Approval Date: March 4, 1992

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 011-315

B. Sponsor

The Upjohn Company
Kalamazoo, Michigan 49001

C. Proprietary Name

NEOMIX® 325 Soluble Powder and NEOMIX® AG 325 Soluble Powder

D. Established Name

Neomycin sulfate

E. Dosage Form

Soluble Powder.

F. Dispensing Status

OTC

G. Dosage Regimen

The drug is administered at 10 mg neomycin sulfate per pound of body weight (equivalent to 7 mg neomycin base) per day in divided doses for a maximum of 14 days.

H. Route of Administration

NEOMIX 325 and NEOMIX AG 325 are administered orally in water or milk.

I. Indication

For the treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin sulfate in cattle (excluding veal calves), swine, sheep and goats.

J. Effect of Supplement

The effectiveness neomycin sulfate was reviewed by the National Academy of Sciences/National Research Council Drug Efficacy Study Implementation (NAS/NRC DESI) and has been deemed effective when labeled as specified in the Indications and Recommended Dosage section of the summary.

II. EFFECTIVENESS

NADA 011-315 was originally approved as safe for use as labeled on March 21, 1958. The drug was the subject of National Academy of Sciences/National Research Council (NAS/NRC) reports which were published in the **FEDERAL REGISTER** of January 19,

1971 (DESI 11-315V, 36 FR 837). The NAS/NRC evaluated the drug as "probably effective" for use in the control and treatment of bacterial enteritis in cattle, horses, sheep, swine, goats, cats, turkeys, chickens, ducks, and mink, and as a wet antibacterial dressing in swine, cattle, sheep, and dogs. The NAS/NRC stated in relevant part: (1) the labeling should warn that treated animals must actually consume enough medicated feed or medicated water to provide a therapeutic dose under the conditions that prevail - as a precaution, the label should state the desired oral dose per unit of animal weight per day for each species as a guide to effective use of the preparation in drinking water or feed; (2) the labeling should warn that oral neomycin sulfate is not indicated if animals have developed a septicemia as systemic levels of neomycin are not obtained because of the low degree of absorption from the gastrointestinal tract; (3) the disease claims for preparations administered orally must be restricted to disease involving the gastrointestinal tract because of the chemical and pharmacological properties of neomycin sulfate; and (4) each disease claim should be properly qualified as "appropriate for use in (name of disease) caused by pathogens sensitive to (name of drug)", and if the disease claim cannot be so qualified the claim must be dropped.

The Food and Drug Administration concurred with the academy's findings, interpreting the phrase " ...cannot be so qualified ..." in paragraph (4) to mean " ...is not supported by adequate data ..." (See 36 Fed. Reg. 837). FDA then proceeded to review all available data relating to the effectiveness of products subject to NADA 011-315 to determine which label claims were supported by the requisite proof of effectiveness. That review resulted ina letter dated December 10, 1985, addressed to the Animal Health Institute (AHI), in whichthe agency stated that it had "concluded that such data supported effectiveness for the treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin sulfate in cattle, sheep, and goats, and porcine colibacillosis caused by E. coli susceptible to neomycin sulfate."

Thereafter, the sponsor complied with the evaluation of NAS/NRC and FDA's conclusions in the following manner:

1. One disease of the gastrointestinal tract (colibacillosis in cattle, swine, sheep and goats) has been properly qualified as being caused by pathogens sensitive to neomycin sulfate. Disease claims which were not so qualified (including all claims involving use in poultry, horses, mink, dogs and cats) have been deleted from labeling.
2. The appropriate oral dose of 10 mg neomycin sulfate per unit of animal weight per day in each species has been incorporated in the labeling.
3. The revised labeling contains the statements that treated animals must have the medicated water adjusted to compensate for variation in age and weight of the animal, the nature and severity of disease signs, and environmental temperature and humidity, each of which affects water consumption.
4. The labeling also contains a statement that the use of oral neomycin is not indicated as a sole treatment, if the animals develop septicemia.

III. TARGET ANIMAL SAFETY

NADA 011-315 was originally approved as safe on March 21, 1958. No further safety data are required.

IV. HUMAN FOOD SAFETY

The NAS/NRC evaluation of the drug is concerned only with the effectiveness and safety of the drug for the treated animal. FDA's approval of the supplemental application did not involve reevaluation or reaffirmation of the human food safety data in the parent application.

Tolerance
A tolerance of 0.25 ppm is already established for edible tissue of calves and 0.15 ppm for milk (21 CFR 556.430). The tolerance of 0.25 ppm in edible tissues also applies to swine,sheep, and goats. The tolerance of 0.15 ppm for milk also applies to goats.

Withdrawal Time
The withdrawal times are those previously established in 21 CFR 558.20: 30 days for cattle (excluding veal calves), and 20 days for swine and sheep. The withdrawal time is 30 days for goats.

Regulatory Methods for Residues
The regulatory analytical method for detection of residues of the drug is a microbiological test using *Staphylococcus epidermidis* suspension. The method is as published by the Food and Drug Administration, "Antibiotic Residues in Milk, Dairy Products and Animal Tissues: Methods, Reports, and Protocols", revised October 1968, reprinted December 1974.

V. AGENCY CONCLUSIONS

This supplemental NADA satisfies the requirements of section 512 of the Act and demonstrates that neomycin sulfate soluble powder, when used under its proposed conditions of use, is safe and effective for the labeled indications. The approval provides for use of neomycin sulfate soluble powder for the treatment and control of colibacillosis (bacterial enteritis) caused by ***Escherichia coli*** susceptible to neomycin sulfate in cattle (excluding veal calves), swine, sheep and goats.

The "probably effective" finding of the NAS/NRC regarding neomycin sulfate which was published in the **FEDERAL REGISTER** of January 19, 1971, was subsequently reviewed by FDA, resulting in the December 10, 1985 letter to AHI discussed above. , the "probably effective" status for neomycin sulfate soluble powder, NADA 011-315, was upgraded to"effective" status with respect to the claims noted in the previous paragraph. The firm submitted revised labeling to conform to the letter to AHI and, therefore, this supplemental NADA complies with the NAS/NRC evaluation and FDA's conclusions.

Neomycin sulfate soluble powder for use in food-producing animals is currently on the market as an over-the-counter product. Accurate diagnosis can be made with a reasonable degree of certainty by the layman, and the conditions for use described in the labeling are likely to be followed in practice. Therefore, the Center for Veterinary Medicine has concluded that this product should retain over-the-counter marketing status.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug and, therefore, did not

require a re-evaluation of the human food or target animal safety data in the parent application.

Under the Generic Animal Drug and Patent Term Restoration Act of 1988, this approval does not qualify for an exclusivity period under section 512(c)(2)(F)(iii) of the Federal, Food, Drug, and Cosmetic Act (21 U.S.C. 360b (c)(2)(F)(iii)) because the supplemental application does not contain reports of new clinical or field investigations or human food safety studies (other than bioequivalence or residue studies) essential to the approval and conducted or sponsored by the applicant.

VI. ATTACHMENTS

Copies of applicable labels may be obtained by writing to the:

Food and Drug Administration
Freedom of Information Staff (HFI-35)
5600 Fishers Lane
Rockville, MD 20857

Or requests may be sent via fax to: (301) 443-1726. If there are problems sending a fax, call (301) 443-2414.

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.