Date of Approval: December 11, 2009

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-221

OPTAFLEXX 45

Ractopamine Hydrochloride
Type A Medicated Article to be Used in the Manufacture of
Type B and C Medicated Top Dress Feeds
Cattle Fed in Confinement for Slaughter

This supplement provides for top dress feeding of ractopamine hydrochloride for increased rate of weight gain and improved feed efficiency in cattle fed in confinement for slaughter during the last 28 to 42 days on feed.

Sponsored by:

Elanco Animal Health,

A Division of Eli Lilly & Co.

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I. GENERAL INFORMATION:

A. File Number:	NADA 141-221
B. Sponsor:	Elanco Animal Health A Division of Eli Lilly & Co. Lilly Corporate Center Indianapolis, IN 46285 Drug Labeler Code: 000986
C. Proprietary Name:	OPTAFLEXX 45
D. Established Name:	Ractopamine hydrochloride
E. Pharmacological Category:	Beta adrenergic agonist
F. Dosage Form:	Type A medicated article to be used in the manufacture of Type B and C medicated top dress feeds
G. Amount of Active Ingredient:	45.4 g per lb (100 g per kg)
H. How Supplied:	25 lb bag
I. How Dispensed:	OTC
J. Dosage:	Type C Medicated Top Dress feed – 70 to 400 mg/head/day, provided in a minimum of 1.0 lb of top dressed Type C medicated feed containing a maximum of 800 g/ton ractopamine
K. Route of Administration:	Oral, in feed
L. Species/Class:	Cattle fed in confinement for slaughter
M. Indications:	**Top Dress Feed:** For increased rate of weight gain and improved feed efficiency in cattle fed in confinement for slaughter during the last 28 to 42 days on feed
N. Effect of Supplement:	This supplement provides for top dress feeding of ractopamine hydrochloride for increased rate of weight gain and improved feed efficiency in cattle fed in confinement for slaughter during the

last 28 to 42 days on feed.

II. EFFECTIVENESS:

A. Dosage Characterization:

The Freedom of Information (FOI) Summary for the original approval of NADA 141-221 dated June 13, 2003, contains dosage characterization information for cattle fed in confinement for slaughter when ractopamine hydrochloride (HCl) is administered in a total mixed ration (complete feed) during the last 28 to 42 days on feed. For the indications of increased rate of weight gain and improved feed efficiency, the dose range of 8.2 to 24.6 g/ton of complete feed, equivalent to 70 to 430 mg/head/day, was approved. As discussed in section IV.B.1.c of this FOI Summary (below), tissue residue depletion data support a zero day withdrawal period for the top dress formulation at doses up to 400 mg/head/day. Thus, a dosage range of 70 to 400 mg/head/day of ractopamine HCl when fed as a top dress to cattle fed in confinement is consistent with the original approval, taking food safety concerns into consideration. Ractopamine HCl would be fed in a minimum of 1.0 lb of top dress containing a maximum of 800 g/ton ractopamine HCl.

B. Substantial Evidence:

1. Dose Confirmation Study

Title: "Clinical Study (GCP): Effectiveness of Ractopamine Hydrochloride (HCl) when Fed as a Top Dress Application in Beef Cattle"

Data from four replicated trials involving 560 steers were pooled and statistically analyzed. Trials were conducted in four locations in the United States. Steers fed in confinement were fed ractopamine HCl at 400 mg/head/day as a top dress for the last 42 days prior to slaughter. Steers were fed typical basal diets common to the feedlot industry. A linear mixed model analysis was conducted on the claim variables, rate of weight gain and feed efficiency. Statistically significant improvements in these variables and no treatment-related adverse effects in this study in steers using the highest intended dose and longest intended duration would adequately demonstrate that ractopamine HCl is effective in increasing rate of weight gain and improving feed efficiency when fed as a top dress to cattle fed in confinement for slaughter at 70 to 400 mg/head/day for the last 28 to 42 days on feed.

Investigators and Locations:

Trial T4V180803: Ronald P. Lemenager, PhD, Purdue University, Department of Animal Sciences, West Lafayette, IN

Trial T4V060804: Terry TerHune, DVM, PhD, HMS Veterinary Development, Inc. Tulare, CA

Trial T4V160805: Matt Edmonds, DVM, PhD, Johnson Research LLC, Parma, ID

Trial T4V180806: John J. Wagner, PhD, Southeast Colorado Research Center, Lamar, CO

Study Design:

a. *Objective:* To evaluate the clinical effectiveness of ractopamine HCl for improving growth performance when fed at 400 mg/head/day to steers as a top dress feed for the last 42 days immediately prior to slaughter.

b. *Study Animals:* A total of 560 healthy steers were enrolled in this study. Steers were acquired from major cattle producing regions of the United States. Breeds of cattle placed on the study were typical of the U.S. beef industry. No ionophores or antibiotics were administered to any of the cattle during the treatment period.

c. *Experimental Design:* The study was conducted at four independent sites. A complete randomized block design was used at each site. The pen was the experimental unit. Study pens were blocked by location in the study facility with each block containing four treatment replicates within each location block. There were 8 pens per treatment group at each site. At the Indiana and California sites there were 8 cattle per pen, at the Idaho site there were 10 cattle per pen, and at the Colorado site there were 9 animals per pen for a total of 64 pens containing 560 steers.

d. *Treatment Groups:* The two treatment groups used in this study were the test article treatment group (ractopamine HCl at 400 mg/head/day fed as a Type C medicated top dress feed) and a negative control treatment group (non-medicated top dress feed). Treatments were randomly assigned to study pens.

e. *Test Article Administration:* Cattle received a top dress feed (either ractopamine HCl or control) once per day for the last 42 days of the study.

f. *Measurements and Observations:* Cattle were observed twice daily for any abnormal conditions.

   Individual animal weights were recorded on Day -1 (assignment to pen), Day 0 (treatment start), and Day 42 (end of treatment). The weights taken on Day -1 and Day 0 were averaged to determine the initial weight. The initial animal

weights and Day 42 weights were used to calculate the average daily weight gain (ADG) of cattle during the treatment period.

Feed issue weights and top dress issued by pen were recorded daily at each issue from Day 0 (treatment start) through Day 42 (end of study).

Carcass data were collected for: Adjusted 12th rib fat thickness, muscle conformation score, marbling score, USDA quality grade, muscle color, firmness and texture score, overall maturity score, ribeye area, percent kidney-pelvis-heart (KPH) fat, hot carcass weight, calculated USDA yield grade, dressing percentage, dark cutter, liver abscess score, and liver condemnation.

Average daily gain (ADG) and feed efficiency {gain to feed (G/F) and feed to gain (F/G)} were evaluated. In order to demonstrate effectiveness of the test article for increased rate of weight gain and improved feed efficiency when fed as a top dress feed, a statistically significant increase in ADG and improved feed efficiency in the ractopamine HCl treated cattle as compared with the negative control cattle, respectively, needed to be demonstrated.

g. *Statistical Analysis:* The effect of ractopamine HCl fed as a top dress feed on growth performance was evaluated using a linear mixed model (the MIXED procedure of SAS, SAS Institute, Cary, NC, Version 9.2). Treatment was included in the model as a fixed effect. Random effects included study site, study site by treatment interaction, and block (study site). The assumption of heterogeneity between sites and among blocks within sites for claim variables (ADG and feed efficiency) was evaluated using Levene's test (the ANOVA procedures in SAS, SAS Institute, Cary, NC, Version 9.2). A P-value ≤ 0.05 was deemed statistically significant. The remaining outcomes were not subjected to this test. If significant, a weighted analysis was conducted.

The effect of treatment on carcass measurements, continuous in nature, was evaluated using a linear mixed model (the MIXED procedure in SAS, SAS Institute, Cary, NC, Version 9.2). Treatment was included in the model as a fixed effect. Random effects included study site, study site by treatment interaction, and block (study site). Where results were converted to a binomial outcome (liver abscess score (present/not present), dark cutter scores (dark/not dark)), the GLIMMIX procedure was used assuming a binomial distribution and using a logit link. Categorical outcomes were also evaluated using GLIMMIX, assuming a multinomial distribution and a cumulative logit link. The statistical model described above was used.

Pooled Results:

Ractopamine HCl was fed at 400 mg/head/day as a top dress feed for the last 42 days prior to slaughter. A total of 555 steers fed in confinement completed the study.

Growth performance results are provided in Table 1. Average daily gain (ADG) was improved in the ractopamine HCl treated group as compared to the control group ($P<0.05$). Feed efficiency, measured as F/G and G/F was improved in the ractopamine HCl treated group as compared to the control group ($P<0.05$).

Table 1. Pooled Statistical Analysis – LSMeans for Growth Performance of Steers Fed Diets Containing Ractopamine HCl

Variables	Ractopamine HCl (mg/head/day)			
	0 mg	400 mg	SEM	P-value
Number of replicates	**32**	**32**		
Number of steers*	**279**	**276**		
Variables				
Rate of weight gain (ADG, lbs/d)	3.71	4.21	0.414	0.0060
Feed efficiency (F/G), as fed	9.08	7.77	0.983	0.0362
Feed efficiency (F/G), 100% DM basis†	6.03	5.28	0.146	0.0129
Gain efficiency (G/F), as fed	0.116	0.134	0.0145	0.0066
Gain efficiency (G/F), 100% DM basis	0.150	0.174	0.0161	0.0057

† The test of heterogeneity of variance for study site was statistically significant; therefore a weighted analysis was conducted.

* Five animals were removed prior to the end of the treatment period. These outcomes were calculated without these animals.

There were no adverse effects of treatment on hot carcass weight, conformation score, ribeye area, USDA yield grade, and incidence of dark cutters.

There were no adverse effects on animal health attributable to the test article.

Conclusions:

Ractopamine HCl fed as a Type C medicated top dress at 400 mg/head/day to steers fed in confinement for 42 days prior to slaughter was effective at significantly ($P<0.05$) increasing rate of weight gain and improving feed efficiency over that of control animals.

The results of the study support that ractopamine HCl fed as a Type C medicated top dress at 70 to 400 mg/head/day to cattle fed in confinement for 28 to 42 days prior to slaughter is effective for increased rate of weight gain and improved feed efficiency.

Individual Trials

T4V180803 (Indiana): One hundred twenty-eight Continental x British crossbred steers were used in this 42-day study. The treatment phase of the study was initiated on August 21, 2008, and final animal weights were collected on October 2, 2008. The study was conducted by Dr. Ronald P. Lemenager, Purdue University, West Lafayette, IN. Cattle were fed a high concentrate ration based on corn, corn silage, dried distillers grains, a protein supplement and the top dress treatment. Two animals were removed from the study. One animal (control treatment group) was removed for lameness and the other (ractopamine HCl treatment group) for severe foot rot.

This site had a large number of lameness problems with the cattle. Twenty-three animals from each treatment group (46 total) were observed to have been lame at some point during the study. This lameness did not require medical treatment, and all animals were observed as being healthy prior to slaughter. As equal numbers of animals per treatment group were affected, environment and not treatment appeared to cause the high level of lameness. Housing conditions may have contributed to this as animals were housed on slatted concrete floors.

Six animals had backfat measurements at the beginning of the study that were outside of the protocol criteria of being between 4 mm and 13 mm. Study animal backfat measurements were between 2.67 mm and 13.67 mm. The number of animals that fell outside of the criteria was equal across treatment groups and likely had limited impact on the study outcome.

Fifty-five percent of the control treated animals and forty-five percent of the ractopamine HCl treated animals had loose stools between the days of August 26 and September 10, 2008. This study was conducted in the late summer months and into early fall. Temperature changes of up to 25 °F between day and night temperatures as well as steady rainfall during the first days of the study may have contributed to the large number of loose stools observed. As loose stools were evenly distributed among treatment groups, the incidence likely had little impact on the outcome of this study.

After the last day of treatment, cattle were individually weighed, loaded on semi-trucks, and hauled 157 miles from the feedlot to a slaughter facility in North Aurora, IL. Cattle were held co-mingled prior to slaughter. All cattle were inspected and passed both the ante-mortem and post-mortem inspections

by USDA inspection staff. No treatment-related adverse conditions were observed during the study, at the end of the study, or during the harvest of the cattle.

Table 2. Site T4V180803 (Indiana):

Variables	**Control[a]**	**Ractopamine HCl[a]**
No of replicates	8	8
Total no. of steers starting on study	64	64
Total no. of steers completing study	63	63
Initial weight, lb	1260.7	1266.9
Final weight, lb	1368	1396.4
Rate of weight gain, lb/d	2.58	3.10
Feed efficiency, pounds of feed/lb of gain, 100% dry matter basis	9.29	7.46

[a] all values are arithmetic means

T4V060804 (California): One hundred twenty-eight Angus and Angus crossbred steers were used in this 42-day study. The study was conducted in the August and September of 2008 by Dr. Terry TerHune, Health Management Services, Tulare, CA. Cattle were fed a high concentrate ration based on corn, alfalfa hay, a protein supplement, molasses and top dress feed. The study was conducted during the summer months with the normal expected high temperatures above 100° F on numerous days.

No animals were removed from the study. At the end of the study, cattle were individually weighed, and moved approximately 100 to 200 yards from the feedlot research pens to the cattle loading area. Cattle were loaded on semi-trucks and hauled approximately 400 miles from the feedlot to the slaughter plant by a commercial livestock hauler. Cattle were held co-mingled prior to slaughter. All cattle were inspected and passed both the ante-mortem and post-mortem inspection by the USDA personnel. There were no animal safety concerns or treatment-related adverse conditions observed during the study, at the end of the study or during the slaughter of the cattle.

Table 3. Site T4V060804 (California)

Variables	Control[a]	Ractopamine HCl[a]
No of replicates	8	8
Total no. of steers starting on study	64	64
Total no. of steers completing study	64	64
Initial weight, lb	1082.1	1082.0
Final weight, lb	1268.2	1293.9
Rate of weight gain, lb/d	4.43	5.04
Feed efficiency, pounds of feed/lb of gain, 100% dry matter	5.49	4.83

[a] all values are arithmetic means

T4V160805 (Idaho): One hundred sixty crossbred steers were used in this 42-day study. The study was conducted by Dr. Matthew Edmonds, Johnson Research LLC, Parma, ID. The treatment phase of this study was initiated on September 23, 2008, and concluded on November 4, 2008. Cattle were fed a high concentrate ration based on rolled corn, high moisture corn with cob, alfalfa hay, dried distillers grains, a liquid molasses based protein supplement, tallow, whey and the top dress treatment assigned to them. Two animals from the ractopamine HCl treatment groups were removed from the study, one due to acute pneumonia and the other died due to acute bloat.

Cattle from this study site were exposed to fall weather conditions. At the end of the study, cattle were individually weighed and moved approximately 160 to 300 yards from the feedlot research pens to the cattle loading area. Cattle were loaded on semi-trucks and hauled approximately 310 miles from the feedlot to a commercial slaughter facility in Toppenish, WA. Cattle were held co-mingled prior to slaughter. All cattle were inspected and passed both the ante-mortem and post-mortem inspection by the USDA personnel. There were no treatment-related adverse conditions observed during the study, at the end of the study or during the slaughter of the cattle.

Table 4. Site T4V160805 (Idaho)

Variables	Control [a]	Ractopamine HCl [b]
No of replicates	8	8
Total no. of steers starting on study	80	80
To no. of steers completing study	80	78
Initial weight, lb	1194.9	1191.9
Final weight, lb	1350.9	1358.1
Rate of weight gain, lb/d	3.72	4.04
Feed efficiency, pounds of feed/lb of gain, 100% dry matter	6.91	6.30

[a] all values are arithmetic means

T4V180806 (Colorado): One hundred forty-four steers were used in this 42-day study. Sixty-nine percent of these were either Angus or Angus-cross steers. Another twenty percent of the steers were of continental breeding with the remaining animals being a mixture of beef breeds. The treatment phase of this study was initiated on July 16, 2008, and concluded on August 27, 2008. The study was conducted by Dr. John J. Wagner, Colorado State University, Lamar, CO. Cattle were fed a high concentrate diet containing corn, dried distillers grains, condensed corn distillers solids, fat, corn silage, protein supplement, and the treatment top dress. One animal in the ractopamine HCl treatment group died from bloat during this study.

This study was conducted during the summer months having 22 days with a high temperature of above 100 °F. Animals were moved several hundred yards to the loading facility prior to loading for shipment to the slaughter facility the day after treatment ended. Animals were transported 164 miles by truck from Lamar, CO to Cactus, TX to be slaughtered. All cattle were inspected and passed both the ante-mortem and post-mortem inspection by the USDA personnel. No treatment-related adverse conditions were observed during the study, at the end of the study, or during the slaughter of the cattle.

Table 5. Site T4V180806 (Colorado):

Variables	**Control[a]**	**Ractopamine HCl[a]**
No of replicates	8	8
Total no. of steers starting on study	72	72
Total no. of steers completing study	72	71
Initial weight, lb	1161.4	1161.3
Final weight, lb	1334.2	1356.6
Rate of weight gain, lb/d	4.11	4.66
Feed efficiency, pounds of feed/lb of gain, 100% dry matter basis	6.14	5.19

[a] all values are arithmetic means

III. TARGET ANIMAL SAFETY:

CVM did not require target animal safety studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-221, dated June 13, 2003, contains a summary of a target animal safety study for beef cattle fed 0, 30, 90, or 300 ppm ractopamine hydrochloride in a complete diet during a 42-day feeding period, and animal health observations in cattle fed in confinement the intended range of doses in a complete diet (8.2 – 24.6 g/ton) during the effectiveness studies.

Additional information related to the evaluation of the safety and effectiveness of ractopamine HCl when fed as a top dress to cattle under feedlot conditions and shipped,

and harvested under commercial conditions is included in the effectiveness section. There were no adverse effects on animal health attributable to the test article.

Additional information regarding animal feeding behavior was used to conduct a risk analysis to establish that cattle are unlikely to over-consume OPTAFLEXX 45 to a toxic level if fed as a top dress.

References:

Gibb, D.J., T.A. McAllister, C. Huisma, and R. Wiedmeier. 1998. Bunk attendance of feedlot cattle with radio frequency technology. Can. J. Anim. Sci. 78:707-710.

Pritchard, R.H. and K.W. Bruns. 2003. Controlling variation in feed intake through bunk management. J. Anim. Sci. 81(E Suppl. 2): E133-E138.

Schwartkopf-Genswein, K.S., K.A. Beauchemin, T.A. McAllister, D.J. Gibb, M. Streeter, and D.A. Kennedy. 2004. Effect of feed delivery fluctuations and feeding time on ruminal acidosis, growth performance, and feeding behavior of feedlot cattle. J. Anim. Sci. 82: 3357-3365.

IV. HUMAN FOOD SAFETY:

A. Toxicology

CVM did not require toxicology studies for this supplemental approval. The FOI Summary for the original approval of NADA 140-863, dated December 22, 1999, contains a summary of all toxicology studies.

B. Residue Chemistry:

1. Summary of Residue Chemistry Studies

a. Total Residue and Metabolism Study

Total residue and metabolism data were described in the FOI Summary for ractopamine hydrochloride (NADA 141-221, dated June 13, 2003).

b. Comparative Metabolism Study

Comparative metabolism data were described in the FOI Summary for ractopamine hydrochloride (NADA 141-221, dated June 13, 2003).

c. Residue Depletion Study

Residue Depletion in Beef Cattle Following Oral Administration of Ractopamine hydrochloride (Optaflexx®) via a 500 mg/head/day or 600 mg/head/day Top Dress for 10 days.

Study Number: MCL-LRL-0704

In-life Facility- Midwest Veterinary Services, Inc., Oakland, NE

Analytical Laboratory- Covance Laboratories, Inc., Madison, WI

Following an acclimation period of 14 days, twenty beef cattle (19 females and one male) were fed Test Article (Type A medicated article incorporated into a Type B medicated top dress feed) administered as a top dress at either a rate of 500 mg/head/day or 600 mg/head/day for ten days. Under Study ABC-0398 (see FOI Summary for NADA 141-221, dated June 13, 2003), total residues of ractopamine in cattle liver reached steady state seven days following initiation of feeding ractopamine hydrochloride. The animals were euthanized and tissues collected at practical zero day withdrawal period(12 hours). Liver tissue was collected and assayed for ractopamine by high performance liquid chromatography with fluorescence detection. It is noted that with the exception of one animal, the data sets contain samples from female cattle only. Previous residue depletion studies for ractopamine in cattle were examined, and no significant gender differences in depletion of ractopamine residues from the liver were observed.

The mean ractopamine residues in the liver at practical zero-time withdrawal were 12.60 ppb for the 500 mg/head/day group and 16.81 ppb for the 600 mg/head/day group. A statistical analysis of the data for livers from each treatment group was conducted to determine the 99th percent tolerance limit with 95% confidence. The calculation for both treatment groups fell well below the tolerance of 90 ppb for ractopamine in cattle liver.

The tissue residue depletion data showed that residues of ractopamine hydrochloride in liver were less than the tolerance at practical zero withdrawal, thereby supporting the assignment of a zero day withdrawal period for the top dress formulation at doses up to 400 mg/head/day.

2. Target Tissue and Marker Residue Assignment

The target tissue is liver. The marker residue is ractopamine hydrochloride.

3. Tolerance Assignments

Tolerances for ractopamine in cattle are 0.09 ppm in liver and 0.03 ppm in muscle (21 CFR 556.570).

4. Withdrawal Time(s)

The withdrawal period for the use of ractopamine hydrochloride in cattle is zero days.

C. Microbial Food Safety

The Agency carefully reviewed information provided by the sponsor regarding microbial food safety associated with a proposed alternative method of feeding ractopamine hydrochloride in a Type C medicated feed as a top-dress for increased rate of weight gain and improved feed efficiency in cattle. Beta agonists like ractopamine hydrochloride are not considered antimicrobial drugs. Mobile genetic elements that could transfer (horizontally or vertically) specific antimicrobial resistance determinants to indigenous bacteria are not known (at this time) for this class of compounds. The Agency concludes that there should not be an increased risk to human health due to antimicrobial resistance issues associated with the new feeding regimen for ractopamine in cattle.

D. Analytical Method for Residues:

The FOI Summary for the original approval of NADA 141-221 dated June 13, 2003, contains the analytical method summaries for ractopamine in cattle.

The validated regulatory methods for detection and confirmation of residues of ractopamine are available from CVM, FDA, 7500 Standish Place, Rockville, MD 20855.

V. USER SAFETY:

The User Safety Concerns section of the FOI Summary for the original NADA 140-863, approved December 22, 1999, states:

> Ractopamine (RACT) is pharmacologically active as a partial beta adrenergic agonist. Acute and chronic exposures of mammals to RACT at sufficiently high levels by the oral, inhalation, or intravenous injection routes results in the signs expected from this class of compounds: increased heart rate, increased blood and pulse pressure, peripheral dilation of blood vessels, and increased cardiac output. Monkeys exposed for four hours per day for 8 days to airborne levels of RACT of 0.38 mg/m^3 or greater experienced increased heart rates while 15 minute inhalation exposures resulted in increased heart rate at concentrations of 13.9 mg/m^3 and greater (2.4 mg/m^3 was a no-effect-level).

The PAYLEAN Type A Medicated Article was formulated with an oil coating to minimize the inhalation exposure during use of the product. To estimate the potential for feed mill operators to experience significant inhalation exposures to ractopamine during handling and mixing operations, an exposure monitoring study was conducted. Under the conservative conditions of the on-site study, measurements from the mill operators' personal air samplers demonstrated mean exposure values of < 0.001 mg/m^3 during short term weighing and bagging operations and long term operations in the mill resulted in exposure values of <0.0002 mg/m^3.

RACT is an eye irritant in rabbits and at very high exposure levels (5,000 mg/kg) is a slight skin irritant. In Guinea pigs, RACT was a contact sensitizer. In rodents there were no effects on mating performance or fertility, but increased mortality, growth retardation, and structural abnormalities were seen in offspring where doses were high enough to be maternally toxic.

User safety concerns associated with effects of accidental inhalation or direct contact have been satisfactorily addressed by formulating the product to minimize dust generation and by establishing label warnings. In addition, a toll-free telephone number will be available on the label to inform users of where they can obtain additional information concerning user safety, request an MSDS, and to report adverse effects.

In addition, labeling for the product contains a warning regarding user safety. This warning states:

The active ingredient in OPTAFLEXX, ractopamine hydrochloride, is a beta-adrenergic agonist. Individuals with cardiovascular disease should exercise special caution to avoid exposure. Not for use in humans. Keep out of the reach of children. The OPTAFLEXX 45 formulation (Type A Medicated Article) poses a low dust potential under usual conditions of handling and mixing. When mixing and handling OPTAFLEXX, use protective clothing, impervious gloves, protective eye wear, and a NIOSH-approved dust mask. Operators should wash thoroughly with soap and water after handling. If accidental eye contact occurs, immediately rinse eyes thoroughly with water. If irritation persists, seek medical attention. The material safety data sheet contains more detailed occupational safety information. To report adverse effects, access medical information, or obtain additional product information, call 1-800-428-4441.

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 and 21 CFR part 514. The data demonstrate that OPTAFLEXX 45, when used according to the label, is safe and effective for increased rate of weight gain and improved feed efficiency when fed as a top dress feed (70-400 mg/hd/day) to cattle fed in confinement for slaughter for the last 28-42 days on feed. Additionally, data demonstrate that residues in food products derived from cattle treated with OPTAFLEXX 45 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 label are reasonably certain to be followed in practice.

B. Exclusivity:

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 date of approval. The three years of marketing exclusivity applies only to the use of OPTAFLEXX 45 (ractopamine hydrochloride) as a top dress feed fed for increased rate of weight gain and improved feed efficiency in cattle fed in confinement for slaughter during the last 28 to 42 days on feed for which this supplement is approved."

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:

The sponsor did not submit any patent information with this application.

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

ATTACHMENTS:

Facsimile Labeling:

A. OPTAFLEXX 45 Type A Medicated Article Bag Label

B. Ractopamine Finishing Cattle Feed Concentrate – TD Type B Medicated Feed Label

C. Ractopamine Finishing Cattle Feed Concentrate – TD Liquid Type B Medicated Feed Label

D. Ractopamine Finishing Cattle Feed Concentrate – TD Type C Medicated Top Dress Feed Label