



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

JUL 27 2007

I-011236-P-0025-EF

• U.S. Department of the Interior
Fish and Wildlife Service
Aquatic Animal Drug Approval Partnership Program
Attention: David Erdahl, Ph.D.
Branch Chief
4050 Bridger Canyon Road
Bozeman, MT 59715

Re: Field effectiveness final study report (MT-05-EFF.3-01)

Dear Dr. Erdahl:

The data from the study submitted on February 12, 2007, entitled "The Efficacy of 17α -methyltestosterone Medicated Feed to Produce Predominately Male Populations of Hybrid Tilapia" (Study Number MT-05-EFF.3-01), are acceptable to provide a portion of the effectiveness data required for the proposed indication. The proposed indication for 17α -methyltestosterone-medicated feed when administered to 6 to 7 day post-hatch tilapia is to produce a predominately male population of fish. While the 17α -methyltestosterone (MT) dose administered during the trial was 5.9 mg/kg of fish/day for 28 consecutive days, the proposed MT dose is 9.0 mg/kg of fish/day for 28 consecutive days. To complete the Effectiveness technical section for the proposed indication, additional data will be required. Therefore, the Effectiveness technical section remains incomplete.

To complete the data requirements for the Effectiveness technical section, at least one additional study with equivalent or better results will be needed. Because the study protocol states that studies will be conducted at a total of three sites, the data from the additional sites will need to be submitted to us and reviewed by us before a conclusion can be reached about the effectiveness technical section.

In your current submission, data from only one site are analyzed. However, the protocol indicates that data from at least three sites would be analyzed together. Please include the data from the current study (Study No. MT-05-EFF.3-01) with data from the other sites, and analyze the data from all the sites together as specified in the protocol. If you have any questions or concerns about the analysis, please contact us.

When submitting data to complete the effectiveness technical section, please include a draft effectiveness section for the Freedom of Information Summary, draft label language, and information to address All Other Information. Please include draft language for the dose characterization section of the effectiveness section of the Freedom of Information Summary, as well as a summary of all of the effectiveness data.

General Comments

We provide the following comments regarding future trials.

1. Fish behavior and appetite data were not collected as described in the protocol during the post-treatment period of the currently submitted study. While the lack of performing this procedure does not affect the determination that the currently submitted trial was adequate and well controlled, the events that led to the data not being collected should be addressed during future trials. The final study report does not state why the on-site investigator did not collect these data.
2. Additionally the final study report does not include a report from the Study Monitor. The Study Monitor should have conducted on-site inspections or been in contact with the Investigator to determine whether study procedures were being conducted according to the study protocol. Information about the Study Monitor contacts with the Investigator should have been recorded in the form of a report, and this report included in the raw data. Please refer to section 5 of Guidance for Industry Number 85 – Good Clinical Practice, available on the CVM website.

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 301-827-7571 or Dr. Donald Prater, Leader, Aquaculture Drugs Team, at 301-827-7567.

Sincerely,



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



U.S. FISH & WILDLIFE SERVICE
AQUATIC ANIMAL DRUG APPROVAL PARTNERSHIP PROGRAM
4050 BRIDGER CANYON ROAD
BOZEMAN, MT 59715
PHONE 406-994-9905/FAX 406-582-0242

February 12, 2007

Dr. Joan Gotthardt
Director, Division of Therapeutic Drugs
for Food Animals
Document Control Unit, HFV-199
Center for Veterinary Medicine
7500 Standish Place, MPN-2
Rockville, MD 20855

Dear Dr. Gotthardt:

The purpose of this submission is to request a formal review of the enclosed Final Study Report (FSR) titled "The efficacy of 17- α methyltestosterone medicated feed to produce predominantly male populations of hybrid tilapia." The FSR is identified by Study Number MT-05-EFF.3-01. Please note that we also request that the FSR be included in the 17- α methyltestosterone (MT) efficacy technical section in support of a New Animal Drug Approval for MT, and that the FSR be filed in the Service's Investigational New Animal Drug (INAD) file #11-236. We refer to your file number INAD I-011236-E-0016 dated May 17, 2006.

The enclosed FSR, including the Freedom of Information (FOI) Summary, demonstrate that MT was effective in producing predominantly male populations of tilapia. The MT efficacy study was conducted under research study protocol MT-05-EFF.3 at SeaPac of Idaho's Idaho Aquatic's tilapia nursery (Buhl, ID) during July – October, 2006. The FSR summarizes results from a study in which "first feeding" tilapia fry were fed MT medicated feed administered at a concentration 40 mg MT/kg feed, and fish were fed at a rate of approximately 15% fish body weight per day for 28 consecutive days. Gonads from test fish were examined (70 days post-treatment and the relative number of fish with gonads containing testis, ovaries, or ovatestis were compared histologically with gonadal tissue from fish fed non-medicated feed (i.e., controls). Specifically, the FSR summarizes the following: 1) In treated tanks, 84% of the fish were characterized as males (gonads contained 100% testis), 3% as females (100% ovary), and 13% as intersex (ovatestis); and 2) In control tanks, 38% were characterized as males, 60% as females, and the remainder as intersex. Please note that, due to improper feed storage conditions, the concentration of MT in the feed used in the study was reduced from the target concentration of



60 mg MT/kg feed (as per the study protocol) to the analytically verified concentration of 40 mg MT/kg feed. We speculate (and believe that this speculation is supported by numerous peer-reviewed journal articles) that if 40 mg MT/kg feed effectively produced predominantly male populations of hybrid tilapia, then the target concentration of 60 mg MT/kg feed would have also produced predominantly male populations of fish.

The current sponsor for INAD #11-236 is Dr. David Erdahl, Branch Chief, U. S. Fish and Wildlife Service, AADAP Program, 4050 Bridger Canyon Road, Bozeman, MT 59715. 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. Erdahl at (406)-994-9904.

Sincerely,



Dr. David Erdahl
Branch Chief, AADAP Program

Enclosure: Three copies of the FSR, including the FOI Summary

