FINDING OF NO SIGNIFICANT IMPACT

for

ADVOCIN®180: Danofloxacin 18% Injectable Solution for the Treatment of Respiratory Disease in Cattle

Pfizer, Inc.
New York, NY 10017

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

Pfizer, Inc. has submitted a new animal drug application (NADA) for the approval of Danofloxacin 18% Injectable Solution at a dose of 6 mg/kg x 2 doses for the treatment of respiratory disease in cattle. Danofloxacin is a fluoroquinolone antimicrobial agent that will be used only under prescription for the therapeutic treatment of cattle. In support of the application, the drug sponsor has submitted an environmental assessment (EA) dated, May 2000, revised March 2002, and signed on March 22, 2002.

The EA provides information on the potential environmental effects from the use of ADVOCIN®180 in cattle. In general, the submitted EA provides sufficient information to assess the potential exposures and effects of danofloxacin in the environment. Introduction of danofloxacin into the environment will be intermittent through the field application of aged cattle manure containing excreted drug residue, with some limited introduction also possible from treated grazing cattle. Environmental fate characterization and estimated environmental concentrations are supported by an adequate data base and conceptual models. Effect characterization is limited to terrestrial organisms and includes toxicity studies on earthworms, microorganisms, seed germination, root elongation and seedling growth. Aquatic toxicity data is not provided. Risk characterization is based on exposure:toxicity ratios and estimated environmental concentrations. Adverse effects on soil microorganisms and the potential for danofloxacin residues to select for resistant bacteria are evaluated.

Only limited amounts of soil incorporated danofloxacin residues would be expected to partition into the atmosphere or surface and ground water. This is based on the low vapor pressure and strong sorption of danofloxacin to manure and soils. Danofloxacin is not expected to bioaccumulate in non-target terrestrial or aquatic organisms. Unbound

danofloxacin residues in soil could be biotransformed and degraded and are not expected to accumulate.

A risk characterization indicates that potential risks to terrestrial organisms are expected to be low. Effects on aquatic organisms appear to be unlikely based on the expected negligible aquatic environmental concentrations. Toxicity data from structurally related fluoroquinolones support this conclusion.

Based on estimated environmental concentrations, exposure:toxicity ratios and decreased availability of sorbed danofloxacin residues, significant environmental effects due to danofloxacin residues in the environment are not anticipated.

The possibility for danofloxacin residues to select for resistant microorganisms in the environment was discussed in the EA. The limited bioavailability and concentrations of danofloxacin in soils and sediments would tend to reduce the selective pressure of residues. In addition, as discussed in the EA, antibiotic resistance in the environment is not considered to have significant impacts on ecological processes.

The EA adequately demonstrates that no significant environmental impacts are expected from the use of ADVOCIN®180 in cattle. We have reviewed the EA and find that it supports a finding of no significant impact (FONSI) for this NADA.

4/30/02
Date

Director, Office of New Animal Drug Evaluation, HFV-100

Attachment: Environmental Assessment, dated May 2000 and revised March 2002