DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

AUG 2 8 2008

I-010987-D-0030-OT

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

Re: Amended authorization to slaughter finfish and mussels treated with calcein

Dear Dr. Erdahl:

You are authorized to slaughter up to 5 million finfish and 10,000 mussels 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 May 15, 2008, submission and find that an investigational exemption for the use of calcein as a skeletal marker in finfish and mussels is consistent with the public health.

AMENDED AUTHORIZATION

DRUG	Calcein
Dosage Form	Liquid
Route of Administration	Bath
SPECIES	Finfish – Body weight of 2 grams or less Mussels – Higgins Eye, Hickory Nut, Black Sandshell, Pocketbook, Fat Mucket, Sheepnose, Maple Leaf
Number of Animals	5 million finfish 10,000 freshwater mussels
MAXIMUM DOSE (or Range)	125 mg/L to 5.0 g/L
Frequency and Duration	1 to 6 hours for doses of 125 to 250 mg/L 1 to 7 minutes for doses of 2.5 to 5.0 g/L
MINIMUM WITHDRAWAL PERIOD	No investigational withdrawal time is assigned for fish weighing less than 2 grams because the body weight restriction ensures a long withdrawal

	time. No investigational withdrawal time is necessary for fish that are classified as endangered. No investigational withdrawal time is assigned for mussels due to their treatment at an early life stage and the limited human consumption of freshwater mussels.
RENDERING	Animals may be rendered at any time.
OTHER RESTRICTIONS	No slaughter authorization is provided for fish weighing greater than 2 grams.

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

We find your claim for investigational use of calcein in freshwater fish and mussels falls within the categorical exclusion in 21 CFR 25.33(e). Your submission states that, to your knowledge, no extraordinary circumstances exist which may significantly affect the human environment. Therefore, neither an environmental assessment (EA) nor an environmental impact statement (EIS) is required. This categorical exclusion from preparation of an EA and an EIS 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. For each of these sites, site investigators may be required to report INAD use of calcein to

the appropriate EPA or State NPDES permitting authority if their facility's effluent is discharged to surface water [see 40 CFR Parts 451.1, 451.2, and 451.3(a)].

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 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.

If you submit correspondence relating to this letter, your correspondence should reference this letter and the principal submission identifier found at the top of this letter. If you have any questions about this letter, please contact Dr. Donald Prater, Acting Director, Division of Therapeutic Drugs for Food Animals, at 240-276-8343.

Sincerely,

Kevin J. Greenlees for

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