

Oxytetracycline Immersion Clinical Field Trials - INAD 9033

2002 Annual Summary Report on the Use of Oxytetracycline Immersion Therapy in Field Efficacy Trials

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Summary

Water soluble antibiotics such as oxytetracycline are routinely used in fisheries programs to control mortality in young fish caused by systemic bacterial infections. Immersion therapy is often the only option when treating young fish not accustomed to feeding on man-made fish diets. The U.S. Food and Drug Administration has authorized the use of oxytetracycline immersion therapy (OIT) under the Compassionate Investigational New Animal Drug (INAD) Exemption #9033 for the purpose of gathering efficacy data to support a new animal drug approval for OIT. Numerous Investigational New Animal Drug (INAD) trials were conducted in calendar year (CY) 2002 to evaluate the efficacy of OIT to control mortality in fish caused by a variety of bacterial diseases. Twenty-six such trials that involved nearly 3.1 million fish were conducted at 3 state fish hatcheries and two private hatcheries during this period. Efficacy was based on whether or not mortality of infected fish decreased when treated with OIT. Overall results showed that 62% of the trials conducted during CY 2002 appeared efficacious, while 38% 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 flavobacteriosis in catfish, sturgeon, paddlefish, temperate basses, sunfishes, and other fish species.

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. Therapeutic treatment can be administered as either 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.

Treatment strategies for the use of OIT have been designed to meet the needs of individual fish species and life stages, the layout of the facility, and environmental conditions. The overall objective of OIT efficacy trials was 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 OIT, data were collected with respect to a number of parameters to help determine appropriate use patterns for OIT under routine fish culture conditions. These data should provide valuable information with respect to potential OIT use patterns in aquaculture.

Purpose

The purpose of this report is to summarize the results of CY 2002 supplemental OIT field efficacy trials. Furthermore, it is expected that these data will be used to enhance the existing OIT database that has been established from previous years trials for the purpose of pursuing an initial label claim for use of OIT aquaculture.

Facilities, Materials, and Methods

1. Participating Facilities

Five aquaculture facilities conducted OIT trials under this INAD during CY 2002, including three state fish hatcheries and two private fish. Water temperature during treatments ranged from 51 to 79.0°F.

2. Oxytetracycline used in trials

All oxytetracycline used in CY 2002 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.

3. Drug dosages

The permissible OIT dosage defined by the Study Protocol for INAD #9033 allowed the Investigator to treat fish with 20 mg/L for 1 hr. Investigators used this treatment regimen in 19 of the 26 OIT trials conducted during CY 2002. In the remaining seven trial, fish were treated with 17 mg/L for 1 hr.

Fish Species

1. Species of fish treated

One salmonid and four non-salmonid fish species were treated during CY 2002.

Treated fish ranged in size from 1.7 - 16.5 in. Species treated included:

1. Atlantic salmon (*Salmo salar*)
2. Muskellunge (*Esox masquinongy*)
3. Smallmouth bass (*Micropterus dolomieu*)
4. Walleye (*Stizostedion vitreum*)
5. White sturgeon (*Acipenser transmontanus*)

2. Diseases treated

Test fish were treated with OIT to control mortality caused by external columnaris, bacterial gill disease, *Aeromonas hydrophila*, and bacterial hemorrhagic septicemia.

Data Collected

Summary results on the efficacy of OIT to control mortality caused by bacterial infections conducted during CY 2002 under INAD #9033. (Note: A summary of the individual OTM studies conducted during CY 2002 under INAD #9033 in which results were efficacious or inconclusive are presented in Tables 1 and 2, respectively; Table 3

describes the number of trials conducted, number of fish and fish species treated, and treatment regimens used; and Table 4 lists all treatment trials conducted during this reporting period).

1. Pathologists Reports

Fish health pathology reports provide essential information with respect to disease confirmation and general fish health. Fish health evaluations should be conducted on a subsample of moribund test fish to ascertain the cause of death prior to recommending treatment therapy. Pathology reports were submitted with 42% of the CY 2002 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 possible.

Discussion of Study Results

1. General observations on the efficacy of OIT

A. Efficacy of OIT at 17.0 mg/L for 1 hour

OIT was used at 17.0 mg/L for 1 hour in 7 trials involving walleye that had been presumptively diagnosed with bacterial gill disease (Tables 1 & 2). Only 1 trial appeared to be efficacious, while 6 trials were characterized as inconclusive. The Investigator noted that trials involving young walleye were characterized as inconclusive because it is difficult to convert young walleye to accept man-made feed, and cumulative mortality among groups of young walleye as high as 50% are not uncommon. Therefore, it was difficult to differentiate whether mortality of test fish was due to gill disease or to starvation and overcrowded conditions.

B. Efficacy of OIT at 20.0 mg/L for 1 hour

OIT was used at 20.0 mg/L for 1 hour in 19 trials involving Atlantic salmon, muskellunge, smallmouth bass, and white sturgeon, diagnosed with bacterial gill disease, columnaris, bacterial hemorrhagic septicemia, or *Aeromonas hydrophila* (Tables 1 & 2). Fifteen trials appeared efficacious, while 4 trials were characterized as inconclusive.

2. Observed Toxicity

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

Summary of Study Results

Oxytetracycline as an immersion therapeutant was used at a dosage of either 17.0 or 20.0 mg/L for 1 hr. One salmonid species and four non-salmonid species were treated with OIT, and trials involved nearly 3.1 million treated fish. Treated fish ranged in size from 1.7 - 16.5 in. Water temperature during treatments ranged from 51 to 79.0°F. Approximately 62% of the trials appeared efficacious, while 38% were characterized as inconclusive. No evidence of toxicity or adverse effects related to OIT treatment were reported. Because trials were not conducted under a pivotal research protocol, these data should be considered as ancillary efficacy data, and should provide useful corroborative data to support an initial label claim for OIT. It is anticipated that additional ancillary efficacy data will continue to be collected 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 CY 2002 Oxytetracycline Immersion Efficacy 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)
Rathbun SFH	1	WAE	10,338	2.80	1	17	BGD	6.2	78.0
Spirit Lake SFH	2	MUE	8,267	5.4 - 6.8	1	20	Bacterial Hemorrhagic Septicemia	8.0 - 8.5	75.0
Jake Wolf Memorial SFH	1	SMB	290	16.5	1	20	Aeromonus Hydrophila	6.8	74.0
Stolt Sea Farm California, LLC	12	WHS	106,150	4.0 - 7.0	1	20	Columnaris & BGD	8.0	69 - 70

Table 2. Summary of CY 2002 Oxytetracycline Immersion Efficacy Results - inconclusive results

Hatchery	Number of Trials	Fish Species	Number of Fish	Fish Size (in)	Treatment Duration (hrs)	Dose (mg/L)	Disease	Dissolved Oxygen	Temp. (°F)
Rathbun SFH	6	WAE	1,779,337	1.7 - 3.5	1	17	BGD	6.0 - 8.2	71 - 79
Kennebec Hatchery	1	ATS	1,146,800	6.5	1	20	BGD	12.0	51.0
Spirit Lake SFH	3	MUE	11,828	5.4 - 6.8	1	20	Bacterial Hemorrhagic Septicemia	8.0 - 8.5	73 - 75

Table 3. Description of number of treatment trials conducted, fish species and number of fish treated, and treatment regimens used during CY 2002 OIT Efficacy Trials

Total Number of Trials Conducted:	26
Number of efficacious trials:	16
Number of inconclusive trials:	10
Total Number of Fish Treated:	3,063,010
Number of fish treated in efficacious trials	125,045
Number of fish treated in inconclusive trials	2,937,965
Treatment Regimes Used:	
17 mg/L static bath for 1 hr	7 trials
20 mg/L static bath for 1 hr	19 trials
Treatment Water Temperature (°F):	
51.0 - 79.0	
Size of Treated Fish (in):	
1.7 - 16.5	
Species Treated:	
Atlantic salmon <i>Salmo salar</i>	
Muskellunge <i>Esox masquinongy</i>	
Smallmouth Bass <i>Micropterus dolomieu</i>	
Walleye <i>Stizostedion vitreum</i>	
White Sturgeon <i>Acipenser transmontanus</i>	
