

Oxytetracycline Immersion Clinical Field Trials - INAD 9033

2001 Annual Summary Report on the Use of Oxytetracycline Immersion Therapy in Field Efficacy Trials

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Summary

A number of Investigational New Animal Drug (INAD) trials were conducted in calendar year (CY) 2001 to evaluate the efficacy of oxytetracycline for immersion therapy (OIT) to control mortality in fish caused by bacterial diseases. Twenty-four such trials that involved approximately 236,000 fish were conducted at one private hatchery during this period. The U.S. Food and Drug Administration has authorized the use of OIT under Compassionate Investigational New Animal Drug Exemption #9033 for the purpose of collecting 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 all trials conducted during CY 2001 appeared efficacious.

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 oxytetracycline for immersion therapy (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 2001 supplemental oxytetracycline for immersion therapy (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 expanding and/or extending the approved label for OIT use in aquaculture.

Facilities, Materials, and Methods

1. Participating Facilities

One private fish hatchery (Stolt Sea Farm California, LLC) used OIT during CY 2001.

2. Oxytetracycline used in trials

All oxytetracycline used in CY 2001 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 CY 2001.

3. Drug dosages

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

Fish Species

1. Species of fish treated

Early life-stages (i.e., 2 - 8" total length) of white sturgeon *Acipenser transmontanus* were the only test fish treated with OIT during CY 2001.

2. Diseases treated

Test fish were treated with OIT to control mortality caused by external columnaris.

Data Collected

A summary of all OIT efficacy trials conducted during CY 2001 under INAD #9033 are listed in Table 3.

1. Pathologists Reports

Fish health pathology reports provide essential information with respect to disease confirmation and general fish health. However, no pathology reports were submitted for CY 2001 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.

In OIT efficacy trials conducted in CY 2001, the Investigator recorded mortality daily during the treatment period and for at least the first 4 days of the post-treatment period.

Discussion of Study Results

1. Summary results on the efficacy of OIT to control mortality caused by columnaris.

Twenty-four trials in which white sturgeon, presumptively diagnosed with columnaris, were treated with the standard dosage of OIT. All trials appeared efficacious.

2. Observed Toxicity

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

Summary of Study Results

OIT was used at the standard dosage in 24 trials to control mortality of white sturgeon caused by columnaris. A total of 236,600 early life stage fish (2 - 8" in length) were treated. Water temperature during treatment was 68 - 70.0° F. All trials appeared efficacious. The Investigator reported no evidence of toxicity or adverse effects related to OIT treatment. Although these data must be considered as ancillary efficacy data, they should provide useful corroborative data to support a future expanded 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 2001 Oxytetracycline Immersion Efficacy Results

| Hatchery | Number of Trials | Fish Species | Number of Fish | Treatment type | Treatment Duration (hrs) | Dose (mg/L) | pH | Dissolved Oxygen | Temp. (°F) |
|--------------------------------|------------------|--------------|----------------|----------------|--------------------------|-------------|-----------|------------------|------------|
| Stolt Sea Farm California, LLC | 24 ¹ | WHS | 236,600 | Therapeutic | 1 | 20 | 6.7 - 6.8 | 8.0 - 9.0 | 68 - 70 |

¹All trials appeared efficacious.

Table 2. Summary Data Regarding CY 2001 Oxytetracycline for Immersion Efficacy Trials

Total Number of Trials Conducted: 24

Number of efficacious trials: 24

Total Number of Fish Treated: 236,600

Treatment Regimes Used:

20 mg/L static bath for 1 hr

Treatment Water Temperature (°F):

68.0 - 70.0

Size of Treated Fish:

2" - 8"

Species Treated:

white sturgeon *A. transmontanus*
