

Oxytetracycline Immersion Clinical Field Trials - INAD 9033

2005 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. In calendar year 2005 (CY05), the efficacy of OTIMM was evaluated under compassionate Investigational New Animal Drug (INAD) #9033 in seven disease control/prevention trials. All trials were conducted at one private hatchery and involved treatment of 54,100 test fish. The purpose of conducting such trials under INAD #9033 was to collect ancillary efficacy data to support a new animal drug approval for OTIMM. Efficacy was based on whether or not mortality of infected fish decreased when treated with OTIMM. Overall results showed mortality decreased following treatment in each trial, indicating that all OTIMM trials appeared efficacious.

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 CY05 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

One private fish hatchery used OTIMM in seven separate field efficacy trials during CY05 to control mortality in white sturgeon caused by bacterial gill disease and external columnaris. Water temperature during treatments at this testing facility was a constant 68°F.

2. Oxytetracycline used in trials

All oxytetracycline used in CY05 trials was Terramycin-343 soluble powder, supplied by Pfizer, Inc., Lee's Summit, Missouri. Pfizer's over-the-counter Terramycin-343 soluble powder contains 343 grams of active oxytetracycline hydrochloride per pound. Pfizer's Terramycin-343 was the only form of oxytetracycline used by fish culturists to treat fish under INAD #9033 during the reporting period.

3. Drug dosages

Two treatment regimens are allowed in the Study Protocol for INAD #9033. During CY05, OTIMM was administered as a bath treatment once per day for

four consecutive days at a concentration of 20 mg/L for 1 hour (i.e., the standard dosage) in all seven trials.

Fish Species

1. Species of fish treated

White sturgeon *Acipenser transmontanus* was the only fish species treated during the reporting period. Approximate length of treated fish was 10 in.

2. Diseases treated

Test fish were treated with OTIMM to control mortality caused by bacterial gill disease and external columnaris.

Data Collected

1. Pathologists Reports

Fish health pathology reports provide essential information with respect to disease confirmation and general fish health. Unfortunately, no pathology reports were submitted with any of the CY05 trials.

2. Mortality data

As stated in the Study Protocol, mortality data was to be collected for at least 10 days prior to treatment, during treatment, and for at least 30 d post-treatment.

Investigators were strongly encouraged to collect mortality data on a daily basis. However, daily collection of post-treatment mortality data was not always collected.

Discussion of Study Results

1. General observations on the efficacy of OTIMM for the control of bacterial diseases in non-salmonid fish (Note: Table 1 provides a summary of all efficacious trials; Table 2 provides summary data for all trials; and Table 3 describes all trials conducted during CY05 under INAD #9033).

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

OTIMM was used at 20.0 mg/L for 1 hour for 4 consecutive days in seven trials involving white sturgeon diagnosed with bacterial gill disease and external columnaris (Table 1). Results indicated that OTIMM treatments appeared efficacious in all trials.

2. Observed Toxicity

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

Summary of Study Results

Oxytetracycline as an immersion therapeutant was used at a dosage of 20.0 mg/L for 1 hr daily, and treatments were administered on four consecutive days. One

fish species was treated with OTIMM, and trials involved 54,100 treated fish. Treated fish size was 10.0 in. Water temperature during treatments was 68.0 °F. All of the trials appeared to be efficacious. No evidence of toxicity or adverse effects related to OTIMM treatment were reported. Although these data will be considered as 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 be directed towards the generation of higher quality data.

Table 1. Summary of CY05 OTIMM Treatment Trial Results - efficacious results

Hatchery	Number of Trials	Fish Species	Number of Fish	Fish Size (in)	Treatment Duration (hrs)	Dose (mg/L)	Disease	Dissolved Oxygen	Temp. (°F)
Stolt Sea Farm California, LLC	7	WHS	54,100	10	1	20	BGD & External Columnaris	9.0	68.0

Table 2. Summary Data Regarding CY05 OTIMM Efficacy Trials

Total Number of Trials Conducted:	7 - All appeared efficacious
Total Number of Fish Treated:	54,100
Treatment Regimes Used:	
20 mg/L static bath for 1 hr	7 trials
Treatment Water Temperature (°F):	680.0
Size of Treated Fish (in):	10.0
Species Treated:	
White Sturgeon <i>Acipenser transmontanus</i>	
