Approval Date: October 22, 1990

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 095-735

B. Sponsor

Elanco Products Company
A Division of Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

C. Proprietary Name

Rumensin

D. Established Name

monensin (as monensin sodium)

E. Dosage Form

Type A medicated article

F. Dispensing Status

OTC

G. Dosage Regimen

The Type A medicated article is to be incorporated into complete feeds to provide levels of 10 to 30 g monensin per ton or may be included in Type B or Type C medicated feeds. Type B or Type C medicated feeds are to be mixed with grain and roughage to provide 10-30 g/ton in complete feed. Feed to provide 100 to 360 mg monensin per head daily.

H. Route of Administration

Oral in feed

I. Indication

For the prevention and control of coccidiosis in feedlot cattle due to *Eimeria bovis* and *Eimeria zuernii*.

J. Effect of Supplement

This supplement provides for an additional claim for the use of monensin in the prevention and control of coccidiosis in feedlot cattle.

II. EFFECTIVENESS

Clinical Effectiveness in Monensin Fed to Cattle Inoculated With Coccidia Oocysts in a Four-Trial Dose Titration Experiment

Investigators:

Study No. 1 (T1F278303)
Bert E. Stromberg, Ph.D.
University of Minnesota
St. Paul, MN 55108

Study No. 2 (T1F178304)
Dr. Paul Fitzgerald
University of Illinois
Urbana, IL 61801

Study No. 3 (T1F398306)
Dr. Gary Davis
Greenbrier Veterinary Services, Inc.
Delaware, Ohio 43015

Study No. 4 (T1F278401)
Bert E. Stromberg, Ph.D.
John E. Schlotthaues, D.V.M., Ph.D
University of Minnesota
St. Paul, MN 55108

One hundred and twenty-three ruminating cattle weighing approximately 150 to 188 pounds were used in 4 trials to confirm the effectiveness of monensin fed at 0, 10, 20 or 30 g/ton against coccidiosis. The cattle were orally challenged with sporulated *Eimeria bovis* and/or *Eimeria zuernii* oocysts on the third day after monensin feeding began. The experimental design used was a randomized block at several locations with the challenge type (coccidia species) as the blocking factor. Oocyst counts and fecal score data were collected over time on several days throughout the 33- to 38-day trials. These data were viewed as sub-sampling units and analyzed accordingly. Animal weights and feed intakes were measured weekly, but analyzed over the entire length of the trial. Mortality within each treatment group was recorded upon occurrence. The least squares treatment means for pair-wise comparisons to the control treatment (0 g/ton monensin) were as follows:

Table 1. Least Squares Treatment Means for Pair-wise Comparisons to the Control Treatment (0 g/ton monensin)

Variable	0 g monensin/ ton	10 g monensin/ ton	20 g monensin/ ton	30 g monensin/ ton
Ave. Daily Weight Gain (lbs/h/d)	1.310	1.592	1.941	1.960
Ave. Daily Dry Matter Intake (lbs/h/d)	5.488	5.578	6.033	6.168
E. bovis oocysts (sq. root,1000 g/feces)	49.936	29.077	15.894	11.163

Variable	0 g monensin/ ton	10 g monensin/ ton	20 g monensin/ ton	30 g monensin/ ton
E. zuernii oocysts (sq. root,1000 g/feces)	18.472	7.032	2.313	2.214
Other oocysts (sq. root,1000 g/feces)	19.275	9.233	8.666	4.710
Feces scores (sq. root, scale 1-5)*	1.40	1.28	1.12	1.09
Mortality (% of initial number)**	16	0	0	0

*1 = normal, 2 = slight diarrhea, 3 = diarrhea, 4 = diarrhea/blood, 5 = diarrhea/mucus
**Calculated percent (No. died/No. initially) x 100); not analyzed statistically

For both *E. bovis* and *E. zuernii* oocyst counts, the 10-gram level showed significant reduction as compared to controls. A statistically significant decrease in both oocyst counts was seen through 20 grams per ton. Although the 30 gram per ton level gave directionally lower oocyst counts than the 20-gram per ton level, the difference was not significant. Medical judgment was utilized in deciding that the 30-gram per ton level was medically meaningful.

Prior to initiation of the above studies, two preliminary studies were conducted as follows:

Study No. 665
L. R. McDougald and W. H. Henry
Lilly Research Laboratories
Greenfield, IN

Study No. 715
L. R. McDougald, W. H. Henry and L. L. Schenck
Lilly Research Laboratories
Greenfield, IN

The design and conduct of each pivotal or preliminary study are discussed under

A. Pivotal Studies - Study No. 1

The Clinical Effectiveness of Monensin in Controlling Bovine Coccidiosis. (T1F278303)

Investigator:

Bert E. Stromberg, Ph.D.
University of Minnesota
St. Paul, MN 55108

1. General Design:

   a. Objective:

      To determine the effect of monensin on coccidial oocysts production, weight gain, feed intake, clinical signs, and mortality of ruminating cattle challenged with *E. bovis* or *E. zuernii* oocysts.

b. Test Animals: Thirty-six male Holstein-Friesian cattle approximately 8 weeks of age.

Each animal constituted an experimental unit. The four non-challenged animals served as controls for baseline performance and were confined in separate tie stalls adjacent to the coccidial challenged animals. The challenged controls and treated animals were blocked by inoculum (*E. zuernii* or *E. bovis*) into treatment groups of four animals each. Treatments (0, 10, 20, or 30 g/ton monensin) were assigned at random to each group as follows:

Table 2. Treatment Groups - Study No. 1

Monensin g/ton	No. of Animals	Coccidial Challenge
0	4	None
0	4	*E. zuernii*
10	4	*E. zuernii*
20	4	*E. zuernii*
30	4	*E. zuernii*
0	4	*E. bovis*
10	4	*E. bovis*
20	4	*E. bovis*
30	4	*E. bovis*

c. Treatment:

Treatment feeds were offered three days prior to *E. bovis* or *E. zuernii* inoculation to establish acceptance and normal intake.

The cattle challenged with *E. zuernii* received an essentially pure inoculum containing about 235,000 sporulated oocysts in an oral gavage.

The cattle challenged with *E. bovis* received an essentially pure inoculum containing about 150,000 sporulated oocysts in an oral gavage.

d. Dosage Form:

Rumensin Premix, 60 g monensin/lb. incorporated into complete feeds at levels of 0, 10, 20 and 30 monensin/ton.

e. Test Duration:

35 days

f. Parameters Measured:

1) Body weights were recorded and average daily gain was calculated.

2) Feed intake was recorded.

3) Fecal character for each animal was recorded daily on the following scale:

1 = normal, 2 = slight diarrhea, 3 = diarrhea, 4 = diarrhea/blood, and 5 =diarrhea/mucus.

4) Oocyst counts were made. Oocysts were identified and recorded by species.

2. Results

Table 3. Results - Study No. 1

Monensin Trt. (g/ton)	Coccidia Challenge	Number of Animals	Mortality	ADG* (lbs)	ADF** (lbs)	Cumulative Oocysts Days 19-23 Post Challenge				Cumulative Fecal Character Days 19-23 Post-Challenge
						E. zuernii	*E. bovis*	Other	Total	
0	None	4	0	1.91	5.93	50	70	10	130	1.25
0	*E.zuernii*	4	0	1.63	5.75	110	100	10	220	1.25
10	*E.zuernii*	4	0	1.62	5.51	0	0	0	0	1.10
20	*E.zuernii*	4	0	1.69	5.70	0	10	0	10	1.10
30	*E.zuernii*	4	0	1.47	5.18	10	0	0	10	1.10
0	*E.bovis*	4	2	1.93	5.46	750	1260	40	2050	2.05
10	*E.bovis*	4	0		5.74	710	1670	0	2380	1.85
20	*E.bovis*	4	0		6.05	20	60	0	80	1.45
30	*E.bovis*	4	0		5.65	0	90	0	90	1.00

*ADG = Average daily gain.
** ADF = Average daily feed.

Animals inoculated with *E. bovis* exhibited more marked signs of bovine coccidiosis than those inoculated with *E. zuernii*. A monensin dose related oocyst passage response was observed in cattle receiving each challenge.

The daily fecal character indicated in reduction in diarrhea of monensin treated cattle when compared to non-treated challenged control animals.

All species of coccidial oocyst isolations following challenge were considerably reduced in the monensin treated groups of cattle when compared to non-treated challenged control animals

There were no mortalities in this study.

3. Statistical Analysis

This trial was part of a four trial experiment. Statistical analysis was performed on the whole experiment run under a common protocol.

4. Conclusions

The cattle in the monensin treated groups demonstrated reduced coccidial oocyst shedding and diarrhea, over the non-treated challenged control animals.

5. Adverse Reactions

There were no adverse reactions attributable to the drug.

B. Pivotal Studies - Study No. 2

The Clinical Effectiveness of Monensin in Controlling Bovine Coccidiosis. (T1F178304)

Investigator:

Dr. Paul Fitzgerald
University of Illinois
Urbana, IL 61801

1. General Design:

a. Objective:

To determine the effect of monensin on coccidial oocysts production, weight gain, feed intake, clinical signs, and mortality of ruminating cattle challenged with *E. bovis* or *E. zuernii* oocysts.

b. Test Animals:

Thirty-six male Holstein-Friesian cattle approximately 8 weeks of age.

Each animal constituted an experimental unit. The four non-challenged animals served as controls for baseline performance and were confined in separate tie stalls adjacent to the coccidial challenged animals. The challenged controls and treated animals were blocked by inoculum (*E. zuernii* or *E. bovis*) into treatment groups of four animals each. Treatments (0, 10, 20, or 30 g/ton monensin) were assigned at random to each group as follows:

Table 4. Treatment Groups - Study No. 2

Monensin g/ton	No. of Animals	Coccidial Challenge
0	4	None
0	4	*E. zuernii*
10	4	*E. zuernii*
20	4	*E. zuernii*
30	4	*E. zuernii*
0	4	*E. bovis*
10	4	*E. bovis*
20	4	*E. bovis*
30	4	*E. bovis*

c. Treatment:

1) Treatment feeds were offered three days prior to *E. bovis* or *E. zuernii* inoculation to establish acceptance and normal intake.

2) The cattle challenged with *E. zuernii* received an inoculum containing about 228,000 sporulated oocysts in an oral gavage as follows: *E. zuernii*, 76%; *E. bovis*, 4%; *E. auburnensis*, 6%; and *E. ellipsoidalis/cylindrica*, 14%.

3) The cattle challenged with *E. bovis* received an inoculum containing about 250,000 sporulated oocysts in an oral gavage as follows: *E. bovis*, 99%; less than 1% of *E. zuernii*, *E. auburnensis*, or *E. ellipsoidalis/cylindrica*.

d. Dosage Form:

Rumensin Premix, 60 g monensin/lb. incorporated into complete feeds at levels of 0, 10, 20 and 30 monensin/ton.

e. Test Duration: 35 days

f. Parameters Measured:

1) Body weights were recorded and average daily gain was calculated.

2) Feed intake was recorded.

3) Fecal character for each animal was recorded daily on the following scale:

1 = normal, 2 = slight diarrhea, 3 = diarrhea, 4 = diarrhea/blood, and 5 =diarrhea/mucus.

4) Oocyst counts were made. Oocysts were identified and recorded by species.

2. Results

Table 5. Results - Study No. 2

Monensin Trt. (g/ton)	Coccidia Challenge	Number of Animals	Mortality	ADG* (lbs)	ADF** (lbs)	Cumulative Oocysts Days 19-23 Post Challenge				Cumulative Fecal Character Days 19-23 Post-Challenge
						E. zuernii	*E. bovis*	Other	Total	
0	None	4	0	2.12	5.84	30	1120	410	1560	1.00
0	*E.zuernii*	4	0	1.36	4.23	1580	3970	6410	11960	1.85
10	*E.zuernii*	4	0	2.28	5.84	110	870	3260	4240	1.15
20	*E.zuernii*	4	0	2.31	6.10	220	270	4030	4520	1.05
30	*E.zuernii*	4	0	2.11	5.24	60	200	3070	3330	1.00
0	*E.bovis*	4	3	0.02	3.71	8107	87493	2227	97827	4.20
10	*E.bovis*	4	0	0.70	3.70	1965	22710	840	25515	3.20
20	*E.bovis*	4	0	1.73	4.49	350	13030	180	13560	1.60
30	*E.bovis*	4	0	1.62	4.85	740	10680	30	11450	1.75

*ADG = Average daily gain.
** ADF = Average daily feed.

Animals inoculated with *E. bovis* exhibited more marked signs of bovine coccidiosis than those inoculated with *E. zuernii*. A monensin dose related response was observed in cattle receiving each challenge.

Monensin treated groups of cattle gained more weight than the non-treated, challenge control animals.

The daily fecal character indicated reduction in diarrhea of monensin treated cattle when compared to non-treated, challenged control animals.

All species of coccidial oocyst isolations following challenge were considerably reduced in the monensin treated groups of cattle when compared to non-treated, challenged control animals.

3. Statistical Analysis

   This trial was part of a four trial experiment. Statistical analysis was performed on the whole experiment run under a common protocol.

4. Conclusions

   The cattle in the monensin treated groups demonstrated improved performance and reduced coccidial oocyst shedding, diarrhea, and mortality over the non-treated, challenged control animals.

5. Adverse Reactions

   There were no adverse reactions attributable to the drug.

C. Pivotal Studies - Study No. 3

The Clinical Effectiveness of Monensin in Controlling Bovine Coccidiosis. (T1F398306)

Investigator:

Dr. Gary Davis
Greenbrier Veterinary Services, Inc.
Delaware, OH 430158

1. General Design:

   a. Objective:

      To determine the effect of monensin on coccidial oocysts production, weight gain, feed intake, clinical signs, and mortality of ruminating cattle challenged with *E. bovis* or *E. zuernii* oocysts.

   b. Test Animals:

      Thirty-six male Holstein-Friesian cattle approximately 8 weeks of age.

      Each animal constituted an experimental unit. The four non-challenged animals served as controls for baseline performance and were confined in separate tie stalls adjacent to the coccidial challenged animals. The challenged animals were blocked both by inoculum (*E. zuernii* or *E. bovis*) and location (four animals/block). Treatments (0, 10, 20, or 30 g/ton monensin) were assigned to each block.

Table 6. Treatment Groups - Study No. 3

Monensin g/ton	No. of Animals	Coccidial Challenge
0	4	None
0	4	*E. zuernii*
10	4	*E. zuernii*
20	4	*E. zuernii*
30	4	*E. zuernii*
0	4	*E. bovis*
10	4	*E. bovis*
20	4	*E. bovis*
30	4	*E. bovis*

c. Treatment:

1) Treatment feeds were offered three days prior to *E. bovis* or *E. zuernii* inoculation to establish acceptance and normal intake.

2) The cattle challenged with *E. zuernii* received an inoculum containing about 475,000 sporulated oocysts in an oral dose.

3) The cattle challenged with *E. bovis* received an inoculum containing about 300,000 sporulated oocysts in an oral dose.

d. Dosage Form:

Rumensin Premix, 60 g monensin/lb. incorporated into complete feeds at levels of 0, 10, 20 and 30 monensin/ton.

e. Test Duration:

35 days

f. Parameters Measured:

1) Body weights were recorded and average daily gain calculated.

2) Feed intake was recorded.

3) Fecal character for each animal was recorded daily on the following scale:

1 = normal, 2 = slight diarrhea, 3 = diarrhea, 4 = diarrhea/blood, and 5 =diarrhea/mucus.

Oocyst counts were made. Oocysts were identified and recorded by species.

2. Results

Table 7. Results - Study No. 3

Monensin Trt. (g/ton)	Coccidia Challenge	Number of Animals	Mortality	ADG* (lbs)	ADF** (lbs)	Cumulative Oocysts Days 19-23 Post Challenge				Cumulative Fecal Character Days 19-23 Post-Challenge
						E. zuernii	*E. bovis*	Other	Total	
0	None	4	0	2.04	6.68	0	0	0	0	1.08
0	*E.zuernii*	4	0	2.12	6.44	25	0	5	70	1.53
10	*E.zuernii*	4	0	2.04	5.88	0	0	0	0	1.08
20	*E.zuernii*	4	0	1.96	6.01	0	5	0	5	1.58
30	*E.zuernii*	4	0	2.46	6.43	15	0	0	15	1.10
0	*E.bovis*	4	2	-0.25	4.11	1067	22008	4831	25420	3.88
10	*E.bovis*	4	0	0.21	4.65	265	2198	1337	10750	3.20
20	*E.bovis*	4	0	2.04	6.18	23	12175	1688	14065	2.23
30	*E.bovis*	4	0	2.25	6.12	0	630	125	2610	1.73

*ADG = Average daily gain.
** ADF = Average daily feed.

Animals inoculated with *E. bovis* exhibited more marked signs of bovine coccidiosis than those inoculated with *E. zuernii*. A monensin dose related response was observed in cattle receiving each challenge.

Monensin *E. bovis* treated groups of cattle gained more weight than the non-treated, challenged control animals.

The daily fecal character indicated reduction in diarrhea of monensin treated cattle when compared to non-treated, challenged control animals.

All species of coccidial oocyst isolations following challenge were considerably reduced in the monensin treated groups of cattle when compared to non-treated, challenged control animals.

3. Statistical Analysis

This trial was part of a four trial experiment. Statistical analysis was performed on the whole experiment run under a common protocol.

4. Conclusions

The cattle in the monensin treated groups demonstrated reduced coccidial oocyst, shedding, diarrhea, and mortality from *E. bovis* over the non-treated, challenged control animals.

5. Adverse Reactions

There were no adverse reactions attributable to the drug.

D. Pivotal Studies - Study No. 4

The Clinical Effectiveness of Monensin in Controlling Bovine Coccidiosis. (T1F278401)

Investigator:

Bert E. Stromberg, Ph.D.
John C. Schlotthaues, D.V.M., Ph.D.
William J. Bemrick, Ph.D.
University of Minnesota
St. Paul, MN 55108

1. General Design:

   a. Objective:

      To determine the effect of monensin on coccidial oocysts production, weight gain, feed intake, clinical signs, and mortality of ruminating cattle challenged with *E. bovis* or *E. zuernii* oocysts.

   b. Test Animals:

      Thirty-six male Holstein-Friesian cattle approximately 8 weeks of age.

      Each animal constituted an experimental unit. The four non-challenged animals served as controls for baseline performance and were confined in separate tie stalls adjacent to the coccidial challenged animals. The challenged controls and treated animals were blocked by inoculum (*E. zuernii* or *E. bovis*) into treatment groups of four animals each. Treatments (0, 10, 20, or 30 g/ton monensin) were assigned at random to each group as follows:

Table 8. Treatment Groups - Study No. 4

Monensin g/ton	No. of Animals	Coccidial Challenge
0	4	None
0	7	Mixed*
10	7	Mixed*
20	7	Mixed*
30	7	Mixed*

*Challenged with both *E. bovis* and *E. zuernii*.

   c. Treatment:

      1) Treatment feeds were offered three days prior to *E. bovis* or *E. zuernii* inoculation to establish acceptance and normal intake.

      2) The cattle were challenged with predominantly (99+%) *E. zuernii* inoculum containing 500,000 sporulated oocysts and a predominantly (99+%) *E. bovis* inoculum containing 300,000 sporulated oocysts. Each animal received these inocula oral gavages.

d. Dosage Form:

Rumensin Premix, 60 g monensin/lb. incorporated into complete feeds at levels of 0, 10, 20 and 30 monensin/ton.

e. Test Duration:

31 days

f. Parameters Measured:

1) Body weights were recorded and average daily gain was calculated.

2) Feed intake was recorded.

3) Fecal character for each animal was recorded daily on the following scale:

1 = normal, 2 = slight diarrhea, 3 = diarrhea, 4 = diarrhea/blood, and 5 =diarrhea/mucus.

4) Oocyst counts were made. Oocysts were identified and recorded by species.

2. Results

Table 9. Results - Study No. 4

Monensin Trt. (g/ton)	Coccidia Challenge	Number of Animals	Mortality	ADG* (lbs)	ADF** (lbs)	Cumulative Oocysts Days 19-23 Post Challenge				Cumulative Fecal Character Days 19-23 Post-Challenge
						E. zuernii	*E. bovis*	Other	Total	
0	None	4	0	1.83	8.56	0	5	145	150	1.05
0	Mixed***	7	0	2.21	8.19	651	8783	123	9614	1.94
10	Mixed***	7	0	2.41	7.90	72	2623	54	4549	2.09
20	Mixed***	7	0	2.39	8.37	0	103	3	106	1.06
30	Mixed***	6****	0	2.49	9.37	3	346	0	349	1.34

*ADG = Average daily gain.
** ADF = Average daily feed.
*** Challenged with both *E. zuernii* and *E. bovis*.
**** One animal was removed due to inability to measure feed consumption.

The signs of bovine coccidiosis exhibited by these animals inoculated with a mixture of *E. zuernii* and *E. bovis* were more severe than previous trials using pure *E. zuernii* inoculation. A monensin dose-related response was observed in the animals.

Monensin-treated groups of cattle gained more weight than the unmedicated, challenged control animals.

The daily fecal character indicated, in most cases, reduction in diarrhea of monensin treated cattle when compared to the unmedicated, challenged control animals.

There were no mortalities in this study.

3. Statistical Analysis

This trial was part of a four trial experiment. Statistical analysis was performed on the whole experiment run under a common protocol.

4. Conclusions

The cattle in the monensin treated groups demonstrated improved performance and reduced coccidial oocyst shedding, and in most cases, diarrhea over the non-treated challenged control animals.

5. Adverse Reactions

There were no adverse reactions attributable to the drug.

E. Preliminary Effectiveness Studies - Study No. 665

Monensin Coccidiosis Experiment No. 665

Investigator:

L. R. McDougald and W. H. Henry
Lilly Research Laboratories
Greenfield, IN

1. General Design

The study was designed as a pilot experiment to evaluate the efficacy of monensin against *Eimeria bovis* and *E. zuernii* in calves. Eight newborn male Holstein calves were acquired from Florida. They were fed milk replacer until weaning onto the calf starter ration and housed in isolation pens.

a. Treatment

Pen 19 Monensin - 30 g/ton
Pen 20 Infected controls

b. Coccidia Challenge

Each calf was orally administered sporulated oocysts of the following species:

E. bovis (LB7) 100,000 oocysts (passed 6-1-76)
E. zuernii (LB6) 100,000 oocysts (passed 6-1-76)

c. Rations and Administration

A calf starter ration containing monensin levels of 0 to 30 g/ton was fed during the 35-day experiment.

d. Experimental Design

Eight calves were divided into 2 groups of 4 calves/group on an equal weight pen basis. Treated calves were on medicated feed (8-3-76, day 1) prior to inoculation (8-10-76, day 7). The following data were collected: weight gains

per pen, feed/gain by pen and mortality. All calves and feed were weighed as shown in the following tables.

2. Results

Table 10. Mean Weight Gain Per Pen (lbs)

Monensin (g/t)	Day 7	Day 14	Day 21	Day 28	Day 35
30	27	69	109	157	168
0	38	76	98	132	170

Table 11. Mean Feed/Gain Per Pen

Monensin (g/t)	Day 7	Day 14	Day 21	Day 28	Day 35
30	2.87	2.39	2.46	2.07	2.68
0	2.38	2.38	2.72	2.38	2.55

Table 12. Oocysts Passage Per Pen*

Days P.I.	Monensin	Infected Controls
15	0	0
16	0	Trace
17	0	Trace
18	0	Trace
19	0	4,442,000
20	0	603,000
21	0	670,000
22	0	Trace
23	0	Trace
24	0	Trace

* Count based on 1 liter of fecal material.

Table 13. Percent Mortality Due to Coccidiosis

Monensin (g/t)	Percent Mortality
30	0
0	0

3. Statistical Analysis

This was a preliminary pilot study. Statistical analysis is not applicable.

4. Conclusions

Monensin was effective in prevention of bovine coccidiosis caused by *Eimeria bovis* when fed to calves at 30 g/ton in finished feed.

5. Adverse reactions

There were no adverse reactions attributable to the drug.

F. Preliminary Effectiveness Studies - Study No. 715

Monensin Coccidiosis Experiment No. 715

Investigators:

L. R. McDougald, W. H. Henry and L. L. Schenck
Lilly Research Laboratories,
Greenfield, IN

1. General Design

The study was designed to test the prophylactic effectiveness of monensin against *Eimeria bovis* infections in calves.

Thirty-two calves, 6 weeks old, male Holstein, obtained as 1-3 day old calves and fed milk replacer until weaning at 4 weeks of age.

a. Treatments

1. Noninfected, nonmedicated controls (2 x 4 calves)
2. Infected, nonmedicated controls (2 x 4 calves)
3. Infected, monensin 15 g/ton (2 x 4 calves)
4. Infected, monensin 30 g/ton (2 x 4 calves)

b. Coccidia Challenge

72 hrs. after initiation of the feeding regiment, each calf was given 100,000 oocysts of *E. bovis* (isolate LB7, Lot 60176) by oral inoculation.

c. Rations and Administration

A pelleted cattle ration containing levels of 0, 15 and 30 g monensin per ton was fed during the 28-day experiment.

d. Experimental Design

Each treatment was fed to two groups of 4 calves each. Calves were distributed to pens on a weight basis, to achieve approximately equal pen weights.

Each pen was supplied with the appropriate feed *ad libitum* and pine shavings used for bedding. At the onset of oocyst passage, bedding material was removed and the total fecal output was collected on a daily basis. Calves were weighed individually at the time of the infection and subsequently at 7-day intervals until termination at 28 days post-infection. The following data were collected: Clinical observations, daily oocyst passage per pen, weight gain, individual weight gain and feed consumption per pen.

2. Results

a. Clinical Observations

Diarrhea and anorexia were noted in both infected control groups from day 12 through day 21 post-infection. No untoward effects were seen in any other treatments.

b. Oocyst Passage per Pen

Substantial oocyst passage was noted on days 19-28 post-infection in both infected control groups.

Table 14. Oocyst Passage

Monensin (g/t)	Infection	Total Oocyst Passage Calf (x 10 degrees)
0	+	58.7
0	-	0
15	+	---*
30	+	0

* Positive, but too few to count

Table 15. Weight Gain/Calf

Monensin Conc (g/t)	Total Gain/Infection	Calf (lbs)	Average Daily Gain (lbs)
0	+	47.75	1.54
0	-	56.75	1.83
15	+	62.67	2.02
30	+	63.00	2.03

Table 16. Feed Consumption and Feed/Gain

Monensin Conc (g/t)	Infection	Feed Consumption (lbs/calf)	Feed/Gain
0	+	142.8	3.00
0	-	157.3	2.77
15	+	155.0	2.48
30	+	154.3	2.45

3. Statistical Analysis

The data from this equipment were not statistically analyzed.

4. Conclusions

Monensin was effective in preventing bovine coccidiosis due to *Eimeria bovis* and *E. zuernii* when fed continuously at 15 and 30 g/ton in a complete feed. Control animals suffered depressed weight gain during the patent period but recovered by the end of the experiment.

5. Adverse Reactions

There were no adverse reactions attributable to the drug.

G. Corroborative Effectiveness Study

Comparison of Two Forms and Two Levels of Lasalocid with Monensin on Feedlot Cattle Performance. Journal of Animal Science, Vol. 53, No. 6, 1981, pages 1440-1445.

Investigators:

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University of Illinois
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1. General Design:

The purpose of these trials as regards anticoccidial activity was to determine the effects of lasalocid and monensin on the incidence and concentrations of coccidia oocysts.

2. Summary and Conclusions

Results: Refer to Tables 17 and 18 below of the study. Monensin and lasalocid decreased the incidence and concentration of coccidial oocysts.

Table 17. Coccidiostatic Effect of Two Forms of Lasalocid and Monensin in Trial 1

	% of Steers with Coccidia Oocysts			**Oocysts/g***		
Treatment	**Day 1**	**Day 40**	**Day 120**	**Day 1**	**Day 40**	**Day 120**
Control	70.8	41.5	58.3	495	275	715
Pure Lasalocid	79	4.2	21.0	883	50	200
Mycelia-Cake Lasalocid	58.3	4.2	8.5	833	50	100
Monensin	62.9	4.2	4.2	1,104	50	100
SE**	7.2	4.6	5.4	172	40.4	105.3

* Average concentration for those steers shedding oocysts.
** Standard error of the mean.

Table 18. Coccidiostatic Effect of Lasalocid at 30 and 45 g/ton and of Monensin at 30 g/ton

	% of Steers with Coccidia Oocysts			Oocysts/g*		
Treatment	**Day 1**	**Day 40**	**Day 120**	**Day 1**	**Day 40**	**Day 120**
Control	66.9	10.2	6.3	742	19.7	12.5
Lasalocid, 30 g/ton	71.5	4.2	0	703	12.0	0
Lasalocid, 45 g/ton	63.1	5.1	0	794	10.3	0
Monensin, 30 g/ton	69.3	0	0	603	0	0
SE**	10.3	2.7	3	179.7	6.3	6.2

* Average concentration for those steers shedding oocysts.
** Standard error of the mean.

III. TARGET ANIMAL SAFETY

Monensin premix is the subject of an approved NADA 095-735. The conditions of the existing approval are described in 21 CFR 558.355. The feeding levels and rates proposed in this supplemental NADA providing for the control of bovine coccidiosis are essentially the same as for the existing approval. The differences involve changing the lower feeding level/rates of 5-30 g/ton and 50-360 mg/hd/day and providing 10-30 g/ton and 100-360 mg/hd/day when used for the control of coccidiosis. The duration of feeding will not exceed that already approved in the cited regulation. There is no reason to conclude that this additional approval at essentially the same levels will adversely affect the safety of animals receiving monensin.

IV. HUMAN FOOD SAFETY

This information is addressed in the original FOI for monensin for cattle in confinement for slaughter (FR 58289-58290, Vol:40, No. 242, December 16, 1975).

V. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA satisfy the requirements of section 512 of the Act and 21 CFR 558 of the implementing regulations. It demonstrates that monensin (Type A medicated article) is safe and effective for the indications stated on the product labeling. The supplement provides for a new claim, the use of monensin in feedlot cattle for the prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii*.

Monensin sodium for use in food producing animals is an over the counter product. Accurate diagnosis can be made with reasonable degree of certainty by the layman, and the conditions for use prescribed on the labeling are likely to be followed in the practice. Therefore, the Center for Veterinary Medicine has concluded that this product remains under over-the-counter marketing status.

According to the Center's provisions of 21 CFR 514.106 (2) (vii) this is a Category II change because the claim was expanded for the use of monensin in feedlot cattle to prevent coccidiosis caused by *E. bovis* and *E. zuernii*. It was concluded that the approval of this supplement neither poses an increased human risk from exposure to the drug nor alters the condition of the drug's safety in cattle.

The approved monensin sodium premix is codified in section 21 CFR 558.355 as a Type A medicated article for use in broiler chickens, turkeys, replacement chickens intended for use as cage layers, bobwhite quail, and goats for the prevention of coccidiosis, and in cattle for the improvement of feed efficiency. The tolerance is codified in section 21 CFR 556.420 (a) and is established at 0.05 part per million for negligible residues of monensin in the edible tissues of cattle and goats. Withdrawal time before slaughter is not required.

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.