DEPARTMENT OF HEALTH & HUMAN SERVICES **Public Health Service**

Food and Drug Administration
Rockville MD 20857

I-008069-P-0089-TS

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

Re: Target Animal Safety technical section complete

Dear Dr. Erdahl:

Based upon the information you submitted on May 2, 2012, and amended on August 7, 2012 (T-0090) and the information contained in INAD 008069, we consider the Target Animal Safety technical section to be complete. The technical section is complete for the use of oxytetracycline dihydrate Type A medicated article when administered at an inclusion rate of 1.5-4.5 g/ kg of feed for 14 consecutive days.

TARGET ANIMAL SAFETY

This technical section complete letter represents our finding that the study data essential to determining target animal safety are complete and accepted. We also evaluate target animal safety in our review of other technical sections, particularly the Effectiveness and All Other Information technical sections.

We have the following comments:

1. The maximum feed rate included on the label should be 5.5% of body weight.

2. Because a reproductive safety study has not been conducted, a precaution statement should be included on the label. The label should include the statement "The safety of oxytetracycline in shrimp used for breeding purposes has not been demonstrated." A reproductive safety study should be conducted and demonstrate the safety of the proposed doses in broodstock shrimp, if you would like to remove the precaution from the label.

BIOSTATISTICS COMMENTS

1. CVM found numerous data entry errors resulting in discrepancies between the raw data and the electronic data. In future submissions please perform adequate quality control procedures to ensure that the electronic data which were used in the statistical analyses accurately represent the information recorded in the raw data collection forms.

2. During our review of the raw data, we found that shrimp were added to several tanks to replace shrimp that died after the study had started. One animal in tank 23 (1.5X), and 2 animals in tank 25 (0X) were replaced on day 2 and 1 animal in tank 5 (0X) was replaced on day 3. These actions caused the tanks to be unevaluable, so that tanks 5, 23, and 25 were excluded from all the summaries and statistical analyses of clinical observations.

3. The data were not analyzed in accordance with the analysis described in the protocol. Although the protocol described only the analysis of terminal weight, tank mortality, and feed consumption, none of these planned analyses were applied to the study data. We also disagree with your analysis of activity and appetite as well as the histopathology assessments. Because these variables are measured repeatedly over time, it is more appropriate to analyze the data using repeated measures models that take into account the correlation among values from the same tank over time.

4. We performed a revised analysis after making the appropriate corrections and data exclusions. Please refer to the revised draft Freedom of Information Summary for a description of the revised statistical analysis and statistical results.

ADDITIONAL COMMENT

We would like to remind you of the following information which may limit the upper end of the dose range. The following was sent in a CVM letter dated February 3, 1997, regarding the Chemistry, Manufacturing, and Controls (CMC) Technical Section.

> "Based on the data presented, a three (3) week expiration date is to be used in the labeling for the 1.5 and 3.0 g oxytetracycline per kg of medicated shrimp feeds."

Additional manufacturing data will be needed in order to approve the higher concentrations. You can contact Mr. Michael Popek, Leader, Biotherapeutics Team at 240-276-8269 for additional information on the CMC Technical Section.

FREEDOM OF INFORMATION (FOI) SUMMARY

We appreciate your cooperation in including the relevant portions of the FOI Summary with this submission. The Target Animal Safety 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. If you request changes other than the correction of errors, CVM may re-open the Target Animal Safety technical section. CVM will prepare the final version of the FOI Summary and will provide you a copy when the last technical section is complete.

DRAFT LABELING

We note that you did not provide draft labeling with your submission. Please submit the Labeling technical section when the last major technical section has been submitted. In the future, please include draft labeling with each technical section.

ALL OTHER INFORMATION

We note that you did not submit additional information pertaining to Target Animal Safety in this submission. Please submit your All Other Information technical section,

containing any additional information not previously submitted, when the last major technical section has been submitted and is likely to be complete. In the future, please include the available relevant "all other information" with each technical section, or note in your cover letter that there is no "all other information" pertaining to the 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, 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, Leader, Aquaculture Drugs Team, at 240-276-8338.

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 Freedom of Information Summary for Target Animal Safety