ENVIRONMENTAL IMPACT
ASSESSMENT REPORT

Sponsor: A. L. Laboratories, Inc.
452 Hudson Terrace
Englewood Cliffs, New Jersey 07632

Sponsor No.: 46573

Drug: Bacitracin, Zinc

NADA: Zinc Bacitracin-50 Medicated Feed Premix
98-452

I. Introduction into the Environment

a) The total quantity of the drug imported for all uses, portion used subtherapeutically in animal feeds, relative magnitude of other uses, uses in humans.

The total quantity of zinc bacitracin that will be imported from A/S Apothekernes Laboratorium, Oslo, Norway is estimated as 12,100 standard kilograms in 1977. Of this amount, 12,000 kg will be used subtherapeutically in animal feeds.

One hundred kg will be used for topical application only for humans.

b) Pollutants generated and resources consumed by the manufacture of the drug, premix, including energy uses.

Any pollutants generated are negligible and controlled. In the manufacture of the product for subtherapeutic purposes in feed, the total fermenter contents goes by closed system into a spray drier. The water vapors, odors and gases are retained in a closed system and passed through an incinerator at 1500°F with only carbon dioxide and water vapor returned to the atmosphere. The manufacture of bacitracin involves a fermentation using harmless nutrients and a non-pathogenic organism. Airborne products involve only carbon dioxide enriched air. (See attachment 1, 2 & 3)

No objections have been raised by any agencies, organizations or individuals to the current operations.

Resources consumed in the manufacture of zinc bacitracin feed grade:

Fermentation Media

%	Resource
8.0	Soya bean meal
3.2	Barley flour
0.25	Calcium carbonate
0.10	Sodium sulfate
0.02	Magnesium sulfate
0.01	Oil sperm
0.005	Polyglycol - 2000 (polypropyleneglycol)
1.2	Zinc chloride

The average fermentation is about 25,000 liters per run.

It is estimated that between 3,500,000 and 3,700,000 BTU are used in the production of each standard kg.

c) Routes through which the drug may pass into the environment, amounts passing through various routes, during manufactures, preparation of premixes, excretion by target animals.

Any dust generated in blending of the premix is subject to pickup by a dust collector and is considered only a minor source going into the environment.

The antibiotic passes through the animal in the excreta. Its disappearance from the faeces is surprisingly rapid.

The following example shows this with broiler chickens fed continuously a mash feed containing 500 g bacitracin MD per ton of feed:

Sample	Bacitracin found* (ppm)
Fresh faeces	6.17
Same held 24 hours RT	5.00
Same held 72 hours RT	4.89
Same held 7 days	1.30
Same held 14 days	0.14
Same held 21 days	0,14

*All values are on a dry matter basis. The experiment was done by Dr. T. Chang, Michigan State University, E. Lansing.

Inactivation of zinc bacitracin in faeces from laying hens was studied by S. Thomassen and K. Vaaji, A/S Apothekernes Laboratorium, Oslo, Norway (1976). In their first experiment, zinc bacitracin was mixed with faeces from laying hens to a final concentration of 10 and 100 ppm. The faeces was stored in plastic bags at 15°C for 15 days and assayed at regular intervals. A rapid inactivation of the antibiotic was observed. The half-life of the antibiotic was estimated to 6 days.

In a second experiment, the hens were fed feeds with 100 ppm zinc bacitracin. The faeces were stored for 11 days in open glass jars. The half-life was estimated at 4 days.

The objective of a third experiment was to study the inactivation of zinc bacitracin in faeces from laying hens after storage under natural conditions in the dung in the hen house. This experiment was in a commercial layer flock of 15,000 birds, half was fed 100 ppm zinc bacitracin in their diet, the other half was fed the same diet without antibiotic. The birds were caged on a mesh floor and the faeces was deposited in a pit under the floor. Sampling was carried out in May and August, 1975. The half-life estimates were 7 and 2 days for the May and August samplings.

From the cited examples, it appears that Bacitracin MD and zinc bacitracin are biologically inactivated rapidly in faeces with rate of disappearance being affected by temperature, moisture and pH.

II. Fate in the environment

a) Mobility of the antibiotic in the environment measured by leaching potentials, vaporization, absorption in soils.

This has not been done, but the physical conditions of the media would cause rapid destruction.

b) Stability and persistence of the antibiotic in those environments where it is determined that it will be introduced or those environments to which it is subsequently transported.

The available data indicates that the antibiotic is not stable in the faeces of animals, and consequently, would not reach or persist in the environment. (See I.c.)

c) Potential for the antibiotic to be accumulated or bioconcentrated by plants, animals and micro-organisms measured by such factors as lipid/water partitioning or studies with animals.

This has not been investigated. The cited work shows that the half-life of the antibiotic is short and that it is not absorbed by target animals.

The antibiotic is not absorbed from the intestinal tract of the animal as shown by the fact that no detectable bacitracin has been found in the tissues or eggs when the feed of chickens, turkeys, and laying hens were consuming feeds containing as much as 1000 grams antibiotic per ton of feed on the day that they were sacrificed for tissue harvest. No detectable bacitracin residues have been found in tissues of cattle or swine when they had been consuming feeds containing 500 g antibiotic per ton. Reference is made to the bacitracin MD submission of January 15, 1971, pp. 440-697 in NADA 46-592.

III. Environmental Effects

a) Effects of antibiotic on organisms important to key ecological processes, such as fresh water algae, nitrogen-fixing bacteria, nitrifying bacteria, soil fungi, and bacteria responsible for nutrient mineralization.

This has not been investigated. The bacitracins are effective against gram-positive organisms, not gram-negative organisms. Most nitrogen-fixing bacteria, nitrifying bacteria, etc., are gram-negative bacteria. For example: the Azotobacter is an aerobic, free-living nitrogen fixer; Rhizobium are aerobic symbiotic nitrogen fixers; Nitrosomonas, nitrobacter, Thiobacillus, pseudomonas, and acetobacter are aerobic organisms that oxidize inorganic and/or organic compounds.

Following is a table which was taken from Microbiology, 2nd ed., Davies, et al, Harper Row, Hagerstown, MD.

GRAM-NEGATIVE BACTERIA, EXCLUDING PHOTOSYNTHETIC FORMS

Cell Shape	Motility	Other distinguishing characteristics		Genera	Families
Cocci	Permanently Immotile	Aerobic		Neisseria	Neisseriaceae
		Anaerobic		Veillonella	
				Brucella	Brucellaceae
				Pasteurella	
				Hemophilus	
				Bordetella	
Straight Rods	Motile with peritrichous flagella, and related immotile forms	Facultative anaerobic	Mixed acid fermentation of sugars	Escherichia Erwinia Shigella Salmonella Proteus	Entero-bacteriaceae
			Butylene glycol fermentation of sugars	Enterobacter Serratia	
		Aerobic	Free-living nitrogen fixers	Azotobacter	Azoto-bacteriaceae
			Symbiotic nitrogen fixers	Rhizobium	Rhizobiaceae
	Motile with polar flagella	Aerobic	Oxidize inorganic compounds; Oxidize organic compounds	Nitrosomonas Nitrobacter Thiobacillus Pseudomonas Acetobacter	Nitro-bacteriaceae Thio-bacteriaceae
		Faculative anaerobic		Photobacterium Zymonmonas Aeromonas	
Curved Rods	Motile with/Polar Flagella	Comma-shaped Spiral	Aerobic Anaerobic	Vibrio Desulfovibrio Spirillum	Spirillaceae

b) Effects on fish, mammals and other vertebrates that are important to man as food, or food for human-food producing animals or organisms that are of aesthetic interest to man, etc.

This has not been investigated. The bacitracins are non-toxic drugs that are used in animals consumed as food by humans, and the animal by-products are consumed by other animals. The antibiotic is not absorbed from the intestinal tract, thus it is concluded that there would be no effect.

c) Indirect effects on populations or organisms and communities that might arise from the subtherapeutic use of the drug.

The requirements have been satisfied for 21 CFR 558.15. The accumulated data showed that the Animal-Human Health criteria have been met for safe use of low levels of bacitracin(s) in animal feeds. Dr. Gerald B. Guest's letter of September 27, 1976 concludes that "the review of required data for bacitracin is hereby concluded. Results indicated that the use of low levels of bacitracin in animal feeds satisfied the animal and human safety criteria for safety as specified by the Antibiotics in Animal Feeds Task Force."

In these investigations, it was shown that the low level feeding of bacitracin to swine and chickens did not affect the salmonella or E. coli populations or mediate a change in resistance or cross resistance to antibiotics used in human medicine. Reports are on record in Bureau of Veterinary Medicine.

A/S APOTHEKERNES LABORATORIUM
FOR SPECIALPRÆPARATER

TELEFON SENTRALBORD: 559390
TELEGRAMADRESSE: ALGROUP
TELEX NR. 11332
BANKFORBINDELSE: BERGENS PRIVATBANK

POSTBOKS 158
SKØYEN, OSLO 2

ENVIRONMENTAL IMPACT ANALYSIS
ZINC BACITRACIN FEED GRADE

Introduction

This Environmental Impact Analysis is being submitted as part of the request published in the Federal Register, Vol. 42, p. 27265, May 27, 1977.

Name of Applicant

A. L. Laboratories, Inc.
452 Hudson Terrace
Englewood Cliffs, New Jersey 07632

Custom Manufacturer

A/S Apothekernes Laboratorium
for Specialpraeparater
P.O. Box 158 (Skoyen)
Oslo 2, Norway

1. Manufacturing Procedure

The manufacture of zinc bacitracin feed grade involves a fermentation using harmless nutrients and a non-pathogenic organism, with subsequent spray drying of the total component; blending, and packaging to obtain the final bulk product.

All steps are carried out at the Oslo Plant of A/S Apothekernes Laboratorium for Specialpraeparater.

2. Probable Impact on the Environment

No significant impact on the environment is believed created, for the following reasons:

a) Airborne by-products involve only (1) Carbon dioxide enriched air having only a slight, non-persistent odor from the fermentation step, and (2) Moisture laden air from the spray dryer.

b) No solvents are utilized in this process.

3. Probable Adverse Environmental Effects Which Cannot be Avoided

No adverse environmental effects are being created.

4. Alternatives to the Current Method of Operation.

No practical alternatives to the current method of operation are known.

5. Relationship-Local Short-Term Uses of Environment; and the Maintenance and Enhancement of Long-Term Productivity

No measurable lasting or cumulative effect on the environment is foreseen, due to the current method of operation.

6. Irreversible or Irretrievable Commitments of Resources Due to Current Operation

Current operations cause no irreversible or irretrievable commitment of resources.

7. Objections Raised by Other Agencies, Organizations or Individuals

No objections to current operations by any agencies, organizations or individuals are known to be in existence.

8. Action Schedule

Since no change is contemplated over the current, long-standing method of operation, no schedule problems are involved.

9. Benefits vs Risk to the Environment

The negligible risks to the environment due to the operations involved are far overshadowed by the benefits to mankind created, by making a valuable food additive and growth stimulant available to the food producing industry, at a time when global food requirements are drastically inadequate.

A/S Apothekernes Laboratorium
for Specialpræparater
Postboks 158, Skøyen

OSLO 2

Deres ref. | Vår ref. (bes oppgitt ved svar) | Dato 22.4.1976 | Vedlegg

POLLUTION FROM THE PRODUCTION OF BACITRACIN FEED GRADE

We hereby confirm that the firm A/S Apothekernes Laboratorium for Specialpræparater, Oslo, comply with the present demands of The State Pollution Control Authority for their production of Bacitracin feed grade.

At the moment pollution from the production of Bacitracin is being considered anew. It is expected that more stringent demands will be made in order to reduce air and water pollution from the above mentioned production.

For The State Pollution Control Authority

John Hatling
senior engineer

Berit Viig
section engineer

Certification

TO WHOM IT MAY CONCERN

This is to certify that A.L.'s production of antibiotics is in compliance with all regulations and laws which relate to the environment, according to the specifications given in the enclosed lists:

"Identification of all manufacturing emissions"
"Details in emission".

Oslo, November 24th 1975

Eigil Løyvaatten

KJEMISEKSJONEN
O.V.K.
OSLO VANN- OG KLOAKKVESEN