



# National INAD Program Overview

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USFWS - AADAP



# Today's Presentation

- Background Information on the NIP
- How to Participate
- AADAP Website
- Your Help is Needed
  - How you can help!



# Investigational New Animal Drugs (INAD) 101

- What are they?
  - Allow the legal use of unapproved drugs under limited and experimental conditions
  - Strictly controlled by FDA's Center for Veterinary Medicine
- Why are they important?
  - Provide fisheries managers access to drugs necessary to meet current management needs
  - Generates the necessary supportive data to demonstrate a drug's safety and effectiveness and support broad (i.e., multiple species/pathogens) approvals

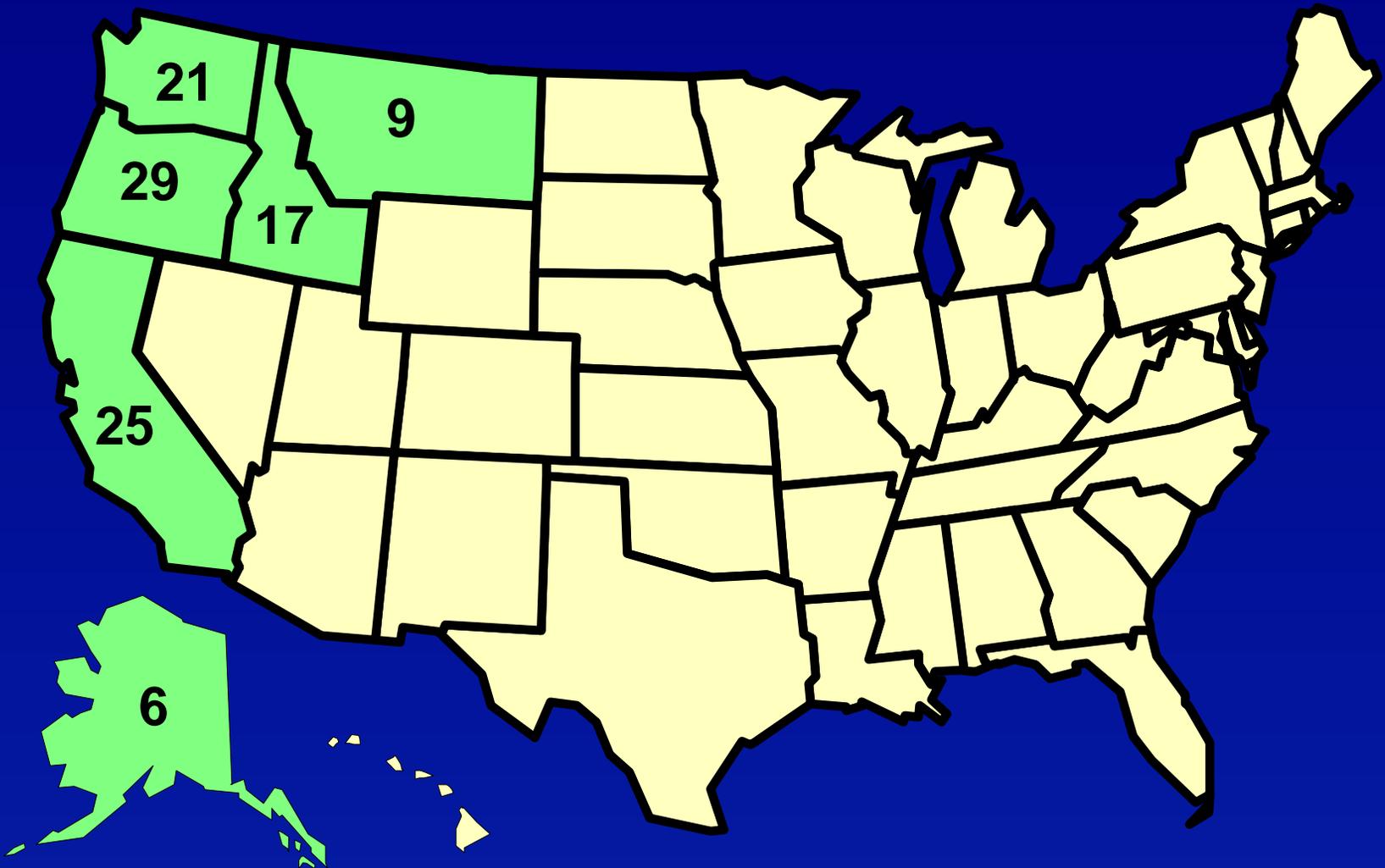


# National INAD Program (NIP)

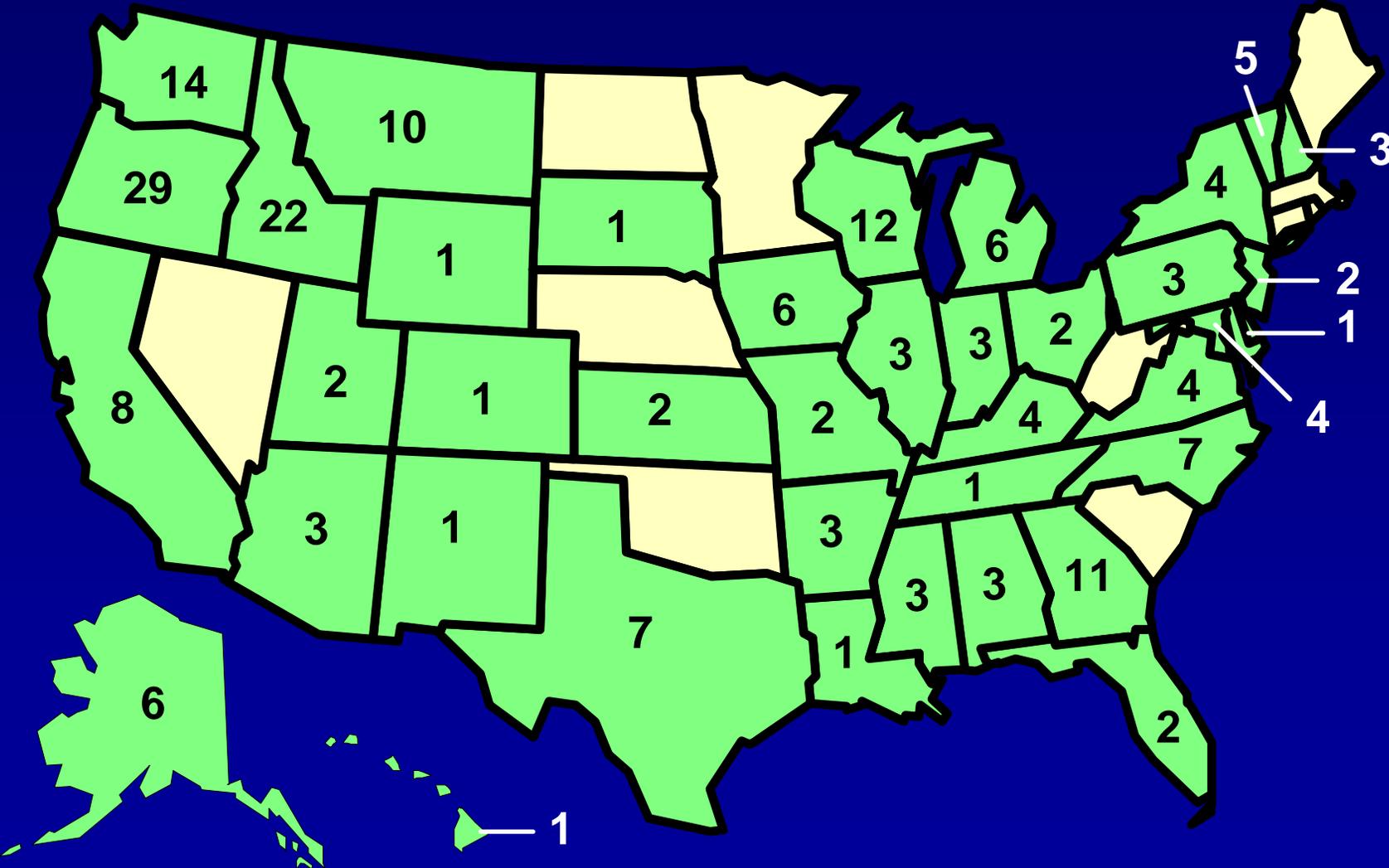
- Established in 1998 to meet the INAD needs of 6 western states
- Expanded in 1999 to include State, Tribal, University, and private aquaculture facilities throughout the entire U.S.
- NIP is a cost-reimbursable program



Map of the United States Showing State, Tribal, and Private Aquaculture Participation (by Number of Facilities) in the National INAD Program **Calendar Year 1998**



Map of the United States Showing State, Tribal, and Private Aquaculture Participation (by Number of Facilities) in the National INAD Program  
Calendar Year 2005/2006



# USFWS INAD Exemptions

- OTC Medicated Feed
- Florfenicol Med. Feed
- Chloramine-T
- Diquat
- OTC Immersion
- OTC Injectable
- Aqui-S
- LHRHa
- CCP
- sGnRHa
- Calcein Bath Mark
- 17-alpha Methyltestosterone
- Formalin
- Slice



# How to Participate

- Fill out & send in the current year sign-up form
- AADAP Office sends
  - Study Protocols, Cooperative Agreements, Standards & Invoice
- AADAP Office notifies FDA & drug sponsors
- Participants *Read* Study Protocols



# INAD Study Protocols

- Heart-and-Soul of INAD Process
- Approved by FDA and required to receive slaughter authorization to treat animals
- Contains all pertinent information regarding drug acquisition, fish treatment and disposition, data collection, etc., etc.



# Key Study Protocol Sections

- Drug Manufacturer
  - source of supply
  - storage & handling procedures
- Entrance Criteria
  - study animals
  - presence of disease
- Treatment Schedules
  - must follow study objectives
- Disposition of Investigational Animals
  - withdrawal time met
  - fish are disposed of properly



# INAD Forms – Data Reporting

- Form “CLT”– W: Worksheet for Designing Individual Field Trials
- Form CLT– 1: Report on Receipt of Drug
- Form CLT– 2: Drug Inventory Form
- Form CLT– 3: Results Report Form
- Addendum 2 - Discharge Worksheet



# Study Worksheet

- 2 page form
- Sent in prior to start of study
- Fish numbers, disease, treatment regimen, etc.
- AADAP reviews & assigns a Study Number

## Chloramine-T Clinical Field Trials CLT-W: Worksheet for Designing Study Numbers - Version 4 Chloramine-T INAD 9321

### INSTRUCTIONS

1. Investigator must fill out Form CLT-W for each trial conducted under this INAD **before** actual use of Chloramine-T. The Investigator is responsible that Form CLT-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 Bozeman NIO for assignment of the Study Number.
4. The Bozeman NIO 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 CLT-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)	
No. 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	
Anticipated date treatment will be initiated			
Check type of treatment method used		___ Flow through ___ Standing bath	
Check type of treatment		___ Disease control ___ Disease prevention	
Intended drug target dosage (mg/L)	<input type="checkbox"/> 10 mg/L <input type="checkbox"/> 15 mg/L <input type="checkbox"/> 20 mg/L	Estimated total amount of drug needed for proposed treatment (Kg)	
Drug manufacturer		Drug lot number	

# Drug Receipt Form

- 1 page form
- Sent in within 10 days of drug receipt
- Fish numbers, date received, amount received
- AADAP reviews & sends a copy to FDA

## FORM CLT-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 CLT-1 **immediately** upon receipt of chloramine-T.
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 Bozeman NIO.
4. **Note:** Both Investigator and Study Monitor should sign and date Form CLT-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	Chloramine-T	INAD Number	9321
Proposed Use of Drug	Treatment or control of bacterial gill disease or certain flavobacteriosis that occur in a variety of fish species		
Date of CVM Authorization Letter	July 11, 2003		
Date of Drug Receipt		Amount of Drug Received	
Drug Lot Number		Study Worksheet Number	
Name of Investigator			
Address of Investigator			
Location of Trial			
Pivotal Study (yes/no)		Non-pivotal Study (yes/no)	
Approximate Number of Treated Animals		Approximate Number of Control Animals	
Number of Animals Used Previously <sup>1</sup>			
Study Protocol Number	9321		
Approximate dates of trial (start/end)			
Species, Size, and Type of Animals			
Maximum daily dose and duration	20 mg/L for 1hour		
Method(s) of Administration	Immersion (static bath or flow-through treatment)		
Withdrawal Period	Zero		

<sup>1</sup> To be filled out by the NIO

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

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

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



# Results Report Form

- 3 page form
- Sent in within 10 days after the completion of the study
- Actual fish numbers, disease, treatment regimen, etc.
- Track mortality
- Results
  - Successful
  - Deviations
- Pathology Reports
- Toxicity/Adverse Effects
- Withdrawal Times
- Signatures
- AADAP reviews & generates 2 pg summary report

# Results Report Form - Page 1

STUDY NUMBER \_\_\_\_\_

Page 1 of 3

**Chloramine-T Clinical Field Trials**  
**CLT-3B: Results Report Form - Version 4**  
*(For use on non-salmonids or salmonids with a disease condition  
 other than BGD and for salmonids with BGD treated at 10ppm)*  
**Chloramine-T INAD 9321**

**INSTRUCTIONS**

1. Investigator must fill out Form CLT-3B no later than 10 days after completion of the 14-day post-treatment observation period. Study Number must be recorded on all pages of Form CLT-3B. Attach lab reports and other information.
2. If Chloramine-T 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 Bozeman NIO for inclusion in the permanent file.
4. **Note:** Both Investigator and Study Monitor should sign and date Form CLT-3B.

**SITE INFORMATION**

Facility	
Reporting Individual	

**TREATMENT INFORMATION AND SCHEDULE**

Drug lot number		Total amount drug used (kg)	
Fish species treated		CLT dosage used (mg/L)	
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	
Check type of treatment	<input type="checkbox"/> Flow through <input type="checkbox"/> Standing bath		
Dates of treatment (disease control)	1st	2nd	3rd
Date treatment started (disease prevention)		Date treatment ended (disease prevention)	

**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)	

# Results Report Form - Page 2

STUDY NUMBER \_\_\_\_\_

Page 2 of 3

## Daily Mortality Record

### INSTRUCTIONS

- Investigator should fill out the Daily Mortality 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.
- Water temperature and individual tank mortality should be recorded on a daily basis.
- If treatment is on 3 consecutive days, fill in only days 1-3 of the "treatment period" and proceed directly to day 1 of the "post-treatment period". If treatment is on 3 alternate days, fill in days 1-5 of the "treatment period" and proceed to day 1 of the "post-treatment period". If less than 3 treatments are used, proceed directly to day 1 of the "post-treatment period" after the final treatment. Please mark all treatment days with an asterisk.
- Use additional copies of this form if more than 6 rearing units are involved in the trial.

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 period	1									
	2									
	3									
	4									
	5									
Post-treatment period	1									
	2									
	3									
	4									
	5									
	6									
	7									
	8									
	9									
	10									
	11									
	12									
	13									
	14									

# Results Report Form - Page 3

STUDY NUMBER \_\_\_\_\_

Page 3 of 3

**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.

**NEGATIVE REPORT** Chloramine-T 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

- 1 page form
- Sent in with corresponding Form 3
- Calculates drug discharge from facility

ADDENDUM 2

## Discharge Worksheet - Chloramine-T

**Instructions:** Use this Worksheet to calculate estimates of 1) the *maximum* amount of Chloramine-T to be used for a single treatment of fish at your facility, and 2) the resulting concentration of Chloramine-T 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 flow of treated and untreated water during treatment period:

1a Number of rearing units to be treated: \_\_\_\_\_

1b Total water volume (at treatment flow rates) to these units during treatment period: \_\_\_\_\_ (gal.) or (cuft.) of treated flow)

1c Total water volume to all other untreated units during treatment period: \_\_\_\_\_ (gal.) or (cuft.) of untreated flow)

1d Grand total hatchery discharge (Treated + Untreated):  
\_\_\_\_\_ (gal.) or (cuft.) of flow during treatment period.

Step 2 - Calculate the amount of Chloramine-T needed:

2a \_\_\_\_\_ gms =  $\frac{\text{_____}}{\text{Amount}} \times \frac{\text{_____}}{\text{Vol. from line 1b}} \times \frac{\text{_____}}{\text{Conv. factor}^*} \times \frac{\text{_____}}{\text{Desired dosage}}$  ppm

Step 3 - Calculate Chloramine-T level in hatchery discharge during treatment period:

3a \_\_\_\_\_ ppm =  $\frac{\text{_____}}{\text{Disch. level}} \div \left( \frac{\text{_____}}{\text{Amt. from line 2a}} \times \frac{\text{_____}}{\text{Total vol. (line 1d)}} \times \frac{\text{_____}}{\text{Conver. factor}^*} \right)$   
\*If in gallons use 0.0038  
If in cubic ft use 0.0283

# Field Data for Years 2004/2005

- 10 Different INADs

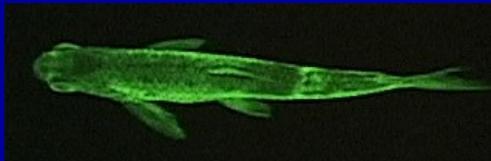
- Aquí-S, CAL, CCP, CLT, DQT, FLOR, LHRHa, OTC, OTIMM, OTINJ

- 23 Coolwater Species

- Walleye, Bass, Perch, sturgeon, etc., etc.

- Total of 443 Studies Conducted

- 82% of the studies appeared to be successful
- 3% of the studies unsuccessful
- 15% characterized as inconclusive



The AADAP Program has developed a website at  
<http://www.fws.gov/fisheries/aadap/>

The website debuted August 2004 as a “one stop shopping” for information on all aquaculture drug approvals and activities

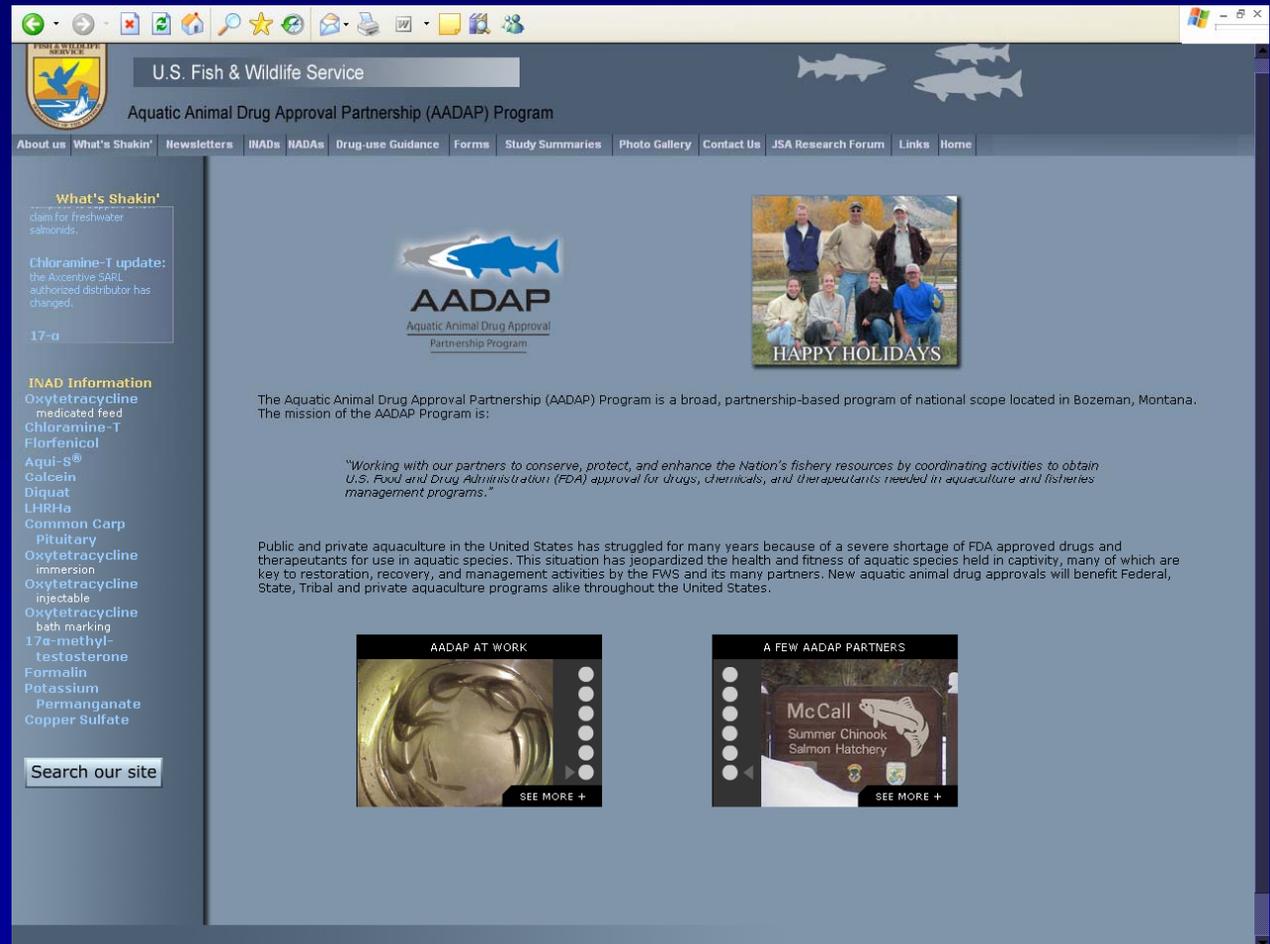
INAD specific features of the website include:

- INAD Sign-up Information
- INAD Fact Sheets (one-pagers)
- Complete INAD Study Protocols
- All INAD Forms
- Annual Reports



# AADAP Website – Welcome Page

- Dynamic
- INAD information available
- Drug guidance forms
- AADAP Newsletters
- Links



The screenshot shows the AADAP website interface. At the top, there is a navigation bar with the U.S. Fish & Wildlife Service logo and the text "Aquatic Animal Drug Approval Partnership (AADAP) Program". Below this is a horizontal menu with links: "About us", "What's Shakin'", "Newsletters", "INADs", "IADAs", "Drug-use Guidance", "Forms", "Study Summaries", "Photo Gallery", "Contact Us", "JSA Research Forum", "Links", and "Home".

The main content area features a large blue fish logo with the text "AADAP Aquatic Animal Drug Approval Partnership Program" below it. To the right of the logo is a photo of a group of people with the text "HAPPY HOLIDAYS".

Below the logo and photo, there is a paragraph: "The Aquatic Animal Drug Approval Partnership (AADAP) Program is a broad, partnership-based program of national scope located in Bozeman, Montana. The mission of the AADAP Program is:"

Below this paragraph is a quote: "Working with our partners to conserve, protect, and enhance the Nation's fishery resources by coordinating activities to obtain U.S. Food and Drug Administration (FDA) approval for drugs, chemicals, and therapeutics needed in aquaculture and fisheries management programs."

Below the quote is another paragraph: "Public and private aquaculture in the United States has struggled for many years because of a severe shortage of FDA approved drugs and therapeutics for use in aquatic species. This situation has jeopardized the health and fitness of aquatic species held in captivity, many of which are key to restoration, recovery, and management activities by the FWS and its many partners. New aquatic animal drug approvals will benefit Federal, State, Tribal and private aquaculture programs alike throughout the United States."

At the bottom of the main content area, there are two small image galleries. The first is titled "AADAP AT WORK" and shows a close-up of a fish in a tank. The second is titled "A FEW AADAP PARTNERS" and shows a sign for "McCall Summer Chinook Salmon Hatchery".

On the left side of the page, there is a sidebar with the following sections:

- What's Shakin'**
  - claim for freshwater salmonids.
  - Chloramine-T update:** the Axcentive SARL authorized distributor has changed.
  - 17-a
- INAD Information**
  - Oxytetracycline medicated feed
  - Chloramine-T
  - Florfenicol
  - Aqui-S®
  - Galcein
  - Diquat
  - LHRHa
  - Common Carp
  - Pituitary
  - Oxytetracycline immersion
  - Oxytetracycline injectable
  - Oxytetracycline bath marking
  - 17α-methyl-testosterone
  - Formalin
  - Potassium Permanganate
  - Copper Sulfate
- Search our site

# AADAP Website – Aqu-i-S Fact Sheet

- Drug name & source
- Treatment regimen
- Withdrawal Period
- Links to:
  - Study Protocol
  - Forms
  - Annual Reports
  - Status of drug approval

The screenshot shows a Microsoft Internet Explorer browser window displaying the AADAP website. The page title is "Fact Sheet: AQU-I-S INAD 10-541 for detailed information, see INAD study protocol, use link on the left". The page features a table with the following information:

<b>Objective/purpose:</b>	Collect supportive and pivotal data needed to establish the effectiveness of AQU-I-STM as an anesthetic for use in a variety of fish species.
<b>Drug name:</b>	AQU-I-STM
<b>Source of drug:</b>	AQU-I-S New Zealand, Ltd.
<b>Address:</b>	P.O. Box 818 San Luis Obispo, CA 93406
<b>Contact:</b>	Bob Campbell Phone: 805-542-0871; Fax: 805-542-0891; email: campbellr@aol.com
<b>Target pathogen(s):</b>	Not Applicable
<b>Method of administration:</b>	Immersion: standing-bath treatment only
<b>Treatment dosage:</b>	5 - 80 milligrams AQU-I-STM per liter
<b>Treatment regimen:</b>	Treatment duration is 1 - 60 minutes. Treatment duration will vary dependent upon species, water temperature, and level of anesthesia desired. AQU-I-STM should be applied as a single treatment event.
<b>Withdrawal period:</b>	21 days
<b>Required test parameters:</b>	Investigator must collect data documenting: 1) time to anesthesia; and 2) time to recovery from anesthesia. Investigator should also report general fish behavior and any adverse effects relating to treatment.
<b>Limitations or restrictions on use:</b>	Treatment is restricted to anesthetic tanks containing a maximum of 75 gallons of water. Investigator must follow all instructions in the Study Protocol for INAD 10-541 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.
<b>Required INAD fee:</b>	none
<b>AADAP contact for other information:</b>	Ms. Bonnie Johnson, FWIS - AADAP Phone: 406-587-9265 ext. 136 Fax: 406-582-0242 bonnie_johnson@fws.gov

At the bottom of the table, there are three buttons: "home", "top", and "close".

# National INAD Program Summary

- ".....of the many drug approval-related activities that AADAP is involved in....if not the most important, the NIP is certainly the most rewarding (at least in the short-term)....as through this program we are able to help fisheries managers meet their immediate needs, and help to make a positive impact on our precious fisheries resources..."



# Help Wanted....Pivotal Studies!!!

- Pivotal Studies are:
  - High quality, scientifically valid studies that are an essential component of all complete NADA packages
  - Considerably more rigorous than typical “INAD” studies (e.g., controls, replication, disease confirmation, dose verification, blinding, etc. etc.)
  - Typically completed at field stations under production conditions.....always conducted with considerable coordination and on-site assistance from AADAP

# Help Wanted!!!

## Pivotal Studies Still Needed

- **Florfenicol**
    - Columnaris on any coolwater species
  - **OTC Medicated Feed**
    - Columnaris on any coolwater species
  - **Chloramine-T**
    - BGD on any coolwater species
- Contact: Jim Bowker  
406/994-9910  
[jim\\_bowker@fws.gov](mailto:jim_bowker@fws.gov)



