

The Investigational New Animal Drug Program – Monitor Guide

As the monitor your job involves assisting the Investigator to complete all necessary steps of the INAD process including reviewing the Study Requests and Results Report before submitting them to AADAP. We encourage Investigator’s to reach out to their Monitor with questions prior to contacting AADAP. This guide is intended to provide Monitor’s with the information needed to help answer those questions and aid them in the INAD process. The following topics are covered below:

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Monitor qualifications

The monitor is responsible for reviewing the study protocols laid out by the FDA and ensuring that they are followed while conducting INAD studies. Ideally, the monitor would be a fish health professional or someone in a supervisory role, this is not required, but it often helps to enforce the protocol or aid in diagnosing fish diseases.

Setting up an account

If you are brand-new to the INAD Program you will first need to set up an account. It is important that the Monitor set up their account before the Investigator initiates theirs. **Each facility can only have one Monitor**; however, a monitor can be responsible for multiple facilities.

New Monitor account – If brand new start here!

Visit our “[How to Enroll in the Investigational New Animal Drug Program](#)” page for step-by-step instructions on the enrollment process.

Go to the [INAD database homepage](#), and select “Study Monitor”.

Enter the requested contact information.

Click “Submit for Approval”.

Contact Investigators so they can select you as their Monitor through their account.

New Monitor taking over pre-existing account

If a facility already has a Monitor it is best for the incoming Monitor to take over the account, rather than create their own. This ensures that the new Monitor will have access to previously conducted studies. To take over an account the previous Monitor will need to share the login information with the new individual. If the login information is unknown [contact AADAP](#).

Log in, select the “Account Info” tab on the top menu bar of the page.

Update the contact information to reflect the new Monitor, change the username and password, then click the “Save Data” button.

The Investigators’ accounts will automatically update their Monitor information to you once this is completed.

Updating the Monitor account

If you need to update your contact information, do the following:

Log into the Monitor account on INAD database, select the “Account Info” tab on the upper-left of the page, and update the Account Information section. Be sure to click the “Save Data” button.

Monitors acting as Investigators

AADAP strongly discourages Monitors from acting in both roles (Investigator and Monitor) however, we realize this is sometimes necessary to meet the data entry requirements. In these rare cases, follow these steps to successfully submit a study.

- The Investigator will need to send the raw data and all required information to the Monitor.
- The Monitor will need to log on to the Investigator’s account on the INAD database to enter the data (**data can only be entered from the Investigator’s account**).
- Once all the required information has been added, the Monitor will need to log out of the Investigator’s account and log into the Monitor’s account to advance the Study Request/ Results Report.
 - This may require closing the web browser and re-opening the website.

The data-entry is a multi-step process which is meant to provide both the Investigator and Monitor opportunities to ensure that the information entered in the studies is complete and accurate.

Yearly enrollment

Each year that a facility would like to participate in the INAD Program they will need to enroll. Enrollment lasts for one calendar year and participants are not limited to the number of studies conducted or the number of species they can treat using an INAD. Each non-USFWS facility/office will be required to pay \$700 to participate in the INAD Program for each INAD they plan to use per year. When enrolling, a facility will need to sign up for each INAD they plan to use as well as each individual species they plan to treat. **Note:** there is no charge for monitor accounts; only for actively participating Investigator accounts.

Enrollment is the responsibility of the Investigator and **can only be added by the Investigator**. Please see the [Investigator's Guide](#) for detailed instructions.

Ordering the INAD drug

Once a facility has enrolled in the INAD Program they will need to contact the drug suppliers to order the INAD. Either the Investigator or the Monitor can order the drug. If the Monitor makes the order, then they should reference the name of the facility(ies) which will be conducting the treatment. If needed, the Monitor **can** order the INAD for their facility(ies), store it at their location, and then send the amount needed to multiple facilities, as long as those facilities were participating in the INAD Program. Contact information for each supplier can be found on the [INAD Fact Sheet page](#). Please note that some INADs require that the Study Request be filled out prior to receiving the INAD. It is important to know that the INAD fee does not pay for the INAD drug and that submitting a Study Request does not automatically order the drug.

The drug suppliers listed on the INAD factsheet pages are working on the specific formulations of drugs which are in the approval process. Therefore, only their product can be used for an INAD treatment.

Submitting a drug receipt

Submitting a drug receipt is the responsibility of the Investigator and must be done from the Investigator's INAD account. Each time an INAD drug is ordered a drug receipt will need to be submitted. All drug receipts need to be submitted within 10 days of receiving the drug. Please note that extra INAD drug **can** be transferred to other facilities participating in the INAD Program.

Please see the [Investigator's Guide](#) for detailed instructions on how to submit a drug receipt.

If the Monitor stores the INAD:

If a Monitor stores the INAD and sends it out as needed, they do not need to submit a drug receipt. However, the Monitor will need to send an email to AADAP each time they receive an INAD drug so AADAP can enter this information in our tracking system. Once the receiving facility obtains the INAD they will then be responsible for submitting a drug receipt. **Note:** When submitting a drug receipt in this way, the date should reflect **the day the facility received the INAD**, not the date that their Monitor received the INAD.

Checklist for Study Requests

A Study Request needs to be submitted each time a facility plans to treat their fish, **before the treatment occurs**. The Investigator is responsible for filling out and submitting Study Requests. Once the Investigator submits the request it will be sent to the Monitor, NOT AADAP (see Study Stages below). The Monitor then reviews the Study Request to ensure that all necessary information is included and accurate. The [study protocol and factsheet](#) webpage contains all the information needed to ensure that the protocol laid out by the FDA is followed. Once the Monitor has reviewed the Study Request, they can submit it to AADAP to assign a study number. Treatment cannot be initiated until a study number has been assigned.

All current and previously conducted studies can be found from the Monitor's Homepage on the INAD database. Study Requests which are waiting for the Monitor's review can be found on the Monitor's Homepage and will be **highlighted in red**.

A complete Study Request needs to contain the following:

- The drug dose must be within the threshold laid out in the study protocol. The correct dose may be species/sex dependent.
- Double check the calculations for the drug dose to ensure they are accurate.
- The number of fish treated must be consistent throughout the form.
- The anticipated number of study dates should include the number of dates which the treatment was administered, not the span of dates from the beginning to end of treatment.
- There are usually multiple options for the Study Protocol Objective. Please be sure to read each option and select the one that is representative of the treatment needed.
- The Study Design section should include a brief description of the planned study including, the reason the fish should be treated, the treatment dates, the number of fish that will be treated, and whether the fish are considered a threatened or endangered species.
- If a deviation from the Study Protocol is unavoidable, please let AADAP know prior to conducting the treatment.**

***If you find anything that does not match up or additional information is needed please contact the Investigator and address the concern before submitting the Study Request to AADAP.**

Once you have completed reviewing the form click "Approve for Testing" which will send the Study Request to AADAP.

Study numbers

A study number is assigned to each Study Request by AADAP. The study number allows AADAP to track and reference each study.

A new study number is needed (e.g., a new Study Request will need to be submitted) anytime a new therapeutic or sex reversal treatment is initiated.

- If the start date of treatments will be staggered over multiple days, then each treatment will need its own study number.

For anesthetic, marking, or spawning INADs there are different guidelines. Generally, a new study number will be needed;

- if there are more than 30 days between treatments,
- different doses will be used,
- different levels of sedation will be used (handleable, surgery, or euthanasia),
- or the treatment crosses into the new year by more than two weeks.

If these guidelines are not followed, AADAP will ask that your studies be broke up into multiple study numbers. Even if the treatment has already occurred AADAP may request additional study requests to be submitted, enabling the data to be better evaluated.

Study stages

The INAD process is broken into seven study stages as described below. In **bold** you will see who is responsible for advancing the study in each stage.

Stage 1: Before treatment can begin, the **Investigator** must fill out and submit a Study Request. The Study Request is advanced to the Monitor.

Stage 2: The **Monitor** will review and advance the Study Request to AADAP.

Stage 3: **AADAP** will review the Study Request and assign a study number.

Stage 4: Treatment can now begin. Once the treatment is completed and all data has been collected, the **Investigator** then enters the data into the Results Report and submits it to the Monitor.

Stage 5: The **Monitor** will review the Results Report and advance the study to AADAP.

Stage 6: **AADAP** will review the study for the last time and determine if it can be approved.

Stage 7: Completed studies will be archived in the database and accessible to study participants.

If information is missing, the protocol is not followed, or forms are not correctly filled out, both the Monitor and AADAP can send the Results Report back to Stage 4 for the Investigator to edit.

Adverse events

Ideally, the Monitor should be present during INAD studies to ensure that the required data is being collected and the protocols are properly followed. We recognize that this is not always realistic, and if that is the case, the Monitor is responsible for contacting the Investigator to ensure that the treatment is going to plan.

If an adverse event occurs (i.e., fish die during/after treatment that is attributed to the INAD) then the Investigator must notify the **Monitor and AADAP immediately**. AADAP will then determine if additional information needs to be collected and submitted to the FDA.

Concomitant drug use

The use of additional drugs (approved or unapproved) are considered concomitant treatment. Some INADs allow concomitant use with specific INADs, however this is not common. The Monitor needs to know if concomitant use ([found in study protocols](#)) is allowed prior to conducting a treatment and enforce that throughout the study.

If concomitant use is NOT allowed then no other drugs can be used for a **minimum of 2 weeks prior to treatment, 2 weeks post-treatment, and during the treatment period**. This ensures that the INAD treatment can be fully evaluated without the efficacy discounted because another drug was applied to the fish.

If concomitant use is allowed for the INAD, or it is necessary to treat threatened or endangered fish which are not available for human consumption, please contact AADAP for additional information on how to conduct the study **prior to the treatment being conducted**.

Fish health reports

Fish health reports are always encouraged to be added to the Results Report form. However, in some situations, a fish health report may be required to be submitted with the study results. AADAP does not have a required form or format for fish health reports. All submitted fish health reports need to be saved as a PDF and attached to the Results Report (bottom of page).

Situations where a Fish Health Report should be included:

- Chloramine-T is used to treat external-Flavobacteriosis
- Mortality caused by INAD use
- Concomitant INAD use occurred (only if AADAP approved it prior to conducting treatment and the species treated was threatened or endangered).

If any of these situations occur and a fish health report is not available, a justification explaining the situation will be needed. This information can be included in the Description of Results within the Results Report.

Checklist for Results Report

Once the Investigator has completed the treatment, they need to submit a Results Report submitted **within 30 days**. If the INAD used required post-treatment evaluation or laboratory results, then the Results Report should be submitted within 30 days of receiving the results or beginning on the last day of the evaluation. It is important that the Results Report be filled out with detail and accuracy. If questions arise the Monitor should contact the Investigator for missing/additional information. Once submitted by the Monitor, AADAP will review the Results Report for final approval. If multiple errors are found or information is missing both the Monitor and AADAP can send the study back to the Investigator for changes. All current and previously conducted studies can be found from the Monitor's Homepage on the INAD database. Studies in Stage 5 (**highlighted in red**) are Results Reports which the Monitor will need to address.

Please note that **data entered on the Study Request is automatically pre-populated** into the Results Report. It is **very important that you double check this information** (i.e., number of fish treated,

treatment dates, number of treatment dates, treatment dose). If any changes occur, then the form will need to be updated to reflect what happened during treatment.

A complete Results Report needs to contain the following:

- The drug inventory (located at the top of the page) should show a record of how much drug was used. The dates in the drug inventory should match the treatment dates, or if the dates were consolidated then a short note needs to be included in the Description of Results section confirming that “x” number of days received treatments.
- The number of treatment dates should reflect the dates which the drug was administered, not the number of dates from the initial to final treatment.
- Some information (i.e., number of fish treated, dose, treatment dates) may be reported multiple times on the report, it is important that this information is consistent throughout the report. Inconsistently reported information will result in the Results Report being sent back for revisions.
- The result section needs to contain;
 - Whether the treatment was successful, if not, explain why.
 - Information regarding the treatment (dose used, treatment dates, and whether mortality changed with treatment).
 - Information regarding fish well-being (the number of fish treated, their behavior post-treatment, and any adverse effects).
 - Whether deviations, or changes from the FDA study protocol from the study design occurred, if so describe.
 - Explanation of any adverse events during the treatment period.
- The last question on the Results Report asks the number of days before availability of treated fish for human consumption, this question enables us to determine whether the withdrawal period was fulfilled. If you notice that the Investigator entered NA (with no additional text) please reach out to them to determine the number of days the fish was held before release.
- Be aware the changes made to the form are not saved unless all the required fields are completed. Therefore, we suggest having all study data available when completing the form.

Special circumstances:

- **Disease related INADs** will require mortality information. **Mortality data will be required for five days of pre-treatment, treatment period, and ten days of post-treatment.** Not reporting the pre and post treatment mortality data is considered a deviation. If there was a reason this information was not collected it will need to be specified in the Study Deviation section of the Results Report.
 - Mortality needs to be reported every day during the treatment period in the Mortality Record. If no mortalities occurred, then enter 0. Each treatment date needs to be evaluated and reported.
 - Disease-related INADs also need to report the percent of fish saved due to the INAD treatment. Since controls are not used in the majority of INAD studies, one cannot truly calculate the percentage of fish which were saved due to the INAD treatment. However, we do ask that Investigators provide an estimate of the percentage of fish they believe were saved due to INAD use. This estimate can be based on past facility history or mortality rates prior to treatment.
- **Aqui-s 20E used in the field** will require that “0-field use” be entered into the number of days before availability of treated fish for human consumption.

- **If the study was conducted on mixed species, then the number of each species treated must be included in the Description of Results in the Results Report.**

Database notifications

The database is programmed to send out an email to the Monitor each time a study is advanced to stage 2; 4; and 5. However, some notifications are being sent to the Junk file in your email account or being blocked by your IT. If you find that you are not receiving your email notifications, and you can't rectify this situation, then please have your Investigators contact you each time they advance a study. This way the studies can be reviewed and advanced in a timely manner.