OFFICE

FINDING OF NO SIGNIFICANT IMPACT

for

V-Max™ (Virginiamycin) for Use in Feedlot Cattle

NADA 140-998

SMITHKLINE BEECHAM
WEST CHESTER, PA

FOR PUBLIC DISPLAY

FINDING OF NO SIGNIFICANT IMPACT

for

VIRGINIAMYCIN TYPE A MEDICATED ARTICLE (V-Max™)

NADA 140-998

SmithKline Beecham
West Chester, PA

The Center for Veterinary Medicine has carefully considered the potential environmental impact of this action and has concluded that this action will not have a significant effect on the quality of the human environment. Therefore, an environmental impact statement will not be prepared.

SmithKline Beecham is requesting approval of their new animal drug application (NADA) for the manufacture and use of V-Max™, containing virginiamycin, in feedlot cattle. Virginiamycin is currently approved, under NADA 91-467, for indications in swine, turkeys, and broiler chickens, as codified under 21 CFR 558.635. The current NADA would provide for the use of the product in feedlot cattle for increased rate of weight gain, improved feed efficiency, and reduction of incidence of liver abscess.

In support of the NADA, SmithKline Beecham has conducted a number of studies to determine the potential environmental fate and effects of virginiamycin and summarized the results of these studies in the attached environmental assessment (EA), dated October 22,1993.

The EA evaluates the potential environmental impacts of the manufacture and use of the product. Precautions taken at the sites of manufacture of the bulk drug substance and the final product are expected to minimize occupational exposures and environmental release. These sites are stated to be in compliance with the applicable national (United States and Belgium), state, and local environmental regulations. Therefore, the manufacture of the bulk drug and final product is not expected to have a significant impact on the environment.

Information in the EA indicates that ingested drug is metabolized in the rumen of cattle. Residues of virginiamycin are expected to be introduced into soil through the application of cattle manure as fertilizer. These residues are expected to be moderately bound to soil and to be biodegraded to a variety of degradates in the soil (in a soil biodegradation study, parent virginiamycin was almost totally degraded into a series of minor components by day 64 of the study).

The sponsor has calculated that the maximum possible concentration of virginiamycin (assuming no metabolism of drug in the animal or degradation of drug in the manure) expected in agricultural soils following the application of manure from cattle which ingest feed containing the product could be 0.56 ppm. Evidence that the drug is metabolized in the cattle rumen indicates that the actual concentration would probably be lower. Additionally, the concentration of the drug is expected to decrease over time because it is biodegraded in soil. Minimum inhibitory concentration (MIC) tests of soil

microorganisms demonstrate that the residues are not expected to have adverse impacts on soil microorganisms.

The major route of entry of virginiamycin residues into water is runoff from feedlots or from agricultural fields to which manure has been applied. Assuming no metabolism of drug in the animal, no degradation of drug in the manure, no sorption of the drug to soil, and no biodegradation of the drug in soil, the estimated maximum concentration in runoff from these soils would be 39.729 ppm. However, because the available data indicate that the drug is metabolized in the animal, is moderately sorbed to soil, biodegrades in soil, and is sparingly soluble in water, the concentration of virginiamycin in the water column should be considerably less than this estimate. Projected concentrations in runoff water are thus considerably less than the LC50's for rainbow trout or bluegill. Therefore, the use of the drug is not expected to have significant impacts on aquatic species. Soil sorption also reduces the likelihood that the chemical will be found in groundwater.

3/7/94
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Attachment: Environmental Assessment, dated October 22, 1993