

## Oxytetracycline-Injectable Clinical Field Trials - INAD 9027

### **Year 2000 Annual Summary Report on the Use of Oxytetracycline-Injectable in Field Efficacy Trials**

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#### **Summary**

Oxytetracycline as an injectable was used at one U.S. Fish and Wildlife Service hatchery and one state fish hatchery during calendar year 2000 to evaluate its effectiveness to prevent pre- and/or post-spawning mortality in paddlefish and pallid sturgeon caused by systemic bacterial infection, and to control mortality caused by furunculosis in chinook salmon broodstocks. The U.S. Food and Drug Administration has authorized the use of this compound under the Compassionate Investigational New Animal Drug Exemption #9027 for the purpose of collecting pivotal and ancillary efficacy data to support a new animal drug approval for oxytetracycline. Oxytetracycline as an injectable was administered in 3 trials and involved a total of 146 fish. All of the trials appeared efficacious.

#### **Introduction**

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 flexibacteriosis 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, fish handling procedures, physiological changes related to the onset and completion of spawning, and other culture related factors can lead to severe disease outbreaks requiring prompt treatment. An injectable drug product can effectively prevent losses in broodstock and other valuable non-feeding fish. Such treatment also reduces 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 oxytetracycline as an injectable have been designed

primarily to prevent or control pre- and post-spawning mortality in valuable broodstock populations. The overall objective of these studies 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 oxytetracycline therapy, data were collected on a variety of parameters to help determine appropriate use patterns for oxytetracycline under routine fish culture conditions. These data should provide valuable information with respect to potential oxytetracycline use patterns in aquaculture.

## **Purpose**

The primary purpose of this report is to summarize the results of calendar year (CY) 2000 supplemental oxytetracycline as an injectable (OTI) field efficacy studies. However, it is also expected that data from these studies will be used to enhance the existing OTI database that has been established from previous years studies for the purpose of expanding and/or extending the approved label for oxytetracycline use in aquaculture.

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

### **1. Facilities**

One U.S. Fish and Wildlife Service National Fish Hatchery (Natchitoches NFH) and one state fish hatchery (Elmendorf Hatchery - AK) used OTI during CY 2000.

### **2. OTI used in trials**

All OTI used in these trials was Liquamycin LA-200 supplied by Pfizer, Inc., Lee's Summit, Missouri. Pfizer's over-the-counter injectable Liquamycin LA-200 contains 200 mg of active oxytetracycline amphoteric per milliliter, and 1.8% magnesium oxide. Pfizer's Liquamycin LA-200 was the only form of injectable oxytetracycline used to treat fish under INAD #9027.

### **3. Drug dosages**

As described in the Study Protocol for INAD #9027, Investigators were allowed to use OTI as either a single injection treatment at the standard terrestrial animal dosage of 20 mg of active oxytetracycline per kg of fish body weight; or at various dosages and multiple treatment frequencies. If used as a single injection at 20 mg/kg body weight, a 30 d withdrawal period was required. All other treatment regimes required a 60 d withdrawal period. Oxytetracycline dosages used in these studies included 20mg OTI/kg (chinook salmon), and 25mg OTI/kg (paddlefish and pallid sturgeon).

## **Fish Species and Diseases Treated**

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

Three fish species were treated during CY 2000. Species treated included paddlefish (*Polydon spathula*), pallid sturgeon (*Scaphirhynchus albus*), and chinook salmon (*Oncorhynchus tshawytscha*).

### **2. Diseases treated**

Paddlefish and pallid sturgeon broodstocks were treated prophylactically to prevent potential bacterial infection. Paddlefish and pallid sturgeon broodstocks have both been shown to be susceptible to bacterial infection prior to, during, and following spawning. Chinook salmon were treated to control furunculosis prior to being spawned.

## **Data Collected**

### **1. Pathologist's reports**

Fish health pathology reports provide essential information with respect disease confirmation. However, in CY 2000 a pathology report was submitted only in the trial for chinook salmon diagnosed with furunculosis.

### **2. Mortality data**

As stated in the Study Protocol, mortality data was to be collected for at least 10 days prior to treatment, during the treatment period, and for at least 30 days post-treatment. Investigators were strongly encouraged to collect mortality data on a daily basis. However, in these trials daily collection of mortality data was not always possible as fish were being held in ponds. Therefore, mortalities were collected, counted, and recorded on an intermittent basis throughout the entire study period.

## **Discussion of CY 2000 Study Results:**

### **1. Summary results on the efficacy of OTI for the control of furunculosis in salmonid fish**

#### **A. Efficacy at 20 mg/kg body weight**

OTI was used at 20 mg/kg body weight in a single trial involving chinook salmon to control furunculosis. Forty fish were injected a single time ten days prior to being spawned. OTI treatment appeared to be efficacious (Table 1) as percent daily mortality decreased from 21.0% (pre-treatment)

to 6.0% (post-treatment).

## **2. Summary results on the efficacy of OTI for the control of bacterial diseases in non-salmonid fish**

### **A. Efficacy at 25 mg/kg body weight**

OTI was used at 25 mg/kg body weight in one trial involving paddlefish and one trial involving pallid sturgeon. Sixty-eight pallid sturgeon and thirty-eight paddlefish were injected a single time immediately following completion of spawning. All females were spawned by caesarian section, which is a quite invasive procedure and can often lead to resultant bacterial infection. Although 28 of 106 treated fish (~26%) died during the post-spawn recovery period, all mortalities were attributed to a mechanical failure due to a damaged pump. Based on previous experience by staff at this facility with respect to the spawning and holding of adult paddlefish and pallid sturgeon, OTI treatment was considered to be efficacious (Table 1).

## **3. Observed Toxicity**

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

### **Summary of Study Results**

Oxytetracycline as an injectable was used at dosages of 20 and 25 mg/kg body weight and was administered as a single injection. Trials involved the prophylactic treatment of paddlefish and pallid sturgeon broodstocks at a U.S. Fish and Wildlife Service National Fish Hatchery, and to control mortality caused by furunculosis in chinook salmon broodstocks at one state hatchery. A total of 146 adult fish were treated. Water temperature during treatment ranged from 50.0 - 65.0°F, with a mean trial treatment temperature of 57.5°F. All trials conducted in CY 2000 appeared to be efficacious. Determination of efficacy was based primarily on previous years' experiences at the hatcheries indicating significant post-spawning mortality of untreated fish, and on the decrease in mortality after treatment. Furthermore, Investigators reported no evidence of toxicity or adverse effects related to OTI treatment. However, based on a lack of untreated control fish, replication, randomization, etc., it is understood that these data can only be considered as ancillary data. None-the-less, the ancillary data described above should provide useful corroborative data to support a future expanded label claim for oxytetracycline. It is anticipated that additional ancillary efficacy data will continue to be collected under INAD #9027. In future trials conducted under INAD 9027, efforts will be directed towards the generation of higher quality data.

**Table 1. Summary of CY 2000 Oxytetracycline-Injectable Efficacy Results (note: all studies appeared efficacious)**

Hatchery	Number of Trials	Fish Species	Number of Fish	Treatment type	Number of treatments	Dose (mg/kg bw)	Temp. (°C)
Natchitoches NFH	1	PAH	38	Prophylactic	1	25	65.0
	1	PLS	68	Prophylactic	1	25	65.0
Elmendorf Hatchery	1	CKS	40	Therapeutic	1	20	50.0

**Table 2. Summary Data Regarding 2000 Oxytetracycline as an Injectable Efficacy Studies**

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<b>Total Number of Fish Treated:</b>	146
<b>Treatment Regimes Used:</b>	
20 mg/kg body weight (1 time)	1 trial
25 mg/kg body weight (1 time)	2 trial
<b>Treatment Water Temperature (°C):</b>	50 - 65
<b>Size of Treated Fish:</b>	Adult
<b>Species Treated:</b>	paddlefish ( <i>Polydon spathula</i> ) pallid sturgeon ( <i>Scaphirhynchus albus</i> ) chinook salmon ( <i>Oncorhynchus tshawytscha</i> )

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