FINDING OF NO SIGNIFICANT IMPACT

for

Aquaflor® (Florfenicol) Type A Medicated Article

for

Freshwater-Reared Salmonids

Supplemental NADA 141-246

Schering-Plough Animal Health
Summit, NJ

FOR PUBLIC DISPLAY
(HFA-305)

FINDING OF NO SIGNIFICANT IMPACT

for

Aquaflor® Type A Medicated Article

for

Control of Mortality in Freshwater-reared Salmonids

Due to Coldwater Disease Associated with *Flavobacterium psychrophilium*

Supplemental NADA 141-246

Schering-Plough Animal Health
Summit, 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. Therefore, an environmental impact statement will not be prepared.

Schering-Plough Animal Health is requesting approval of a supplemental new animal drug application (NADA) for the use of Aquaflor® (florfenicol) Type A Medicated Article in freshwater-reared salmonids. Aquaflor® is used to control mortality caused by coldwater disease associated with *Flavobacterium psychrophilium* and will be fed as the sole ration for 10 consecutive days at a dose rate of 10 mg florfenicol/kg body weight of fish.

Florfenicol is also approved for use in catfish as codified under 21 CFR 558.261 and for use in swine and cattle as codified under 21 CFR 520.955 and 522.955.

In support of their application, Schering-Plough Animal Health has provided the attached Environmental Assessment (EA), dated January 31, 2007. The EA examines the potential environmental impacts of florfenicol in receiving waters as a result of use in, and discharge from, intensive freshwater aquaculture facilities using flow-through water systems (i.e., raceways) to rear salmonids. The assessment consists of (1) a summary of the scientific literature relevant to the proposed use, pharmacokinetics, and environmental fate and effects of florfenicol; (2) estimates of predicted environmental concentrations (PECs) for typical and worst-case exposure scenarios; (3) initial and refined risk characterizations for freshwater organisms under both typical and worst-case exposure scenarios; and (4) supporting tables, figures, and appendices with cited references.

Environmental fate data in the EA indicate that the majority of florfenicol will remain in the aqueous phase if released to water, however, 20 to 30% may rapidly partition to solids and/or sediment. Half-lives in three sediment:water test systems ranged from 8 to 19 days, with degradation to smaller, more polar compounds observed in both water and sediment.

The EA addresses potential risks for aquatic organisms, microorganisms, terrestrial plants, and earthworms. Risks to sediment-dwelling and most terrestrial organisms were not considered in the EA because florfenicol and its metabolites are not likely to significantly adsorb to sediment or be transported to a terrestrial environment. Additionally, the EA does not address potential risks to avian species because no significant bioaccumulation of florfenicol is expected and direct exposure is unlikely.

Quantitative risk characterization data are presented in the EA for aquatic organisms. The initial risk characterizations indicate that populations of algae and bacteria in receiving waters are potentially at risk, but that no impacts on fish and invertebrates populations are expected, even with worst-case exposure conditions. The refined risk characterizations show that only the most sensitive species of algae and bacteria (i.e., *Skeletonema costatum* and *Pasteurella multocida*) are potentially at risk and then only with worst-case exposure conditions that would be expected to exist at less than 5% of all aquaculture facilities expected to use Aquaflor® for treatment of freshwater salmonids.

Potential risks to algae and bacteria populations are mitigated by several factors discussed in the EA, including the fact that dilution in receiving waters has not been accounted for in the analyses. Even if effects on algae and bacteria occur, these effects are not likely to be ecologically significant, widespread, or long-lasting in receiving waters for several reasons. First, the effects of florfenicol on algae and bacteria are largely inhibitory so a rapid recovery in population growth is expected shortly after release is completed. Second, although toxicity data are somewhat limited, particularly for algae, it is apparent from the existing data that there is a very wide range of sensitivity to florfenicol. The algal and bacterial species used in the risk characterizations, *S. costatum* and *P. multocida*, appear to be at one extreme. Most species will likely not be affected by florfenicol under the expected exposure conditions. Third, because there is significant functional redundancy in communities of these organisms, even if sensitive species are affected, the overall productivity and functionality of the affected ecosystems are likely to remain relatively constant.

Based on data submitted in the EA, risk analyses for florfenicol and its metabolites indicate that there is a potential for short-term inhibitory effects on sensitive algae and bacteria downstream of a very small percentage (<5%) of locations where Aquaflor® is used. Adverse effects on fish, aquatic invertebrates and terrestrial organisms are not expected under any conditions. The information provided in the EA is adequate to conclude that the use of Aquaflor® in intensive aquaculture of freshwater-reared salmonids and its disposal not expected to have a significant impact on the environment.

Steven D. Vaughn

Director, Office of New Animal Drug Evaluation, HFV-100
FDA, Center for Veterinary Medicine

February 13, 2007
Date

Attachment: Environmental Assessment dated January 31, 2007