

Oxytetracycline Medicated Feed Clinical Field Trials - INAD 9332

Year 2005 Annual Summary Report on the Use of Oxytetracycline Medicated Feed as a Marking Agent in Field Efficacy Trials

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Summary

Oxytetracycline medicated feed (OTF-M) has been shown to be an effective and convenient agent for marking skeletal tissue of early life stages of fish. Large numbers of young fish can be marked simultaneously by feeding fish a standard dosage of OTF-M for a period ranging up to 14 d. In many cases, OTF-M is the only viable option, other than immersion marking with water-soluble oxytetracycline, for permanently marking large numbers of small fish for the purpose of evaluating fishery management strategies. Oxytetracycline medicated feed has been approved for use in aquaculture for limited therapeutic uses and for marking skeletal tissue in Pacific salmon in the United States by the U.S. Food and Drug Administration (FDA). For uses other than those for which OTF-M is approved, the FDA has authorized its use under Compassionate Investigational New Animal Drug (INAD) Exemption #9332 for the purpose of collecting pivotal and ancillary clinical field data on OTF-M for the marking skeletal tissue in a variety of salmonid species. Five such trials were conducted at one

state fish hatchery involving two species and approximately 0.38 million fish under INAD #9332 during calendar year 2005 (CY05). Efficacy was determined by whether or not a “readable” mark could be observed on skeletal tissue of treated fish. Standard treatment regimens allowed under the INAD included the use of OTF-M at 2.5 - 3.75 g/100 lbs fish/d for 11 d; and 10.0 g/100 lbs fish/d for 13 - 14 d. Overall results of trials conducted in CY05 showed that all of the trials appeared efficacious.

Introduction

The current U. S. Food and Drug Administration (FDA) approved label for OTF-M in aquaculture limits its use to marking of skeletal tissue in Pacific salmonids using the following treatment regimen: administer at dosages of 250 mg/kg of fish/d (i.e., 11.4 g OTF-M/100 lbs fish/d) for 4 d in salmon less than 30 gm followed by a 7 d withdrawal period. These label restrictions severely limit the overall utility of approved OTF-M use in aquaculture.

Historically, fish culturists have reported that OTF-M treatment is a useful tool for marking the skeletal tissue in rainbow and cutthroat trout, and kokanee salmon when treated at a size in which fish body weight does not exceed 2 gms. Marks were visible on skeletal tissue of fish immediately after the treatment period, and had still been visible for several months afterwards. In addition, studies have been conducted in which different OTF-M drug dosages were used to mark skeletal tissue of test fish. Summary conclusions from such studies indicated that not only did various dosages of

OTF-M effectively mark skeletal tissue, but there were also no evidence of any toxic or adverse effects to the fish.

Purpose of Report

The primary purpose of this report is to summarize the results of CY05 supplemental OTF-M field efficacy studies. Furthermore, it is expected that data from these studies will be used to enhance the existing OTF-M database that has been established from previous years studies for the purpose of expanding and/or extending the approved label for OTF-M.

Facilities, Materials, and Treatment Procedures

1. Participating Facilities

OTF-M was used under INAD #9332 during CY05 to mark skeletal tissue of test fish in five trials conducted at one state fish hatchery. Water temperature during treatments at these testing facilities ranged from 55.0 - 58.0 °F, with a mean treatment temperature of 57.4 °F.

2. OTF-M used in efficacy trials

The OTF-M used was either Terramycin 100 or Terramycin 100D, both of which contained 100 g active oxytetracycline quaternary salt per pound of premix. All Terramycin 100/100D was supplied by Pfizer, Inc., 1107 South 291 Highway,

Lee's Summit, MO. All OTF-M was prepared with Pfizer brand product by one of several commercial fish feed manufacturers (e.g., Nelson and Sons, Inc., Rangen Inc.)

3. Drug dosages and duration

As described in the Study Protocol for INAD #9332, Investigators were allowed to use OTF-M either within the current label range of 2.5 - 3.75 gm of active drug per 100 lbs of fish/d for 11 d (1 of 5 studies used this treatment regimen), or at 10.0 gm of active drug per 100 lbs of fish/d for 13 - 14 d (4 of 5 studies used this treatment regimen).

Fish Species Involved in CY05 Efficacy Trials

1. Species of fish treated

Two salmonid species were treated during CY05. Treated fish ranged in length from 2.8 - 4.6 in. A total of approximately 0.38 M test fish were treated during this period. Species treated included:

(1) rainbow trout *Oncorhynchus mykiss*

(2) kokanee salmon *O. nerka*

2. Marking

Fish were treated with OTF-M to provide a readable mark on skeletal tissue.

Data Collected

1. Pathologist's reports

No pathology reports were submitted during CY05 studies.

2. Efficacy of marking procedure

Samples of treated fish were collected, processed, and evaluated for a mark on skeletal tissue using standard procedures.

Discussion of Study Results:

- 1. General observations on the efficacy of OTF-M for marking of skeletal tissue of salmonids** - Efficacy was determined by whether or not a “readable” mark could be observed on skeletal tissue of treated 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 #9332).

- A. Efficacy at 2.5 - 3.75 g/100 lbs fish/d for 11 d at water temperatures above 48.2° F**

OTF-M was used at 2.5 - 3.75 g/100 lbs of fish/d for 11 d in 1 trial involving kokanee salmon (Table 1). Results from this trials indicated that treatment was efficacious.

B. Efficacy at 10g/100lbs fish/d for 13 - 14 d at water temperatures above 48.2°F

OTF-M was used at 10 g/100lbs fish/d for 13 - 14 d in four trials involving rainbow trout (Table 1). Results from these trials indicated that all treatments were efficacious.

2. Observed Toxicity

No toxicity or adverse effects relating to OTF-M treatments were reported in any of the trials conducted in CY05.

Summary of Study Results

Oxytetracycline medicated feed was used to mark skeletal tissue of test fish at dosages ranging from 2.50 to 10.0 g/100lbs fish/d for durations ranging from 11 to 14 d. Two different salmonid species were treated with OTF-M in five trials, and trials involved approximately 0.38 million fish. Treated fish ranged in size from 2.8 - 4.6 in. Overall mean water temperature during treatments was 57.4 °F (range, 55.0 - 58.0 °F). None of the trials included a pathologist's report documenting health of test fish prior to or after treatment. Overall results of trials conducted in CY05 showed that all of the trials appeared effective in creating a readable mark on the skeletal tissue of the treated fish in all trials. Furthermore, Investigators reported no evidence of toxicity or adverse

effects related to OTF-M treatment. However, based on a general lack of untreated control fish, replication, randomization, etc., it is understood that these data will only be considered as ancillary data. None-the-less, the ancillary data described in this report should provide useful corroborative data to support a future expanded label claim for OTF-M. It is anticipated that additional ancillary skeletal tissue marking efficacy data will continue to be collected under INAD #9332. In future trials conducted under INAD #9332 for the purpose of marking fish, efforts will be directed towards the generation of higher quality data.

Table 1. Summary of CY05 Oxytetracycline Medicated Feed Efficacy Results - Efficacious Studies

Hatchery	Number of Trials	Fish Species	Fish Size (inches)	Fish Number	Use of Feed	Dose (g/100 lbs)	Treatment Duration (days)	Temp. (°F)
Big Springs Trout SFH	1	KOE	2.80	220,000	Marking	2.50 - 3.75	11	55.0
Big Springs Trout SFH	4	RBT	3.1 - 4.6	158,000	Marking	10	13 - 14	58.0

Table 2. Summary Data Regarding CY05 OTF-M Efficacy Studies

Total Number of Fish Treated:	<u>378,000</u>	
Number of fish in efficacious studies	378,000	
Total number of studies:	5	
Number of efficacious studies	5	
Treatment Regimens Used:		
2.5 - 3.75 g/100 lbs fish/day for 11 days (above 48.2°F)		1 trial
10.0 g/100 lbs fish/day for 13 -14 days (above 48.2°F)		4 trials
Treatment Water Temperature (°F):		
Temperature Range	55.0 - 58.0	
Mean Temperature	57.4	
Size of Treated Fish (in.):		
Size Range	2.8 - 4.6	
Species Treated:		
rainbow trout <i>Oncorhynchus mykiss</i>		
kokanee salmon <i>O. nerka</i>		