DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

INAD 010687 P 0022

David A. Erdahl
National INAD Coordinator
USFWS, National INAD Office
Bozeman Fish Technology Center
4050 Bridger Canyon Rd.
Bozeman, MT 59715

MAR 4 2003

Dear Dr. Erdahl:

We refer to your submission dated September 9, 2002, to the Investigational New Animal Drug (INAD) file for the use of florfenicol (Aquaflor™) as an oral antibacterial in fish. You requested our review of a study completed to demonstrate the effectiveness of florfenicol to control mortality in fingerling steelhead trout, *Oncorhynchus mykiss,* due to coldwater disease caused by *Flavobacterium psychrophilum.*

We have completed our review and have the following comments. The results of this study, combined with previously submitted data, demonstrate the effectiveness of florfenicol-medicated feed administered at a dose of 10 mg/kg of fish/day for 10 consecutive days to control mortality in freshwater-raised salmonids due to coldwater disease caused by *F. psychrophilum.*

You used a two sample, one-tailed t-test to analyze the difference in the cumulative mortality between the florfenicol-treated and control group. We analyzed the cumulative mortality data using the mixed model with treatment group, day and the interaction between treatment group and day as fixed effects and the tanks within treatment as a random effect for treatment period, for post-treatment period and for total study period. There was a marginally significant mortality difference between the treatment group and the control group for treatment period (P=0.0500), but not in the post-treatment period (P=0.1142). The mortality during the total study period was significantly less in the treated group as compared to the control group (P=0.0332). The study day was very significant only in the total study period (P=0.0003), but the interaction of study day by treatment group was not statistically significant for treatment, post-treatment and total study periods (P=0.7118, P=0.4269 and P=0.6779, respectively). Because the mortality of the tanks may differ among days, the variability of the study day within tanks should not be ignored. The analysis using the mixed model accounts for the variability between and within tanks using treatment group, study day and an interaction between the treatment group and study day as fixed effects and the tanks within treatment as a random effect.

The study included in this submission as well as the studies included in the December 12, 2001 (Study FLOR-01-EFF-01, Submission H 0007), and April 10, 2002 (Study FLOR-01-EFF-05, Submission P 0016), submissions should be included in the Freedom of Information Summary. A final decision on the effectiveness technical section for this claim will be made following our review of studies submitted to us on January 7, 2003, and February 5, 2003.

Future correspondence regarding your submission to the Investigational New Animal Drug file should include the date of this letter and our file number, INAD 010697 P 0022, and should be addressed to the Document Control Unit, HFV-199. Please include only one request per submission, and clearly state the request in the first paragraph of the submission.

If you need further information regarding this letter, please contact Dr. Susan Storey, Aquaculture Drugs Team, at 301-827-7581.

Sincerely yours,

Joan C. Gotthardt

Joan C. Gotthardt, D.V.M.
Director, Division of Therapeutic
Drugs for Food Animals
Office of New Animal Drug Evaluation
Center for Veterinary Medicine

United States Department of the Interior

FISH AND WILDLIFE SERVICE
FISH TECHNOLOGY CENTER
4050 BRIDGER CANYON ROAD
BOZEMAN, MONTANA 59715
(406) 587-9265/FTS 585-4900

September 9, 2002

Dr. Andrew J. Beaulieu
Acting Director, Division of Therapeutic Drugs for Food Animals
Document Control Unit, HFV-199
Center for Veterinary Medicine
7500 Standish Place
Rockville, MD 20855

Dear Dr. Beaulieu:

The purpose of this submission is to request a formal review of the enclosed Final Study Report (FSR) titled "The efficacy of florfenicol-medicated feed to control mortality of fingerling steelhead trout (*Oncorhynchus mykiss*) caused by bacterial coldwater disease, causative agent *Flavobacterium psychrophilum*." The FSR is identified by Study Number FLOR-01-EFF-06. Please note that we also request that the FSR be included in the florfenicol medicated feed efficacy technical section in support of a New Animal Drug Approval for florfenicol, and that the FSR be filed in the U. S. Fish and Wildlife Service's Investigational New Animal Drug (INAD) file #10-697. We refer to your file number INAD 10-697 E-0015, dated July 12, 2002.

The enclosed FSR (3 copies) demonstrates the efficacy of florfenicol-medicated feed to control mortality in steelhead trout caused by bacterial coldwater disease when administered at a dosage of 10 mg florfenicol/kg of fish/day for 10 consecutive days. This florfenicol-medicated feed study was conducted under research study protocol FLOR-01-EFF (2nd revision, submitted to CVM on April 1, 2002) at the Makah National Fish Hatchery, Neah Bay, WA. A copy of study protocol FLOR-01-EFF including standard operating procedures not contained within the FSR is also enclosed.

The current sponsor of INAD #10-697 is William Knapp, Deputy Assistant Director - Fisheries, U. S. Fish and Wildlife Service, 4401 N. Fairfax Dr., Arlington, VA 22203. We would like to thank you in advance for your time and consideration with respect to the above-described request. If you have questions, please contact Dr. David Erdahl, National INAD Office, Bozeman, MT at (406) 587-9265, ext. 125.

Sincerely,

Dr. David Erdahl
National INAD Coordinator

enclosures