ENVIRONMENTAL ASSESSMENT FOR THE USE OF COBAN® PREMIX IN THE FEED OF BOBWHITE QUAIL

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

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TABLE OF CONTENTS

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1. DATE — January 1988

2. APPLICANT — Elanco Products Company
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3. ADDRESS — Lilly Corporate Center
Indianapolis, Indiana 46285

4. DESCRIPTION OF THE PROPOSED ACTION

A Supplemental New Animal Drug Approval has been requested for use of COBAN premix in the feed of bobwhite quail. Monensin sodium is the active ingredient in COBAN premix. It is proposed that monensin be fed to quail at 73 g monensin/ton of complete feed (80 ppm) for the prevention of coccidiosis acquired from normal infection. The species to be controlled are Eimeria dispersa and E. lettyae. Prevention of coccidiosis in bobwhite quail is especially important since quail subjected to confinement rearing are very susceptible to infection. Outbreaks are characterized by diarrhea, weight loss, unthriftiness and increases in mortality. Approval of the use of COBAN premix in the feed of bobwhite quail would result in a small increase in the total amount of monensin sodium sold in the United States.

COBAN premix is already approved for use in the rations of chickens at 90 to 110 g/ton (21 CFR558.355; Federal Register, May 20, 1970) and turkeys at 54 to 90 g/ton (21 CFR558.355; Federal Register, April 30, 1987). RUMENSIN® premixes also contain monensin and are approved for use in the rations of cattle (up to 360 mg/head/day) fed in confinement for slaughter (21 CFR558.355; Federal Register, December 16, 1975) and for use in the rations of growing cattle in pastures (up to 200 mg monensin/head/day [21 CFR558.355; Federal Register, July 28, 1978]). In 1983 approval for use of RUMENSIN premixes in pastured cattle was expanded to include beef and dairy replacement heifers.

COBAN® (monensin sodium, Elanco)

An Environmental Impact Analysis Report (1) has been provided for RUMENSIN premixes fed to cattle. An Environmental Assessment for the use of COBAN premix in turkeys (2) and for the use of RUMENSIN premixes in the feed of reproducing beef cattle (3) were both submitted in 1986 to support the request for approval of NADA's 130-736 and 95-735. The current Environmental Assessment is abbreviated since it addresses the use of COBAN premix to prevent disease in bobwhite quail, a minor species (21CFR514.1[d]).

Approval of the proposed action would authorize the use of COBAN premix to be expanded to include bobwhite quail. Approval of the proposed action would also authorize the fermentation and processing plants of Eli Lilly and Company at Clinton and Lafayette, Indiana to manufacture and package the COBAN premix to be sold in the United States for use in the rations of bobwhite quail.

Based on the proposed action, monensin could potentially be introduced into the following environments:

a) The environment adjacent to the manufacturing plants.

b) The environment adjacent to facilities which mix COBAN with feed.

c) Agricultural lands where waste products from quail may be used as fertilizer.

d) Aquatic systems where runoff may flow from sites receiving waste products of quail.

RUMENSIN® (Monensin sodium, Elanco)

5. IDENTIFICATION OF CHEMICAL SUBSTANCE

A. COBAN PREMIX

COBAN premix will be incorporated into rations of bobwhite quail maintained in confinement. Monensin sodium is the active ingredient in the COBAN premix and is produced in dried mycelial biomass and crystalline forms. The raw material is added to the premix to achieve a monensin concentration of 45 g/lb. COBAN premix may contain diluents such as rice hulls.

B. MYCELIAL MONENSIN

Monensin is produced by the fermentation of a strain of Streptomyces cinnamonensis, an organism isolated from soil (4). The most economical procedure to prepare a usable form of monensin is to harvest the fermentation culture in such a way as to combine monensin with the mycelial cells of the producing organisms and the unused components of the feed-stock used in the fermentation to achieve growth of the organism. Thus, the dried mycelial or biomass form of monensin may contain nutrients which can commonly be found in bobwhite feedstuff.

C. MONENSIN (References 4 and 5)

Monensin consists primarily of monensin factor A, but small amounts of monensin factor B and very small amounts of factors C and D do occur. Monensin factor A accounts for at least 90 percent of the microbiologically active material of mycelial monensin. The characteristics of monensin factor A are discussed in this section. Monensin is a monocarboxylic polyether compound which complexes with monovalent alkali cations and shows ionophorous activity with a selectivity of $Na^+ > K^+ > Rb^+ > Li^+ > Cs^+$.

Monensin Sodium:

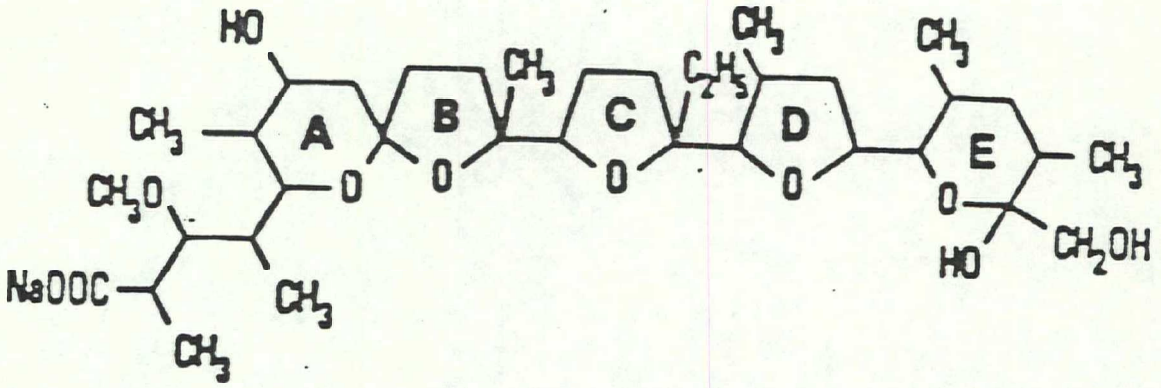
During the manufacturing process, monensin is exposed to sodium ions during a pH adjustment giving rise to monensin sodium which is the chemical form in the product.

Chemical Name (acid form):

Stereoisomer of 2-[2-ethyloctahydro-3'-methyl-5'-tetrahydro-6-hydroxy-6-(hydroxymethyl)-3,5-dimethyl-2H-pyran-2-yl][2,2'-bifuran]-5-yl]-9-hydroxy-β-methoxy-α,γ,2,8-tetramethyl-1,6-dioxaspiro[4,5]decane-7-butanoic acid.

CAS Registry Number:	17090-79-8
Molecular Formula:	$C_{36}H_{62}O_{11}$ (acid), $C_{36}H_{61}O_{11}Na$ (salt)
Molecular Weight:	670 (acid), 692 (sodium salt)

Structural Formula:



Solubility

water	pH 7 63 mg/L
	pH 9 0.85 mg/L
ethyl acetate	very soluble
chloroform	very soluble
acetone	very soluble
benzene	very soluble
methanol	very soluble
hexane	slightly soluble

Melting Point: 103-105°C (acid)
267-269°C (sodium salt)

UV absorption: None

pKa value: 6.65 (66% DMF)

Specific Rotation: + 47.7° (acid), + 57.3° (sodium salt)

Vapor pressure: Non-volatile solid based on molecular weight, melting point, and thermogravimetric analysis.

6. INTRODUCTION OF SUBSTANCE INTO THE ENVIRONMENT

A. INTRODUCTION OF SUBSTANCES FROM THE MANUFACTURING SITE

The manufacturing process for monensin, in conjunction with the corresponding pollution control practices at each of the plant sites, is designed to have minimal environmental impact. These plant sites are located near Clinton and Lafayette, Indiana. Monensin is produced by a fermentation process and is recovered by processes utilizing unit operations such as evaporation, centrifugation or filtration, drying, pelletizing, granulation by crushing, screening and blending.

Essentially no monensin will be released from the manufacturing process. The only releases of monensin from manufacturing operations will be in dilute washwaters used to rinse the empty fermentation and processing facilities. At these plant sites, these washwaters would be treated by wastewater concentration and pyrolysis, by land application or by microbiological degradation.

Residual biodegradable fermentation nutrients from the manufacture of other fermentation products at each of the plant sites are discharged to receiving rivers at rates significantly below permitted limitations. Since monensin will not be the only fermentation-based product manufactured at these plant sites, it will account for a small portion of the permitted discharge of residual nutrients expressed as biological oxygen demand (BOD).

Essentially no other wastewater pollutants or liquid, solid or gaseous pollutants from the manufacture of monensin will be allowed to enter the environment. Therefore, the manufacture of monensin will have a minimal effect on the environment at these plant sites.

Limitations for atmospheric pollutant emissions and wastewater pollutant discharges, and disposal practices for other liquid and solid wastes applicable to these plant sites, are defined by regulations administered, in certain instances, by the U.S. Environmental Protection Agency and, in certain other instances, by Indiana's Department of Environmental Management (IDEM).

The following operating permits for those manufacturing emission sources and control facilities which would produce monensin at these plants currently are administered by IDEM's Office of Air Management.

Location	Permit Identification No.	Issued	Expiration
Clinton	83-09-87-0067	Dec. 13, 1983	Sept. 01, 1987*
Clinton	83-09-87-0068	Dec. 13, 1983	Sept. 01, 1987*
Clinton	83-09-87-0073	Dec. 13, 1983	Sept. 01, 1987*
Lafayette	79-04-90-0372	Oct. 09, 1986	Apr. 01, 1990
Lafayette	79-04-90-0386	Oct. 09, 1986	Apr. 01, 1990

*(These permits are being extended administratively by IDEM until it issues the renewal permit, for which a timely application has been submitted by Eli Lilly and Company.)

The following NPDES permits for the discharge of wastewaters from these plants to the Wabash River currently are administered by IDEM's Office of Water Management.

Location	NPDES Permit No.	Issued	Expiration
Clinton	IN 0002852	Sept. 23, 1985	Aug. 31, 1990
Lafayette	IN 0002861	Sept. 30, 1987	Sept. 30, 1992

No hazardous wastes and essentially no solid wastes will be generated in these manufacturing operations. Processes which use organic solvents provide for recovery and reuse of solvents, and those operations where solvents are present are served by condensers, carbon adsorbers or scrubbers to prevent solvent emissions from being discharged to the atmosphere. Those manufacturing operations which use dry procedures are served by dust control facilities to prevent particulate matter emissions from being discharged to the atmosphere. Packaging materials, nonrecyclable tailings and floor sweepings from these plants either are incinerated at the Clinton plant with industrial and domestic trash from other sources or are landfilled.

Based on the information above, any atmospheric emissions, wastewater pollutant discharges and disposal practices for other wastes from the manufacturing processes for monensin will comply with appropriate statutes, regulations, and permits.

B. INTRODUCTION OF SUBSTANCE FROM FEED MIXING LOCATIONS

Commercial feed mills will be a major site of feed mixing. The marketing of COBAN premixes to bobwhite quail producers would be through a few mills producing game bird feed, minimizing environmental exposure during the product distribution process. These feed mills have to meet Good Manufacturing Practice Standards for feeds. With the required manufacturing controls for feed, inventory accountability, and quality assurance procedures, the potential for release of monensin sodium into the environment at these locations should be minimal.

C. INTRODUCTION OF SUBSTANCE AT THE USE SITE

Dr. M. D. Ruff of the USDA estimates that about 10 million game type quail are raised in the United States each year. Not all of these would be bobwhite quail. The quail industry is concentrated in the southern and eastern states, similar to the broiler industry.

COBAN would be used in the rations of bobwhite quail maintained in confinement. The only feeding level recommended is 73 g per ton (80 mg/kg) total diet. Each bobwhite quail raised under confinement will consume about 5 pounds of feed. If all 10 million game quail were bobwhite quail and all their feed contained COBAN, the total consumption of treated feed would be 25,000 tons. At 73 gms of monensin sodium per ton of feed, total consumption of compound would be 1,825 kgs per year. This is less than 0.1% of the monensin sodium already sold in the United States.

For additional information pertaining to the fate of monensin in the environment, please refer to Public Master File 5014.

12. LIST OF PREPARERS

The following Lilly personnel are responsible for the preparation of this Environmental Assessment:

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13. CERTIFICATION

The undersigned official certifies that the information presented in the Environmental Assessment is true, accurate, and complete to the best of his knowledge.

Merle E. Amundson, Ph.D.
Executive Director
Toxicology Division
Lilly Research Laboratories

January 29, 1988
Date

14. REFERENCES

1. Elanco Products Company. 1975. Environmental impact analysis report for use of monensin in the feed of beef cattle. NADA 95-735.

2. Elanco Products Company. 1986. Environmental assessment for the use of COBAN 45 in the feed of turkeys. NADA 130-736.

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4. Haney, Jr., M. E. and M. M. Hoehn. 1967. Monensin, a new biologically active compound. I. Discovery and isolation. In Antimicrobial Agents and Chemotherapy. pp. 349 to 352.

5. Pressman, B. C. 1976. Biological applications of ionophores. Ann. Rev. Biochem. Vol. 45: 925.