Oxytetracycline Immersion Clinical Field Trials - INAD 9033

2000 Annual Summary Report on the Use of Oxytetracycline Immersion in Field Efficacy Trials

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Summary

Oxytetracycline for immersion was used at only one private fish hatchery during the year 2000 to evaluate its efficacy to control mortality caused by columnaris in white sturgeon. The U.S. Food and Drug Administration has authorized the use of this compound 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 oxytetracycline. Oxytetracycline for immersion was administered in 5 studies and involved a total of 110,750 fish. Approximately 40% of the studies appeared efficacious, while 60% were characterized as inconclusive.

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 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. An immersion drug product can effectively prevent losses in a variety of cultured fish species. 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 immersion therapy 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 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 with respect to a number 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 purpose of this report is to summarize the results of calendar year (CY) 2000 supplemental oxytetracycline for immersion (OXIM) field efficacy studies. However, it is also expected that these data will be used to enhance the existing OXIM 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

Only a single private fish hatchery (Stolt Sea Farm California, LLC) used OXIM during CY 2000.

2. Oxytetracycline used in trials

All oxytetracycline used in these 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.

3. Drug dosages

As described in the Study Protocol for INAD #9033, oxytetracycline was administered as a single bath treatment for 1 hour at a dosage of 20 mg/L.

Fish Species

1. Species of fish treated

Only one fish species, the white sturgeon (*Acipenser transmontanus*), was treated during CY 2000.

2. Diseases treated

All fish were treated therapeutically to control external columnaris and bacterial gill disease.

Data Collected

A summary of all OXIM studies conducted during CY 2000 under INAD #9033 is presented in Table 1.

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 during CY 2000 studies.

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. The Investigator did not record daily mortalities for every treatment; however, comments/observations were made on treatment days.

Discussion of Study Results

1. Summary results on the efficacy of OXIM for control of columnaris and bacterial gill disease.

A total of 5 studies (104 outbreaks) of presumptively diagnosed cases of columnaris or bacterial gill disease were treated with 20 mg/L of oxytetracycline. Approximately 40% of the studies appeared efficacious, while 60% were characterized as inconclusive in controlling mortality in white sturgeon. The Investigator noted that symptoms of viral infections can mimic bacterial infection, and that the bacterial infections often occurred as secondary infections.

2. Observed Toxicity

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

Summary of Study Results

OXIM was used as a single bath treatment for 1 hour at a dosage of 20 mg/L in 5 studies involving white sturgeon. A total of 110,750 early life stage fish (2 - 8" in length) were treated. Water temperature during treatment was 68 - 70.0^{o} F. Approximately 40% of the studies appeared efficacious, while 60% were characterized as inconclusive in controlling mortality in white sturgeon. Trials were characterized as inconclusive due to lack of mortality data and the presence of secondary infections. Investigators reported no evidence of toxicity or adverse effects related to OXIM 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 oxytetracycline. 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 2. Summary of CY 2000 Oxytetracycline Immersion Efficacy Results

Hatchery	Number of Studies	Fish Species	Number of Fish	Treatment type	Treatment Duration (hrs)	Dose (mg/L)	pH	Dissolved Oxygen	Temp. (ºF)
Stolt Sea Farm California, LLC	5[1]	WHS	110,750	Therapeutic	1	20	6.8 - 7.0	7.0 - 9.0	68 - 70

[1]Two studies appeared to be efficacious, while results of 3 studies were inconclusive.

Table 3. Summary Data Regarding CY 2000 Oxytetracycline for Immersion Efficacy Studies

Total Number of Fish Treated: 110,750

Treatment Regimes Used:

20 mg/L static bath for 1 hr 5 studies

Treatment Water Temperature (ºF): 68.0 - 70.0

Size of Treated Fish: 2" - 8"

Species Treated: white sturgeon (*Acipenser transmontanus*)