

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 Oxytetracycline Medicated Feed. The Investigator is responsible that Form OTC-W is completed accurately.
2. Investigator should keep the original on file, and Fax a copy to the Study Monitor for review.
3. After review, the Study Monitor will Fax a copy to the AADAP Office for assignment of the Study Number.
4. The AADAP Office will review the worksheet, and then fax the assigned trial Study Number to both the Investigator and Study Monitor, at which time the trial may be initiated.
5. Note: Both Investigator and Study Monitor should sign and date Form OTC-W.

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: Describe in detail the purpose of the clinical trial. For example you might compare OTC dosage, number of fish per unit, or disease to be treated. Study design must be carefully focused and lend itself to rigorous evaluation. If more space is required to describe study details, title additional page(s) "Study Design" and attach them to this Worksheet.

Study designed by _____

DISPOSITION OF TREATED FISH (Human Food Safety Considerations):

Check applicable box(es):

- Study Objective A - Current label: salmonids; 21 day withdrawal period
- Study Objective B - 10 gram dosage: all freshwater and marine species; 70 day withdrawal period
- Study Objective C - Current label: non-salmonid freshwater and marine species; 40 day withdrawal period
- Study Objective D - 6.0 gram dosage: abalone 35 day withdrawal period
- Study Objective E - Mark skeletal tissue in a variety of fish species; 21 days for standard dose (salmonids); 40 days for standard dose (non-salmonids); 70 days for high dose (all species)

Investigator should initial here to indicate awareness that fish disposition must be in compliance with FDA-mandated withdrawal times as described in Section VI. of the Study Protocol.

WORKER SAFETY CONSIDERATIONS:

Investigator should initial here to indicate that all personnel handling drug have read Material Safety Data Sheet for Terramycin® 200 for Fish and have been provided protective equipment, in good working condition, as described in the MSDS.

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 Terramycin® 200 for Fish medicated feed.
2. Investigator should keep the original on file, and send one copy to the Study Monitor for review.
3. Within 10 days of receipt, the Study Monitor should send a copy to the AADAP Office.
4. **Note:** Both Investigator and Study Monitor should sign and date Form OTC-1.

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	Terramycin® 200 for Fish	INAD Number	9332
Proposed Use of Drug	Treatment of certain bacterial diseases that occur in a variety of fish species; mark skeletal tissue in a variety of freshwater and marine 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	Yes	Non-pivotal Study	----
Approximate Number of Treated Animals		Approximate Number of Control Animals	
Number of Animals Used Previously ¹			
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 times based on specific treatment regimen)		

¹ To be filled out by the AADAP Office

Date Prepared: _____ Investigator: _____

Date Reviewed: _____ Study Monitor: _____

Date Reviewed: _____ Sponsor: _____

Form OTC-3b: Results Report Form for use of Terramycin® 200 for Fish under INAD 9332- All therapeutic use excluding salmonids with coldwater disease and *Oncorhynchus mykiss* with columnaris treated at 3.75g/100 lb fish/day

INSTRUCTIONS

- Investigator must fill out Form OTC-3b no later than 10 days after completion of the 20-day post-treatment observation period. Study Number must be recorded on all pages of Form OTC-3b. Attach lab reports and other information.
- If Oxytetracycline Medicated Feed was not used under the assigned Study Number, fill out only the Site Information portion on this page, and skip to the end of page 4 and fill out only the "Negative Report" section.
- Investigator should keep the original on file, and send a copy to the Study Monitor. Within 10 days of receipt, the Study Monitor should send a copy to the AADAP Office for inclusion in the permanent file.
- Note:** Both Investigator and Study Monitor should sign and date Form OTC-3b.

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 ₃ (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. 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									
	Day	Date	Water Temp (F°)	Mortality						
re-treatment	1									
	2									
	3									
	4									
	5									
	1									
	2									
	3									
	4									
	5									
	6									
	7									
	8									
	9									
	10									
11										
12										
13										
14										

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

Post-treatment Period

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.

DRUG DISCHARGE RESULTING FROM THIS TREATMENT: Use Addendum 2: Discharge Worksheet for calculations and attach completed Discharge Worksheet to this form. Enter the value from Addendum 2 step 3 in this space.

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). _____

NEGATIVE REPORT Oxytetracycline Medicated Feed was not used at this facility under this Study Number during the reporting period. (Investigator should initial for negative reports as soon as the Study Number is known to be no longer needed or valid.)

Date Prepared: _____ Investigator: _____

Date Reviewed: _____ Study Monitor: _____

**Form OTC-3c: Results Report Form for use of Terramycin[®] 200 for Fish
under INAD 9332- For use in the marking of skeletal tissue**

INSTRUCTIONS

1. Investigator must fill out Form OTC-3c no later than 10 days after completion of the 20-day post-treatment observation period. Study Number must be recorded on all pages of Form OTC-3c. Attach lab reports and other information.
2. If Oxytetracycline Medicated Feed was not used under the assigned Study Number, fill out only the Site Information portion on this page, and skip to the end of page 3 and fill out only the "Negative Report" section.
3. Investigator should keep the original on file, and send a copy to the Study Monitor. Within 10 days of receipt, the Study Monitor should send a copy to the AADAP Office for inclusion in the permanent file.
4. **Note:** Both Investigator and Study Monitor should sign and date Form OTC-3c.

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	skeletal tissue mark		
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 ₃ (mg/L)	

Marking Record

INSTRUCTIONS

1. Investigator should fill out the Marking 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. 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.
4. Use additional copies of this form if more than 6 rearing units are involved in the trial.

		Rearing Unit ID							
		Number of Fish							
		<u>T</u> reated or <u>C</u> ontrol							
		Skeletal Tissue Evaluated							
Fish Number	Date	Days Post-treatment	Mark	Mark	Mark	Mark	Mark	Mark	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. Was mortality considered "normal" during the treatment and post-treatment periods? If unanticipated mortality was observed, explain possible cause(s). Were there any mitigating environmental conditions that may have impacted treatment results? Were there any deviations from the Study Protocol?

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

DRUG DISCHARGE RESULTING FROM THIS TREATMENT: Use Addendum 2: Discharge Worksheet for calculations and attach completed Discharge Worksheet to this form. Enter the value from Addendum 2 step 3 in this space.

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). _____

NEGATIVE REPORT Oxytetracycline Medicated Feed was not used at this facility under this Study Number during the reporting period. (Investigator should initial for negative reports as soon as the Study Number is known to be no longer needed or valid.)

Date Prepared: _____ **Investigator:** _____

Date Reviewed: _____ **Study Monitor:** _____

Discharge Worksheet - Oxytetracycline

Instructions: Use this Worksheet to calculate estimates of 1) the *maximum* amount of Oxytetracycline (in grams) to be fed each day during treatment of the fish at your facility, and 2) the resulting average daily concentration of Oxytetracycline in your total hatchery wastewater discharge.

Handy conversion factors: 1 part per million (ppm) = 0.0283 grams/cuft; or, 0.0038 grams/gallon.

Calculations:

Step 1 - Calculate the total volume of treated and untreated water:

- 1a Number of rearing units to be treated: _____
- 1b Total water volume through these treated units during 24
hours: _____ (gal.) or (cuft.) of treated flow
- 1c Total water volume through all other untreated units during 24
hours: _____ (gal.) or (cuft.) of untreated flow
- 1d Grand total hatchery discharge (Treated + Untreated):
_____ (gal.) or (cuft.) of flow during 24 hours.

Step 2 - Calculate the daily amount of Oxytetracycline administered each day (24 hours) in this trial:

$$2a \quad \text{Amount} \quad \text{gms} = \left(\frac{\text{Pounds of fish treated}}{100} \right) * \text{Oxytet dosage given} \quad \text{gms Oxytet/100 lbs of fish}$$

Step 3 - Calculate Oxytetracycline level resulting in hatchery discharge during treatment period:

$$3a \quad \text{Disch. level} \quad \text{PPM} = \frac{\text{Amt. from line 2a}}{\left(\frac{\text{Total vol. (line 1d)}}{\text{Conver. factor}} \right)}$$

* If in gallons use 0.0038
If in cubic ft use 0.0283