ENVIRONMENTAL IMPACT ANALYSIS REPORT
AND ENVIRONMENTAL ASSESSMENT REPORT
FOR
THE USE OF THE ANTIBIOTIC VIRGINIAMYCIN
IN POULTRY FEED

The Environmental Impact Analysis Report and the Environmental Assessment Report are attached. The latter has been accomplished on the basis of a complete Environmental Impact Analysis Report and it is concluded that the action will not significantly affect the quality of the human environment and that no Environmental Impact Statement is required.

10/19/79
Date

Edison L. Monk
Edison L. Monk, Ph.D.
Primary Action Officer

10/19/79
Date

K. E. Taylor
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Director
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Enclosures:

Environmental Impact Analysis Report
Environmental Assessment Report

ENVIRONMENTAL ASSESSMENT REPORT

FIRM: Smith Kline Animal Health Products,
West Chester, PA.

NADAs: 91-467 'Stafac' 500 Medicated Premix
91-513 'Stafac' 22 and 110 Medicated Premixes

The 'Stafac' Medicated Premixes are approved for the following claims: treatment of swine dysentery in non-breeding swine weighing over 120 pounds at 100 grams per ton for 2 weeks; treatment and control of swine dysentery in swine weighing up to 120 pounds at 100 grams per ton for 2 weeks followed by 50 grams per ton; aid in the control of swine dysentery in animals weighing up to 120 pounds at 25 grams per ton; increased rate of weight gain and improved feed efficiency from weaning to 120 pounds body weight at 10 grams per ton; increased rate of weight gain from 120 pounds to market weight at 5 to 10 grams per ton; and improved feed efficiency from 120 pounds to market weight at 5 grams per ton. The firm is requesting via a supplemental application to each NADA that the present virginiamycin regulation (21 CFR 558.635) be amended to provide for the use of virginiamycin in broiler chickens for increased rate of weight gain at 5 to 20 grams per ton and for improved feed efficiency at 5 grams per ton. Environmental consideration of these supplemental applications is necessary as per 21 CFR 25.1(b)(15).

A review of the information present in the firm's EIAR has been completed and it is concluded that based on the low order of toxicity of virginiamycin and the rapid degradation of virginiamycin upon exposure to the environment that no impairment of the quality of the human environment should result from the use of this drug. The following statements describe in more detail the reasons for this conclusion:

1. The bulk drug and primary premix ('Stafac' 500) are produced in Genval, Belgium. The firm stated that the waste water conforms with provincial and local requirements.

2. Smith Kline stated that with respect to the manufacturing operations performed in this country, i.e. blending of the lesser concentrated premixes ('Stafac' 22 and 'Stafac' 110) from the primary premix, the manufacturing facilities comply with all local and state regulations for waste water and air filtration systems.

3. The firm has certified that, during the course of the above mentioned manufacturing operations, effluent emissions into the environment will be within the limits set forth by Federal, State and local regulations.

4. The only other expected source of potential environmental impact is that arising from the disposal of the droppings and litter from virginiamycin-fed broiler chickens.

5. Based on the information generated from the following studies conducted by the firm it appears that virginiamycin will degrade rapidly when exposed to the environment and, as such, has a limited potential for bioaccumulation.

   a. Poultry droppings were fortified to a level of 30 ppm of virginiamycin, and maintained at room temperature (18-22°C). After three days, more than 79% of the virginiamycin had degraded and by the 14th day more than 94% degradation had occurred.

   b. Poultry droppings were spiked to a level of 30 ppm of virginiamycin and maintained at ambient temperatures (8-24°C). After seven and 14 days, the virginiamycin activity was reduced 77% and 94%, respectively.

   c. Poultry litter (a combination of droppings and straw from the pens) was spiked with 30 ppm virginiamycin and maintained at room temperature (18-22°C). After three and seven days the virginiamycin activity was reduced 68% and 83%, respectively.

   d. Several studies were presented that indicate that virginiamycin rapidly loses activity upon addition to water.

6. The firm provided calculcations showing that the application of manure from virginiamycin-fed broilers to agricultural land should result in very low concentration (ppb) of this drug in the soil. This low level of virginiamycin should not have an impact on soil microflora since they are below that level necessary to inhibit microbial growth as determined <u>in vitro</u>.

7. Based on the information generated from the following studies conducted by the firm it appears that virginiamycin contaminated soil would have little if any effect on plant and animal life.

   a. Phytotoxicity studies utilizing wheat, barley, fescue, peppers, tomatoes and corn grown in soil containing 4-10 tons of manure from virginiamycin-fed broilers (20 g/ton of feed) indicated no adverse effects.

   b. A housefly toxicity study utilizing fly eggs grown on litter from poultry fed virginiamycin, showed no decrease in viability of eggs.

   c. An earthworm toxicity study utilizing red earthworms in soil containing virginiamycin-medicated poultry litter indicated no adverse effects.

8. The results from a n-octanol/water partitioning study on virginiamycin indicate that the drug is lipophilic. The significance of this finding is difficult to assess at this time. Residue studies have indicated very low levels of the drug and its metabolites in animal tissue suggesting poor absorption across the gastro-intestinal tract. Further studies would be necessary to clarify this matter. However, studies designed to assess the toxicological effects of virginiamycin have revealed a very low order of toxicity. This is based on oral LD_{50} work in mice (>1500 mg/kg) and swine (nontoxic at 1600 mg/kg), 3-month toxicity studies in rats and beagle dogs (up to 100 mg/kg with no effect) and in swine (up to 500 mg/kg with no effect), and extremely high level feeding (20,000 grams/ton) to swine for a two-week period with no effect.

9. Although no information has been provided with regard to the identity of the virginiamycin metabolites (either as excreted or from degradation of the voided intact drug), it is not likely that they would be of concern for two reasons. First, the microbiological activity of virginiamycin is reduced considerably when the two factors (factors M and S) which comprise this drug are separated, and second, it is generally agreed that catabolism of antibiotics results in less (if any at all) antibiotic activity.

10. No adverse environmental condition has resulted from virginiamycin use in swine.

11. Virginiamycin is not used in this country in human medicine.

Since the requested uses of virginiamycin should not impair the human environment, it is concluded that no Environmental Impact Statement is necessary.