Date of Approval: June 17, 2010

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-225

OPTAFLEXX plus RUMENSIN

(Ractopamine Hydrochloride and Monensin USP)
Type A medicated article to be used in the manufacture of Type C medicated feeds
Cattle fed in confinement for slaughter

Provides for top dress application of ractopamine hydrochloride Type C medicated feed administerd on Type C medicated feed containing monensin USP for increased rate of weight gain, improved feed efficiency, and prevention and control of cocciodiosis due to *Eimeria bovis* and *E. zuernii* 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 141-225
B. Sponsor:	Elanco Animal Health A Division of Eli Lilly & Co. Lilly Corporate Center Indianapolis, IN 46285 Drug Labeler Code: 000986
C. Proprietary Names:	OPTAFLEXX plus RUMENSIN
D. Established Names:	Ractopamine hydrochloride Monensin USP
E. Pharmacological Categories:	Ractopamine hydrochloride - Beta adrenergic agonist Monensin USP - Ionophore/anticoccidial
F. Dosage Form:	Type A medicated article to be used in the manufacture of Type C medicated feed
G. Amount of Active Ingredients:	Ractopamine hydrochloride - 45.4 grams per pound (100 grams per kilogram) Monensin USP - 90 grams per pound
H. How Supplied:	Ractopamine hydrochloride - 25 lb bag Monensin USP - 55 lb bag
I. How Dispensed:	OTC
J. Dosage:	Ractopamine is fed at 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 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. Monensin is added to diets for cattle fed in confinement for slaughter at concentrations of

	10 to 40 g of monensin per ton of complete feed for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* at a rate of 0.14 to 0.42 mg monensin/lb of body weight, depending on the severity of the coccidiosis challenge, up to 480 mg/head/day.
K. Route of Administration:	Oral, in feed
L. Species/Class:	Cattle fed in confinement for slaughter
M. Indication:	For increased rate of weight gain, improved feed efficiency, and prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* 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 application of ractopamine hydrochloride Type C medicated feed administered on Type C medicated feeds containing monensin USP for increased rate of weight gain, improved feed efficiency, and prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* in cattle fed in confinement for slaughter during the last 28 to 42 days on feed.

II. EFFECTIVENESS:

In accordance with the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Animal Drug Availability Act (ADAA) of 1996, if the animal drugs or active ingredients intended for use in combination in an animal feed have already been separately approved for the particular uses and conditions for which they are intended for use in combination, the Center for Veterinary Medicine (CVM) will not refuse to approve an NADA for the combination on effectiveness grounds unless the FDA finds that the sponsor fails to demonstrate that:

- there is substantial evidence to indicate that any active ingredient or animal drug intended only for the same use as another active ingredient or animal drug in the proposed combination makes a contribution to the labeled effectiveness
- each of the active ingredients or animal drugs intended for at least one use that is different from all other active ingredients or animal drugs used in the combination provides appropriate concurrent use for the intended target population
- where the combination contains more than one nontopical antibacterial active ingredient or animal drug, there is substantial evidence that each of the nontopical antibacterial active ingredients or animal drugs makes a contribution to the labeled effectiveness.

Ractopamine hydrochloride, as provided by Elanco Animal Health, A Division of Eli Lilly & Co., has previously been separately approved for use in feed for cattle fed in confinement for slaughter, during the last 28 to 42 days on feed, for increased rate of weight gain and improved feed efficiency (21 CFR 558.500(e)(2)(xi)). Monensin USP, as provided by Elanco Animal Health, A Division of Eli Lilly & Co., has previously been separately approved for use in feed for cattle fed in confinement for slaughter for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* (21 CFR 558.344(f)(3)(vii)). Effectiveness of each drug, ractopamine hydrochloride and monensin USP when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Elanco Animal Health, A Division of Eli Lilly & Co's approved NADAs 141-221 and 095-735 for ractopamine hydrochloride and monensin USP, respectively.

Because ractopamine hydrochloride and monensin USP each have at least one use that is different from all other animal drugs used in the combination, the NADA must also demonstrate that ractopamine hydrochloride plus monensn USP provide appropriate concurrent use for the intended target population. The use of ractopamine hydrochloride plus monensin USP provides appropriate concurrent use because these drugs are intended to treat different conditions (ractopamine hydrochloride for increased rate of weight gain and improve feed efficiency and monensin sodium for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*) likely to occur simultaneously with sufficient frequency in cattle fed in confinement for slaughter. There is no more than one nontopical antibacterial contained in this combination animal drug intended for use in Type C medicated feed.

III. TARGET ANIMAL SAFETY:

In accordance with the FFDCA, as amended by the ADAA of 1996, if the animal drugs or active ingredients intended for use in combination in animal feed have previously been separately approved for the particular uses and conditions of use for which they are intended for use in combination, CVM will not refuse to approve an NADA for the combination on target animal safety grounds unless:

- there is a substantiated scientific issue specific to an active ingredient or animal drug used in the combination that cannot adequately be evaluated based on the information contained in the application for the combination, and CVM finds that the application fails to show that the combination is safe, or
- there is a scientific issue raised by target animal observations contained in the studies submitted to the NADA for the combination, and CVM finds that the application fails to show that the combination is safe.

Ractopamine hydrochloride, as provided by Elanco Animal Health, A Division of Eli Lilly & Co., has previously been separately approved for use in feed for cattle fed in confinement for slaughter, during the last 28 to 42 days on feed, for increased rate of weight gain and improved feed efficiency (21 CFR 558.500(e)(2)(xi)). Monensin USP, as provided by Elanco Animal Health, A Division of Eli Lilly & Co., has previously been separately approved for use in feed for cattle fed in confinement for slaughter for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* (21 CFR 558.355(f)(3)(vii)).

Under the provisions of ADAA, this supplemental approval allows for the combination of ractopamine hydrochloride (as provided by Elanco Animal Health, A Division of Eli Lilly & Co.) and monensin USP (as provided by Elanco Animal Health, A Division of Eli Lilly & Co.). Target animal safety for each drug, ractopamine hydrochloride and monensin USP when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Elanco Animal Health, A Division of Eli Lilly & Co's approved NADAs 141-221 and 095-735 for ractopamine hydrochloride and monensin USP, respectively. The Agency has found no substantiated scientific issue relating to the target animal safety of ractopamine hydrochloride and monensin USP when used in combination under this NADA and no scientific issue has been raised by target animal observations submitted as part of the NADA for this combination. Therefore, in accordance with the FFDCA, as amended by the ADAA of 1996, no specific target animal safety studies are required for approval of this application.

IV. HUMAN FOOD SAFETY:

In accordance with the FFDCA, as amended by the ADAA of 1996, if the animal drugs or active ingredients intended for use in combination in animal feed have already been separately approved for the particular uses and conditions of use for which they are intended for use in combination, CVM will not refuse to approve an NADA for the combination on human food safety grounds unless CVM finds that the application fails to establish that:

- none of the active ingredients or animal drugs used in combination at the longest withdrawal for any of the active ingredients or animal drugs in the combination exceeds the established tolerance, or
- none of the active ingredients or animal drugs in combination interferes with the method of analysis for another active ingredient or animal drug in the combination.

A. Toxicology:

CVM did not require toxicology studies for this supplemental approval. Safety of the individual drugs in this combination product has been established by data in NADA 141-221 (FOI Summary dated June 13, 2003) for ractopamine hydrochloride and NADA (FR 58289-58290, Vol: 40, No. 242, December 16, 1975) for monensin.

B. Residue Chemistry:

CVM did not require residue chemistry studies for this supplemental approval. NADA 141-221 (FOI Summary dated June 13, 2003; supplement dated December 11, 2009) for ractopamine hydrochloride and NADA 095-735 (FR 58289-58290, Vol: 40, No. 242, December 16, 1975) for monensin contain summaries of the residue chemistry studies for ractopamine hydrochloride and monensin in cattle.

C. Microbial Food Safety:

The Agency determined that an assessment of microbial food safety associated with this combination of ractopamine hydrochloride and monensin, USP approvable pursuant to the provisions of the Animal Drug Availability Act (1996), was not necessary at this time.

D. Analytical Method for Residues:

1. Analytical Method

The approvals of NADA 141-221 (FOI Summary dated June 13, 2003) for ractopamine hydrochloride and NADA 095-735 (FR 58289-58290, Vol: 40, No. 242, December 16, 1975) for monensin contain the analytical method summaries for ractopamine hydrochloride and monensin in cattle.

2. Availability of Methods

Analytical methods for detection of residues of ractopamine and monensin in cattle are available from CVM, FDA, 7500 Standish Place, Rockville, MD 20855.

V. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to the Type C medicated feed:

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 contained in the previously approved NADAs for OPTAFLEXX plus RUMENSIN demonstrate that, when they are used according to the label, they are safe and effective for increased rate of weight gain and improved feed efficiency, prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* in cattle fed in confinement for slaughter during the last 28 to 42 days on feed. Additionally, data demonstrate that residues in food products derived from cattle fed in confinement for slaughter treated with OPTAFLEXX plus RUMENSIN 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 following in practice.

B. Exclusivity:

This approval does not qualify for marketing exclusivity under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act.

C. Supplemental Applications:

This supplemental NADA did not require a reevaluation of the safety or effectiveness data in the original NADA (21 CFR §514.106(b)(2)).

D. Patent Information:

No patents were submitted with this application.

VII. ATTACHMENTS:

Facsimile Labeling:

Ractopamine Finishing Cattle Feed Concentrate – TD + M Type C Medicated Top Dress Feed
Monensin Medicated Feedlot Cattle Feed Type C Medicated Feed