FINDING OF NO SIGNIFICANT IMPACT
for
Finaplix® (trenbolone acetate) Ear Implant
NADA 138-612
for
Feedlot Heifers and Steers

Hoechst-Roussel Agri-Vet Company
Summerville, NJ

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 and that an environmental impact statement therefore will not be prepared.

Hoechst-Roussel Agri-Vet Company is the U.S. agent requesting approval for Rousgel-Uclaf, Paris, France, of NADA 138-612 for the use of Finaplix®-H (trenbolone acetate) in finishing heifers for improved body weight and feed efficiency and Finaplix®-S in finishing steers for improved feed efficiency. The product is to be administered to heifers at a dose of 200 mg during the last 63 days prior to slaughter and to steers at a dose of 140 mg every 63 days.

The firm has submitted an environmental assessment (EA) dated April 1987 (copy attached) in support of the approval of the NADA. The active drug substance is produced in the Roussel-Uclaf facility in Vertolaye, France. The finished product is to be produced in Compiegne, France. Therefore, introductions of the drug substance into the U.S. environment from manufacturing are not expected.

The firm has submitted information which describes the waste control measures utilized during the production of the product and has certified compliance with the environmental requirements of the appropriate French government. Additionally, information has been provided in the EA which indicates that appropriate precautions are taken to protect employees from exposure to the active substance and adverse occupational effects at manufacturing facilities are not anticipated. Adverse effects to individuals utilizing the finished product are not expected because of the nature of the packaging and delivery of the finished drug product.

Trenbolone acetate could be introduced into the environment of the U.S. through use of the product. However, data contained in the EA indicate that trenbolone acetate is extensively metabolized after administration. Of the initial dose of tritium-labelled trenbolone acetate administered to heifers, none was detected in the bile. The primary route of excretion is through the bile, therefore, significant quantities of trenbolone acetate would not be expected in cattle waste and would not be expected to enter the environment as a result of its use in feedlot heifers and steers.

The major metabolite detected in the bile was the 17a-hydroxy-estra-4,9,11-trien-3-one (17-alpha) metabolite. This metabolite was detected at 34.7% of the excreted radioactivity. Other metabolites were also detected, but at less than or equal to 3.0% of excreted radioactivity. Based on this finding, the chemical of environmental concern is the 17-alpha metabolite of trenbolone acetate.

The firm has calculated that the maximum amount of the 17-alpha metabolite which could be expected in heifer waste as a result of the the use of trenbolone acetate is 0.1 parts per million (ppm). The maximum concentration of the 17-alpha metabolite which could be expected in runoff from a feedlot is 0.0371 ppm and the maximum concentration which could appear in agricultural soils following incorporation of waste from cattle given trenbolone is 0.0017 ppm. The maximum amount which would enter runoff, however, would be expected to be less based on the expected adsorption of the 17-alpha metabolite to organic matter (Koc range 420-1100) in cattle waste. Additional data contained in the EA indicate that the 17-alpha metabolite can be expected to undergo biodegradation in agricultural soils with less than or equal to 2% of the initial concentration remaining after 56 days. This degradation would result in approximately 0.00003 ppm of the 17-alpha metabolite remaining in agricultural soils after 56 days.

The EA contains information which indicates that the 17-alpha metabolite of trenbolone acetate has a low vapor pressure (7×10^{-10} mmHg) and is low-moderately sorbed to three soils. Therefore, it is not expected that this metabolite will enter the atmosphere following the incorporation of cattle waste containing the metabolite in agricultural soils.

Based on the octanol/water partition coefficient (Kow = 510), the 17-alpha metabolite has a low-moderate tendency to bioaccumulate in fatty tissue. However, organisms which could be threatened by bioaccumulation would not be expected to have access to the molecule and its relatively rapid degradation would reduce the likelihood of bioaccumulation.

Data in the EA indicate that the 17-alpha metabolite is not expected to have any adverse impacts on carbon and nitrogen cycling environmental organisms. The 17-alpha metabolite at 0.015 and 0.15 ppm did not have any adverse effects on soil microorganisms associated with environmental nitrogen and carbon cycling in two soils. These concentrations are considerably higher then those expected in agricultural soils. Additional toxicity testing for the target species and for various laboratory species (mouse, rat, pig, monkeys) also indicate that the only adverse effects associated with trenbolone were hormonal in nature. No-effect dietary levels for trenbolone acetate's hormonal activity were determined to be 0.5 ppm for the rat and 0.24 ppm for the Rhesus monkey. These concentration are both greater than the concentrations of the 17-alpha metabolite which could occur in the environment. Additionally, information in the EA indicates that the 17-alpha metabolite is expected to exhibit considerably less hormonal activity than the parent compound. Adverse effects on higher environmental organisms would therefore not be expected.

Based on (1) the lack of parent compound expected in the environment, (2) the low concentrations of the major metabolite, 17-alpha, expected in aquatic and terrestrial environments, (3) the low vapor pressure and moderate soil sorption of the 17-alpha metabolite, (4) a demonstrated lack of adverse impacts to nitrogen and carbon circling organisms, and (5) a lack of adverse effects on target and laboratory species, it is expected that the use of trenbolone acetate in feedlot heifers and steers will not have a significant impact on the quality of the environment.

5/8/87
Date

Preparer, HFV-152

5/11/87
Date

Primary Action Officer, HFV-126

5-8-87
Date

Chief, Environmental Staff, HFV-152