

November 28, 1979

ENVIRONMENTAL ASSESSMENT REPORT OF BACITRACIN METHYLENE DISALICYLATE
IN CHICKENS AND TURKEYS

The environmental assessment of this action has been accomplished on the basis of a complete environmental impact analysis report. It is concluded that the proposed action will not have a significant impact on the quality of the human environment and that an environmental impact statement is not needed.

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Enclosures:

Environmental Impact Analysis Report
Environmental Assessment Report

cc: Hearing Clerk HFA-305 ✓

NADA Orig, Dup HFV-16

HFV-1

HFV-102

HFV-9

HFV-147

MCTHOMAS/ls/8/27/80

NADA 65-280 and 65-470
Bacitracin Methylene Disalicylate
A. L. Laboratories, Inc.
452 Hudson Terrace
Englewood Cliffs, New Jersey 07632
November 20, 1979

ENVIRONMENTAL ASSESSMENT REPORT OF BACITRACIN METHYLENE
DISALICYLATE IN CHICKENS AND TURKEYS

November 9, 1979

A. L. Laboratories, Inc. is requesting approval of bacitracin methylene disalicylate in the drinking water of chickens (100-400 mg/gal) for the prevention and/or control of necrotic enteritis and in the drinking water of turkeys (400 mg/gal) for the control of transmissible enteritis.

The drug was evaluated by the National Academy of Science, National Research Council, Drug Efficacy Study Group as probably effective for increased rate of weight gain and improved feed efficiency in poultry and probably not effective for the therapeutic claims in poultry. The firm has supplemented their NADA 65-280 to provide adequate safety and efficacy data to support therapeutic claims in broiler chickens and growing turkeys.

Chemical and Physical Characteristics:

Bacitracin methylene disalicylate is prepared by the reaction of two moles of methylenedisalicylic acid and one mole of bacitracin. It is a white to grayish-brown powder that is less bitter than bacitracin and has a slightly disagreeable odor. It is soluble in water to about 50 mg of bacitracin per gram of water at a pH range of 3.5 to 5.0; more soluble in dilute alkaline solutions; and soluble in pyridine and ethanol. Bacitracin MD is insoluble in pentane and benzene. Molecular weight of bacitracin is 1411, bacitracin methylene disalicylate molecular weight is 1985.

Pharmacological and Toxicological Properties:

The bacitracins are effective against gram-positive organisms of the digestive tract. Bacitracin MD is a larger polypeptide (MW 1411) plus two moles of methylene disalicylate with a combined molecular weight of 1985 and is very poorly absorbed. Blood levels are not detectable when fed up to 5 times recommended dosage level in poultry or in swine.

The first sign of an overdose in the feed is a reduction in feed intake resulting in a lowered rate of weight gain and reduced feed efficiency. This occurs at about 5,000 g/ton. Levels of the bacitracins in the drinking water above one gram per gallon will reduce the consumption of water in swine due to palatability.

The Purpose and Benefit of the Proposed Action:

The firm did not specifically address this question. However, the purpose of the action is to provide the poultry industry with an approved product for the prevention and/or control of two diseases that are commonly found in poultry; necrotic enteritis in young chickens and transmissible enteritis (blue comb, mud fever) in growing turkeys. The approval will provide the poultry industry with a product that is safe to the animal, the environment and does not present a tissue residue problem to the human food supply. It is easily administered, relatively economical and animal losses are reduced due to necrotic enteritis and transmissible enteritis.

Estimate the Potential Market Penetration and Product Distribution:

This product is eligible for enterim marketing under Title 21 CFR 558.15(g). The annual production of bacitracin methylene disalicylate for all uses is about 135,000 kgs. The subtherapeutic use accounts for approximately 125,000 kg in animal feeds and 10,000 kgs are used therapeutically in animal drinking water. This is enough bacitracin to provide medication for 25-50 million birds. None is manufactured for use in man.

Manufacturing Evaluation:

The bacitracins are antimicrobial metabolic products resulting from the fermentation of a soybean flour and degerminated cornmeal, plus essential minerals in a liquid media by Bacillus subtilis licheniformis. The media is filtered and the bacitracin containing liquid is spray-dried. The solid by-product is the water-wet filter cake containing filter aids, Bacillus mycetium, and insoluble broth nutrients. This solid material is biodegradable or harmless inert mineral and is disposed of via sanitary landfill. The liquid waste and wash water is discharged into a treatment system before releasing it into the environment.

The spray-dryer is equipped with air filters, dust bags and anti-air pollution devices. The packaging of the product is also done under an air pollution control system. Copies of permits are attached to the Environmental Impact Analyses Report.

A/S Apothekernes Laboratorium for Specialpraeparater Skoyen, Oslo, Norway is approved as an alternate manufacturer and supplier of the bulk drug to A. L. Laboratories, Inc. under Master File 3663. The Master File contains copies of permits for the manufacture of the product and a certificate that the firm is in compliance with the existing regulations.

Environmental Evaluation:

The drug (bacitracin MD) passes into the environment through the animal by way of excretion in the feces. Studies were conducted to determine the rate of inactivation of bacitracin in broiler and laying chicken feces. Bacitracin was mixed with feces to a concentration of 10 and 100 ppm. The drug treated feces were assayed at regular intervals over a 15 day period. A rapid inactivation of the antibiotic was observed. The half-life of bacitracin was estimated to be 6 days. In another study hens were fed feeds containing 100 ppm bacitracin. The feces were stored and assayed for 11 days. The half-life was estimated to be 4 days. A study was conducted with layer feces stored in a pit under a wire mesh floor. Sampling was carried out in May and the half-life estimate was 7 days. Using the same facilities and sampling in August the half-life estimate was 2 days.

Drug stability data for water soluble bacitracin shows that fresh solution of bacitracin must be made daily to maintain adequate dosages. This demonstrates that the water soluble product breakdown at about the same rate to somewhat faster than in feces.

Most nitrogen-fixing bacteria of the soil are gram-negative bacteria, therefore are not affected by bacitracins in that they are effective against gram-positive organisms. Mobility of bacitracin through the soil leaching does not pose a problem in that conditions for leaching are also conditions for degradation of the molecule. Bacitracins breakdown rather rapidly in dilute solutions.

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The large molecule is very poorly absorbed and is not detected in tissues or eggs when fed as much as 1000 g/ton of feed. A review of the literature did not reveal any report that bacitracin is taken up by plants.

The Animal-Human Health Criteria requirements described in Title 21 CFR 558.15 have been satisfied according to a letter issued by Dr. Gerald Guest dated September 27, 1976. It was shown that the low level feeding of bacitracin to chickens and swine did not affect the Salmonella or E. coli population or mediate a change in the resistance or cross-resistance to antibiotics used in human medicine.

We conclude that it is unlikely that long term bio-accumulation would occur with environmental residues of bacitracin.

The data submitted are sufficient to permit the determination of potential impacts. We have concluded from these data that an Environmental Impact Statement is not required.


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cc: Orig. (HFV-16)
Dup. (HFV-16)
Branch File HFV-147
HFV-101
HFV-X 9
HFC-20 HFA-385 ✓
MCTHOMAS/dc/11/27/79