



I-009321-P-0149-EF
I-009321-P-0150-EF

U.S. Fish & Wildlife Service
Aquatic Animal Drug Approval Partnership Program
Attention: David Erdahl, Ph.D.
Branch Chief, AADAP
4050 Bridger Canyon Road
Bozeman, MT 59715

Re: Effectiveness technical section complete

Dear Dr. Erdahl:

Based upon the information you submitted on December 15, 2014 (P-0149), and amended on March 5, 2015 (T-151), and June 10, 2015 (T-0154); the request you submitted on January 22, 2015 (P-0150); and the information contained in Investigational New Animal Drug (INAD) files I-010974, I-004000, and I-009321, we consider the Effectiveness technical section to be complete. The technical section is complete for the use of HALAMID (chloramine T powder for immersion) Aqua for the control of mortality due to external columnaris disease associated with *Flavobacterium columnare* in freshwater-reared coolwater finfish when administered at a concentration of 20 milligrams per liter water in a continuous flow water supply or as a static bath once per day for 60 minutes on consecutive or alternative days for three treatments.

COMMENTS REGARDING THE EFFECTIVENESS STUDY REPORT CHLT 07 EFF.1 09

1. Section 5.12 of the protocol states that "A representative number of fish from the reference population (10 fish) will be sampled and necropsied before the start of the study" and that "Necropsies will include using appropriate diagnostic techniques to 1) presumptively confirm presence of external bacterial infections and (2) assess whether there is a systemic bacterial infection that could confound test results (such as microscopic examination of kidney imprints or culturing kidney streaks on appropriate media)". No examination or culture of internal organs was recorded for the 10 fish selected for a pre-study fish health evaluation. Based on the severity of the external infections, the external nature of the treatment, and the internal observations recorded during the treatment and post-treatment necropsies, the absence of these observations in the pre-study fish was acceptable for this study. We remind you that it is important to follow all of the necropsy procedures described in the protocol in order to clearly define the disease and cause of mortality in the study population. Any protocol deviations should be described in the study report, along with an explanation of how they did or did not impact the outcome of the study.
2. Page 12 of the final study report states that general fish behavior was normal throughout the study; however, the raw data (Form 2, Appendix H) and the

summary table found in Appendix I show that abnormal behavior was observed in some tanks throughout the experiment. The abnormal behavior was mainly reported as "hanging high" in the water column and lethargy, and was disproportionately associated with the fish in the untreated control tanks. Similarly, page 12 states that fish appetite behavior was "semi-aggressive" throughout the study; however, the raw data (Form 6) and the summary table found in Appendix I show that non-aggressive feeding behavior was observed in a number of the tanks throughout the study. As with the abnormal behavior, non-aggressive feeding was seen more often in the untreated control tanks.

Observations of abnormal behavior and non-aggressive feeding in the untreated tanks are not surprising because these tanks had higher mortality and more sick fish; however, the observations were misreported in the study report. In future reports please verify that the text of the study report matches the raw data.

3. Deviation #6 reports that pencil was used on several forms in order to avoid the potential for ink to smear when working around water. We recognize the advantages of using pencil and waterproof paper when working in a hatchery environment, and we agree that this deviation did not impact the outcome of the current study. However, please be sure to use only blue or black ink in all future studies. The use of ink for recording all raw data is one of the characteristics of a GCP compliant study.

DRAFT LABELING

We reviewed the draft label language related to effectiveness. Please revise your proposed labeling per the changes listed below. CVM may request additional revisions after reviewing the other technical sections.

1. In order to match the language used on the currently approved label, the wording of the indication should be revised to read "For the control of mortality in freshwater-reared coolwater finfish due to external columnaris disease associated with *Flavobacterium columnare*".
2. The dosing regimen for this indication will be "20 milligrams per liter water in a continuous flow water supply or as a static bath once per day for 60 minutes on consecutive or alternative days for three treatments".
3. The currently labeled dose regimen for walleye includes concentrations as low as 10 mg/L; however, 20 mg/L was the lowest concentration used for the current study in tiger musky. Therefore, 20 mg/L will be the lowest labeled concentration for a grouping that includes all freshwater-reared coolwater finfish. You will need to determine if you would like to retain the labeled option to treat walleye at a 10 mg/L separately from the rest of all freshwater-reared coolwater finfish.

FREEDOM OF INFORMATION (FOI) SUMMARY

We appreciate your cooperation in including the relevant portions of the FOI Summary with this submission. The Effectiveness section of the FOI Summary has been revised, and a copy is enclosed. Please review the FOI Summary for accuracy and notify us if you find errors.

ALL OTHER INFORMATION

The "all other information" provided in this submission is acceptable. You do not need to re-submit the information provided in this submission again when you submit your All Other Information technical section.

Include a copy of this technical section complete letter when you submit your new animal drug application. Please contact us if there are changes in the product development plan (e.g., indication, dosage, duration of use) or you become aware of any issues that may impact the status of this technical section or your application. We will make a final decision on whether we can approve your application after we have reviewed all of the data for all applicable technical sections and any other information available to us, as a whole, and determined whether the requirements for approval described in the Federal Food, Drug, and Cosmetic Act have been met.

If you submit correspondence relating to this letter, you should reference the date and the principal submission identifiers found at the top of this letter. If you have any questions or comments, please contact me at 240-402-0817. You may also contact Dr. Jennifer Matysczak, Leader, Aquaculture Drugs Team, at 240-402-0588.

Sincerely,

{ see appended electronic signature page }

Cindy L. Burnsteel, DVM
Director, Division of Therapeutic
Drugs for Food Animals
Office of New Animal Drug Evaluation
Center for Veterinary Medicine

Enclosure:

Draft Section of Freedom of Information (FOI) Summary: Effectiveness