

Form MT-W: Worksheet for Designing Individual Field Trials Under MT INAD 11-236

INSTRUCTIONS

1. Investigator must fill out Form MT-W for each trial conducted under this INAD **before** actual use of MT medicated feed. The Investigator is responsible for accurate completion of Form MT-W.
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 MT-W.

SITE INFORMATION

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

FISH CULTURE AND DRUG TREATMENT INFORMATION

Manufacturer of MT medicated feed		Rangen Inc.	
MT medicated feed batch number		MT medicated feed manufacture date	
Treatment dosage	9 mg/kg bw/day	Treatment duration	28 days
Fish species to be treated		Number of fish to be treated	
Fish age (days post-hatch)		Average fish length (mm)	
Number of rearing units to be treated		Number of fish per treated rearing unit	
Number of control rearing units		Number of fish per control rearing unit	
Feed rate (% body weight fed per day)	15	Estimated total weight of fish treated (kg)	
Estimated amount of MT medicated feed needed for proposed treatment (kg)			
Anticipated date treatment will be initiated			

Worksheet for Designing Individual Field Trials (cont.)

STUDY DESIGN: Describe in detail the purpose of the clinical trial. 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):

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

USE AND DISPOSITION OF MT MEDICATED FEED (Environmental Safety Considerations):

Investigator should initial here to indicate awareness that MT medicated feed usage and disposition must be in compliance with requirements described in the Study Protocol.

WORKER SAFETY CONSIDERATIONS:

Investigator should initial here to indicate that all personnel handling MT medicated feed have read the Material Safety Data Sheet for 17-alpha methyltestosterone and have been provided personal protective equipment, in good working condition, as described in the Study Protocol.

Date Prepared: _____ Investigator: _____

Date Reviewed: _____ Study Monitor: _____

FORM MT-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 MT-1 **immediately** upon receipt of 17-alpha methyltestosterone 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 MT-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. The following information is submitted in triplicate:

Name of Drug	17-alpha methyltestosterone medicated feed		
INAD Number	11-236	Study Number	
Proposed Use of Drug	Production of tilapia populations comprised of greater than 90% male fish (i.e. sex reversal)		
Date of CVM Authorization Letter	December 20, 2007		
Date of Medicated Feed (MF) Receipt		Amount MF Received (kg)	
Medicated Feed (MF) Batch Number		MF Manufacture Date	
Location of Trial (facility name)			
Name of Investigator			
Address of Investigator			
Pivotal Study (yes/no)		Non-pivotal Study (yes/no)	
Approximate Number of Treated Animals		Approximate Number of Control Animals	
Number of Animals Used Previously¹			
Study Protocol Number	11-236		
Approximate dates of trial (start/end)			
Species, Size, and Type of Animals			
Maximum daily dose and duration	9 mg/kg body weight for 28 consecutive days		
Methods(s) of Administration	Medicated feed		
Withdrawal Period	Batch culture = 120 days Partial harvest/restock culture = 350 g fish weight		

¹ To be filled out by the NIO

Date Prepared: _____ **Investigator:** _____

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

Date Reviewed: _____ **Sponsor:** _____

STUDY NUMBER: _____

Form MT-2a. Daily Record of MT Medicated Feed Use *(for use as a supplement to Form MT-2)*

- Instructions:**
1. Form MT-2a should be used by the Investigator to supplement data on Form MT-2.
 2. A separate Form MT-2a should be used for each treatment event.
 3. Form MT-2a should be appended directly to Form MT-2.

Study Number	Treatment Day	Date	MT-Medicated Feed Used (kg)	Feed Administered by (initials)
	1			
XXXX	2			
XXXX	3			
XXXX	4			
XXXX	5			
XXXX	6			
XXXX	7			
XXXX	8			
XXXX	9			
XXXX	10			
XXXX	11			
XXXX	12			
XXXX	13			
XXXX	14			
XXXX	15			
XXXX	16			
XXXX	17			
XXXX	18			
XXXX	19			
XXXX	20			
XXXX	21			
XXXX	22			
XXXX	23			
XXXX	24			
XXXX	25			
XXXX	26			
XXXX	27			
XXXX	28			

Date Prepared: _____

Investigator: _____

Date Reviewed: _____

Study Monitor: _____

Form MT-3: Results Report Form for Clinical Field Trials Using MT Medicated Feed Under INAD 11-236

INSTRUCTIONS

- Investigator must fill out Form MT-3 no later than 10 days after completion of treatment. Study Number must be recorded on all pages of Form MT-3. Attach lab reports and other information.
- If MT 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 2 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 MT-3.

SITE INFORMATION

Facility	
Reporting Individual	

FISH CULTURE AND DRUG TREATMENT INFORMATION

MT medicated feed batch number		MT medicated feed manufacture date	
Treatment dosage	9 mg/kg bw/day	Treatment duration	28 days
Fish species treated		Total number of fish treated	
Number of rearing units treated		Number of fish per treated rearing unit	
ID of all treated rearing units (e.g. Tank 5, Pond 6B)			
Number of control units		Number of fish per control unit	
Fish age (days post-hatch)		Average fish length (mm)	
Treatment date (initiated)		Treatment date (completed)	
Sample collection ¹ (yes/no)		Sample collection date	
Number of fish remaining at the completion of the treatment period (i.e. number of fish treated minus treatment period mortality)			

¹ Sample of 60 fish collected for determination of sex ratio and sent to AADAP Office for histological evaluation

WATER QUALITY PARAMETERS

Mean Treatment Temperature (°F)		Mean Dissolved Oxygen (mg/L)	
Mean pH		Mean Hardness - CaCO ₃ (mg/L)	

RESULTS: Describe in brief detail treatment results. Did treatment go as planned? Did all fish readily consume MT medicated feed? Was any unusual fish behavior or unexpected mortality associated with the treatment?? 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?

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

OBSERVED WITHDRAWAL PERIOD OF TREATED FISH:

Observed withdrawal period for BATCH CULTURE: _____ **120 days** (Investigator should initial)

Observed withdrawal period for PARTIAL HARVEST/RESTOCK CULTURE: _____ **350 g fish weight** (Investigator should initial)

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 MT MEDICATED FEED

Use and disposition of all MT medicated feed followed Study Protocol guidelines and has been clearly identified on Form MT-2 (Investigator should initial)

_____ **NEGATIVE REPORT** MT 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 MT-5: Transfer Record of MT-treated Fingerling Tilapia Under MT INAD 11-236

INSTRUCTIONS

1. Form MT-5 must be completed by Investigators for all sales of MT-treated fingerling tilapia to other producers for grow-out of fish to market size. The purpose of this form is to formally establish that all purchasers of MT-treated fingerling tilapia are aware of, and agree to comply with, the FDA-mandated withdrawal period(s) that must be observed before MT-treated tilapia may be slaughtered for processing or released for possible human consumption.
2. This form should be completed and signed by both the Investigator and purchaser **prior** to the transfer of fish.
3. The original should be returned to the Investigator and maintained on file. Within 10 days of fish transfer, the Investigator should send a copy to the AADAP Office for inclusion in the permanent file.

INVESTIGATOR (i.e. seller) INFORMATION

Investigator			
Facility			
Number of MT-treated fingerlings transferred		Transfer date	
Treatment dates (i.e., start date - end date)		Study Number Corresponding to MT-treated fingerlings	

PURCHASER (i.e. buyer) INFORMATION

Name of purchaser			
Facility address			
Phone Number			

As described in the FDA-approved Study Protocol for MT INAD 11-236:

a.) **The investigational withdrawal period for fish reared under a batch culture regime will be 120 days.** Batch culture is defined as when all fish in a group/lot enter and leave the lot at the same time (sometimes referred to as “all in/all out” culture). In batch culture a defined group of similar age/size fish are stocked simultaneously for a prescribed grow-out period, which is followed by a complete harvest of the production unit. This withdrawal period is determined based on the last day of treatment with 17-alpha methyltestosterone medicated feed.

b.) **The investigational withdrawal period for fish reared under partial harvest/restock culture will be until such time that harvested fish reach an individual minimum weight of 350 g.** Partial harvest/restock culture is defined as the mixing of different lots of fish during the grow-out period, and the selective harvest of fish from the production unit at various times.

The purchaser acknowledges his/her responsibility to comply with the above-stated withdrawal periods:

Purchaser: _____

Date: _____

Investigator: _____

Date: _____