

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

**Year 2010 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 2010 (CY10) the efficacy of oxytetracycline (Terramycin® 200 for Fish) medicated feed (OTFS) was evaluated in three trials involving 28,400 shrimp to control mortality caused by vibriosis. Trials were conducted at one university research 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 CY10 indicated that treatments appeared to be efficacious in approximately 67% of the trials and were characterized as inconclusive in 33% of the 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 CY10 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**

Three trials were conducted at one university research facility. Water temperature during treatments ranged from 79.9 - 84.3 °F, with a mean treatment temperature of 82.8°F.

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

The OTFS used in CY10 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. All trials followed this treatment regimen.

## **Shrimp Species and Shrimp Diseases Involved in CY10 Trials**

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

The Pacific white shrimp was the only shrimp species treated during CY10. Treated shrimp ranged in weight from 17.0 - 25.0 g. and the average weight of all treated shrimp was 21.3 g.

### **2. Disease treated**

Shrimp were treated with OTFS to control mortality caused by vibriosis.

## **Data Collected**

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

A pathologist's report was submitted for 100% of the 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 study monitor for review, and then sent to the AADAP Office for review, data analysis and report writing, entering data into a database, 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; Table 2 provides a summary of all trials characterized as inconclusive ; Table 3 provides summary data for all trials; Table 4 provide a summary of all trials conducted during CY10 under INAD #9332).

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

Pacific white shrimp were treated with 4.5 g OTC/kg feed/day for 14 days in three trials (Tables 1 - 2). Investigators used OTFS to control mortality caused by vibriosis. OTFS treatments appeared effective in two trials and was characterized as inconclusive in one trial.

## **2. Observed Toxicity**

No toxicity or adverse effects relating to OTFS treatment were reported in any of the trials conducted in CY10.

## **3. Observed Withdrawal Period**

All withdrawal times were either met or exceeded.

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

Please see the attached current study protocol for Oxytetracycline (Terramycin® 200 for Fish) INAD #8069 . Please note no changes have occurred to this study protocol.

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

Please see “Table 5. Facilities and Names of Investigators” for facilities that signed-up to participate in the Oxytetracycline (Terramycin® 200 for Fish) INAD #9332 during CY10. 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 CY10.

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

Total number of shrimp treated during CY10 was 28,400. The total number of treated fish to count against the Oxytetracycline (Terramycin® 200 for Fish) treatment use authorization dated August 15, 2003 is 36,528,400.

## **Summary of Study Results**

Oxytetracycline (Terramycin<sup>®</sup> 200 for Fish) medicated feed was used at 4.5 g OTC/kg feed/day for 14 days. Treatment trials involved one shrimp species and 28,400 shrimp. Treated shrimp ranged in weight from 17.0 - 25.0 g. Water temperature during treatment ranged from 79.9 - 84.3 °F, with a mean treatment temperature of 82.8 °F. Overall results showed that treatment in approximately 67% of trials appeared to be efficacious while treatment in 33% was characterized as inconclusive. 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 2010 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)
AgriLife Research Mariculture Lab	2	PWS	17.0 - 25.0	6,400	Vibriosis	4.5	14	79.9 - 84.3

**Table 2. Summary of CY 2010 OTFS Treatment Results - Inconclusive 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)
AgriLife Research Mariculture Lab	1	PWS	22.00	22,000	Vibriosis	4.5	14	84.1

**Table 3. Summary Data Regarding Summary of CY 2010 OTFS Treatment Trials**

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<b>Total Shrimp Treated:</b>		<b><u>28,400</u></b>
Number of fish treated in efficacious trials		6,400
Number of fish treated in inconclusive trials		22,000
<b>Total number of trials:</b>		<b>3</b>
Efficacious trials		2 (67%)
Inconclusive trials		1 (33%)
<b>Treatment Regimens Used:</b>		
4.5 g OTC/kg feed/day for 14 days		3 trials
<b>Treatment Water Temperature (°F):</b>		
Temperature Range	79.9 - 84.3	
Average Temperature	82.8	
<b>Size of Treated Fish (g.):</b>		
Size Range	17.0 - 25.0	
Average Weight	21.3	
<b>Shrimp Species Treated:</b>		
Pacific white shrimp		