Approval Date: March 23, 1990

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 130-736

B. Sponsor

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

C. Proprietary Name

COBAN®

D. Established Name

monensin

E. Dosage Form and Route of Administration

Medicated premix for inclusion in finished feeds

F. Dosage Regimen

Monensin, 54 through 90 g/ton (60 to 100 ppm) of feed

G. Indication

For the prevention of coccidiosis in growing turkeys caused by *Eimeria adenoeides, E. meleagrimitis* and *E. gallopavonis*.

H. Effect of Supplement

This supplemental NADA (130-736) provides for a change in treatment regimen from a ten-week feeding period to a continuous feeding for growing turkeys.

II. EFFECTIVENESS

Efficacy data may be found in the FOI Summary made available following initial approval of NADA 130-736 on April 24, 1987, as published in the Federal Register (Vol. 52, No. 83, pg. 15718) April 30, 1987.

III. ANIMAL SAFETY

Target animal safety data may be found in the FOI Summary made available following initial approval of NADA 130-736 on April 24, 1987, as published in the Federal Register (Vol. 52, No. 83, pg. 15718) April 30, 1987.

Succinctly, these data previously summarized in the April 24, 1987, FOI Summary show that monensin is not toxic to growing turkeys when fed at 110 g/ton for 17 weeks (20 g/ton above highest approval level).

A. Pivotal Study

A pivotal study was conducted in mature turkeys under simulated use conditions in support of the extended use of monensin in growing turkeys. Six hundred Nicholas White turkeys, 12 weeks of age and naive to monensin, were purchased and acclimated for an additional 12 weeks. Two hundred toms and 200 hens were then randomly selected and distributed to 16 floor pens of 25 birds each in the poultry house. Treatment groups were 0, 90, 180, and 450 g/ton monensin, with two pens of each sex per treatment group as follows:

Treatment Group	Monensin (g/ton)	Treatment (ppm)	No.Replicates -Hens	No. Replicates –Toms	No. of Turkeys- Per Replicate	No. of Turkeys –Per Group- Hens	No. of Turkeys – Per Group- Toms
00	0	0	2	2	25	50	49*
01	90	99	2	2	25	50	50
02	180	198	2	2	25	50	50
03	450	495	2	2	25	50	50
					Totals:	200	199

* One turkey died prior to start of study.

A turkey ration with these monensin treatments was provided *ad libitum* during the four-week treatment period.

Birds were observed twice daily for any changes in general physical condition or behavior during the study. Body weight, feed consumption, and feed conversion data were collected and analyzed. Daily mortality was recorded. A gross post-mortem examination was conducted on all birds that died or were killed *in extremis* during the study, as well as five/sex/dose randomly-preselected birds from each replicate killed for necropsy at study termination. Findings were recorded and tabulated.

There was a dose-related increase in the incidence and severity of physical signs of toxicity at the 180 and 450 g/ton monensin treatment levels. Recumbency and dyspnea were the most consistent clinical signs observed. Anorexia was evident from the decreased food consumption values from the 180 and 450 g/ton dose groups. Body weight gain and feed efficiency were depressed at these levels. Mortality increased in a dose-related manner. The average mortality rates for the 0, 90, 180, and 450 g/ton treatment groups were 0, 0.5, 23, and 65%, respectively. One turkey in the 90 g/ton group showed dyspnea and recumbency

during the second week of the study, but subsequently was apparently normal and had no gross lesions on necropsy at the end of the study. Gross postmortem lesions were nonspecific. The incidence of pallor in cardiac and skeletal muscles was present at all monensin levels and appeared to increase with increasing doses of monensin levels and appeared to increase with increasing doses of monensin in the feed.

In conclusion, mature turkeys continuously fed a complete ration containing 180 and 450 g monensin/ton of feed for one month had increased mortality. Clinical signs of anorexia, dyspnea, and recumbency, together with pallor of cardiac and skeletal muscles, also increased in incidence and severity. Dose-related decreases in body weight gain, feed consumption, and feed consumption, and feed efficiency occurred. These compound-related effects were restricted to the exaggerated dose levels of 180 and 450 g/ton, equivalent to 198 and 495 ppm monensin, respectively. The data from this study, coupled with that shown in the referenced FOI Summary, show that monensin at 90 g/ton can be safely fed to growing turkeys with the restriction of "do not feed to mature turkeys," as provided by product labeling.

Names and address of investigators who did the study:

Dr. M. N. Novilla and Mr. R.L. Van Duyn
Lilly Research Laboratories
Greenfield, IN 46140

B. Corroborative Study

Dr. Malcolm Reid, University of Georgia, Athens, Georgia 30602, in a noncontrolled study, dosed monensin-naive turkeys of various ages above ten weeks with the range of monensin dosages approved for coccidiosis prevention in turkeys up to ten weeks of age.

To ensure consumption, these monensin-naive turkeys were starved for 24 hours, fed the appropriate monensin concentration for two or three weeks, starved 36 hours, and again fed monensin for another two to three weeks.

In this series of three experiments with turkeys from 14 to 70 weeks of age fed either 54 or 90 grams monensin per ton of feed, no mortality or morbidity occurred. Data are shown in Table 1.

Table 1 Feeding of Monensin to Older Turkeys Naive to Monensin

Expt. No.	Age and Sex	No.	First Starvation	Monensin -g/ton	Monensin -Wks	Second Starvation	Monensin -Wks.	Monensin Mortality
1	14-wk. hens;	12	24 hr.	0	0	36 hr.	0	0
1	½ large	12	24 hr.	54	2	36 hr.	2	0

Expt. No.	Age and Sex	No.	First Starvation	Monensin -g/ton	Monensin -Wks	Second Starvation	Monensin -Wks.	Monensin Mortality
1	½ small	12	24 hr.	90	2	36 hr.	2	0
	Whites	24	0	0	0	36 hr	0	0
		24	0	54	2	36 hr.	2	0
		24	0	90	2	36 hr.	2	0
2	70-wk. toms	15	24 hr.	54	3	36 hr.	2	0
	Large, white	15	24 hr.	90	3	36 hr.	2	0
3	14-wk. toms	10	24 hr.	54	2	36 hr.	3	0
	24-wk. toms	10	24 hr.	90	2	36 hr.	3	0

IV. HUMAN SAFETY

Human safety data may be found in the FOI Summary made available following initial approval of NADA 130-736 on April 24, 1987, as published in the Federal Register (Vol. 52, No. 83, pg. 15718) April 30, 1987.

V. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA comply with the requirements of Section 512 of the act and demonstrate that COBAN (monensin), when used under its proposed conditions of use, is safe and effective.

Coban (monensin), was previously approved in chickens and turkeys with a ten-week feeding period (21CFR558.355). This supplemental provides for a change in the dosing regimen from the 10 week feeding period to growing turkeys. In support of the safe use of Coban in growing turkeys, the firm submitted a pivotal study and a corroborative study which demonstrated the drug is safe for use in growing turkeys. No additional efficacy are necessary. Data generated in turkeys up to 10 weeks of age are sufficient to approve Coban in growing turkeys.

Proper use by non-veterinarians can be expected because poultry producers routinely use medicated feed containing an animal drug for the prevention of coccidiosis in growing turkeys. Directions are clearly written and there is reasonable certainty that the conditions for use, including mixing directions, on the label can and will be followed by the producer. The Agency has concluded that this product can be approved for over-the-counter use.

Approval of this supplemental NADA will not significantly increase human exposure to residues of the drug in edible tissues because the product is already regulated for use in

turkeys under 21CFR558.355. Because total monensin residues will not exceed the safe concentration at zero withdrawal, establishing a tolerance for a marker residue in a target tissue is not necessary.

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.