I-011365-P-0007-EF

U.S. Geological Survey
Upper Midwest Environmental Sciences Center
Attention: Mark Gaikowski
Interim Registration Officer
2630 Fanta Reed Road
La Crosse, WI 54603

Re: Effectiveness technical section complete

Dear Mr. Gaikowski:

Based upon the information you submitted September 11, 2009, and amended on January 15, 2010 (T-0008), and April 14, 2010 (T-0009), we consider the Effectiveness technical section to be complete. The technical section is complete for the use of PARASITE-S (formalin) solution for the control of mortality in freshwater-reared finfish due to saprolegniasis associated with fungi in the family Saprolegniaceae when administered at a dose of 150 ppm for 60 minutes per day on alternate days for three treatments in tanks and raceways.

EFFECTIVENESS

As stated in the end review amendment (ERA) request email dated March 19, 2010, CVM needs additional information to determine that the lower formalin doses (*i.e.*, 50 ppm, 100 ppm) will be effective when used in the field. The 50 ppm dose in this study had a P-value = 0.0566 and information within INAD files suggest that 50 ppm may not be effective in the field. Without an additional study, this dose can not be included on the label. While there was statistical significance with the 100 ppm dose, data in your Public Master File (PMF) 5693 (C-0002, October 22, 2003), data submitted to PMF 5228 (C-0008, April 22, 1998), and general INAD data were not sufficient to support a dose of 100 ppm when used in the field. We can accept the 100 ppm dose if enough supporting documentation is provided that shows that this dose is effective in the field. This justification should be supported with published literature, INAD or PMF information, or other data or information. Please reference any files previously shared with CVM that are relevant.

ADDITIONAL COMMENT

You proposed the use of an adaptive design to allow for an extension of the post• treatment period. CVM is open to the proper use of adaptive methods when designing a study. Adaptive methods should be outlined and discussed at the protocol stage and should include when interim analyses or evaluations will be employed, how that

information will be used (sample size adjustment, dropping treatments, variable selection, etc.), define any alpha adjustment appropriate for the additional testing, and describe any criteria that may be used to determine exclusion criteria for sites or trials.

The type of changes employed in the study submitted in this technical section could not be considered part of an adaptive design strategy. The multi-trial protocol was written and approved by CVM to collect data and assess pivotal effectiveness at Day 15 and no provisions were made for the use of adaptive design methods. Therefore, the deviations from the protocol once the study began were necessarily not *a priori* deviations.

DRAFT LABELING

We note that you did not submit draft labeling. Please submit your labeling technical section when the last major technical section has been submitted and is likely to be complete. In the future, please include draft labeling with each major technical section.

FREEDOM OF INFORMATION (FOI) SUMMARY

A copy of the draft effectiveness section of the FOI Summary is enclosed. Please review the FOI Summary for accuracy and notify us if you find any errors. We will prepare the final version of the FOI Summary and will provide you a copy when the last technical section is complete.

ALL OTHER INFORMATION (AOI)

We note that you did not submit additional information pertaining to Effectiveness in this submission. In the future, please include the available relevant AOI with each technical section, or note in your cover letter that there is no AOI pertaining to the technical section. We encourage you to submit AOI related to effectiveness prior to requesting the AOI technical section complete. The AOI, along with your justification, may also help support the lower dose of 100 ppm. Please submit your AOI technical section, containing any additional information not previously submitted, when the last major technical section has been submitted and is likely to be complete.

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, your correspondence should reference the date and the principal submission identifier found at the top of this letter. If you have any questions or comments, please contact me at (240) 276-8341. You may also contact Dr. Jennifer Matysczak, Team Leader, Aquaculture Drugs Team, at (240) 276-8338.

Sincerely,

Cindy L. Burnsteel DVM 6/16/10

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

Enclosure:
Draft Effectiveness section of the Freedom of Information (FOI) Summary