



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
Rockville MD 20857

INAD 10697 H-0007

Dr. David Erdahl  
Bozeman National INAD Office  
US Fish and Wildlife Service  
4050 Bridger Canyon Road  
Bozeman, MT 59715

FEB 8 2002

RE: Your submission dated December 12, 2001, amended December 19, 2001, requesting review of a study completed to demonstrate the efficacy of florfenicol administered at 10 mg/kg body weight for 10 consecutive days to control mortality of coldwater disease caused by *Flavobacterium psychophilum* in fingerling westslope cutthroat trout, *Oncorhynchus clarki*.

Dear Dr. Erdahl:

We have completed our review and have concluded that while this study is supportive of the effectiveness of florfenicol, additional effectiveness data will be required for the proposed claim. We have the following specific comments about the study.

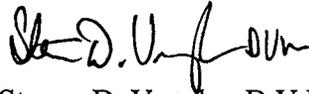
1. We agree that fish were randomly allocated to the test tanks at the start of the study. However, the method used to assign treatments to the test tanks makes the study a randomized block design rather than a completely randomized design.
2. Treatment groups did not include a sufficient number of replicates. Each treatment group should include a minimum of three replicates to allow for adequate statistical analysis.
3. The final study report and the raw data submitted do not indicate if fish were collected from each of the four tanks included in the study. For future studies, each population of fish used in a study should be positively diagnosed with the disease under consideration through appropriate testing prior to the start of the study. Along with the examination and diagnostic test results, the raw data should indicate the number of fish collected, examined and tested and from which tank the fish originated.
4. A representative number of dead and moribund fish should be collected during the treatment and post-treatment periods for necropsy including appropriate diagnostics to confirm the continued presence of the disease under study and the cause of death.
5. Florfenicol was present in an adequate concentration in the medicated feed. However, raw data of the clinical observations describing the appetite of the fish were not submitted. Without this data we cannot correlate the consumption of the medicated feed with the improvement seen in the mortality rate in the treated fish.

6. All feeds used in a study should be analyzed for the approved antimicrobial, oxytetracycline, as well as florfenicol.
7. For future studies, please include a copy of the protocol used to conduct the study with the final study report. A previously submitted protocol may not be the same as the protocol used for the study.
8. A copy of the standard operating procedures (SOPs) or a brief description of the SOP procedures mentioned in the final study report should also be included. The final study report mentions two SOPs used for medicated feed preparation. Neither SOP is included with the final study report. A full description of the feed preparation should be included, especially in a study report concerning the effectiveness of a medicated feed.

Future correspondence regarding this submission to the files for your INAD exemption should be identified by the date of the submission and our file number, INAD 10697 H-0007, and be addressed to the Document Control Unit, HFV-199. Please include only one request per submission, clearly stating the request in the first paragraph of the submission.

If you have any questions or comments regarding this correspondence, please telephone Dr. Joan Gotthardt, Leader, Aquaculture Drugs Team at 301-827-7571.

Sincerely yours,



Steven D. Vaughn, 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

December 12, 2001

Dr. Steven Vaughn  
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. Vaughn:

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 westslope cutthroat trout (*Oncorhynchus clarki*) caused by bacterial coldwater disease, causative agent *Flavobacterium psychophilum*." The FSR is identified by Study Number FLOR-01-EFF-03. 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 Investigational New Animal Drug (INAD) file #10-697. We refer to your file number INAD 10-697 E-0004, dated September 12, 2001.

The enclosed FSR is intended to demonstrate the efficacy of florfenicol-medicated feed to control mortality in cutthroat trout caused by coldwater disease when administered at a dosage of 10 mg florfenicol/kg of fish/day for 10 days. This study was conducted under the currently active research study protocol FLOR-01-EFF at the Montana Fish, Wildlife, and Parks Washoe State Fish Hatchery in Anaconda, MT. **It should be noted that although total mortality in treated tanks was lower than in untreated tanks, the differences were not significant.** Furthermore, treatment conditions in this study were replicated only in duplicate. If it is determined that either of these conditions preclude study results for being considered "pivotal", we then request that the FSR receive only informal review and the data be considered supportive.

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 for your time and consideration with respect to the above-described request. If you have any questions, please contact Dr. David Erdahl, National INAD Office, Bozeman, MT at (406) 587-9265 ext. 125.

Sincerely,

Dr. David Erdahl  
National INAD Coordinator

enclosure