

PHARMACOLOGY/TOXICOLOGY DATABASE USER GUIDE

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Introduction

The Pharmacology/Toxicology database was developed to provide investigators with information on preclinical toxicology and biodistribution studies (that are testing specific vectors planned for clinical gene therapy trials). It has two different functions:

- Allows data from preclinical toxicology and biodistribution studies to be viewed
- Allows data to be entered into the system by investigators who have completed these studies and would like to share this information with the field.

The data can be used to facilitate the cross-referencing of relevant studies in support of new Investigational New Drug Applications (INDs). Investigators may discover a study in the database that is relevant to their specific vector and study of interest. Once the study is found, they can then utilize this data by acquiring a letter of cross-reference from the Study PI, allowing then the FDA to review the data and assess whether a specific study would need to be conducted.

The Pharmacology/Toxicology Database

Accessing the Database

To access the database select Toxicology Database on the navigation menu (see figure 1).

You will be presented with a screen displaying general information about the database and the studies. At the end of the page you will see a link that will take you to the database.

To access the database click [here](#)



Figure 1 - Accessing the Tox Database

Viewing Summary Information

You will then see the Toxicology Reports screen. Unless you are authorized to see detailed information (in other words, you have a username and password to login to the site), you will see the public view of the system, which allows you to search for specific reports, but will only display summary information (a partial view of the screen is shown in figure 2).

[Home](#) > [Toxicology Database](#) > Toxicology Reports

Toxicology Reports

Welcome to the Toxicology database. This area holds a summary of Toxicology studies that have been submitted to our database.

The information contained here is for public view. You may search for a study by selecting an option on the right. If you wish to see details of the data or share your own data then you would need to obtain a user account and log-in [click here](#). Once you have acquired your user name and password you can then enter your own study into the database by choosing "Submit a New Report, or you can view reports that you have already entered by choosing "View Your Reports". You can also view a detailed version of all the studies entered by selecting the search options.

Investigators wishing to obtain a letter of cross reference from the

Search for Reports by:

Vector System:

Animal Species:

Vector Grade:

Clinical Indication:

Route of Administration

Figure 2 - Public view of the Tox database. It will only display summary data

Viewing Detailed Information and Submitting Reports

Requesting an account

If you do not have an account, you will not be able to submit or access data. To request an account, please click on “click here” from the Toxicology Report screen (see figure 2). This will generate contact information to gain full access to the data. After receiving your information, you will receive a form via email to complete, sign and return. Upon return of the form you will be issued a user name and password via email. Once you have obtained a user name and password you can login to the database from the website. You will be asked to agree to a Disclaimer. If you select Disagree you will not be allowed access.

Viewing Detailed Information

Login to the website by scrolling down on the navigation menu and enter the required information. Go to the Toxicology Reports the usual way, and you will see two links below the Search Report button, as indicated in figure 3

Toxicology Reports

Welcome to the Toxicology database. This area holds detailed Toxicology studies that have been submitted to our database.

The information contained here is for view by valid site users only. As a valid site user you have obtained a username and password. Now you can:

- Search for a detailed version of the study by selecting an option on the right.
- Submit data into the database by choosing "Submit a New Report"
- View your existing reports by choosing "View Your Reports"

Investigators wishing to obtain a letter of cross-reference from the Principal Investigator of a particular study may do so by emailing lrubin @ iupui.edu stating the title of the study in question.

Search for Reports by:

Vector System:
Select a vector system...

Animal Species:
Select a species...

Vector Grade:
Select a grade...

Clinical Indication:
Select an indication...

Route of Administration:
Select a route...

Search Reports

[Submit a New Report](#)

[View Your Reports](#)

Figure 3 - Links to New Report Submission and the user's reports

At this point, you can view the reports you created, as well as the detailed information from the searched reports.

Submitting a New Report

To enter your own data into the system select "Submit a New Report" (see figure 3). A new browser window will appear. Please read the initial screen. Once you are ready, please proceed to the next screen by clicking on "Start".

You will now be presented with a number of data entry screens, to which you will add data.

Notes:

- Do not use the back, forward, and reload buttons during this process, as you might lose or enter wrong information in the database.
- Most fields are straight forward data entry and are self explanatory. Please note on the fields marked “required” data must be entered in order to generate data in subsequent fields.
- After you have completed each screen, pressing “Next” to submit the data form will finalize the contents for that screen. At this point you cannot go back and fix errors you will need to continue through to the end of the screens. Errors and incomplete reports must be corrected through the edit mechanism on each page. You will get a personal list of submitted reports that will be automatically created when you reach the end of the submission.

Study Administration

This section will contain data on the Sponsor, address, IND information, Protocol number and date of study initiation and completion (Figure 4)

Study Administration

Sponsor:	<input type="text"/>		
Institution:	<input type="text"/>		
Contact Person:	<input type="text"/>		
Address:	<input type="text"/>		
Phone:	<input type="text"/>	Fax:	<input type="text"/>
Email:	<input type="text"/>		
IND Number:	<input type="text"/>		(Optional for Corporate Sponsor)
IND Status	Go <input type="button" value="Go"/>	(Optional for Corporate Sponsor)	
Cross File Numbers:	<input type="text"/>		
Study Conducted By:	<input type="text"/>		
Address Of Study Site:	<input type="text"/>		
Study Protocol #:	<input type="text"/>		
Study In Compliance With GLP?	<input type="radio"/> Y	<input checked="" type="radio"/> N	
Date of Study Initiation:	<input type="text"/>	<input type="text"/>	<input type="text"/>
Date of Study Completion:	<input type="text"/>	<input type="text"/>	<input type="text"/>

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next ->

Figure 4 - Study Administration screen

Study Summary

Study Title

Enter the study title.

Transgene:

Enter name of the transgene.

The following fields MUST BE completed in order to generate data in subsequent fields:

Clinical Indication:

Enter disease diagnosis.

Vector System:

Example: AAV, HSV

Number of Vectors Used:

Choose number from pull down menu.

Number of Drugs Used:

Choose number from pull down menu. (Enter only drugs that are included as part of the study design).

Number of Controls Used:

Choose number from pull down menu.

Number of Study Groups:

Choose number from pull down menu. (This creates the Study Groups in subsequent field).

Note: It is important that the above fields are completed correctly before selecting the “NEXT” button.

Overall Study Design

Enter the design of the study and the aims that the study sets out to achieve.

Results/Findings

Add overall study results and findings.

See figure 5

Study Summary

Study Title:

Transgene:

Clinical Indication: Other:

Vector System:

Number of Vectors Used: required

Number of Drugs Used: required (Enter only drugs that are included as part of the study design)

Number of Controls Used: required

Number of Study Groups: required

Overall Study Design:

Results/Findings:

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next →

Figure 5 - Study Summary screen

Dose Level Assessment

Complete the following:

- *Initial Dose (ADH)*
- *Maximum Dose (MHD)*
- *Safety Margin (NOAEL/MHD)*
- *NOAEL/AHD Initial Dose*
- *NOAEL/MHD Maximum Dose*
- *Therapeutic Index (LOED/NOAEL)*
- *LOED Lowest Observable*
- *ED Minimal Dose*

AHD = Anticipated Human Dose

MHD – Maximum Human Dose

NOAEL = No Observable Adverse Effect in Animals

LOED = Lowest Observable Effective Dose in Animals

ED = Minimal Effective Dose in Animals

See figure 6

Dose Level Assessment

Initial Dose (AHD):	<input type="text"/>
Maximum Dose (MHD):	<input type="text"/>
Safety Margin (NOAEL/MHD):	<input type="text"/>
NOAEL/AHD Initial Dose:	<input type="text"/>
NOAEL/MHD Maximum Dose:	<input type="text"/>
Therapeutic Index (LOED/NOAEL):	<input type="text"/>
LOED Lowest Observable:	<input type="text"/>
ED Minimal Dose:	<input type="text"/>

AHD = Anticipated Human Dose
MHD = Maximum Human Dose
NOAEL = No Observable Adverse Effect in Animals
LOED = Lowest Observable Effective Dose in Animals
ED = Minimal Effective Dose in Animals

Enter NA (not applicable) or ND (not done) in the fields you do not have data to enter.

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next →

Figure 6 - Dose Level Assessment screen

Vector Information

Complete the following:

- *Vector name*
- *Vector Role in the Study (Test or Control)*
- *Vector Grade (Select from pull down menu Phase I/II GMP, etc.)*
- *Manufacturer*
- *Lot #*
- *Batch Number*
- *Exp. Date*
- *Titer*
- *Purity*
- *Storage (Temperature)*

- *Production Method*
- *Titer Determination Method*
- *Method for Assaying Purity*

Vector Information

Vector 1

Vector Name	<input type="text"/>
Vector Role In Study	<input type="checkbox"/> Control <input type="checkbox"/> Test
Vector Grade	<input type="text" value="Phase I/II GMP"/>
Manufacturer	<input type="text"/>
Lot Number	<input type="text"/>
Batch Number	<input type="text"/>
Exp. Date	<input type="text"/>
Titer	<input type="text"/>
Purity	<input type="text"/>
Storage	<input type="text"/>

Production Method:

Titer Determination Method:

Method For Assessing Purity:

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next →

Figure 7 - Vector Information screen. Observe that only one vector is displayed, since only one was specified (see fig. 5)

Controls used

Enter control name, i.e. Saline

Control Information

Control Name

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next →

Figure 8 - Control Information screen. Notice that only one control was specified (Fig. 5)

Drugs Used

Enter drug name, i.e. Ganciclovir

Drug Information

Drug Name

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next →

Figure 9 - Drug Information screen. Notice that only one drug was specified (Fig. 5)

Animal Information

Complete the following:

- *Animal Species*
- *Species Strain*
- *Age at Study Initiation*
- *Weight Range*
- *Animal Facility Accreditation (IACUC etc.)*
- *Identification (ear tattoo etc.)*
- *Randomization (Yes/No)*
- *Environment*
- *Quarantine Duration*
- *Disease Model (describe model used, i.e. xenograft, transgenic/ko etc.)*

Animal Information

Animal Species: Other Species:

Species Strain: Other Strain:

Age At Study Initiation:

Weight Range:

Animal Facility Accreditation:

Identification:

Randomization:

Environment:

Quarantine Duration:

Disease Model: (Describe the model used, i.e. xenograft, transgenic/ko etc.)

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next →

Figure 10 - Animal Information screen

Study Groups

Sacrifice Days for this Study

Enter days, example 20, 60, 80

Clinical Observation (daily, weekly, etc).

Select from pull down menu

Note: A table of the number of groups will be created in this section based on data entered in the Study Summary section.

Agents Used

Vector (this data will be filled in)

Route of Administration

Select from a pull down menu

Dosing Regimen

Enter dose, ie 1x10e6 vp

Number of Male Animals

Enter the number in each group

Number of Female Animals

Enter the number in each group

Number of Animals Died or Sacrificed Moribund

Enter deaths that occurred other than those required for the study

Study Methodology:

Enter the study plan, experimental design, testing parameters, hematologies, chemistries etc.

Summary of Findings:

Enter any specific outcomes.

Study Groups

Sacrifice Days for this Study

Clinical Observation Schedule

Group 1

Agents Issued

Route of Administration

Dosing Regimen

Number of Male Animals

Number of Female Animals

Number of Animals Died or Sacrificed Moribund

Study Methodology:

Summary of Findings:

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Figure 11 - Study Groups screen

Necropsy and Histopathology Results

Necropsy Results

Add information pertaining to results obtained from tissues analysed. Add list of tissues collected.

Histopathology Results

Add information pertaining to results obtained from tissues analysed. Add list of tissues collected.

Necropsy & Histopathology Results

Necropsy Results:

Histopathology Results:

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next →

Figure 12 - Necropsy and Histopathology Results screen

Biodistribution

Assay (s) Used:

Example, rtPCR, DNA PCR etc.

Validated Assays

yes/no/na

Level of Assay Sensitivity

Tissues Examined with Positive Findings

Add information pertaining to results obtained from tissues analysed. If data includes both a toxicology study and biodistribution study and the same tissues have been used for both, then refer to data entered in the Necropsy/Histopathology fields.

Assay Methodology

Pharmacokinetics (transgene)

Rt-PCR

Enter data on results from PCR analysis.

Biodistribution

Assay(s) Used:

Validated Assays? Y N NA

Level Of Assay Sensitivity:

Tissues Examined With Positive Findings:

Assay Methodology:

Pharmacokinetics (transgene)

rt-PCR:

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next →

Figure 13 - Biodistribution screen

Laboratory

Choose the specific laboratory tests carried out on the study by checking the box to the left of the text. Select "Other" if selection is not available. This will generate the laboratory fields. Enter a summary of noteworthy findings in each field that you have selected.

- *Hematology*
- *Coagulation*
- *Chemistry*
- *PFT's*
- *BAL Cell Counts*
- *In situ PCR*
- *DNA PCR*
- *Rt PCR*
- *ELISA titer*
- *Blood Gases*
- *Ophthalmology*
- *Cardiovascular Assessment*
- *Neurobehavioural*
- *Other Lab*

Select all pertinent studies performed.

- Hematology
- Coagulation
- Chemistry
- PFT's
- BAL Cell Counts
- In situ PCR
- DNA PCR
- Rt-PCR
- ELISA titer
- Blood Gases
- Opthamology
- Cardiovascular Assessment
- Neurobehavioural
- Other Lab

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next →

Figure 14 - Laboratory screen. Hematology was selected as an example

Hematology

Noteworthy Findings for Hematology:

NOTE: By pressing this button, you are verifying that the information entered on this screen is correct and accurate. In order to fix any mistakes you may have made after pressing this button, you will have to edit the report after it has been fully completed.

Next →

Figure 15 - Example of a lab entry

Report Completion

The laboratory results are the last entry in the database. You will see the screen entitled “Report Complete” (figure 16). To edit or finalize that report select “Click here for your reports”

You will then be given a list of your specific reports that have been entered into the system.

Report Complete

You have completed the toxicology report, and your results have been saved to the database.

In order to make this report available for administrative review, **you must authorize its contents by finalizing it**. You can do this when you select your report list below. **NOTE:** After you have finalized your report, it will no longer be available for editing. Please make sure that all information is correct and ready for administrative review.

[Click here for your reports.](#)

Figure 16 - Report complete screen

Editing and Finalizing Reports

You can now go back into your reports and make any necessary edits before finalizing the data. To edit the report, click on its title.

Once you have completed the data entry you will then select FINALIZE (do not selected this until the data entry is fully completed). At this point you will not be able to make any changes unless you contact the database Administrator.

If you select DELETE, the whole document will be deleted, which means all its contents will be lost. Use this option wisely.

Toxicology Reports for

Incomplete Reports:

<p>No Title Specified Added: Wed Jan 24, 2007 @ 4:57PM</p>	<p>delete FINALIZE</p>
<p>No Title Specified Added: Tue Feb 6, 2007 @ 1:45PM</p>	<p>delete FINALIZE</p>
<p>No Title Specified Added: Thu Feb 15, 2007 @ 1:52PM</p>	<p>delete FINALIZE</p>

Search for Reports by:

Vector System:

Animal Species:

Vector Grade:

Clinical Indication:

Route of Administration

[Submit a New Report](#)

[View Your Reports](#)

Figure 17 - List of Incomplete reports