

## **Oxytetracycline Immersion Clinical Field Trials - INAD 9033**

### **2003 Annual Summary Report on the Use of Oxytetracycline Immersion Therapy in Field Efficacy Trials**

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#### **Summary**

Oxytetracycline for immersion therapy (OIT) 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 man-made feed. In calendar year 2003 (CY03), the efficacy of OIT was evaluated under compassionate Investigational New Animal Drug (INAD) #9033 in 19 disease control/prevention trials. Efficacy trials were conducted at two state fish hatcheries and two private hatcheries and involved approximately 0.7 million fish. The purpose of conducting such trials under INAD #9033 was to collect pivotal and ancillary efficacy data to support a new animal drug approval for OIT. Efficacy was based on whether or not mortality of infected fish decreased when treated with OIT. Overall results showed that 74% of the OIT trials appeared efficacious, 16% appeared ineffective, and 10% 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.

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.

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.

Treatment strategies for the use of OIT 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 OIT 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 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 CY03 supplemental OIT field efficacy trials. However, it is also 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 supporting an approval of an initial label claim for OIT use in aquaculture.

## **Facilities, Materials, and Methods**

### **1. Participating Facilities**

Two state fish hatcheries and two private fish hatcheries used OIT during CY03 to control mortality in a variety of fish caused by a variety of bacterial and other infectious pathogens in 19 separate field efficacy trials. Water temperature during treatments at the various testing facilities ranged from 64.4 - 78.0 °F, with a mean treatment temperature of 73.4 °F.

### **2. Oxytetracycline used in trials**

All oxytetracycline used in CY03 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 CY03.

### **3. Drug dosages**

As described in the Study Protocol for INAD #9033, OIT was administered as a bath treatment at a concentration of 20 mg/L for 1 hour (i.e., the standard dosage) in 11 trials, and at a concentration of 17 mg/L for 1 hour in 8 trials.

## **Fish Species**

### **1. Species of fish treated**

Four fish species, including one salmonid and three non-salmonids, were treated during CY03. Treated fish ranged in length from 2.0 - 8.0 in. Species treated included:

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

### **2. Diseases treated**

Test fish were treated with OIT to control mortality caused by either external columnaris, bacterial gill disease, or bacterial hemorrhagic septicemia.

## **Data Collected**

### **1. Pathologists Reports**

Fish health pathology reports provide essential information with respect to disease confirmation and general fish health. Pathology reports were submitted with 21% of the CY03 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 OTI for the control of bacterial diseases in salmonid and non-salmonid fish** (Note: Table 1 provides a summary of all efficacious trials; Table 2 provides a summary of all ineffective trials; Table 3 provides a summary of all inconclusive trials; Table 4 provides summary data for all trials; and Table 5 describes all trials conducted during CY03 under INAD #9033).

### **A. Efficacy of OIT at 17.0 mg/L for 1 hour on 1, 2, or 3 days**

OIT was used at 17.0 mg/L for 1 hour on 1, 2, or 3 days in eight trials involving walleye presumptively diagnosed with bacterial gill disease (Tables 1 - 3). OIT treatments appeared efficacious in five trials, ineffective in one trial, and inconclusive in two trials.

### **B. Efficacy of OIT at 20.0 mg/L for 1 hour on 1, 2, 3, or 4 days**

OIT was used at 20.0 mg/L for 1 hour on 1, 2, 3, or 4 days in 11 trials involving Atlantic salmon, muskellunge, and white sturgeon diagnosed with either bacterial gill disease, columnaris, or bacterial hemorrhagic septicemia (Tables 1 & 2). OIT treatments appeared to be efficacious in nine trials and ineffective in two trials.

## **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 17.0 or 20.0 mg/L for 1 hr daily, and treatments were administered on 1 - 4 d. Four fish species, including one salmonid and three non-salmonids were treated with OIT, and trials involved approximately 0.7 million treated fish. Treated fish ranged in size from 2.0 - 8.0 in. Water temperature during treatments ranged between 64.4 and

78.0 °F. Approximately 74% of the trials appeared efficacious, 16% appeared ineffective, and 10% were characterized as inconclusive. No evidence of toxicity or adverse effects related to OIT treatment were reported. Although these data will be considered as ancillary efficacy data, they should provide useful corroborative data to support a future initial label claim for OIT. 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 CY03 OIT 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)
Rathbun SFH	5	WAE	152,715	3.2 - 3.5	1	17	BGD	8.0 - 8.1	76 - 78
Spirit Lake SFH	2	MUE	21,851	4.7 - 7.6	1	20	Bacterial Hemorrhagic Septicemia	7.9	74.1 - 75
Stolt Sea Farm California, LLC	7	WHS	63,000	2.0 - 8.0	1	20	Columnaris & BGD	9.0	70.0

**Table 2. Summary of CY03 OIT Treatment Trial Results - ineffective 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	181,195	3.20	1	17	BGD	8.1	78.0
Oquossoc Hatchery	1	ATS	248,500	4.50	1	20	Columnaris	12.0	64.4
Spirit Lake SFH	1	MUE	1,659	7.50	1	20	Bacterial Hemorrhagic Septicemia	7.9	75.0

**Table 3. Summary of CY03 OIT Treatment Trial 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	2	WAE	49,622	3.0 - 3.5	1	17	BGD	8.0 - 8.2	76.0

**Table 4. Summary Data Regarding CY03 OIT Efficacy Trials**

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**Total Number of Trials Conducted: 19**

Number of efficacious trials: 14

Number of efficacious trials: 3

Number of inconclusive trials: 2

**Total Number of Fish Treated: 718,542**

Number of fish treated in efficacious trials 237,566

Number of fish treated in inefficacious trials 431,354

Number of fish treated in inconclusive trials 49,622

**Treatment Regimes Used:**

17 mg/L static bath for 1 hr 8 trials

20 mg/L static bath for 1 hr 11 trials

**Treatment Water Temperature (°F):**

64.4 - 78.0

**Size of Treated Fish (in):**

2.0 - 8.0

**Species Treated:**

Atlantic salmon *Salmo salar*

Muskellunge *Esox masquinongy*

Walleye *Stizostedion vitreum*

White Sturgeon *Acipenser transmontanus*

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