DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

OCT 01 2007

I-009033-D-0098-OT

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

Re: Amended authorization for oxytetracycline hydrochloride (Terramycin 343®)

Dear Dr. Erdahl:

You are authorized to slaughter up to 2 million fish, species listed in Appendix VI (a) and (b) of submission I-009033-D-0098-OT to (1) market for human food use the edible tissues derived from experimental animals or (2) release into public waters for possible human consumption experimental animals treated as described in this letter. We have completed our review of your June 12, 2007, submission and find that an investigational exemption for the use of oxytetracycline hydrochloride (Terramycin 343®) as an antimicrobial to treat certain bacterial diseases in certain species of finfish is consistent with public health.

AUTHORIZATION

DRUG	Oxytetracycline hydrochloride
Dosage Form	Powder
Route of Administration	Immersion
SPECIES	Finfish
Class	Fish species as described in submission D-0098
Number of Animals	2 million
MAXIMUM DOSE (or Range) Frequency and Duration	20 mg of oxytetracycline per liter of water OBJECTIVES A and B- single treatment for 1 hour OBJECTIVES C and D: 1 hour administered on 1 to 4 consecutive days

MINIMUM WITHDRAWAL PERIOD	OBJECTIVES A and B- 21 days. No withdrawal period is required for fish that will not be catchable for 21 or more days after release, or are illegal for harvest. OBJECTIVES C and D- 60 days. No withdrawal period is required for fish that will not be catchable for 60 or more days after release, or are illegal for harvest.
RENDERING	Fish may be rendered at any time.
COMMENTS	The investigational withdrawal periods may be incorporated into grow-out periods for the treated fish.
Reference to other authorizations	All previous authorizations are superseded.

Clinical investigations for this INAD cover only the treatment regimen stated above. The combining of this treatment with any other drug will require a separate authorization. Drugs given to control animals must be administered in full compliance with the currently approved use. Your investigators should be made aware of their responsibilities under Section 511.1(b)(7)(ii) and Section 511.1(c)(1).

Clinical tests conducted under the provisions of this letter do not exempt investigational animals and their products from compliance with any other applicable inspection requirements.

In order for us to complete our files, the disposition of all investigational animals and unused drug must be reported to this office, as well as adverse reactions observed. Please refer to this letter by date and INAD number when reporting the details of clinical investigations or the disposition of investigational animals.

ENVIRONMENTAL CONSIDERATIONS

The investigational use of oxytetracycline hydrochloride (Terramycin 343®) as an antimicrobial in certain finfish continues to fall within the categorical exclusion in 21 CFR 25.33(e). Therefore, neither an environmental assessment (EA) nor an environmental impact statement is required. A categorical exclusion from preparation of an EA and an environmental impact statement does not relieve you of the responsibility for determining and meeting all Federal, state, and local environmental and occupational laws and regulations that apply to the manufacturing, use, and disposal of the investigational drug.

You are responsible for complying with the Federal Clean Water Act as implemented under the National Pollutant Discharge Elimination System (NPDES), as well as any applicable ground-water pollution requirements, for all investigational sites covered under this INAD. You must contact the offices responsible for issuing NPDES permits, and other similar permits, to be certain they have no objection to the use and release of the investigational drug.

Please notify CVM if the scope of your investigation changes (e.g., if additional facilities will treat fish, and/or if the protocol changes in ways which could result in increased environmental exposure, etc.).

INVESTIGATIONAL LABELING

We remind you that the investigational new animal drug must be manufactured, processed, packaged, and labeled in such a way as to maintain appropriate standards of identity, strength, quality, and purity as needed for safety and to give significance to investigations made with the drug.

The investigational labeling, as provided in your June 12, 2007 submission, should be affixed to your investigational drug product prior to shipment for studies conducted under 21 CFR 511.1(a) or (b), as appropriate. The investigational labeling should be affixed to each individual drug container.

SHIPMENT AND DELIVERY NOTIFICATION

The new animal drug regulations, Section 511.1(b)(3) and (4) require the sponsor to submit specific information prior to each shipment or other delivery of the drug for clinical investigation in animals. The agency has devised a form (Form FDA 3458) which you as the sponsor may use to report shipments for clinical trials. You may file the notice of the drug shipment electronically to CVM. Please refer to the Center's electronic submission information on the CVM website at http://www.fda.gov/cvm/esubstoc.html.

You must maintain records of dates, amount of drug received in each shipment, and batch or code mark of each shipment for a period of 2 years after such shipment and delivery. These records should be made available for inspection and copying upon our request.

COUNTING NUMBERS OF FISH

You should note that this authorization is for a specific number of fish in total. Additional numbers of animals may be requested in the future. Having a specific number of animals, rather than annual numbers, facilitates our tracking under the INAD. We remind you that an animal that has been treated more than once still only counts as a single animal toward the authorization.

You should begin counting the number of animals used from the date you receive our letter. Previous authorizations are superseded. In the future, it would be helpful if you would supply the total number of animals used along with your reports.

As you track the total number of animals used by your investigators, a request for additional animals should be made with sufficient lead time to allow us to process an amended authorization. Upon receipt of the letter containing an amended authorization, you may begin counting the number of animals used from zero.

ANNUAL REPORTS

We remind you of the continued necessity to provide annual reports under the FDA/CVM Aquaculture Workload Plan. Your annual report should comprise: a) a brief summary of the past year's activities and accomplishments in each of the technical sections for the NADA; b) certification of accountability of all drugs shipped under the INAD, records maintenance for FDA inspection, compliance with the provisions of 21 CFR Part 511, including notification of adverse effects relative to humans, target animals, or the environment resulting from the use of the investigational drug; c) a list of all investigators, facilities, and species treated; and d) a copy of the current study protocol(s) noting any modification or revision. We recommend that any changes to pivotal study protocols be reviewed by CVM prior to initiating further investigations.

PROTOCOL COMMENTS

The revised protocol is adequate for the development of supportive effectiveness data and a pivotal protocol. The protocol does contain a few minor errors that should be corrected prior to delivering the protocol to investigators.

1. In section IX. Entrance Criteria, section V. Pathogen/disease considerations, part C. states "Typical disease signs should be detectable in at least a few fish and the causative pathogen should be identified." CVM would like a more definitive number (i.e. percentage or actual number) than "at least a few fish". CVM recommends a pre-submission conference to discuss the data necessary for a pivotal study.

2. Form OTIMM-1 includes the date of a previous authorization. With the granting of this authorization, the date of the CVM authorization letter will need to be changed to the date of the letter sent in response to this submission.

If you submit correspondence relating to this letter, you should reference this letter by date and the principal submission identifier found at the top of this letter. If you have any questions or comments, please contact Dr. Joan C. Gotthardt, Director, Division of Therapeutic Drugs for Food Animals, at 301-827-7571.

Sincerely,

Steven D. Vaughn, DVM

Steven D. Vaughn, DVM
Director
Office of New Animal Drug Evaluation
Center for Veterinary Medicine