

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

### **2006 Annual Summary Report on the Use of Oxytetracycline Immersion Therapy in Field Efficacy Trials**

Prepared by:

Bonnie Johnson, Biologist  
U.S. Fish and Wildlife Service  
Bozeman National INAD Office  
Bozeman, Montana

#### **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 2006 (CY06), the efficacy of OTIMM was evaluated under compassionate Investigational New Animal Drug (INAD) #9033 in nine disease control/prevention trials. Efficacy trials were conducted at four state fish hatcheries and one private hatchery and involved approximately 0.8 million 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 that 67% of the OTIMM trials appeared efficacious, 11% appeared ineffective, and 22% 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 CY06 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**

Four state fish hatcheries and one private hatchery used OTIMM in nine separate field efficacy trials during CY06 to control mortality in a variety of fish caused by a variety of bacterial and other infectious pathogens in nine separate field efficacy trials. Water temperature during treatments at the various testing facilities ranged from 48.0 - 75.0 °F, with a mean treatment temperature of 62.2 °F.

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

All oxytetracycline used in CY06 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 CY06, OTIMM was administered as a bath treatment at a concentration of 20 mg/L for 1 hour for one day (i.e., the standard dosage) in six trials; or once per day for four consecutive days in three trials.

## **Fish Species**

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

Five fish species, including three salmonid and two non-salmonids, were treated during CY06. Treated fish ranged in length from 1.1 - 10.0 in; mean length was 4.9 in. Species treated included:

1. Brook trout (*Salvelinus fontinalis*)
2. Rainbow trout (*Oncorhynchus mykiss*)
3. Steelhead trout (*O. mykiss*)
3. Walleye (*Sander vitreum*)
4. White sturgeon (*Acipenser transmontanus*)

### **2. Diseases treated**

Test fish were treated with OTIMM to control mortality caused by either external columnaris, bacterial gill disease, external bacterial coldwater disease, *Aeromonas hydrophila*, 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 67% of the CY06 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 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 CY06 under INAD #9033).

### **A. Efficacy of OTIMM at 20.0 mg/L for 1 hour for 1 day**

OTIMM was used at 20.0 mg/L for 1 hour for 1 day in six trials involving brook trout, rainbow trout, steelhead trout, and walleye diagnosed with bacterial gill disease, external bacterial coldwater disease, bacterial hemorrhagic septicemia, and *Aeromonas hydrophila* (Tables 1 - 3). Results indicated that OTIMM treatments appeared efficacious in three trials, ineffective in one trial, and was characterized as inconclusive in two trials.

### **B. 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 three 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 for either one or four consecutive days. Five fish species were treated with OTIMM, and trials involved approximately 0.8 million treated fish. Treated fish ranged in size from 1.1 - 10.0 in. Water temperature

during treatments ranged between 48.0 and 75.0 °F. Approximately 67% of the trials appeared efficacious, 11% appeared ineffective, and 22% were characterized as inconclusive. 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 high quality data.

**Table 1. Summary of CY06 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)
Crystal Springs SFH	1	BKT	64,000	1.50	1	20	1	BGD	48.0
French River SFH	1	RBT	116,866	3.48	1	20	1	A. Hydrophila	57.0
	1	STT	34,320	3.05	1	20	1	A. Hydrophila	57.0
Sterling Caviar LLC	3	WHS	32,400	10	1	20	4	BGD & External Columnaris	68.0 - 70.0

**Table 2. Summary of CY06 OTIMM Treatment Trial Results - ineffective 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)
Hagerman SFH	1	RBT	125,676	1.10	1	20	1	CWD	58.0

**Table 3. Summary of CY06 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)
Hagerman SFH	1	RBT	388,000	1.10	1	20	1	CWD	59.0
Spirit Lake SFH	1	WAE	26,487	3.80	1	20	1	Bacterial Hemorrhagic Septicemia	75.0

**Table 4. Summary Data Regarding CY06 OTIMM Efficacy Trials**

---

<b>Total Number of Trials Conducted:</b>	<b>9</b>
Number of efficacious trials:	6
Number of ineffective trials:	1
Number of inconclusive trials:	2
<b>Total Number of Fish Treated:</b>	<b>787,749</b>
Number of fish treated in efficacious trials	247,586
Number of fish treated in inefficacious trials	125,676
Number of fish treated in inconclusive trials	414,487
<b>Treatment Regimes Used:</b>	
20 mg/L static bath for 1 hr	9 trials
<b>Treatment Water Temperature (°F):</b>	48.0 - 75.0
<b>Size of Treated Fish (in):</b>	1.10 - 10.0
<b>Species Treated:</b>	
Brook trout ( <i>Salvelinus fontinalis</i> )	
Rainbow trout ( <i>Oncorhynchus mykiss</i> )	
Steelhead trout ( <i>O. mykiss</i> )	
Walleye ( <i>Sander vitreum</i> )	
White Sturgeon ( <i>Acipenser transmontanus</i> )	

---