

# **Oxytetracycline (Terramycin® 200 for Fish) Medicated Feed Clinical Field Trials - INAD 8069**

## **Year 2013 Annual Summary Report on the Use of Oxytetracycline (Terramycin® 200 for Fish) Medicated Feed in Field Efficacy Trials**

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### **Summary**

Oxytetracycline (Terramycin® 200 for Fish) medicated feed has been used effectively in the U. S. under compassionate INAD Exemption #8069 to control mortality in marine penaeid shrimp caused by common bacterial diseases. In calendar year 2013 (CY13) the efficacy of oxytetracycline (Terramycin® 200 for Fish) medicated feed (OTFS) was evaluated in two trials involving 9.5 million shrimp to control mortality caused by necrotizing hepatopancreatitis. Trials were conducted at one private facility. The compassionate study protocol under which treatments were administered allowed the investigator to use OTFS at a dosage of 4.5 g OTC/kg feed/day for 14 days. Overall, results of trials conducted in CY13 indicated that treatments appeared to be efficacious in both trials.

## Introduction

In addition to the use patterns listed on the current label, oxytetracycline has often been the drug of choice when diagnostic evidence shows that penaeid shrimp populations (marine shrimp of the genera *Litopenaeus*, *Penaeus* and *Farfantepenaeus*) are afflicted with vibriosis, necrotizing hepatopancreatitis (NHP) or other bacterial diseases. Discounting viral diseases, the two most important maladies of shrimp are caused by bacteria of the genus *Vibrio*, and the unclassified Gram-negative, pleomorphic, intracellular Alphaproteobacterium (the etiological agent of NHP).

Integrated aquatic animal health management practices usually prevent the occurrence of these diseases. However, adverse environmental conditions, physiological changes associated with molting or spawning, uncontrollable water conditions and unforeseen factors can lead to severe disease outbreaks requiring prompt treatment to prevent significant losses. Such treatment also reduces the discharge of infectious agents into the natural environment thereby reducing the spread of disease.

Treatment strategies for the use of Oxytetracycline (Terramycin® 200 for Fish; hereafter referred to as TM200) in penaeid shrimp shall be designed to meet the needs of each species or lot, the size and numbers of shrimp to be treated, the layout of the facility, and environmental conditions. In all cases, the objective shall be to minimize the impacts of disease on shrimp health, shrimp quality and survival, and to fully meet aquaculture objectives. Because there are many factors that can affect the success or

failure of TM200 therapy, data are needed to determine the best ways to use the drug to obtain effective disease control in route to developing an extended label claim. These data should provide valuable information with respect to potential OTFS use patterns in aquaculture.

### **Purpose of Report**

The purpose of this report is to summarize the results of CY13 OTFS field efficacy trials conducted under INAD #8069. Furthermore, it is expected that data from these trials will be used to enhance the existing OTFS database that has been established from studies conducted in previous years for the purpose of expanding and/or extending the approved label for OTFS.

### **Facilities, Materials, and Treatment Procedures**

#### **1. Facilities**

Two trials were conducted at one private facility. Water temperature during treatments ranged from 86.0 - 88.0°F, with a mean treatment temperature of 87.0°F.

#### **2. Test article used**

The OTFS used in CY13 efficacy trials was Terramycin® 200 which contained 200 g active oxytetracycline (from oxytetracycline dihydrate) per pound of Type A Medicated Article. All Terramycin® 200 was supplied by Phibro Animal Health, 75 Challenger Road Ridgefield Park, NJ. OTFS was prepared with Phibro brand

product by one of several commercial fish feed manufacturers (e.g., Nelson and Sons, Inc., Rangen Inc.).

### **3. Treatment regimen**

As described in the Study Protocol, Investigators were allowed to use OTFS at a dosage of 4.5 g OTC/kg feed/day for 14 days. Deviations did occur to the number of treatment days in both trials. In one trial shrimp were treated between 8 and 10 days due to a decline in water quality. In the other trial shrimp were fed the 14 day treatment over a 19 day period due to poor water quality issues.

## **Shrimp Species and Shrimp Diseases Involved in CY13 Trials**

### **1. Species of shrimp treated**

The Pacific white shrimp was the only shrimp species treated during CY13. Treated shrimp ranged in weight from 8.0 - 16.0 g

### **2. Disease treated**

Shrimp were treated with OTFS to control mortality caused by necrotizing hepatopancreatitis.

## **Data Collected**

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

No pathologist's reports were submitted for either of these studies. Pathology reports are important for accurate interpretation of study results because they typically contain the following information:

- A. A description of how the identity of disease agent(s) was verified,
- B. Disease identification records that confirm the presence of the disease agent,
- C. The name and title of the individual performing the diagnosis.

Additionally, evidence would typically be provided to document that there were no secondary infections or infestations caused by unrelated disease agents in the population of test fish. As a result, pathology reports provide essential information if efforts are to expand/extend an existing approved label.

### **2. Treatment response and drug accountability data**

Drug receipt reports, drug use reports, diagnosis, treatment, and mortality reports (including adverse effects/toxicity observations), and shrimp disposition reports were prepared by study investigators. Such reports were routed through the online INAD database for the study monitor to review, and then send to the AADAP Office for review, data analysis and report writing, and archiving in permanent files.

## **Discussion of Study Results:**

- 1. General observations on the efficacy of OTFS for the control of bacterial diseases in shrimp species** (Note: Table 1 provides a summary of all trials characterized as effective; and Table 2 provides summary data for all trials conducted during CY13 under INAD #8069).

### **A. Efficacy at 4.5 g OTC/kg feed/day for 8 - 14 days**

Pacific white shrimp were treated with 4.5 g OTC/kg feed/day for 8 - 14 days in two trials (Table 1). Investigators used OTFS to control mortality caused by necrotizing hepatopancreatitis. OTFS treatments appeared effective in both trials.

## **2. Observed Toxicity**

No toxicity or adverse effects relating to OTFS treatment were reported in any of the trials conducted in CY13.

## **3. Observed Withdrawal Period**

All withdrawal times were either met or exceeded.

## **Current Study Protocol for Oxytetracycline (Terramycin® 200 for Fish) INAD #8069**

No changes have occurred to the current study protocol for Oxytetracycline (Terramycin® 200 for Fish) INAD #8069.

### **Facility Sign-up List**

Please see “Table 3. Facilities and Names of Investigators” for facilities that signed-up to participate in the Oxytetracycline (Terramycin® 200 for Fish) INAD #9332 during CY13. Please note this facility is in compliance with their reporting requirements to the NPDES authority.

### **Correspondence sent to Oxytetracycline (Terramycin® 200 for Fish) Participants**

Please see the attached correspondence that was sent to all Oxytetracycline (Terramycin® 200 for Fish) participants after the AADAP Office received their sign-up form for CY13.

### **Number of Treated Shrimp under Treatment Use Authorization**

Total number of shrimp treated during CY13 was 9,500,000. The total number of treated fish to count against the Oxytetracycline (Terramycin® 200 for Fish) treatment use authorization dated August 15, 2003 is 45,958,800.

### **Summary of Study Results**

Oxytetracycline (Terramycin® 200 for Fish) medicated feed was used at 4.5 g OTC/kg feed/day for 8 - 14 days. Treatment trials involved one shrimp species and 9,500,000 shrimp. Treated shrimp ranged in weight from 8.0 - 16.0 g. Water temperature during treatment ranged from 86.0 - 88.0 °F. Overall results showed that

treatment appeared to be efficacious in both trials. No evidence of toxicity or adverse effects related to OTFS treatment were reported in any of the trials. However, based on a general lack of untreated control animals, replication, randomization, etc., it is understood that these data will only be considered as supportive or ancillary data. None-the-less, the data described above should provide useful corroborative data to support a future expanded label claim for OTFS for this disease indication. It is anticipated that additional ancillary efficacy data will continue to be collected under INAD #8069. In future trials conducted under this INAD, efforts will continue to be directed towards the generation of high quality data.

**Table 1. Summary of CY 2013 OTFS Treatment Results - Efficacious Trials**

Hatchery	Number of Trials	Shrimp Species	Fish Size (g)	Number of Shrimp	Disease	Dose (g OTC/kg feed/day )	Number of Treatment Days	Temp. (°F)
Kappa Aquafarms	2	PWS	8.0 - 16.0	9,500,000	necrotizing hepatopancreatitis	4.5	8 - 14	86.0 - 88.0

**Table 2. Summary Data Regarding Summary of CY 2013 OTFS Treatment Trials**

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<b>Total Shrimp Treated:</b>		<b><u>9,500,000</u></b>
Number of fish treated in efficacious trials		9,500,000
<b>Total number of trials:</b>		<b>2</b>
Efficacious trials	2	
<b>Treatment Regimens Used:</b>		
4.5 g OTC/kg feed/day for 8 - 10 days		1 trial
4.5 g OTC/kg feed/day for 14 days		1 trial
<b>Treatment Water Temperature (°F):</b>		
Temperature Range	86.0 - 88.0	
<b>Size of Treated Fish (g.):</b>		
Size Range	8.0 - 16.0	
<b>Shrimp Species Treated:</b>		
Pacific white shrimp		