Date of Approval: November 18, 2011

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 095-735

RUMENSIN 90

Monensin
Type A medicated article to be used in the manufacture of Type C free-choice feeds
Growing cattle on pasture or in dry lot (stocker and feeder cattle and dairy and beef replacement heifers)

This supplement provides for approval of free-choice feeds for growing cattle on pasture or in dry lot (stocker and feeder cattle and dairy and beef replacement heifers) for increased rate of weight gain and for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*.

Sponsored by:

Elanco Animal Health
A Division of Eli Lilly & Co.

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I. GENERAL INFORMATION:

A. File Number:	NADA 095-735
B. Sponsor:	Elanco Animal Health A Division of Eli Lilly & Co. Lilly Corporate Center Indianapolis, IN 46285 Drug Labeler Code: 000986
C. Proprietary Name:	RUMENSIN 90
D. Established Name:	Monensin
E. Pharmacological Category:	Anticoccidial/Ionophore
F. Dosage Form:	Type A medicated article to be used in the manufacture of Type C free-choice feeds
G. Amount of Active Ingredient:	90.7 g/lb
H. How Supplied:	25 kg bag
I. How Dispensed:	OTC
J. Dosage:	50 – 200 mg per head per day
K. Route of Administration:	Oral, in feed
L. Species/Classes:	Growing cattle on pasture or in dry lot (stocker and feeder cattle and dairy and beef replacement heifers)
M. Indications:	For increased rate of weight gain and for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*.
N. Effect of Supplement:	This supplement provides for approval of free-choice feeds for growing cattle on pasture or in dry lot (stocker and feeder cattle and dairy and beef replacement heifers) for increased rate of weight gain and for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*.

II. EFFECTIVENESS:

A. Dosage Characterization:

This supplemental approval does not change the previously approved dosage range. The Freedom of Information (FOI) Summaries for the supplemental approvals of NADA 095-735 dated October 22, 1990, September 23, 1993, March 15, 1996, and December 16, 1998, contain dosage characterization information for growing cattle on pasture or in dry lot (stocker, feeder cattle and dairy and beef replacement heifers).

B. Substantial Evidence:

1. Clinical Field Study

Five pasture studies across five different states utilizing 257 crossbred and purebred yearling steers and heifers were used to establish a coefficient of variation (CV) for monensin intake from free-choice feeds. The studies represent three different delivery forms (molasses mineral block, loose mineral and protein block) and three different concentrations of monensin provided in a free-choice feed (350, 800, and 1620 g/ton). All studies included replicates of non-medicated control and medicated animals to evaluate monensin effectiveness when offered in free-choice feeds. The initial weights of the growing cattle used ranged from 420 to 694 pounds. Study duration ranged from 96 to 112 days in length. Pasture (pen) was the experimental unit in all studies. The studies were not designed to collect consumption at the same time periods; however, all data were transformed into fourteen day intake periods and the pooled analysis used the first six periods for a total of 84 days on study.

Study No. Barr_IA_T1
800 g/ton monensin provided in free-choice mineral block
Investigator: Dr. G. Barr
Cooperative Research Farms
Land O'Lakes Inc.
Ft. Dodge, IA

Forty-eight crossbred yearling steers weighing approximately 672 lb were used to evaluate the effect of monensin in molasses mineral blocks on block intake and performance of cattle on pasture in a 96 day trial. Block consumption was determined on a three and four day interval throughout the study. The molasses mineral blocks containing monensin were consumed at a rate that provided 97 mg/head/day monensin. Monensin provided in a molasses mineral block improved average daily gain 0.110 lb (6.8 %).

Table 1: Performance Data for Study No. Barr_IA_T1		
Item	**Control**	**Monensin**
Average Daily Gain, lb/head	1.628	1.738
Monensin Consumption, mg/head/day	0	97

Study No. Caswell_MFA_T2
800 g/ton monensin provided in free-choice mineral block
Investigator: Dr. L. Caswell
Missouri Farmers Association Inc.
Columbia, MO

Thirty-nine Angus yearling heifers weighing approximately 694 lb, thirty crossbred yearling heifers weighing approximately 584 lb and eight crossbred yearling steers weighing approximately 562 lb were used to evaluate the effect of monensin in molasses mineral blocks on block intake and performance of cattle on pasture in a 97 day trial. Block consumption was determined every seven days. Blocks containing monensin were consumed at a rate providing 104 mg/head/day monensin. Monensin provided in a molasses mineral block improved average daily gain 0.154 lb (15.7 %).

Table 2: Performance Data for Study No. Caswell_MFA_T2		
Item	**Control**	**Monensin**
Average Daily Gain, lb/head	0.978	1.132
Monensin Consumption, mg/head/day	0	104

Study No. Cmarik_IL_T3
800 g/ton monensin provided in free-choice mineral block
Investigator: Dr. George Cmarik
University of Illinois
Dixon Springs, IL

Forty crossbred yearling steers weighing approximately 584 lb were used to evaluate the effect of monensin in molasses mineral blocks on block intake and performance of cattle on pasture in a 112 day trial. Block consumption was determined every seven days. Blocks containing monensin were consumed at a rate providing 86 mg/head/day monensin. Monensin provided in a molasses mineral block improved average daily gain 0.184 lb (24.9 %).

Table 3: Performance Data for Study No. Cmarik_IL_T3		
Item	**Control**	**Monensin**
Average Daily Gain, lb/head	0.739	0.923
Monensin Consumption, mg/head/day	0	86

Study No. T1F217647
1620 g/ton monensin provided in free-choice mineral
Investigator: Dr. D. P. Leach
Dunmor, KY

A study was conducted using thirty-two mixed crossbred steers weighing approximately 420 lb to determine the effect of monensin on growing cattle on pasture when incorporated into a loose mineral offered free-choice. Loose mineral consumption was determined every fourteen days. The experiment was conducted over a period of 112 days. Loose mineral containing monensin was consumed at a rate providing 102 mg/head/day monensin. Monensin provided in a loose mineral improved average daily gain 0.22 lb (11.9 %).

Table 4: Performance Data for Study No. T1F217647		
Item	**Control**	**Monensin**
Average Daily Gain, lb/head	1.85	2.07
Monensin Consumption, mg/head/day	0	102

Study No. R&D 290 NE
350 g/ton monensin provided in free-choice protein block
Investigator: Dr. John Ward
University of Nebraska
Mead, NE

Sixty crossbred yearling heifers weighing approximately 538 lb were used to evaluate the effect of monensin in protein blocks on block intake and performance of cattle on pasture in a 112 day trial. Block consumption was determined every seven days. Blocks containing monensin were consumed at a rate providing 141 mg/head/day monensin. Monensin provided in a protein block improved average daily gain 0.10 lb (6.6 %).

Table 5: Performance Data for Study No. R&D 290 NE		
Item	**Control**	**Monensin**
Average Daily Gain, lb/head	1.51	1.61
Monensin Consumption, mg/head/day	0	141

POOLED STUDY RESULTS

Within each of the five studies, study animals were randomly assigned to pens. Pens were then randomly assigned to one of two treatment groups. Pen was the experimental unit. This data set was analyzed as a randomized complete block design with a one-way treatment structure. Study number (location) was used as the blocking effect. The one-way treatment structure was treatment with two levels: monensin and control.

Average daily gain was analyzed using PROC MIXED in the SAS® system version 9.2. Treatment group was the fixed effect in the model with random effects being study number and the interaction of treatment group and study number. Levene's test of homogeneity was used to test homogeneity of variances between treatment groups.

Product consumption (mg/head/day) for the monensin treatment group was analyzed using PROC MIXED in the SAS® system version 9.2. Period was the fixed effect in the model and the random effects included study number and pen within study number.

Average Daily Gain:

Average daily gain (lb) was calculated by taking the final weight of each pen minus the initial weight for each pen and dividing by the total head-days (head-days = total head times the total number of days on study) for each pen. Results of the pooled analysis demonstrated that cattle consuming an average of 110 mg/head/day monensin during the five studies had an average daily gain 0.15 lb per head per day greater than cattle receiving a non-medicated control free-choice feed (11.2 %; $P \leq 0.0012$). Levene's test of homogeneity ($P \leq 0.9846$) demonstrated no evidence that the variances between treatment groups were different.

Consumption of Monensin:

The average monensin consumption for each of the six 14-day periods throughout the study was 115, 100, 109, 126, 117 and 93 mg/head/day for the treated groups during periods 1 through 6, respectively. Overall average consumption across these six 14-day periods was 110 mg/head/day. The coefficient of variation (CV) was estimated to be 32.4% and was calculated by taking the square root of the residual variance divided by the overall average consumption across the six periods.

Table 6: Five Study Pooled Analysis		
Item	**Control**	**Monensin**
Average Daily Gain, lb/head	1.34[a]	1.49[b]
Monensin Consumption, mg/head/day	0	110

[a,b] Means within a row with different superscripts differ ($P \leq 0.0012$)

Prevention and Control of Coccidiosis Due to *Eimeria bovis* and *E. zuernii*:

Because the monensin dosage for increased average daily gain is the same as the monensin dosage for prevention and control of coccidiosis (due to *Eimeria bovis* and *E. zuernii*), it is appropriate to approve both indications based on the above studies.

In conclusion, this supplement provides for approval of free-choice feeds for growing cattle on pasture or in dry lot (stocker and feeder cattle and dairy and beef replacement heifers) for increased rate of weight gain and for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*.

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 095-735 dated December 16, 1975, contains a summary of target animal safety studies for cattle fed in confinement for slaughter.

IV. HUMAN FOOD SAFETY:

A. Toxicology:

CVM did not require toxicology studies for this supplemental approval. The original approval of NADA 095-735 dated December 16, 1975 (40 FR 58289), supplemental approvals for NADA 095-735 (FOI summaries dated December 16, 1998, October 28, 2004, and December 1, 2006), and the original approval of NADA 38-878 dated May 20, 1975 (35 FR 7734) contain a summary of all toxicology studies for monensin.

B. Microbial Food Safety:

CVM did not require additional information for microbial food safety (antimicrobial resistance) for this supplemental approval. The agency does not think that the nature of this supplement – providing free-choice feeds to growing cattle on pasture or drylot – will impact antimicrobial resistance among bacteria of public health concern in or on treated cattle; therefore, evaluation of microbial food safety (antimicrobial resistance) is not warranted for this supplement.

C. Impact of Residues on Human Intestinal Flora:

CVM did not require additional information for the impact of residues on human intestinal flora for this supplemental approval. The original approval of NADA 095-

735 dated December 16, 1975 (40 FR 58289), and FOI summaries for supplemental approvals dated December 16, 1998, October 28, 2004, and December 1, 2006, contain summaries of all information used to assess the impact of residues on human intestinal flora.

D. Assignment of the Final ADI:

No reassessment of the toxicological ADI, or microbiological ADI was needed for this supplemental approval. The toxicological ADI was established as part of the supplemental approval of NADA 095-735 (FOI Summary Dated December 16, 1998). Information used to assess the impact of residues on human intestinal flora provided under the supplemental approval dated October 28, 2004, concluded that a microbiological ADI was not necessary. The final ADI is the toxicological ADI, 12.5 micrograms per kilogram of body weight per day.

E. Safe Concentrations for Total Residues (Edible Tissues and Injection Sites, If Applicable):

No reassessment of the safe concentrations for total residues was needed for this supplemental approval. Safe concentrations for total residues were established as part of the supplemental application for NADA 095-735 (FOI Summary dated October 28, 2004).

F. Residue Chemistry:

CVM did not require residue chemistry studies for this supplemental approval. The original approval of NADA 095-735 dated December 16, 1975 (40 FR 58289), and FOI summary for the supplemental approval dated October 28, 2004, contain summaries of residue chemistry studies for cattle. Tolerances for monensin residues in cattle tissues were established under supplemental approval for NADA 141-233 (FOI summary dated September 11, 2007). Tolerances for monensin residues in cattle are 0.1 ppm in liver, and 0.05 ppm in muscle, kidney, and fat. A tolerance for monensin residues in milk is not required.

G. Analytical Method for Residues:

The original approval of NADA 095-735 dated December 16, 1975 (40 FR 58289), and FOI summary for the supplemental approval dated October 28, 2004, contain the analytical method summaries for monensin in cattle.

V. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to RUMENSIN 90:

WARNING: When mixing and handling Rumensin 90, use protective clothing, impervious gloves and a dust mask. Operators should wash thoroughly with soap and water after handling. If accidental eye contact occurs, immediately rinse with water.

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 RUMENSIN 90, when used according to the label, is safe and effective for increased rate of weight gain and for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*. Additionally, data demonstrate that residues in food products derived from growing cattle on pasture or in dry lot (stocker and feeder cattle and dairy and beef replacement heifers) treated with RUMENSIN 90 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:

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 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.