this implant formulation over a 210 day period in healthy beef heifers following implantation (Day 0).
 - 2) Study Animals: Fifty-six crossbred beef heifers, aged six to eight months of age, were included in this study. The animals were blocked by weight and distributed to outdoor, uncovered, concrete-floored pens. Each pen contained a single water tank and adequate bunk space and the cattle received a normal feedlot diet. All cattle were observed at least once daily prior to feeding.
 - 3) Experimental design: The study utilized a randomized complete block design. Animals were blocked on the basis of weight and randomly assigned to one of seven treatment groups.
 - 4) Treatment Groups: There were seven different explant day treatment groups: Day 0, 36, 70, 105, 140, 175, or 210.
 - 5) Drug Administration: The test article was administered subcutaneously in the middle third of the back of the ear.
 - 6) Measurements and Observations: Implants were explanted from the animals on their specified explant day (Day 0, 36, 70, 105, 140, 175, or 210).
- d. Evaluation Criteria: For evidence of a 200+ day availability of the active ingredients, upon explant of the final implants at Day 210 post implantation, the means of both actives (on a per dose basis) would be present in measureable amounts greater than or equal to 2 mg trenbolone acetate and greater than or equal to 0.5 mg estradiol. For evidence of payout over the 200+ Day period, there would need to be: 1) A statistically significant ($P < 0.05$) reduction in the mean concentration of both actives over the 0 to 210 day period, and 2) A measurable drop in the means of both actives over Days 0 to 105 and 105 to 210 of greater than or equal to 3 mg trenbolone acetate and greater than or equal to 1 mg estradiol.

e. Results:

Table II.5. Mean residual active concentration at day 210 from heifers implanted with Revalor®-XH

Active Ingredient	Mean Amount (mg) on Day 210	Criteria Met?
Trenbolone acetate	26.28	Yes
Estradiol	3.18	Yes

Table II.6. Difference in mean active ingredient concentration recovered from heifers implanted with Revalor®-XH

Active Ingredient	Day 0 to 210 (mg)	P-value for Day 0 to 210 Change	Day 0 to 105 (mg)	Day 105 to 210 (mg)	Criteria Met?
Trenbolone acetate	152.6	0.002	81.02	71.62	Yes
Estradiol	15.86	0.002	6.54	9.32	Yes

- f. Conclusions: The results of the payout study provided evidence of the extended release of Revalor®-XH by the presence of measurable amounts of both active ingredients on Day 210.

III. TARGET ANIMAL SAFETY

CVM did not require target animal safety studies for this supplemental approval. The new animal drug application for Revalor®-XH (trenbolone acetate and estradiol extended-release implant) references the target animal safety studies summarized in the FOI Summaries for NADAs 138-612, 140-992 and 140-897. The data from the field effectiveness study reported in this FOI Summary, in conjunction with the previously reported target animal safety study data for NADAs 138-612, 140-992 and 140-897, demonstrate the safety of the new animal drug for the indication and dosage regimen as described in the "General Information" section.

IV. HUMAN FOOD SAFETY

A. Antimicrobial Resistance

The Agency evaluated the need to address the impact of the use of trenbolone acetate and estradiol on microbial food safety (antimicrobial resistance) among bacteria of public health concern in or on treated cattle. We considered that:

- Trenbolone acetate and estradiol are not normally considered to have properties that would exert antimicrobial resistance pressure towards the emergence or selection of bacteria of public health concern;
- Trenbolone acetate and estradiol are not used to treat zoonotic gastroenteritis or other diseases in humans;

- Trenbolone acetate and estradiol (or a similar compound) are not under development to treat diseases in humans; and
- Trenbolone acetate and estradiol are not indicated for a bacterial disease in a food-producing animal species.

Therefore, the Agency determined there was no need to develop or submit for review any microbial food safety (antimicrobial resistance) information regarding this proposed use of trenbolone acetate and estradiol in cattle.

B. Impact of Residues on Human Intestinal Flora

Residues and metabolites of trenbolone acetate and estradiol are not known to have antimicrobial properties. Additionally, residues and metabolites of trenbolone acetate and estradiol have not been shown to impact bacterial populations. Therefore, at this time, the Agency does not think that residues and metabolites of trenbolone acetate and estradiol in or on edible food products from cattle treated with the compounds will impact the intestinal flora of human consumers, and there was no need to submit additional information or data to define a microbiological acceptable daily intake.

C. Toxicology

Trenbolone Acetate:

Reassessment of the toxicological acceptable daily intake (ADI) was not needed for this approval. The FOI Summary for the original approval of NADA 138-612, dated July 2, 1986, contains summaries of all toxicology studies and information.

The final ADI of trenbolone acetate (TBA) is the toxicological ADI of 0.4 µg per kg of body weight per day derived from a chronic toxicity study in female Rhesus Macaque. The ADI for trenbolone is codified under 21 CFR 556.739.

The safe concentration of total TBA residues in each edible tissue of steers and heifers is 80 ppb for muscle, 240 ppb for liver, 480 ppb for kidney, and 480 ppb for fat, based on the revised food consumption values (NADA 141-269 dated January 19, 2007).

Estradiol:

Estradiol is regulated on the basis of allowable incremental increase limits for residues. Based on the old food consumption values, residues of estradiol or any of the related esters are not permitted in excess of the following increments above the concentrations of estradiol naturally present in untreated animals: In uncooked edible tissues of heifers, steers, and calves, (1) 120 parts per trillion (ppt) for muscle; (2) 480 ppt for fat; (3) 360 ppt for kidney; and (4) 240 ppt for liver.

Using the revised food consumption values, the updated allowable incremental increase limits for residues of estradiol in edible tissues of heifers, steers, and calves to 200 ppt for muscle, 600 ppt for liver, 1200 ppt for kidney, and 1200 ppt for fat.

D. Residue Chemistry

1. Summary of Residue Chemistry Studies

a. Total Residue and Metabolism Studies

CVM did not require total residue and metabolism studies for this approval. The FOI Summary for the original approval of NADA 138-612, dated July 2, 1987 (52 FR 24994, July 2, 1987), contains a summary of total residue and metabolism studies for trenbolone in cattle. The highest concentration of total trenbolone residues in the edible tissues was found in the liver of cattle treated with trenbolone acetate implants. Lower concentrations of total trenbolone residues were found in the kidneys, muscle, and fat.

b. Comparative Metabolism Study

CVM did not require comparative metabolism studies for this approval. The FOI Summary for the original approval of NADA 138-612, dated July 2, 1987 (52 FR 24994, July 2, 1987), contains a summary of comparative metabolism studies for trenbolone.

c. Study to Establish Withdrawal Period

(1) Tissue Residue Depletion Study

In addition to the residue depletion study summary that follows, the NADA for Revalor[®]-XH references residue depletion studies summarized in the FOI Summaries for the approvals of NADAs 138-612, 140-897, 140-992, and 141-269 to demonstrate Human Food Safety. Because studies conducted for the previous approvals did not include the slow release formulation, the following study was conducted to provide data in heifers at Day 70 and Day 105 following implantation of Revalor[®]-XH implant.

Study Title: "Evaluation of Tissue Residue Depletion of Trenbolone and Estradiol Following Implantation of Feedlot Heifers with a Long-Acting Formulation (Revalor[®]-XH)" - Intervet Study #S12061-00.

Objectives: To determine the concentrations of the two metabolites of trenbolone acetate (trenbolone-17 α and trenbolone-17 β) and 17 β -estradiol in the edible tissues of heifers at Day 70 and Day 105 following implantation of Revalor[®]-XH.

In-Life Testing Facility: Terre Haute, IN

Analytical Testing Facility: Summit, NJ

Test Article: Revalor[®]-XH implant

Test Animals: 14 feedlot heifers weighing 258 to 294 kg at 7 days prior to implantation

Test Article Administration: For each implantation period (70 days and 105 days), six heifers were implanted in the ear with one Revalor[®]-XH implant per animal on Day 0 of the study, and one heifer served as untreated control animal.

Duration of Implantation: 70 days and 105 days

Tissue Sampling: On each of Day 70 and Day 105 after the animals were euthanized, muscle, liver, and fat tissue samples were collected from six implanted animals and one control animal for residue determination. Based on the data on file with FDA under NADAs 138-612, 140-897, 140-992, and 141-269, FDA determined that sampling liver, muscle, and fat for analyses of trenbolone and estradiol residues is adequate to ensure safety of all the edible tissues of cattle treated with Revalor[®]-XH.

Residue Analysis: The tissues were analyzed for 17 α -trenbolone and 17 β -trenbolone and 17 β -estradiol concentrations using both radioimmunoassay (RIA) methods and LC-MS/MS methods. The RIA methods were used for residue analyses for previous approvals. However, FDA concluded that in the study (Intervet Study #S12061-00), the RIA methods could not reliably quantitate the residues because key reagents (antibodies) for the methods were not of uniform quality. FDA concluded that the residue concentrations determined using the LC-MS/MS methods in the study were acceptable for residue evaluation. An approximately 1:1 ratio for 17 β -trenbolone concentrations in the liver samples quantitated using the RIA method to those quantitated using the LC-MS/MS method is supported by the sponsor's data on file with FDA. Therefore, only the residue concentrations quantitated using the LC-MS/MS methods were used for residue evaluation.

Results: The limit of detection (LOD) and lower limit of quantitation (LLOQ) for analysis of 17 α -trenbolone, 17 β -trenbolone, and 17 β -estradiol in heifer tissues by the LC-MS/MS methods are summarized in Table IV.1 below.

Table IV.1. The limit of detection (LOD) and lower limit of quantitation (LLOQ) of LC-MS/MS methods for analysis of 17 α -trenbolone, 17 β -trenbolone, and 17 β -estradiol in heifer tissues

Analyte	Liver LOD/LLOQ (pg/g)	Muscle LOD/LLOQ (pg/g)	Fat LOD/LLOQ (pg/g)
17α-Trenbolone	26.7/81.5	17.5/53.4	10.0/30.6
17β-Trenbolone	18.8/57.4	17.9/54.5	11.1/33.9
17βEstradiol	14.9/45.4	3.7/11.3	8.3/25.2

The means and standard deviations (SDs) of 17 α -trenbolone, 17 β -trenbolone and 17 β -estradiol concentrations in muscle, liver, and fat tissues of heifers at Day 70 and Day 105 after implantation are summarized in Table IV.2., Table IV.3., and Table IV.4 below. Only the residue concentrations that are at or above the LLOQs are included in the calculation for the means and SDs. The SD is not calculated where only one sample had a residue value at or above the LLOQs.

Table IV.2. Mean concentration (pg/g) \pm SD of 17 α -trenbolone in tissues of heifers at day 70 and day 105 after implantation of Revalor[®]-XH

Days of Implantation	Animal Number	Muscle	Liver	Fat
Day 70	6	<LLOQ	395.7 \pm 157.9	58.5 \pm 11.3
Day 105	6	<LLOQ	279.7 \pm 52.8	<LLOQ

Table IV.3. Mean concentration (pg/g) \pm SD of 17 β -trenbolone in tissues of heifers at day 70 and day 105 after implantation of Revalor[®]-XH

Days of Implantation	Animal Number	Muscle	Liver	Fat
Day 70	6	88.0 \pm 21.4	229 \pm 100.9	196.3 \pm 84.8
Day 105	6	59	267.8 \pm 73.7	179.5 \pm 18.0

Table IV.4. Mean concentration (pg/g) \pm SD of 17 β -estradiol in tissues of heifers at day 70 and day 105 after implantation of Revalor[®]-XH

Days of Implantation	Animal Number	Muscle	Liver	Fat
Day 70	6	33.0 \pm 23.4	97.0	64.0 \pm 23.6
Day 105	6	<LLOQ	<LLOQ	35.7 \pm 4.9

Conclusions: The incurred total trenbolone residue concentrations in the liver of cattle treated with Revalor[®]-XH were calculated from the 17 β -trenbolone concentrations reported in this study by applying a correlation of 1% for 17 β -trenbolone concentration to total trenbolone residue concentration in the liver previously applied to support the original approval of Revalor[®]-XS (NADA 141-269, approved January 19, 2007). The calculated concentrations of total residues of trenbolone in the liver at Day 70 and Day 105 after the implantation were well below half of the safe concentration for total residues of trenbolone in the liver.

The incremental increases of estradiol-17 β concentrations in the edible tissues at Day 70 and Day 105 after implantation were below the codified allowable incremental increases for estradiol in the respective edible tissues (21 CFR 556.240).

(2) Implant Payout Profile

The implant payout study, Intervet Study #2034-004-01, was summarized in the effectiveness section of this FOI Summary. Seven groups of animals with seven or eight heifers in each group were implanted with Revalor[®]-XH on Day 0. Implants were collected from the heifers in one of the seven groups on explantation Days 0, 36, 70, 105, 140, 175, and 210 following implantation. Concentrations of trenbolone acetate and estradiol remaining in the explants were quantitated.

Conclusions: Data for trenbolone and estradiol concentrations remaining in explants at 0, 36, 70, 105, 140, 175, and 210 days after implantation demonstrated a gradual and steady payout of the steroids from the implants over the tested implantation period.

2. Target Tissue and Marker Residue

Neither a target tissue nor a marker residue assignment is needed for trenbolone acetate in cattle (see the FOI Summary for NADA 138-612, approved July 2, 1987).

A specific target tissue is not identified for residues of estradiol in cattle. Allowable incremental increases for estradiol residues are assigned for each of the edible tissues.

3. Tolerances

A tolerance for trenbolone in cattle is not needed (21 CFR 556.739; see also the FOI Summary for NADA 138-612, approved July 2, 1987).

Residues of estradiol are regulated on the basis of the codified allowable incremental increases (21 CFR 556.240).

4. Withdrawal Period

No withdrawal period is required (*i.e.*, zero-day withdrawal).

E. Analytical Method for Residues

A regulatory analytical method for monitoring trenbolone residues in cattle is not required.

A regulatory analytical method for monitoring estradiol residues in cattle is not required.

V. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to Revalor[®]-XH:

Not for Use in Humans. Keep this and all drugs out of the reach of children.

VI. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR part 514. The data demonstrate that Revalor[®]-XH, when used according to the label, is safe and effective for increased rate of weight gain and improved feed efficiency for up to 200 days after implantation in beef heifers fed in confinement for slaughter. Additionally, data demonstrate that residues in food products derived from species treated with Revalor[®]-XH will not represent a public health concern when the product is used according to the label.

A. Marketing Status

This product can be marketed over-the-counter (OTC) because the approved labeling contains adequate directions for use by laypersons and the conditions of use prescribed on the labeling are reasonably certain to be followed in practice.

B. Exclusivity

This supplemental approval for Revalor[®]-XH qualifies for THREE years of marketing exclusivity under section 512(c)(2)(F)(iii) of the FD&C Act because the supplemental application included safety and effectiveness studies. This exclusivity begins as of the date of our approval letter and only applies to the use of Revalor[®]-XH (trenbolone acetate and estradiol extended-release implants) for increased rate of weight gain and improved feed efficiency for up to 200 days after implantation in beef heifers fed in confinement for slaughter.

C. Supplemental Applications

This supplemental NADA required a reevaluation of the safety or effectiveness data in the original NADA (21 CFR 514.106(b)(2)).

D. Patent Information:

For current information on patents, see the Animal Drugs @ FDA database or the Green Book on the FDA CVM internet website.

E. Analytical Method for Residues

A regulatory analytical method for monitoring trenbolone residues in cattle is not required.

A regulatory analytical method for monitoring estradiol residues in cattle is not required.

V. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to Revalor[®]-XH:

Not for Use in Humans. Keep this and all drugs out of the reach of children.

VI. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR part 514. The data demonstrate that Revalor[®]-XH, when used according to the label, is safe and effective for increased rate of weight gain and improved feed efficiency for up to 200 days after implantation in beef heifers fed in confinement for slaughter. Additionally, data demonstrate that residues in food products derived from species treated with Revalor[®]-XH will not represent a public health concern when the product is used according to the label.

A. Marketing Status

This product can be marketed over-the-counter (OTC) because the approved labeling contains adequate directions for use by laypersons and the conditions of use prescribed on the labeling are reasonably certain to be followed in practice.

B. Exclusivity

This supplemental approval for Revalor[®]-XH qualifies for THREE years of marketing exclusivity under section 512(c)(2)(F)(iii) of the FD&C Act because the supplemental application included safety and effectiveness studies. This exclusivity begins as of the date of our approval letter and only applies to the use of Revalor[®]-XH (trenbolone acetate and estradiol extended-release implants) for increased rate of weight gain and improved feed efficiency for up to 200 days after implantation in beef heifers fed in confinement for slaughter.

C. Supplemental Applications

This supplemental NADA required a reevaluation of the safety or effectiveness data in the original NADA (21 CFR 514.106(b)(2)).

D. Patent Information:

For current information on patents, see the Animal Drugs @ FDA database or the Green Book on the FDA CVM internet website.