

**STUDY PROTOCOL FOR AN AQUACULTURE INVESTIGATIONAL NEW  
ANIMAL DRUG (INAD) EXEMPTION FOR OXYTETRACYCLINE  
(TERRAMYCIN® 200 for Fish) MEDICATED FEED (INAD #9332)**

**Sponsor:**

U.S. Fish and Wildlife Service, Fish and Aquatic Conservation

\_\_\_\_\_  
Sponsor Signature

\_\_\_\_\_  
Date Approved

**Manufacturer:**

Phibro Animal Health Cooperation  
Glenpointe Centre East, 3<sup>rd</sup> Floor  
300 Frank W. Burr Blvd., Ste. 21  
Teaneck, NJ 07666 USA

**Office for Coordination of Terramycin® 200 for Fish INAD:**

Aquatic Animal Drug Approval Partnership Program  
4050 Bridger Canyon Road  
Bozeman, Mt 59715

Proposed Starting Date: April 1, 2008  
Proposed Ending Date: December 31, 2026  
Study Director: Ms. Bonnie Johnson

**Clinical Field Trial Location:**

Facility \_\_\_\_\_  
Type or Print Name

Investigator \_\_\_\_\_  
Type or Print Name

## TABLE OF CONTENTS

I. STUDY ID AND TITLE:.....	4
II. SPONSOR:.....	4
III. INVESTIGATORS/FACILITIES:.....	4
IV. PROPOSED STARTING AND COMPLETION DATES:.....	5
V. BACKGROUND/PURPOSE:.....	5
VI. SPECIFIC OBJECTIVES:.....	6
VII. MATERIALS:.....	7
VIII. EXPERIMENTAL UNIT.....	10
IX. ENTRANCE CRITERIA.....	10
X. TREATMENT GROUPS.....	12
XI. TREATMENT SCHEDULES.....	12
XII. TREATMENT RESPONSE PARAMETERS.....	14
XIII. FORMS FOR DATA COLLECTION.....	15
XIV. RECORD KEEPING PROCEDURES.....	16
XV. DISPOSITION OF INVESTIGATIONAL ANIMALS.....	16
XVI. DISPOSITION OF INVESTIGATIONAL DRUG.....	17
XVII. DATA HANDLING, QUALITY CONTROL, MONITORING, ADMINISTRATIVE RESPONSIBILITIES.....	17
XVIII. PLANS FOR DATA ANALYSIS.....	18
XIX. PROTOCOL AND PROTOCOL AMENDMENTS.....	18
XX. PROTOCOL DEVIATIONS.....	19
XXI: E.O. 13891.....	19
LITERATURE CITED.....	19
APPENDIX I.....	20
APPENDIX II.....	21
APPENDIX IIIA.....	22
APPENDIX IIIB.....	23
APPENDIX IV.....	24
APPENDIX V.....	25
APPENDIX VIA.....	26
APPENDIX VIB.....	27
ALL DATA MUST BE ENTERED THROUGH THE ONLINE INAD DATABASE:.....	28
FORM OTC-W: WORKSHEET.....	29
FORM OTC-1. REPORT ON RECEIPT OF DRUG.....	31

FORM OTC-2A. CHEMICAL USE LOG.....	32
FORM OTC-2B. CHEMICAL USE LOG.....	33
FORM OTC-3A: RESULTS REPORT FORM.....	34
FORM OTC-3B: RESULTS REPORT FORM.....	38

## STUDY PROTOCOL FOR AN AQUACULTURE INVESTIGATIONAL NEW ANIMAL DRUG (INAD) EXEMPTION FOR TERRAMYCIN® 200 FOR FISH MEDICATED FEED UNDER INAD #9332

### I. STUDY ID AND TITLE:

Clinical field trials to determine the efficacy of Terramycin® 200 for Fish when fed as a medicated feed to 1) control mortality caused by bacterial diseases in a variety of freshwater and marine fish species; and 2) mark skeletal tissue in a variety of freshwater and marine fish species. **Note: No clinical field trials will be conducted under this INAD for use patterns for which Terramycin® 200 for Fish has already received FDA-approval (e.g., treatment of ulcer disease, furunculosis, bacterial hemorrhagic septicemia, or pseudomonas disease in salmonids; treatment of bacterial hemorrhagic septicemia or pseudomonas disease in catfish; treatment of gaffkemia in lobster; treatment of coldwater disease in freshwater-reared salmonids; treatment of columnaris disease in freshwater-reared *Oncorhynchus mykiss*; marking Pacific salmon; and marking freshwater-reared salmonids weighing up to 55 grams (NADA 038-439)).**

### II. SPONSOR:

Dr. Marilyn Blair, U.S. Fish and Wildlife Service, Branch Chief, Aquatic Animal Drug Approval Partnership Program, 4050 Bridger Canyon Road, Bozeman, MT 59715; Phone: 406-994-9904; Fax: 406-582-0242; Email: [marilyn\\_j\\_blair@fws.gov](mailto:marilyn_j_blair@fws.gov)

**Manufacturer:** Phibro Animal Health Corporation  
Glenpointe Centre East, 3<sup>rd</sup> Floor  
300 Frank W. Burr Blvd., Ste. 21  
Teaneck, NJ 07666 USA

**Contact:** Sean Parker  
Phone: 201-329-7377  
Email: [sean.parker@pahc.com](mailto:sean.parker@pahc.com)

**Study Director:** Ms. Bonnie Johnson, U.S. Fish and Wildlife Service, Aquatic Animal Drug Approval Partnership (AADAP) Program, 4050 Bridger Canyon Road, Bozeman, MT 59715; Phone: 406-994-9905; Email: [bonnie\\_johnson@fws.gov](mailto:bonnie_johnson@fws.gov)

**Principal Clinical Field Trial Coordinator:** Ms. Paige Maskill, USFWS – AADAP Program  
4050 Bridger Canyon Road, Bozeman, MT 59715;  
Phone: 406-994-9911; Email: [paige\\_maskill@fws.gov](mailto:paige_maskill@fws.gov)

**Study Monitors:** See Appendix II for names and addresses.

### I. INVESTIGATORS/FACILITIES:

See Appendix IIIa for names and addresses.

**IV. PROPOSED STARTING AND COMPLETION DATES:**

Reauthorization Starting Date: April 1, 2008

Reauthorization Expiration Date: December 31, 2026

**V. BACKGROUND/PURPOSE:**

Terramycin® 200 for Fish is currently approved in the United States for treatment of ulcer disease, furunculosis, bacterial hemorrhagic septicemia, or pseudomonas disease in salmonids; treatment of bacterial hemorrhagic septicemia or pseudomonas disease in catfish; treatment of gaffkemia in lobster; treatment of coldwater disease in freshwater-reared salmonids; treatment of columnaris disease in freshwater-reared *Oncorhynchus mykiss*; marking Pacific salmon; and marking freshwater-reared salmonids weighing up to 55 grams (NADA 038-439). If your treatment is for an approved use then the INAD will not be used.

In addition to the use patterns listed on the current label, Oxytetracycline historically has often been the drug of choice when diagnostic evidence shows salmonids to have enteric redmouth (ERM) caused by *Yersinia ruckeri*; flavobacteriosis caused by *Flavobacter columnaris*, *Flavobacter psychrophilus*, or closely related yellow pigmented gliding bacteria as described in U. S. Food and Drug Administration Public Master File #5456; or, vibriosis caused by *Vibrio anguillarum*, *Vibrio ordalli* or other closely related bacteria. Oxytetracycline also has been useful for the control of bacterial hemorrhagic septicemia caused by *Aeromonas hydrophila* and other closely related bacteria, pseudomonas disease caused by *Pseudomonas* sp., or flavobacteriosis in several other families of fishes including sturgeons, pikes, sunfishes (bass), and perches.

In recent years, studies have shown evidence that Oxytetracycline may be effective in controlling bacterial kidney disease (BKD) caused by *Renibacterium salmoninarum* (John Cvitanich, 1995 personal communication). Additional clinical field trials are needed to follow up on this lead.

Integrated fish health management practices usually prevent the occurrence of these diseases. However, adverse environmental conditions, physiological changes related to smoltification or the onset of spawning, uncontrollable water conditions, and unforeseen factors can lead to severe disease outbreaks requiring prompt treatment to prevent significant losses in excess of 50 percent of fish in public, tribal and private aquaculture. 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) in fish shall be designed to meet the needs of each species or lot, the size and numbers of fish 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 fish health, fish quality and survival, and to fully meet fishery management or aquaculture objectives. Because there are many factors that can affect the success or failure of Terramycin® 200 for Fish therapy, data is needed to determine the best ways to use the drug to obtain effective disease control enroute to developing an extended label claim. Complete documentation of studies that are well conceived and well carried out will be of great value.

The primary purpose of this Investigational New Animal Drug (INAD) exemption application is to obtain additional clinical field trial data to demonstrate the efficacy and target animal safety of Terramycin® 200 for Fish therapy to control mortality caused by bacterial diseases of freshwater and marine fish that may occur in a variety of environmental conditions, at a wide range of temperatures, and in a variety of cultured fish species. Specifically, the objective of clinical field efficacy trials is to evaluate the efficacy of Terramycin® 200 for Fish medicated feed treatment to control mortality in a variety of fish species caused by diseases susceptible to oxytetracycline. Efficacy trials will be conducted at a number of different study sites, on a variety of fish species infected with a variety of fish pathogens. Diseases of interest include, but are not limited to: 1) coldwater disease; 2) columnaris; 3) furunculosis, 4) enteric septicemia in catfish; 5) enteric redmouth; 6) vibriosis, and 7) bacterial hemorrhagic septicemia caused by Aeromonads and Pseudomonads. Another purpose of this INAD exemption is to obtain additional clinical field trial data to demonstrate the efficacy and target animal safety of Terramycin® 200 for Fish therapy to mark skeletal tissue in a variety of freshwater and marine fish species.

The U.S. Fish and Wildlife Service (USFWS) anticipates that it may require several years to carry out all clinical field trials and laboratory studies required to extend and expand the current label to cover major aquaculture needs. Therefore, the USFWS may request that the U. S. Food and Drug Administration (FDA) grant re-authorization of this Terramycin® 200 for Fish medicated feed INAD sometime in the future. In the interim, the USFWS will continue to work closely with the sponsor and other research and conservation agencies to develop other required New Animal Drug Application (NADA) research data to support expanded labels claims for Terramycin® 200 for Fish. Therefore, clinical field trials planned under this particular INAD are but one part of a larger coordinated and diligent inter-agency effort that will eventually meet all Terramycin® 200 for Fish NADA data requirements.

## VI. SPECIFIC OBJECTIVES:

The two major objectives of this study protocol are as follows:

1. Collect scientific data necessary to support pivotal efficacy trials to further establish the effectiveness of Terramycin® 200 for Fish to 1) control certain bacterial diseases of freshwater and marine fish that occur under a variety of environmental conditions, at a wide range of temperatures, and in a variety of cultured fish species; and 2) mark skeletal tissue in a variety of freshwater and marine fish species. **Note: No clinical field trials will be conducted under this INAD for use patterns for which Terramycin® 200 for Fish has already received FDA-approval (e.g., treatment of ulcer disease, furunculosis, bacterial hemorrhagic septicemia, or pseudomonas disease in salmonids; treatment of bacterial hemorrhagic septicemia or pseudomonas disease in catfish; treatment of gaffkemia in lobster; treatment of coldwater disease in freshwater-reared salmonids; treatment of columnaris disease in freshwater-reared *Oncorhynchus mykiss*; marking Pacific salmon; and marking freshwater-reared salmonids weighing up to 55 grams (NADA 038-439)).**
2. Provide an opportunity for fish culturists to legally use Terramycin® 200 for Fish medicated feed to control certain bacterial diseases of fish that occur under a variety of environmental conditions, at a wide range of temperatures, and in a variety of cultured fish species so that they can maintain healthy stocks of fish during the

period of time necessary for collection of data that will be used to support expanded label claims for the use of Terramycin® 200 for Fish on freshwater and marine fish.

## VII. MATERIALS:

### A. Test and Control Articles:

#### 1. Drug Identity

##### a. Active ingredient

Common Name: Oxytetracycline (from oxytetracycline dihydrate)

Product Name: **Terramycin® 200 for Fish** (Type A Medicated Article)

Chemical Family: Tetracycline derivative

CAS Number: 79-57-2

Appearance: Uniform tan meal

Odor: Cereal odor

##### b. Strength and dosage form

Terramycin® 200 for Fish is a broad-spectrum anti-infective with a specially designed formula for fish. It has been proven highly effective in controlling diseases caused by Gram-positive and Gram-negative organisms that adversely affect salmonids, catfish, and lobsters. **Terramycin® 200 for Fish contains 200g oxytetracycline (from oxytetracycline dihydrate) per pound of Type A Medicated Article.**

##### c. Manufacturer, source of supply

Phibro Animal Health Corporation  
Glenpointe Centre East, 3<sup>rd</sup> Floor  
300 Frank W. Burr Blvd., Ste. 21  
Teaneck, NJ 07666 USA

**Contact:** Sean Parker  
Phone: 201-329-7377  
Email: [sean.parker@pahc.com](mailto:sean.parker@pahc.com)

**Note:** A Veterinarian Feed Directive (VFD) is not needed when Terramycin® 200 is used under the INAD. Investigators will need to fill out Form OTC-W (study request) in the online database and advance the study to stage 3. AADAP will then review the study; assign a study number; then email a copy of the approved Form OTC-W to the feed mill to show use will be under an INAD. The feed mill will retain a copy of Form OTC-W for their records.

## 2. Verification of Drug Integrity/Strength:

The manufacturer, Phibro Animal Health Corporation, will provide the analytical data necessary to establish the purity of each lot of Terramycin® 200 for Fish Type A Medicated Article supplied. The lot number and date of manufacture for each batch of Terramycin® 200 for Fish will be placed on the label of each container. The form "Report on Receipt of Drug - Guide for Reporting Investigational New Animal Drug Shipments for Poikilothermic Food Animals" (Form OTC-1) will clearly identify the lot number and date of manufacture of Terramycin® 200 for Fish shipments (i.e., Type A Medicated Article or medicated feed). If the integrity of the Terramycin® 200 for Fish is compromised (i.e., by spilling or contamination of the stock container or feed bags) the event will be carefully recorded, dated, and signed in the Chemical Use Log (Form OTC-2a or Form OTC-2b). The Study Monitor assigned to the Investigator involved will be immediately notified.

Based on discussions with Investigators concerning planned feed rate and kg of fish to be medicated, commercial fish feed manufacturers shall prepare feed with dosages of Terramycin® 200 for Fish to assure the desired target dose is achieved (see Section XI for dosage options).

The Investigator may also prepare his/her own drug-treated feed by top-coating feed on-hand (or specially ordered feed) with Terramycin® 200 for Fish. If the Investigator chooses this option, they are encouraged (but not required) to have a sample of the top-coated feed assayed for oxytetracycline concentration by a certified, analytical testing laboratory. Results of drug-treated feed assays should be appended to a Form OTC-3.

## 3. Storage Conditions

Terramycin® 200 for Fish Type A Medicated Article must be stored in the original container supplied by the Manufacturer with the appropriate investigational label attached. The container should be stored out of direct sunlight in a well ventilated area at room temperature. The storage unit for Terramycin® 200 for Fish Type A Medicated Article must be labeled to indicate that it contains hazardous material and that "*NO Food or Drink is to be Stored in this unit*". Terramycin® 200 for Fish medicated feed should be stored at temperatures and for periods of time not to exceed limits set by the feed manufacturer. Medicated feed should be ordered only as needed and not stored for possible future use.

## 4. Handling Procedures

Each Study Monitor and Investigator will be required to have a current copy of the Safety Data Sheet (SDS) for Terramycin® 200 for Fish Type A Medicated Article (see Appendix IV). Each person involved with the study and each person who may be present during the use of Terramycin® 200 for Fish medicated feed shall be required to read the SDS. Safety precautions as outlined in the SDS will be followed at all times when working with Terramycin® 200 for Fish.

## 5. Investigational Labeling

A copy of the label to be attached to each container of Terramycin® 200 for Fish Type A Medicated Article and all bags of Terramycin® 200 for Fish medicated feed is provided in Appendix V. Although investigational labels will be affixed to medicated feed containers



be the feed manufacturer, it is the responsibility of the Investigator to ensure proper labeling of all containers of Terramycin® 200 for Fish Type A Medicated Article and Terramycin® 200 for Fish medicated feed.

#### 6. Accountability

Phibro Animal Health Corporation will be the sole supplier of Terramycin® 200 for Fish Type A Medicated Article to all Investigators under INAD 9332.

***The Online INAD Database must be used by Investigators for ALL INAD reporting. The online INAD database has a built-in system of checks, balances, and email notifications to ensure that all information/data reporting and accountability follows established INAD Study Protocol guidelines. Unless data is entered directly into the online INAD database (i.e., not captured elsewhere at the time of observation or measurement and transcribed into the online INAD database) investigators must archive hard copies of all raw data.***

1. All facilities using Terramycin® 200 for Fish Type A Medicated Article or Terramycin® 200 for Fish medicated feed:

Immediately upon receiving an order/shipment of Terramycin® 200 for Fish Type A Medicated Article or Terramycin® 200 for Fish medicated feed, the Investigator must complete Form OTC-1 "Report on Receipt of Drug - Guide for Reporting Investigational New Animal Drug Shipments for Poikilothermic Food Animals" (located in the "Manage/View Drug Inventory" section of the investigator account). The Study Director will forward a copy of this form to the FDA. Arrangements should be made between Investigators and Study Monitors to insure completed Form OTC-1s are received by the Study Director within 10 days of drug receipt.

All Investigators are also responsible for maintaining an accurate inventory of Terramycin® 200 for Fish Type A Medicated Article or Terramycin® 200 for Fish medicated feed. A Chemical Use Log (Form OTC-2a or OTC-2b) must be completed and maintained by each Investigator. Each time Terramycin® 200 treated feed is used, it must be recorded by the Investigator in the Results Report form in the "Amount Of Drug Used" table.

At the conclusion of field trials, all remaining Terramycin® 200 for Fish Type A Medicated Article or Terramycin® 200 for Fish medicated feed will be destroyed by following the SDS (note: unless medicated feed is planned for use in another approved field trial, and planned usage is within the storage guidelines established by the manufacturer). Disposition of all Terramycin® 200 for Fish Type A Medicated Article or Terramycin® 200 for Fish medicated feed must be properly recorded and accounted for on the Chemical Use Log (Form OTC-2a or OTC-2b). The Study Monitor will be responsible for verifying the quantity of Terramycin® 200 for Fish Type A Medicated Article or Terramycin® 200 for Fish medicated feed remaining on hand versus the amount indicated on Form OTC-2. **Note:** Terramycin® 200 for Fish Type A Medicated Article or Terramycin® 200 for

Fish medicated feed can be transferred to other facilities that are participating under INAD 9332. Transfers must be shown in the Drug Inventory section of the database (formerly Form OTC-2a or OTC-2b).

#### 7. Preparation Procedures

Oxytetracycline will be supplied to Investigators either as Terramycin® 200 for Fish Type A Medicated Article or Terramycin® 200 for Fish medicated feed. Neither product should be adulterated in any manner prior to use. If Investigators are using Terramycin® 200 for Fish Type A Medicated Article to make their own oxytetracycline medicated feed, Terramycin® 200 for Fish Type A Medicated Article should be top-coated on feed. Top-coating procedures should include “finishing” with 0.5% vegetable oil.

#### B. Items Needed for Treatment, Data Collection, Etc.:

Sampling techniques and diagnostic equipment will most likely be provided by trained fish health biologists serving as Study Monitors or their designee(s). Equipment and supplies needed would include items to sample, culture, grow and identify culture growths microscopically. Standard fish culture supplies and equipment would also be required.

When the Study Protocol has been approved and treatments are scheduled, the Investigator at each facility covered by the Terramycin® 200 INAD will need to complete several forms located in the online INAD database. These forms are described in Section XIII. Copies of these forms are attached to this Study Protocol and will be used as a guide only for collecting the data that will be entered into the online INAD database.

### VIII. EXPERIMENTAL UNIT

The experimental unit in these clinical field trials will consist of contained or isolated groups of fish. This will generally be a groups of fish contained in tanks, raceways, or ponds. However, the experimental unit in clinical field trials may also be **individual animals**. If individual animals are considered to be the experimental unit, treatment response parameters for each animal must be evaluated separately.

### IX. ENTRANCE CRITERIA

#### A. Facilities/Investigators

The proposed facility and the Investigator must be listed in Appendix IIIa of the Study Protocol for the current calendar year before Terramycin® 200 for Fish medicated feed can be ordered and dispensed under this INAD. Last minute deviations can be requested by the Sponsor, Study Director, or by an Investigator in case emergency use-pattern needs should arise (See Section XX). However, poor planning and/or a lack of preparation will not be considered an emergency situation.

#### B. The characteristics of the study animals (species, number, etc.) is presented in Appendix VIb.

## C. Environmental conditions

Environmental conditions will be variable and include a broad spectrum of water temperatures and water quality parameters. Environmental conditions will be reported on a Form OTC-3. Drug discharge must be in compliance with local **NPDES** permitting requirements.

## D. Ability of Investigator to fulfill all the requirements of the Study Protocol

See Appendix IIIb for example of knowledge required of hatchery managers (i.e., Investigators).

**Prior to initiating each treatment event**, the Investigator must first complete Form OTC-W. "Worksheet for Designing Individual Field Trials" (located under the "New Study Request" tab in the investigator account) that pertains to each specific treatment event. The worksheet should be filled out and forwarded to the Study Monitor through the online INAD database. The Study Monitor will review the planned treatment (worksheet) and forward it to the Study Director at the AADAP Office. The Study Director will then review the worksheet, assign the approved treatment a Study Number, and then the online INAD database will notify both the Investigator and the Study Monitor of the assigned number and approval to proceed. In most cases, this entire process should be able to be accomplished within a single working day. After initiation of the field trial, the Investigator should also record the assigned study number on any paper forms that are being used as a guide to collect the data to enter in the online database (i.e., Form OTC-2 and OTC-3), as well as on any additional correspondence regarding that specific treatment event. If for some reason the Investigator is unable to reach the Study Monitor with regards to Worksheet approval and the need for treatment is immediate, the Investigator should contact the AADAP Office for permission to proceed.

Note: The online INAD database, which must be used by Investigators for all INAD reporting, has a built-in system of checks, balances, and email notifications to ensure that all information/data reporting follows established INAD Study Protocol guidelines.

## E. Pathogen/disease considerations

1. Bacterial fish pathogens should be presumptively identified by procedures described in Section 3 of the "Blue Book" (Procedures for the Detection and Identification of Certain Fish Pathogens, Third Edition, Fish Health Section/American Fisheries Society, 1985). Other, more sensitive methods described elsewhere in peer-reviewed references, or as mutually determined by the local fish health biologist, in consultation with the Study Monitor, also may be used. **(Note: Diagnostic methods other than those in the Third Edition of the "Blue Book" should be described on a separate sheet attached to a Form OTC-3 "Results Report Form").**
2. There should be increased mortality rates among fish in a rearing unit(s) for three or more consecutive days. Note: Station history and the experience of the investigator, monitor, or the fish health biologist may over-ride this

criterion to halt potentially explosive disease outbreaks. In such cases, however, careful diagnostic surveillance should be carried out in all rearing units proposed for treatment and controlled tests should be carried out if at all possible.)

3. Typical disease signs should be detectable in at least a few fish and the causative bacterial pathogen must be identified.

## X. TREATMENT GROUPS

- A. A treatment group or experimental unit may be an entire tank, pond, raceway, or group of fish, or it may be individual animals.
- B. Separately confined, untreated control fish will not be required in supplementary field studies conducted to determine the effectiveness and safety of Terramycin® 200. Fish from a group or lot will first be examined to determine if treatment with Terramycin® 200 is required. When treatment is underway or has been completed, fish from the same group will be examined to determine the effect of treatment on the parameters used to initially sanction the treatment. Evaluation will in all cases consist of determining fish mortality, although in some cases degree or severity of bacterial infestation may also be quantified.
- C. Although as stated above untreated control groups are not a required element of treatment under this INAD exemption, **it is important for all investigators to note that field trials conducted under a more stringent study protocol (i.e. including requirements for non-treated controls groups, replication, blinding, dose verification, etc.) will ultimately be required in order to support a NADA for Terramycin® 200. It is also important to note that the INAD sponsor fully expects that a limited number of facilities/investigators listed under this INAD exemption will agree to participate in such “pivotal” efficacy studies.** These studies will be initiated only after direct consultation between facilities/investigators and the sponsor. These studies will be conducted under a separate FDA-approved study protocol (i.e. not the INAD study protocol), and will also be conducted with assistance from, and under the direct supervision of, the sponsor. **If for any reason it becomes apparent to the sponsor that facilities/investigators listed under this INAD are not willing to participate in such “pivotal” studies, the sponsor will request that FDA terminate the INAD.**

## XI. TREATMENT SCHEDULES

- A. Route of administration

Terramycin® 200 for Fish will be administered only as a medicated feed treatment.

- B. Dosage and treatment duration

**Objective A** Salmonids treated for the control of mortality caused by bacterial diseases

Treatment at 2.5 - 3.75 grams of active drug per 100 pounds of fish per day for 10 consecutive days.

**Objective B** Freshwater and marine fish treated for the control of mortality caused by bacterial diseases **in water temperatures not below 4°C**

Treatment at 10 grams of active drug per 100 pounds of fish per day for 14 consecutive days.

**Objective C** Non-salmonid freshwater and marine species treated for the control of mortality caused by bacterial diseases

Treatment at 2.5 - 3.75 grams of active drug per 100 pounds of fish per day for 10 consecutive days.

**Objective D** Abalone treated for the control of withering syndrome

Treatment at up to 6.0 g active drug per 100 lbs body weight per day for 14 consecutive days.

**Objective E** Salmonid and non-salmonid (freshwater or marine) treated to apply a skeletal mark

Treatment at 2.5 - 3.75 grams of active drug per 100 pounds of fish per day for 10 consecutive days; or

Treatment at 10 grams of active drug per 100 pounds of fish per day for 14 consecutive days.

C. Dosing interval and repetition

Terramycin® 200 for Fish will be administered as a single treatment regimen, with no repetition of treatment.

D. Fish species

Fish stocks listed in Appendix VIa may be fed Terramycin® 200 for Fish treated feed in clinical field trials.

E. Drug preparation and administration procedures

Terramycin® 200 for Fish Medicated Feed Article will typically be incorporated into standard diets by an established feed manufacturer. However, in certain situations, Terramycin® 200 for Fish Medicated Feed Article may be top-coated on feed by investigators. Standard personal protective equipment such as gloves, lab coats or aprons, eye protection, etc. should be worn at all times when preparing or administering Terramycin® 200 for Fish medicated feed. Medicated feed for each individual lot of fish should be accurately weighed prior to treatment. Fish should be

fed in such a manner as to ensure optimal consumption of Terramycin® 200 for Fish medicated feed (see Feeding Regimen below).

#### F. Feeding Regimen

During the course of therapy fish may be fed only treated feed, or a combination of treated and untreated feed. The actual feeding regimen used will be left to the discretion of the investigator, and will be dictated by the feeding behavior of the fish to be treated and level of premix incorporated in the feed. In most cases it is anticipated that use of only treated feed will work best. However, in some cases, treated feed followed by untreated feed may be determined to be the optimal feeding regimen. In still other cases, a small amount of untreated feed followed by a “full course” of treated feed may be utilized. In all cases, the daily feeding regimen should be designed to maximize consumption of the treated feed to result in fish receiving the target dosage.

Specify on source data sheets how fish were fed (e.g. % treated feed vs % untreated feed, by hand, using automatic feeders, utilizing demand feeders), amount of feed offered (% body weight), and whether feed was well accepted or poorly utilized.

#### G. Permissible concomitant therapy

Since efficacy data are being collected during the INAD process, there should be little or no concomitant therapy. Preferably, there should be no other therapy during a period extending from 2 weeks prior to treatment to 2 weeks after treatment. Investigators must be prepared to minimize changes in fish cultural procedures or environmental conditions, and apply no other treatments following treatment with Terramycin® 200.

However, if concomitant therapy is required in order to protect valuable fish stocks (i.e., threatened and endangered species not for human consumption) it should be fully documented and the efficacy data from the Terramycin® 200 treatment involved should be appropriately labeled. Contact the AADAP Office for the information that will need to be provided in the Form OTC-3 if concomitant therapy is conducted.

## XII. TREATMENT RESPONSE PARAMETERS

The collection and reporting of source data begins with the decision to treat valuable fish based on hatchery records or other pertinent species information indicating treatment is warranted. Daily morbidity and mortality records, case history records, as well as any extenuating or mitigating circumstances that may affect treatment response need to be documented. All pertinent treatment response parameters should be reported on Form OTC-3. Treatment response parameters that should be addressed include the following:

#### 1. Primary Parameters

Morbidity and mortality data, coupled with case history and analyses of bacterial load, usually indicate when Terramycin® 200 for Fish medicated feed treatment is needed. **Source data must be collected for 5 days before treatment, during**

**treatment, and for 10 days after the treatment period has ended.** Collection of this data is critically important in all cases. Samples of kidney or other tissue will be removed from groups of representative fish and tested by bacteriological, serological, or other methods to determine the presence of target pathogens.

## 2. Secondary Parameters

Secondary parameters may also include general observations on fish behavior and response to routine culture/handling activities. This would include such responses as feeding activity, feed consumption, apparent level of stress, negative fish behavior, etc.

## 3. Adverse Reactions

Any adverse reaction to treatment should be reported **immediately** to the Study Monitor, who will in turn notify the Study Director. Such responses might include extremely negative responses/behavior by the fish or hazards to the applicator. Although oxytetracycline medicated feed has been used extensively for many years with beneficial effect in fish culture, it is possible adverse reactions may occur under certain environmental conditions or with respect to specific species/strains of fish. Carefully observe all treated fish for any signs of any adverse reaction to treatment. The Investigator should carefully document all observations of adverse reactions. **If any signs of drug toxicity are detected, they should also be documented and immediately reported to the Study Monitor, who will in turn notify the Study Director.**

**Note:** Investigators are strongly encouraged to record observations/comments with respect to all phases of treatment. This may include a description of events before, during, and post-treatment. All extenuating or mitigating treatment circumstances need to be described in detail. Such information is imperative so that accurate study/data analysis can be performed.

## XIII. FORMS FOR DATA COLLECTION

When the Study Protocol for Terramycin® 200 for Fish medicated feed has been approved and treatments are scheduled, the Investigator at each facility covered by the INAD will need to complete the following forms:

Form OTC-W. Worksheet for Designing Individual Field Trials under Terramycin® 200  
INAD 9332 - located in the New Study Request tab

Form OTC-1. Report on Receipt of Drug - Guide for Reporting Investigational New  
Animal Drug Shipments for Poikilothermic Food Animals – located in the  
Manage/View Drug Inventory tab

Form OTC-2a. Chemical Use Log for Clinical Field Trials Using Terramycin® 200 INAD  
9332- Terramycin® 200 Type A Medicated Article – located in the  
Manage/View Drug Inventory tab and filled out in Form OTC-3 to show  
use

Form OTC-2b. Chemical Use Log for Clinical Field Trials Using Terramycin® 200 INAD 9332 - Terramycin® 200 Medicated Feed – located in the Manage/View Drug Inventory tab and filled out in Form OTC-3 to show use

Form OTC-3a. Results Report Form for Clinical Field Trials Using Terramycin® 200 INAD 9332 – located in the Active Studies table on the home page

Form OTC-3b. Results Report Form for Clinical Field Trials Using Terramycin® 200 INAD 9332 – located in the Active Studies table on the home page

Copies of these forms are attached to this Study Protocol. Actual reporting is accomplished on forms located in the online INAD database.

#### XIV. RECORD KEEPING PROCEDURES

As stated immediately above, all data reporting are accomplished via forms located in the online INAD database. All current and completed studies conducted under the investigator account will be stored and available in the online INAD database to the current study monitor, study investigator, and AADAP.

#### XV. DISPOSITION OF INVESTIGATIONAL ANIMALS

Animals that die during treatment should be disposed of by burial or incineration. All fish treated with Terramycin® 200 for Fish medicated feed must be maintained in culture facilities for a specified withdrawal time following completion of therapy before stocking/release or harvest. Specific withdrawal time is based upon treatment objective as defined in Section XI.B of this study protocol and are as follows:

- Objective A: **21 days** – salmonids treated at standard dose (2.5 - 3.75 grams of active drug per 100 pounds of fish per day for 10 consecutive days)
- Objective B: **70 days** – freshwater and marine species treated at high dose (10 grams of active drug per 100 pounds of fish per day for 14 consecutive days)
- Objective C: **40 days** – non-salmonid freshwater and marine fish at standard dose (2.5 - 3.75 grams of active drug per 100 pounds of fish per day for 10 consecutive days)
- Objective D: **35 days** – abalone treated up to 6.0 g active drug per 100 lbs body weight per day for 14 consecutive days
- Objective E: **21 days** for standard dose (salmonids); **40 days** for standard dose (non-salmonids); **70 days** for high dose (all species)

No withdrawal period will be required for stocked fish that will not be harvestable/catchable after release, or are illegal for harvest, during the withdrawal times specified above (e.g., if fish are treated under Objective A and are not susceptible to harvest for a minimum of 21 days following completion of treatment, they may be stocked/released immediately). No withdrawal period shall be required for dead fish that will be buried or rendered into non-edible products.



The Investigator must verify compliance with requirements regarding the disposition of all treated fish on Form OTC-3. Also, note that the Investigator is also requested to estimate the predicted number of days/months before treated fish will be susceptible to harvest and/or human consumption on Form OTC-3.

## **XVI. DISPOSITION OF INVESTIGATIONAL DRUG**

Terramycin® 200 for Fish medicated feed will be used only in the manner and by the individuals specified in the Study Protocol. If any unused Terramycin® 200 for Fish medicated feed remains at the end of the study period, Investigators should contact Study Monitors for instructions regarding drug disposal. Drug disposal information is available in the Safety Data Sheet (SDS) located in Appendix IV of this protocol. Disposition of all Terramycin® 200 for Fish Type A Medicated Article or Terramycin® 200 for Fish treated feed must be properly recorded and accounted for on the Chemical Use Log (Form OTC-2a or OTC-2b). The Study Monitor will be responsible for verifying the quantity of Terramycin® 200 for Fish Type A Medicated Article or Terramycin® 200 for Fish treated feed remaining on hand versus the amount indicated on Form OTC-2a or OTC-2b. The investigational drug may not be redistributed to others not specified by the protocol and should not be retained by the Investigator after completion of the study (note: unless Terramycin® 200 treated feed is planned for use in another approved field trial, and planned usage is within the storage guidelines established by the manufacturer).

## **XVII. DATA HANDLING, QUALITY CONTROL, MONITORING, ADMINISTRATIVE RESPONSIBILITIES**

### **A. Drug distribution**

See Section VII.A.6. Accountability for information and details.

### **B. Study Monitors**

Study Monitors are generally fish health professionals with experience in diagnosing and treating fish diseases, and the ability to monitor overall fish health with respect to ongoing fish culture practices. A study monitor will be selected by each facility that is authorized to treat fish with Terramycin® 200 for Fish medicated feed. A list of Study Monitors, along with addresses and phone numbers, can be found in Appendix II. Study Monitors are responsible for supervision of the trials, adherence of the Investigator to the Study Protocol, and inspection of the site.

### **C. Special equipment and materials**

Most of the equipment and materials required for this study (with the exception of the Terramycin® 200 for Fish medicated feed itself) are already available at each participating fish hatchery. The use of various drugs, chemicals, and therapeutants to meet management and/or production goals is a common occurrence at most fish hatcheries. Fish hatchery managers (i.e., Investigators) are well trained and well equipped to handle these situations (see Appendix IIIb). If any additional equipment or materials are required, they will be provided by the Study Monitors (See Section VII.B. Items needed for sample collection, observations, etc.).

## D. Administrator of the drug

Terramycin® 200 for Fish medicated feed will be administered directly by the assigned Investigator (fish hatchery manager) or under the Investigator's direct supervision (see Appendix IIIa for names). Terramycin® 200 for Fish medicated feed will be maintained in a secure location, and only the Investigator or persons under his/her direct supervision will have access.

## E. Drug accountability records

See protocol Section VII.A.6. Accountability for details and the following forms will be used as guides for data collection: Form OTC-W, Form OTC-1, Form OTC-2a, Form OTC-2b, and Form OTC-3.

## F. Recording observations

The Investigator or a person under his/her direct supervision will be responsible for implementing the Study Protocol, making observations, collecting samples, and recording data during the clinical field trials. After the data have been collected and recorded on the forms, the Investigator will send the data to the Study Monitor who will ensure that all required information is provided. The Study Monitors will in turn send the data to the Study Director. The Study Director will analyze and summarize the data and prepare summary reports that will be submitted to the FDA. **Note: If the Study Monitor does not think all required information has been provided, or forms have not been satisfactorily completed, he/she should contact the Investigator and rectify the situation before forwarding the package to the Study Director.**

## G. Data storage

The Investigator is responsible for complete and accurate data collection, and must complete all required data forms (see protocol Section XIII). The Investigator should forward all completed forms to the Study Monitor for review. Study Monitors should carefully check each set of data for accuracy and completeness. If a form is incomplete or inaccurate, it should be returned to the Investigator. If a form is complete and accurate, it should be forwarded to the Study Director at the AADAP Office. **Note:** data that is entered through the online INAD database will be archived in the database. These archived forms will be available as long as the study participant accounts remain open.

**XVIII. PLANS FOR DATA ANALYSIS**

Data analysis will be completed by the Study Director located at the AADAP Office. Data from the treatment year will be summarized through tabulation and appropriate statistical analysis. INAD reports will be prepared and submitted to the FDA as required. This submission may include a request for an extension of the INAD based on the data collected during that year. When sufficient data are collected, the entire INAD data set will be summarized in a final report for submission to support a full NADA.

## XIX. PROTOCOL AND PROTOCOL AMENDMENTS

A signed copy of the Study Protocol must be retained by each Investigator. At any time before a field trials begins, desired changes in the Study Protocol should be brought to the attention of the Study Director. The desired changes will be fully described in the form of an amendment along with the reason for the change. The amendment will be signed by the Sponsor (or its representative) and forwarded to FDA for review. Copies of the signed amendment will be attached to each copy of the Study Protocol. **Investigators will be liable for non-compliance violation if drugs are used without a Study Protocol or in a manner different than specified in the Study Protocol, if forms are not filed out on time, or if the study data are not properly collected, maintained, and reported.** The Study Monitor is responsible for ensuring that all INAD procedures are being followed as defined by the Study Protocol.

## XX. PROTOCOL DEVIATIONS

Deviations from the established Study Protocol occasionally cannot be avoided. If deviations occur, the Study Monitor should be notified immediately. **Protocol deviations should be fully documented and should be accompanied by a written explanation of what happened, why, and what steps were taken to mitigate the deviation.** Deviations should be documented on Form OTC-3 in the *Description of Results* section and in the *Study Deviation* field.

## XXI: E.O. 13891

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way. This document is intended only to provide clarity to the public regarding existing requirements under the law or agency policies.

## Literature Cited

This information is currently not available.

## Appendix I. Sponsor Contact Information for Terramycin® 200 for Fish INAD #9332

**Sponsor:** Dr. Marilyn Blair, U.S. Fish and Wildlife Service, Aquatic Animal Drug Approval Partnership (AADAP) Program  
Phone: (406) 994-9904  
Fax: (406) 582-0242  
Email: [marilyn\\_j\\_blair@fws.gov](mailto:marilyn_j_blair@fws.gov)

**Sponsor Address:** 4050 Bridger Canyon Road, Bozeman, MT 59715

**Study Director:** Ms. Bonnie Johnson  
Aquatic Animal Drug Approval Partnership (AADAP) Program  
Phone: (406) 994-9905  
Fax: (406) 582-0242  
Email: [bonnie\\_johnson@fws.gov](mailto:bonnie_johnson@fws.gov)

### Principal Clinical Field

**Trial Coordinator:** Ms. Paige Maskill  
Aquatic Animal Drug Approval Partnership (AADAP) Program  
Phone: (406) 994-9911  
Fax: (406) 582-0242  
Email: [paige\\_maskill@fws.gov](mailto:paige_maskill@fws.gov)

## <sup>1</sup>Appendix II. Study Monitors for Terramycin® 200 for Fish INAD #9332

**Note:** This information will be provided directly to CVM

## **1Appendix IIIa. Facilities and Names of Investigators Participating under Terramycin® 200 for Fish INAD #9332**

**Note:** This information will be provided directly to CVM

## **Appendix IIIb. Sample of Knowledge Required for Position of Hatchery Manager (i.e. Investigators)**

Professional knowledge of all facets of fishery biology as well as the ability to apply new scientific findings, developments, and advances toward the resolution of critical propagation problems involving the rearing a variety of fish species under a variety of water quality conditions, water temperatures, water chemistry, etc.

Knowledge of general bacteriology, parasitology, and water chemistry sufficient to treat fish for various diseases.

Skill in interpreting biological observations and ability to draw sound conclusions from available data.

Skill in developing and coordinating available resources to ensure effective management and utilization of manpower, equipment, and funds relative to established priorities and needs.

Skill in coordination of sometimes divergent resource issues to obtain common objectives, including interaction with other Federal, State, Tribal, and private agencies/facilities.

Knowledge of and skill in the use of effective management and supervisory techniques to provide support, guidance, and motivation to hatchery staff.

## **Appendix IV. Safety Data Sheet (SDS) for Terramycin® 200 for Fish INAD #9332**

The SDS for Oxytetracycline (Terramycin 200 Fish) can be found at the drug sponsors website:

[Terramycin-SDS-11-2015.pdf \(syndel.com\)](#)

## **<sup>1</sup>Appendix V. Investigational Label for Terramycin<sup>®</sup> 200 for Fish INAD #9332**

1. Investigational label for tests in vitro and in laboratory research animals [511.1(a)]:

"Caution. Contains a new animal drug for investigational use only in laboratory animals or for tests in vitro. Not for use in humans."

2. Investigational label for use in clinical field trials [511.1(b)]:

"Caution. Contains a new animal drug for use only in investigational animals in clinical field trials. Not for use in humans. Edible products of investigational animals are not to be used for food unless authorization has been granted by the U.S. Food and Drug Administration or by the U.S. Department of Agriculture."



## **1Appendix VIa. Fish Species Treated under Terramycin® 200 for Fish INAD #9332**

Select freshwater finfish:

Salmonidae  
Acipenseridae  
Catostomidae  
Cyprinodontidae  
Esocidae  
Ictaluridae  
Moronidae  
Percidae  
Poeciliidae  
*Polyodon spathula* (paddlefish)  
*Lepisosteus spatula* (alligator gar)

Select marine finfish:

*Paralichthys* spp.  
*Seriola* spp.  
*Haliotis rufescens* (abalone)  
*Alosa sapidissima* (American shad)  
*Gadus morhua* (Atlantic Cod)  
*Hippoglossus hippoglossus* (Atlantic halibut)  
*Centropristis striata* (black sea bass)  
*Scorpaenichthys marmoratus* (cabezon)  
*Semicossyphus pulcher* (California sheephead)  
*Rachycentron canadum* (cobia)  
*Dicentrarchus labrax* (European sea bass)  
*Sparus aurata* (gilthead seabream)  
*Alosa mediocris* (hickory shad)  
*Atractoscion nobilis* (white sea bass)  
*Hypomesus transpacificus* (delta smelt)  
*Lates calcarifer* (barramundi)

## **<sup>1</sup>Appendix VIb. Table of Facilities and Fish Stocks Treated under Terramycin® 200 for Fish INAD #9332**

**Note:** This information will be provided directly to CVM

**All data must be entered through the online INAD database:**

The following forms are to be used as a guide for collecting data that will be entered into the **online INAD database**. Any paper forms that are submitted to AADAP will be sent back to the study participants.

## Form OTC-W: Worksheet for Designing Individual Field Trials under INAD 9332

### INSTRUCTIONS

1. Investigator must fill out Form OTC-W for each trial conducted under this INAD **before** actual use of Terramycin® 200 for Fish treated feed.
2. Investigator should forward a copy of OTC-W to the Study Monitor for review.
3. After review, the Study Monitor should forward a copy to the AADAP Office for review and assignment of the Study Number.

### SITE INFORMATION

Facility			
Address			
Investigator			
Reporting Individual (if not Investigator)			
Phone		Fax	

### FISH CULTURE AND DRUG TREATMENT INFORMATION

Fish species to be treated		Disease to be treated	
Average fish weight (gm)		Average fish length (in)	
Number of fish per unit (e.g. 10,000 fish/raceway)			
Number of treated units		Number of treated fish	
Number of untreated control units		Number of control fish	
Estimated total weight of fish to be treated (lbs)		Projected % body weight to be fed	
Planned % TM pre-mix (e.g. 2, 4, 6%) in feed (see feed company order sheet)		Intended OTC dosage (gm/100 lbs fish/day)	
Planned duration of drug treatment (days)		Estimated total amount of medicated feed needed for proposed treatment (lbs)	
Anticipated date treatment will be initiated			
OTC-Feed manufacturer		OTC-Feed lot number	

**STUDY DESIGN:** Provide a brief description of your planned study. The description should

include the reason you feel fish should be treated, the treatment dates, the number of fish that will be treated, and if the fish are a threatened or endangered species.

Study designed by \_\_\_\_\_

**DISPOSITION OF TREATED FISH** (Human Food Safety Considerations):

Check applicable box(es):

<input type="checkbox"/>	Study Objective A - Current label (salmonids): 21 day withdrawal period
<input type="checkbox"/>	Study Objective B - 10 gram dosage: 70 day withdrawal period
<input type="checkbox"/>	Study Objective C - Current label (non-salmonids): 40 day withdrawal period
<input type="checkbox"/>	Study Objective D - Abalone; 6.0 gram dosage; 35 day withdrawal period
<input type="checkbox"/>	Study Objective E - Mark skeletal tissue 1in a variety of fish species; 121 days for standard dose (salmonids); 40 days for standard dose (non-salmonids); 70 days for high dose (all species)
<input type="checkbox"/>	Investigator should initial here to indicate awareness that fish disposition must be in compliance with FDA-mandated withdrawal times as described in Section XV. of the Study Protocol.

**WORKER SAFETY CONSIDERATIONS:**

<input type="checkbox"/>	Investigator should initial here to indicate that all personnel handling drug have read Safety Data Sheet for Terramycin® 200 for Fish and have been provided protective equipment, in good working condition, as described in the SDS.
--------------------------	---

Date Prepared: \_\_\_\_\_

Investigator: \_\_\_\_\_

Date Reviewed: \_\_\_\_\_

Study Monitor: \_\_\_\_\_

# **FORM OTC-1. Report on Receipt of Drug - Guide for Reporting Investigational New Animal Drug Shipments for Poikilothermic Food Animals**

## **INSTRUCTIONS**

1. Investigator must fill out Form OTC-1 **immediately** upon receipt of oxytetracycline-medicated feed.
2. Investigator should forward a copy of Form OTC-1 to the Study Director at the AADAP Office.

*The sponsor, **U.S. Fish and Wildlife Service**, submits a notice of claimed investigational exemption for the shipment or delivery of a new animal drug under the provisions of Section 512 of the Federal Food, Drug, and Cosmetics Act.*

Name of Drug	<b>Terramycin® 200 for Fish</b>	INAD Number	<b>9332</b>
Proposed Use of Drug	Treatment of certain bacterial diseases that occur in a variety of fish species; 1mark skeletal tissue in a variety of freshwater fish species		
Date of CVM Authorization Letter	June 25, 2007		
Date of Drug Receipt		Amount of Drug Received	
Drug Lot Number		Trial Number	
Name of Investigator			
Address of Investigator			
Location of Trial			
Pivotal Study	<b>Yes</b>	Non-pivotal Study	----
Approximate Number of Treated Animals		Approximate Number of Control Animals	
Number of Animals Used Previously <sup>1</sup>			
Study Protocol Number	9332		
Approximate dates of trial (start/end)			
Species, Size, and Type of Animals			
Maximum daily dose and duration	10 g oxytetracycline per 100 lb of fish per day for 14 days		
Methods(s) of Administration	Medicated-feed		
Withdrawal Period	Salmonids = 21-70 days; Non-salmonids = 40 - 70 days; Abalone = 35 days (see INAD 9332 Study Protocol for specific salmonid times)		

<sup>1</sup> To be filled out by the AADAP Office

Date Prepared: \_\_\_\_\_

Investigator: \_\_\_\_\_

Date Reviewed: \_\_\_\_\_

Study Monitor: \_\_\_\_\_

Date Reviewed: \_\_\_\_\_

Sponsor: \_\_\_\_\_

# Form OTC-2a. Chemical Use Log for Clinical Field Trials Using Terramycin® 200 for Fish Under INAD #9332 - Terramycin® 200 for Fish Type A Medicated Article

- Instructions:**
1. Initiate Form OTC-2a immediately upon receipt of Terramycin® 200 for Fish Type A Medicated Article.
  2. Each lot number of Terramycin® 200 for Fish Type A Medicated Article may be used for multiple treatment regimens.

Quantity on Hand  
From Previous Page (g):

Facility:

Reporting  
Individual:

Terramycin® 200 for Fish Type A Medicated Article Lot Number	Date Received	Amount Received (g)	Date Used	Study Number	Terramycin® 200 for Fish Type A Medicated Article Used for Treatment (g)	Terramycin® 200 for Fish Type A Medicated Article Shipped <sup>1</sup> (g)	Terramycin® 200 for Fish Type A Medicated Article Disposal <sup>2</sup> (g)	Terramycin® 200 for Fish Type A Medicated Article On-hand (g)	Inventoried by (initials)

<sup>1</sup> Unused Terramycin® Type A Medicated Article that is shipped to another facility participating in Terramycin® INAD #9332 (**Note:** Terramycin® Type A Medicated Article can only be shipped to another facility with prior authorization by the AADAP Office).

<sup>2</sup> Unused Terramycin® Type A Medicated Article that is disposed of by burial or in a landfill.

Investigator: \_\_\_\_\_  
Signature and Date

Study Monitor: \_\_\_\_\_  
Signature and Date

**Instructions:**

1. Initiate Form OTC-2b immediately upon receipt Terramycin® 200 for Fish Medicated Feed.
2. Each lot number of Terramycin® 200 for Fish Medicated Feed should be used for a single treatment regimen.

**Facility:**

**Individual:** \_\_\_\_\_ **Reporting**

[illegible]

<sup>1</sup> Unused Terramycin® 200 for Fish medicated feed that is shipped to another facility participating in Terramycin® 200 for Fish INAD #9332 (Note: Terramycin® 200 for Fish medicated feed can only be shipped to another facility with prior authorization by the AADAP Office).

<sup>2</sup> Unused Terramycin® 200 for Fish medicated feed that is disposed of by burial or in a landfill.

Investigator: \_\_\_\_\_  
Signature and Date

**Study Monitor:** \_\_\_\_\_

**Signature and Date**



1STUDY  
NUMBER

## Form OTC-3a: Results Report Form for use of Terramycin® 200 for Fish under INAD 9332

### INSTRUCTIONS

1. Investigator must fill out Form OTC-3a no later than 30 days after completion of treatment. Attach lab reports and other information.
2. If Terramycin® 200 for Fish was not used under the assigned Study Number, contact the Study Director at the AADAP Office on how to close-out the study.
3. Investigator should forward a copy of Form OTC-3a to the Study Monitor. Within 10 days of receipt, the Study Monitor should forward a copy to the Study Director at the AADAP Office.

### SITE INFORMATION

Facility	
Reporting Individual	

### TREATMENT INFORMATION AND SCHEDULE

OTC-Feed lot number		Total amount OTC-Feed used (lbs)	
Fish species treated		Daily percent body-weight fed	
Planned % TM pre-mix (e.g. 2, 4, 6%) in feed		OTC dosage (gm/100lb fish/day)	
Disease treated		Disease diagnosed by	
Average fish weight (gm)		Average fish length (in)	
Number of fish per unit (e.g. 10,000 fish/raceway)			
Number of treated units		Total number of treated fish	
Number of control units		Total number of control fish	
Date treatment started		Date treatment ended	

### WATER QUALITY PARAMETERS

Ave pre-treatment temp (°F)		Dissolved Oxygen (mg/L)	
Ave treatment temp (°F)		pH	
Ave post-treatment temp (°F)		Hardness - CaCO <sub>3</sub> (mg/L)	

## Daily Mortality Record

### INSTRUCTIONS

1. Investigator should fill out the Daily Mortality Record as completely as possible.
2. Prior to initiation of the trial, fill out Rearing Unit ID, whether a rearing unit is Treated or Control, and the number of fish in each rearing unit.
3. Water temperature and individual tank mortality should be recorded on a daily basis.
4. Enter treatment period mortality only for days which fish were treated. For example, if fish were treated for ten days enter mortality for treatment days 1 - 10 and then proceed directly to post-treatment day 1 and leave days 11 - 14 of the treatment period blank.
5. **Even if mortality is zero an entry is still needed for that day.**

FACILITY										
	Rearing Unit ID									
	Treated or Control									
	Number of Fish									
	Day	Date	Water Temp (F°)	Mortality	Mortality	Mortality	Mortality	Mortality	Mortality	Daily Observer Initials
Pre-treatment	1									
	2									
	3									
	4									
	5									
Treatment	1									
	2									
	3									
	4									
	5									
	6									
	7									
	8									
	9									
	10									
	11									

FACILITY										
	Rearing Unit ID									
	Treated or Control									
	Number of Fish									
	Day	Date	Water Temp (F°)	Mortality	Mortality	Mortality	Mortality	Mortality	Mortality	Daily Observer Initials
	12									
	13									
	14									
Post-treatment	1									
	2									
	3									
	4									
	5									
	6									
	7									
	8									
	9									
	10									
	11									
	12									
	13									
	14									
	15									
	16									
	17									
	18									
	19									
	20									

**RESULTS:** Describe in detail treatment results. Was treatment successful? If treatment did not appear to be successful, explain why not? Were there any mitigating environmental conditions that may have impacted treatment results? Were there any deviations from the Study Protocol?

**Pathology Report:** Attach pathology report to this form. Report should include: 1) a description of how the pathogen(s) was identified; 2) disease identification records that confirm the presence of the pathogen; and 3) the name and title of the individual performing the diagnosis.

Pathology Report  
included:

☐

pre-treatment

☐

post-treatment

**Toxicity observations:** Report any apparent drug toxicity including a description of unusual fish behavior.

**OBSERVED WITHDRAWAL PERIOD:**

Observed withdrawal period: \_\_\_\_\_ 21 days \_\_\_\_\_ 35 days \_\_\_\_\_ 40 days \_\_\_\_\_ 70 days

Estimated number of days between last treatment and first availability of fish for human consumption (ensure this time period meets the withdrawal period). \_\_\_\_\_

**Disposition of Unused or Spoiled Terramycin® 200 for Fish Treated Feed:**

	Use and disposition of all Terramycin® treated feed followed Study Protocol guidelines and has been clearly identified on Form OTC-2b (Investigator should initial)
--	---

☐ **Negative Report:** Terramycin® treated feed was not used at this facility under this Study Number during the reporting period. The study will be closed out in the online INAD database.

Date  
Prepared: \_\_\_\_\_

Investigator: \_\_\_\_\_

Date  
Reviewed: \_\_\_\_\_

Study Monitor: \_\_\_\_\_



STUDY \_\_\_\_\_

**Form OTC-3b: Results Report Form for use of Terramycin® 200 for Fish  
under INAD 9332- For use in the marking of skeletal tissue****1in  
a variety of fish species****INSTRUCTIONS**

1. Investigator must fill out Form OTC-3b no later than 30 days after completion of treatment. Attach lab reports and other information.
2. If Terramycin® 200 for Fish was not used under the assigned Study Number, contact the Study Director at the AADAP Office on how to close-out the study.
3. Investigator should forward a copy of Form OTC-3b to the Study Monitor. Within 10 days of receipt, the Study Monitor should forward a copy to the Study Director at the AADAP Office.

**SITE INFORMATION**

Facility	
Reporting Individual	

**TREATMENT INFORMATION AND SCHEDULE**

OTC-Feed lot number		Total amount OTC-Feed used (lbs)	
Fish species treated		Daily percent body-weight fed	
Planned % TM pre-mix (e.g. 2, 4, 6%) in feed		OTC dosage (gm/100lb fish/day)	
Purpose of OTC Treatment	<b>skeletal tissue mark</b>		
Average fish weight (gm)		Average fish length (in)	
Number of fish per unit (e.g. 10,000 fish/raceway)			
Number of treated units		Total number of treated fish	
Number of control units		Total number of control fish	
Date treatment started		Date treatment ended	

**WATER QUALITY PARAMETERS**

Ave pre-treatment temp (°F)		Dissolved Oxygen (mg/L)	
Ave treatment temp (°F)		pH	

Ave post-treatment temp (°F)		Hardness - CaCO <sub>3</sub> (mg/L)	
------------------------------	--	-------------------------------------	--

## Marking Record

### INSTRUCTIONS

- Investigator should fill out the Marking Record as completely as possible.
- Prior to initiation of the trial, fill out Rearing Unit ID, whether a rearing unit is Treated or Control, and the number of fish in each rearing unit.
- Enter the **Marking Grade for each unit** in the proper column to indicate the quality of the mark:  
3 = excellent, 2 = good, 1 = poor, and 0 = no mark.
- Use additional copies of this form if more than 6 rearing units are involved in the trial.

		Facility:							
		Rearing Unit ID							
		<u>T</u> reated or <u>C</u> ontrol							
		Number of Fish							
Fish Number	Date	Days Post Treatment	Mark (pectoral fin ray)	Mark (pelvic fin ray)	Mark (opercula)	Mark (Jaw)	Mark (scale)	Mark (other)	Observer Initials
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									
16									
17									
18									

19									
20									

**RESULTS:** Describe in detail treatment results. Was treatment successful? If treatment did not appear to be successful, explain why not? Were there any mitigating environmental conditions that may have impacted treatment results? Were there any deviations from the Study Protocol?

**Pathology Report:** Attach pathology report to this form. Report should include: 1) a description of how the pathogen(s) was identified; 2) disease identification records that confirm the presence of the pathogen; and 3) the name and title of the individual performing the diagnosis.

Pathology Report included: ☐ pre-treatment ☐ post-treatment

**Toxicity observations:** Report any apparent drug toxicity including a description of unusual fish behavior.

**OBSERVED WITHDRAWAL PERIOD:**

Observed withdrawal period: \_\_\_\_\_ 21 days \_\_\_\_\_ 40 days \_\_\_\_\_ 70 days

Estimated number of days between last treatment and first availability of fish for human consumption (ensure this time period meets the withdrawal period). \_\_\_\_\_

**Disposition of Unused or Spoiled Terramycin® 200 for Fish Treated Feed:**

Use and disposition of all Terramycin® treated feed followed Study Protocol guidelines and has been clearly identified on Form OTC-2b (Investigator should initial)
---

☐ **Negative Report:** Terramycin® treated feed was not used at this facility under this Study Number during the reporting period. The study will be closed out in the online INAD database.

Date Prepared: \_\_\_\_\_ Investigator: \_\_\_\_\_

Date Reviewed: \_\_\_\_\_ Study Monitor: \_\_\_\_\_



## NOTICES

### Paperwork Reduction Act

In accordance with the Paperwork Reduction Act (44 U.S.C. 3501 *et seq.*), the U.S. Fish and Wildlife Service collects information necessary to permit the use of an investigational new animal drug to generate data to support a new animal drug approval (NADA) as part of the Fish and Aquatic Conservation fish health network. Your response is voluntary, but is required to obtain or retain a benefit. According to the Paperwork Reduction Act of 1995, an agency may not conduct or sponsor and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. OMB has approved this collection of information and assigned Control No. 1018-####.

### ESTIMATED BURDEN STATEMENT

We estimate public reporting for this collection of information to average 5 hours, including time for reviewing instructions, gathering and maintaining data, and completing and reviewing the form. Direct comments regarding the burden estimate or any other aspect of the form to the Service Information Clearance Officer, Fish and Wildlife Service, U.S. Department of the Interior, 5275 Leesburg Pike, MS: PRB (JAO/3W), Falls Church, VA 22041-3803, or via email at [Info\\_Coll@fws.gov](mailto:Info_Coll@fws.gov). Please do not send your completed form to this address.

### FREEDOM OF INFORMATION ACT STATEMENT

Information provided to the Service is generally subject to release to the public under the Freedom of Information Act (FOIA). Certain information, however, may be subject to withholding if the Service determines that the information is a trade secret and/or commercial or financial information that is privileged or confidential. To the extent you are submitting business information that falls into one of these categories, you must clearly mark this information as "Business Confidential" in order for the Service to assess the applicability of FOIA Exemption 4. Any information provided by you that is not marked as "Business Confidential" will be considered releasable to the public under the FOIA [43 CFR 2.26 – 2.33].