

Oxytetracycline Immersion Clinical Field Trials - INAD 9033

2012/2013 Annual Summary Report on the Use of Oxytetracycline Immersion Therapy in Field Efficacy Trials

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Summary

Oxytetracycline for immersion therapy (OTIMM) has been used in aquaculture to control mortality in a variety of fish caused by certain bacterial pathogens, particularly among fish not yet trained to consume medicated feed. The U.S. Food and Drug Administration has authorized the use of OTIMM under the Compassionate Investigational New Animal Drug (INAD) Exemption #9033 for the purpose of gathering efficacy data to support a new animal drug approval. In calendar year 2012/2013 (CY12/13) the efficacy of OTIMM to control mortality was evaluated in four trials involving 46,213 fish. Trials were conducted at two different hatcheries, including one state hatchery and one private hatchery during this period. The compassionate study protocol under which treatments were administered allowed the investigator to use OTIMM at a dosage of 20 mg/L for 1 h for 1 - 4 days. Efficacy was based on whether or not mortality of infected fish decreased when treated with OTIMM. Overall results

showed that 50% of the OTIMM trials appeared efficacious, while 50% of the trials were characterized as inconclusive.

Introduction

Oxytetracycline has historically been the drug of choice when diagnostic evidence shows salmonids to have furunculosis, caused by *Aeromonas salmonicida*; bacterial hemorrhagic septicemia, caused by *A. hydrophila* and other closely related bacteria; pseudomonas disease, caused by *Pseudomonas sp.*; enteric redmouth, caused by *Yersinia ruckeri*; flavobacteriosis, caused by *Flavobacteria columnare*, *F. psychrophila*, or closely related yellow pigmented gliding bacteria as described in U. S. Food and Drug Administration (FDA) Public Master File #5456; or vibriosis caused by *Vibrio anguillarum*, *V. ordalli* or other closely related bacteria.

In warmwater fish culture, oxytetracycline has been found to be efficacious for the control of bacterial hemorrhagic septicemia, pseudomonas disease, and enteric septicemia of catfish caused by *Edwardsiella ictaluri*. Fish culturists have also reported oxytetracycline to be effective against systemic and external flavobacteriosis in catfish, sturgeon, paddlefish, temperate basses, sunfishes, and other fish species.

Oxytetracycline treatment therapy has been shown to be effective, whether administered as a medicated feed or as a bath immersion. Immersion therapy is often the only option when treating young fish not accustomed to feeding on man-made fish

diets. Reluctance or refusal of young fish to consume such feed excludes medicated feed treatment as a therapy option.

Although integrated fish health management practices are often successful in preventing the occurrence of the above-described diseases, adverse environmental conditions, uncontrollable water supplies, and other culture-related factors can lead to severe disease outbreaks requiring prompt treatment to prevent significant losses of fish valuable to natural resource stewardship. Treatment with antibacterial therapeutants can effectively prevent losses of cultured fish species caused by a variety of fish diseases. Such treatments also reduce the discharge of infectious agents into the environment, thereby reducing the spread of disease to both cultured and wild fish. Although relying on administering therapeutic treatment to sick fish if and when they get sick is not the preferred option, it is critical that such an option exists.

Treatment strategies for the use of OTIMM have been designed to meet the needs of individual fish species and life stages, the physical configuration of the fish culture facility, and environmental conditions. The overall objective of OTIMM efficacy trials were to minimize the impact of disease on fish health, fish quality, and survival in order to fully meet fishery management objectives. As many factors can affect the success or failure of OTIMM, data were collected with respect to a number of parameters to help determine appropriate use patterns for OTIMM under routine fish culture conditions. These data should provide valuable information with respect to potential OTIMM use patterns in aquaculture.

Purpose

The purpose of this report is to summarize the results of CY12/13 supplemental OTIMM field efficacy trials. However, it is also expected that these data will be used to enhance the existing OTIMM database that has been established from previous years trials for the purpose of supporting an approval of an initial label claim for OTIMM use in aquaculture.

Facilities, Materials, and Methods

1. Participating Facilities

Two different hatcheries, including one state hatchery and one private hatchery used OTIMM in four separate field efficacy trials during CY12/13 to control mortality in sturgeon species caused by a columnaris. Water temperature during treatments at the testing facilities ranged from 68.9 - 73.0 °F, with a mean treatment temperature of 71.0 °F.

2. Oxytetracycline used in trials

Oxytetracycline hydrochloride used in CY12/13 trials was supplied by either 1) Terramycin-343[®] soluble powder, supplied by Pfizer, Inc., Lee's Summit, Missouri, or 2) Pennox 343[®] soluble powder, supplied by PennField Animal Health, Omaha, Nebraska. Both of these over-the-counter water-soluble powder products contains 343 grams of active oxytetracycline hydrochloride per pound.

3. Drug dosages

According to the Study Protocol, investigators were allowed to administer OTIMM at 20 mg/L for one hour for a single treatment or one hour daily for up to 4 consecutive days. During CY12/13, OTIMM was administered as a bath treatment at a concentration of 20 mg/L for 1 hour for 1 - 4 days in four trials.

Fish Species

1. Species of fish treated

Two fish species were treated during CY12/13. Treated fish ranged in length from 1.5 - 7.1 in; mean length was 3.8 in. Species treated included:

Non-salmonids

pallid sturgeon (*Scaphirhynchus albus*)

white sturgeon (*Acipenser transmontanus*)

2. Diseases treated

Test fish were treated with OTIMM to control mortality caused by columnaris.

Data Collected

1. Pathologists Reports

Fish health pathology reports provide essential information with respect to disease confirmation and general fish health. Pathology reports were not submitted with the CY12/13 trials.

2. Mortality data

As stated in the Study Protocol, mortality data was to be collected 5 days prior to treatment, during treatment, and 10 d post-treatment. Investigators were strongly encouraged to collect mortality data on a daily basis.

Discussion of Study Results

1. General observations on the efficacy of OTIMM for the control of bacterial diseases in treated fish (Note: Table 1 provides a summary of all efficacious trials; Table 2 provides a summary all inconclusive trials; and Table 3 provides summary data for all trials conducted during CY12/13 under INAD #9033).

A. Efficacy of OTIMM at 20.0 mg/L for 1 hour for 1 - 4 days

OTIMM was used at 20.0 mg/L for 1 hour for 1 - 4 days in four trials involving pallid sturgeon and white sturgeon diagnosed with columnaris (Tables 1 - 2).

OTIMM treatments appeared effective in two trials while two trials were characterized as inconclusive.

2. Observed Toxicity

No toxicity or adverse effects relating to OTIMM treatment were reported.

3. Observed Withdrawal Period

All withdrawal times were either met or exceeded.

Current Study Protocol for OTIMM INAD #9033

No changes have occurred to the current study protocol for OTIMM INAD #9033.

Facility Sign-up List

Please see “Table 4. Facilities and Names of Investigators” for facilities that signed-up to participate in the OTIMM INAD #9033 during CY12/13. Please note all of these facilities are in compliance with their reporting requirements to the NPDES authority.

Correspondence sent to OTIMM Participants

Please see the attached correspondence that was sent to all OTIMM participants after the AADAP Office received their sign-up form for CY12/13.

Number of Treated Fish under Treatment Use Authorization

Total number of treated fish during CY12/13 was 46,213. The total number of treated fish to count against the treatment use authorization dated October 1, 2007 is 1,367,117.

Summary of Study Results

Oxytetracycline as an immersion therapeutant was used at a dosage of 20 mg/L for 1 hr, and treatments were administered for 1 - 4 days. Two fish species were treated with OTIMM, and trials involved 46,213 treated fish. Treated fish ranged in size from 1.5 - 7.1 in. Water temperature during treatments ranged between 68.9 and 73.0 °F. Overall results showed that 50% of the OTIMM trials appeared efficacious while 50% of the trials were characterized as inconclusive. No evidence of toxicity or adverse effects related to OTIMM treatment were reported. Although these data will be considered ancillary efficacy data, they should provide useful corroborative data to support an initial label claim for OTIMM. It is anticipated that additional ancillary efficacy data will continue to be collected in the future under INAD #9033. In future trials conducted under INAD #9033, efforts will continue to be directed towards the generation of high quality data.

Table 1. Summary of CY12/13 OTIMM Treatment Trial Results - efficacious results

Facility	Number of Trials	Fish Species	Number of Fish	Fish Size (in)	Treatment Duration (hrs)	Dose (mg/L)	Number of Treatments	Disease	Temp. (°F)
Blind Pony SFH	1	PLS	10,500	1.5	1	20	1	Columnaris	73.0
Sterling Caviar LLC	1	WST	26,000	7.1	1	20	3	Columnaris	68.9

Table 2. Summary of CY12/13 OTIMM Treatment Trial Results - inconclusive results

Facility	Number of Trials	Fish Species	Number of Fish	Fish Size (in)	Treatment Duration (hrs)	Dose (mg/L)	Number of Treatments	Disease	Temp. (°F)
Blind Pony SFH	2	PLS	9,713	1.8 - 4.8	1	20	2 - 4	Columnaris	69.5 - 72.5

Table 3. Summary Data Regarding CY12/13 OTIMM Efficacy Trials

Total Number of Trials Conducted:	4
Number of efficacious trials:	2
Number of inconclusive trials:	2
Total Number of Fish Treated:	46,213
Number of fish treated in efficacious trials	36,500
Number of fish treated in inconclusive trials	9,713
Treatment Regimens Used:	
20 mg/L static bath for 1 hr; 1 day	1 trial
20 mg/L static bath for 1 hr; 2 days	1 trial
20 mg/L static bath for 1 hr; 3 days	1 trial
20 mg/L static bath for 1 hr; 4 days	1 trial
Treatment Water Temperature (°F):	68.9 - 73.0
Size of Treated Fish (in):	1.5 - 7.1
Species Treated:	
<u>Non-salmonids</u>	
pallid sturgeon (<i>Scaphirhynchus albus</i>)	
white sturgeon (<i>Acipenser transmontanus</i>)	
