

Ginkgo Manual

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Introduction

Welcome to the Ginkgo App! In this document we will walk you through the functionality of each part of our application. Also, if you need a reminder of what a function does, there is a info button for each tool. Below is a picture of what the icon looks like.

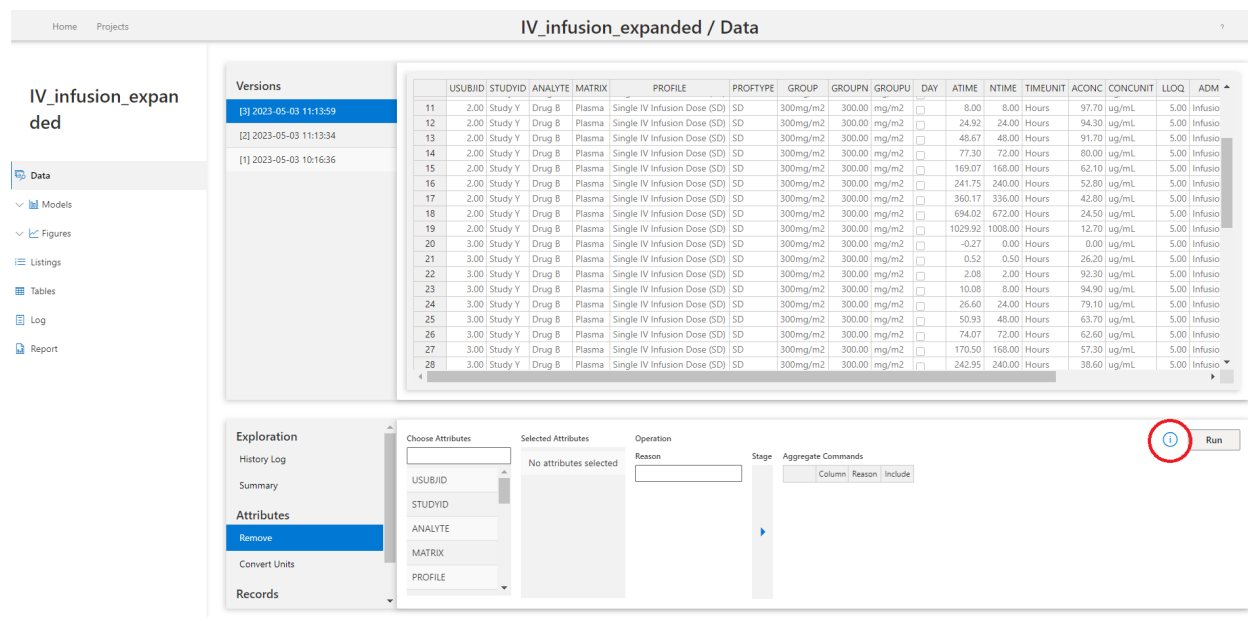


Figure 1: Red Circle is the Info Icon

Installation

1. Let's navigate to the Gitlab page at this link
2. Next, let's clone the repo! We will do this by clicking the Clone button in the top right-hand corner. From here, we can clone via SSH or HTTPS; either one is fine. Below is a screenshot of the repository being downloaded via HTTPS:
3. Now that we have a copy of the repository let's open it up! Launch the project by clicking on the icon named `ginkgo-project.Rproj`. This will launch the application inside of RStudio.
4. Once we are in Rstudio, let's run the script below.

```
$ git clone https://a2pg-gitlab.a2pg.com/ginkgo/ginkgo-shiny.git
Cloning into 'ginkgo-shiny'...
remote: Enumerating objects: 1777, done.
remote: Counting objects: 100% (563/563), done.
remote: Compressing objects: 100% (286/286), done.
remote: Total 1777 (delta 411), reused 360 (delta 257), pack-reused 1214
Receiving objects: 100% (1777/1777), 1.58 MiB | 19.78 MiB/s, done.
Resolving deltas: 100% (1114/1114), done.
```

Figure 2: Downloading via HTTPS

```
# Helps with dependent libraries. y for "yes" for the updates.
renv::restore()
y
# The following packages Ginkgo is dependent on.
package_names_pt1 <- c('tidyr', 'readxl', 'ggplot2', 'echarts4r')

# For loop that will download the dependent packages.
for (package in package_names_pt1) {
  install.packages(package)
}

# IQnca package
install.packages("IQnca",
  repos = c("https://iqnca.intiquan.com/rrepo", "https://cran.r-project.org/"),
  dependencies = TRUE)

package_names_pt2 <- c('rhandsontable', 'psych', 'measurements',
  'shinyBS', 'flextable', 'shinycssloaders')

for (pkg_name in package_names_pt2) {
  install.packages(pkg_name)
}
```

5. We are finished with the installation!

Projects Page

Users use the Projects page to navigate to and create new projects. Users can also delete projects from this page.

Creating a Project

Click the New Project button to open a project creation interface.

Upload Data

Data must be uploaded as an .xlsx file. Please reference the **Data Specification** section of the IQnca documentation to find which columns are required for analysis(<https://iqnca.intiquan.com/>). Data in columns can be named before importing data, or can be adjusted in the app at a later time.

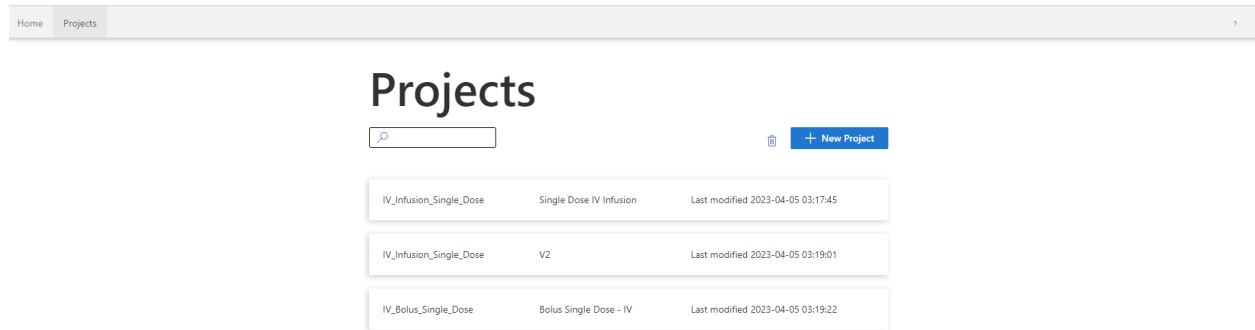


Figure 3: Picture of the projects page

Project Tags

Give an appropriate name and description to the project.

Click **Create New Project** to initialize and open the new project.

Opening A Project

Double click on a project to open it.

Deleting Data

To delete projects, single-click the project, and then click the bin icon. A prompt will ask to confirm this action.

DATA IS NOT SAVED

Persistent data storage is a feature that is currently being worked on. Projects are currently tied to a session.

Data Panel

After the user imports data, they will be directed to the **Data** panel. In the **Data** panel, users are able to make modifications to their dataset before generating models.

Versions

Every time a modification is made to a dataset, a new version of that dataset is created. Users can traverse versions by clicking on versions under the **Versions** header.

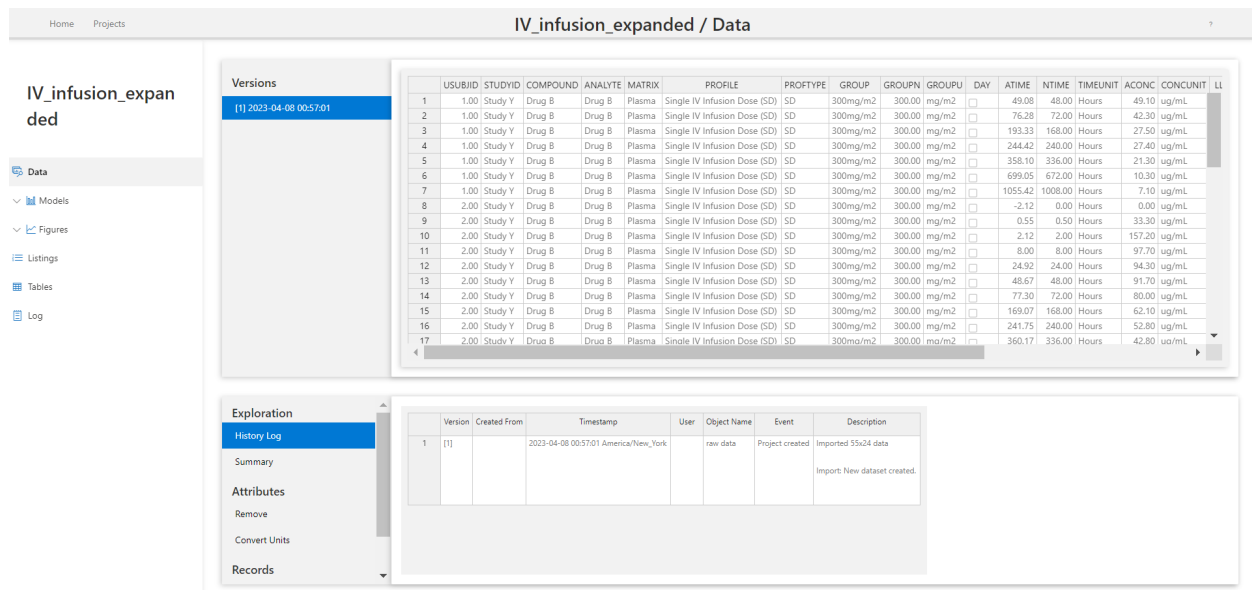


Figure 4: Picture of data frame

Data Page

The currently selected version's dataset is shown in the top frame. In the bottom frame, users can navigate across and perform various dataset modification operations.

Exploration

Exploration contains the **History Log** for the current version, which can also be viewed in the **Log** panel. The user can also view summary statistics under the **Summary** tab.

History Log

The History Log is a log of all the modifications made to the current version's dataframe. It provides information like time modified and a description of the operation.

Summary

The summary tab current uses the **psych** R package to display summary statistics.

Attributes

The Attributes section contains the **Remove** and **Convert Units** operations.

Remove

Remove is used to remove any attributes from the dataset. This operation will be recorded in the History Log and will create a new version of the data.

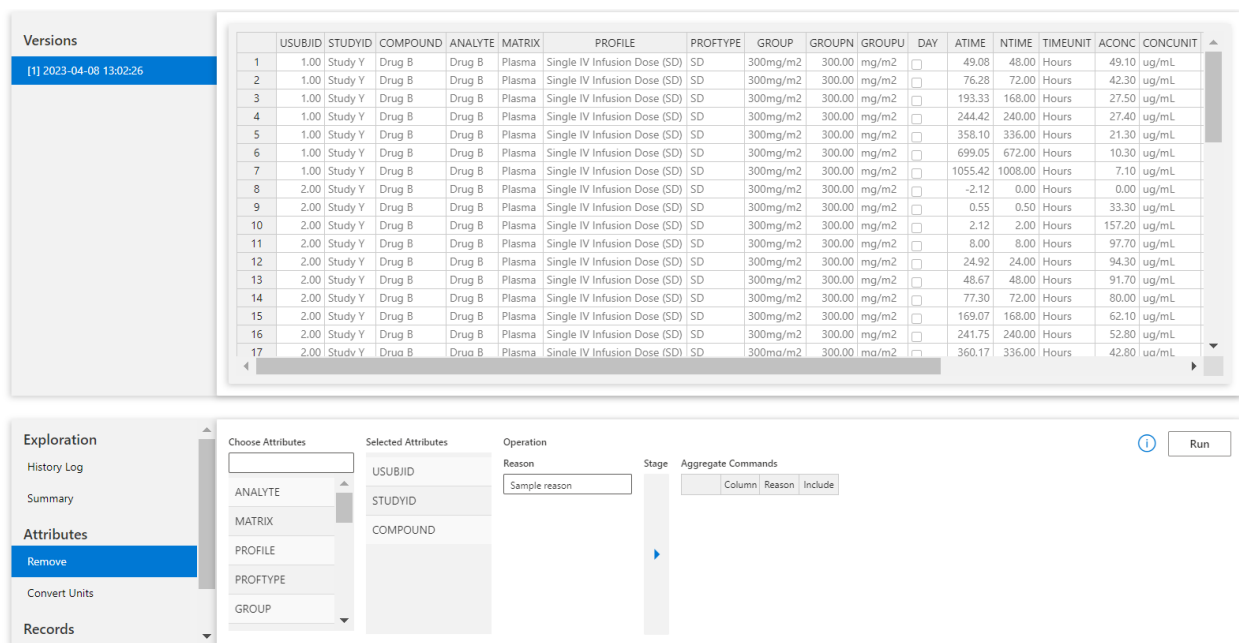


Figure 5: Picture of remove attributes functionality

1. Use **Choose Attributes** to select attributes for removal.
2. Provide a reason for removal.
3. Stage attributes for removal using the **Stage** button.
4. When done staging, use the **Run** button to carry out the operation. This will create a new version of the data with selected attributes removed.

Convert Units

Convert Units can be used to change the units of attributes in the dataset. This operation will be recorded in the History Log and will create a new version of the data. Unit conversions take place in two steps, specification and conversion.

Specifying Units

- Units must be specified before the app can perform unit conversions.
1. Under **Choose attributes**, select an attribute you wish to specify a unit for.
 2. Under **Operation**, select the attribute using the **Column** dropdown.
 3. Select a unit from the units builder. Hit the **Add** button to preview that unit. You may also use the **Operator** buttons to further configure your unit.
 4. Once the unit is completed, stage the operation using the **Stage** button.
 5. Run the operation with the **Run** button. This will create a new column of data specified to your unit.

Figure 6: Picture of units functionality

Converting Units

- Unit conversions are performed similarly to unit specifications.
- To perform a conversion, follow the same steps as specification, except now selecting the newly created column with specified units.

Records

The Records section contains the “Remove” and “Filter” operations.

Remove

Remove is used to remove any records from the dataset. This operation will be recorded in the History Log and will create a new version of the data.

1. Use **Select Row(s)** to select records for removal. Acceptable formats are shown in the example, and may be comma separated to remove multiple ranges of records.
2. Provide a reason for removal.
3. Stage records for removal using the **Stage** button.
4. When done staging, use the **Run** button to carry out the operation. This will create a new version of the data with selected records removed.

Versions

[1] 2023-04-08 13:14:27

	USUBJID	STUDYID	COMPOUND	ANALYTE	MATRIX	PROFILE	PROFTYPE	GROUP	GROUPN	GROUPU	DAY	ATIME	NTIME	TIMEUNIT	ACONC	CONCUNIT
1	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	49.08	48.00	Hours	49.10	ug/mL
2	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	76.28	72.00	Hours	42.30	ug/mL
3	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	193.33	168.00	Hours	27.50	ug/mL
4	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	244.42	240.00	Hours	27.40	ug/mL
5	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	358.10	336.00	Hours	21.30	ug/mL
6	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	699.05	672.00	Hours	10.30	ug/mL
7	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	1055.42	1008.00	Hours	7.10	ug/mL
8	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	-2.12	0.00	Hours	0.00	ug/mL
9	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	0.55	0.50	Hours	33.30	ug/mL
10	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	2.12	2.00	Hours	157.20	ug/mL
11	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	8.00	8.00	Hours	97.70	ug/mL
12	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	24.92	24.00	Hours	94.30	ug/mL
13	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	48.67	48.00	Hours	91.70	ug/mL
14	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	77.30	72.00	Hours	80.00	ug/mL
15	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	169.07	168.00	Hours	62.10	ug/mL
16	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	241.75	240.00	Hours	52.80	ug/mL
17	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	360.17	336.00	Hours	42.80	ug/mL

Summary

Attributes

Remove

Convert Units

Records

Remove

Filter

Operation

Select Row(s)

9:10

Of: 14, 7

Reason

Sample reason

Stage

Aggregate Commands

Row(s)	Reason	Include
1	14, 7	Sample reason <input checked="" type="checkbox"/>

Run

Figure 7: Picture of remove records functionality

Versions

[1] 2023-04-08 13:14:27

	USUBJID	STUDYID	COMPOUND	ANALYTE	MATRIX	PROFILE	PROFTYPE	GROUP	GROUPN	GROUPU	DAY	ATIME	NTIME	TIMEUNIT	ACONC	CONCUNIT
1	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	49.08	48.00	Hours	49.10	ug/mL
2	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	76.28	72.00	Hours	42.30	ug/mL
3	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	193.33	168.00	Hours	27.50	ug/mL
4	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	244.42	240.00	Hours	27.40	ug/mL
5	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	358.10	336.00	Hours	21.30	ug/mL
6	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	699.05	672.00	Hours	10.30	ug/mL
7	1.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	1055.42	1008.00	Hours	7.10	ug/mL
8	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	-2.12	0.00	Hours	0.00	ug/mL
9	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	0.55	0.50	Hours	33.30	ug/mL
10	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	2.12	2.00	Hours	157.20	ug/mL
11	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	8.00	8.00	Hours	97.70	ug/mL
12	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	24.92	24.00	Hours	94.30	ug/mL
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14	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	77.30	72.00	Hours	80.00	ug/mL
15	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	169.07	168.00	Hours	62.10	ug/mL
16	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	241.75	240.00	Hours	52.80	ug/mL
17	2.00	Study Y	Drug B	Drug B	Plasma	Single IV Infusion Dose (SD)	SD	300mg/m2	300.00	mg/m2	<input type="checkbox"/>	360.17	336.00	Hours	42.80	ug/mL

Summary

Attributes

Remove

Convert Units

Records

Remove

Filter

Choose Attributes

COMPOUND

ANALYTE

MATRIX

PROFILE

PROFTYPE

Selected Attributes

USUBJID

STUDYID

Operation

Column

STUDYID

Filter

=

Value

Study B

Reason

Sample Reason

Stage

Aggregate Operations

	Column	Filter	Value	Reason	Include
1	USUBJID	<=	3	Sample Reason	<input checked="" type="checkbox"/>

Run

Figure 8: Picture of filter functionality

Filter

Filter is used to filter the data based on user-set parameters.

1. Use **Choose Attributes** to select columns you wish to filter by.
2. Select a column using the **Column** dropdown
3. Select a filter using the **Filter** dropdown.
4. Input a value to filter by.
 - Ex. A filter operation of Column X \geq 2 will remove all records with Column X value less than 2.
5. Enter a reason for this operation.
6. Hit run to carry out the operation. This will create a new version with the filter applied.

Models Page

The Models page is used for generating exploratory plots and other TLFs. Users should visit the models page once they finish making modifications to their data.

General Models Workflow

The general workflow to generate models is as follows: 1. Import a dataset 2. Define custom NCA Parameters 3. Apply any-order operations if desired 4. Generate desired graphs and NCA data

Implement Analysis Plan

On this tab the user will import a dataset and define custom NCA parameters.

Import Data

1. Under **Versions** select a version of data you wish to use for analysis. You can review this data under **Data**.
2. If your column names are not automatically recognized, match your column names to the appropriate attributes using the dropdown menus. This includes columns that have undergone a unit change.
3. Hit the **Run** button to import your selected data.

-After hitting **Run** the dataframe should pop up in the **NCA Data** frame, as in the picture in the next section.

Define NCA Parameters Use this page to define custom parameters for NCA. Hitting **Run** will generate exploratory graphs in the **Figures** tab as seen below.

Reference IQnca IQdataNCA() function documentation for more information about what each parameter does(<https://iqnca.intiquan.com/book/reference/IQdataNCA.html>).

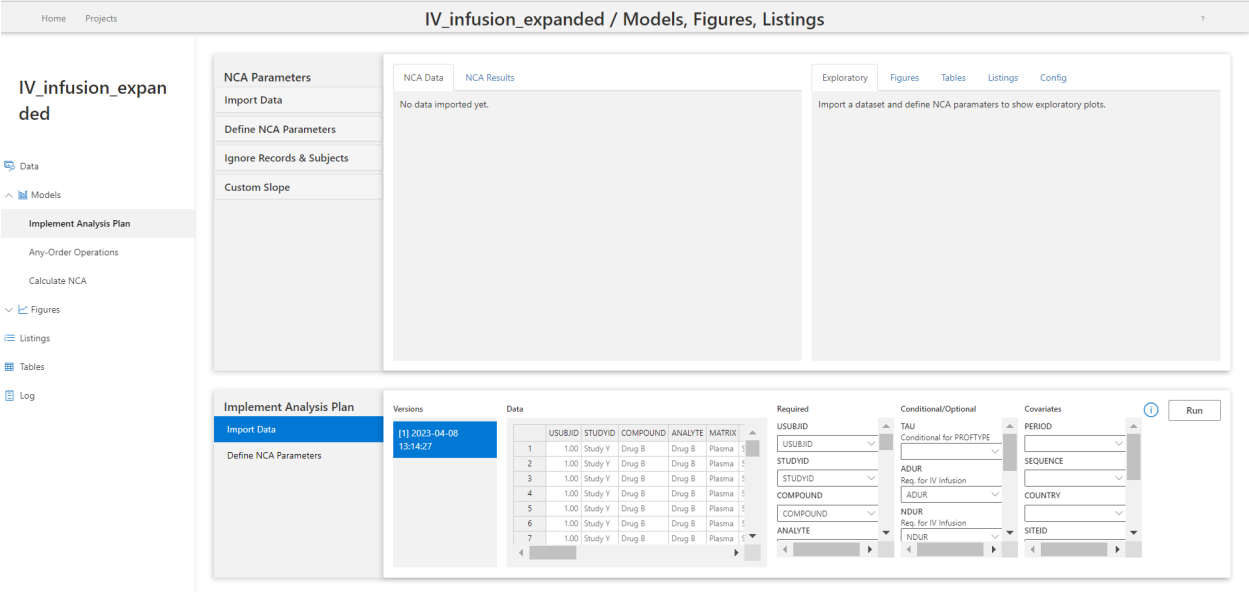


Figure 9: Picture of Import page

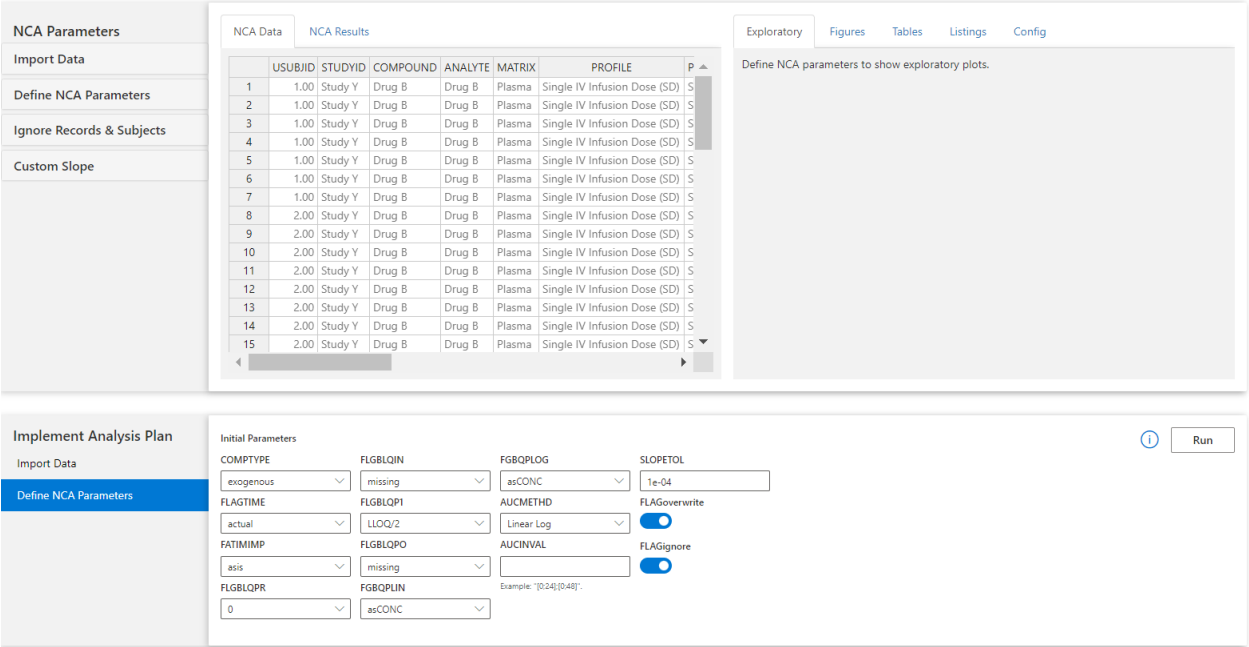


Figure 10: Picture of Define page

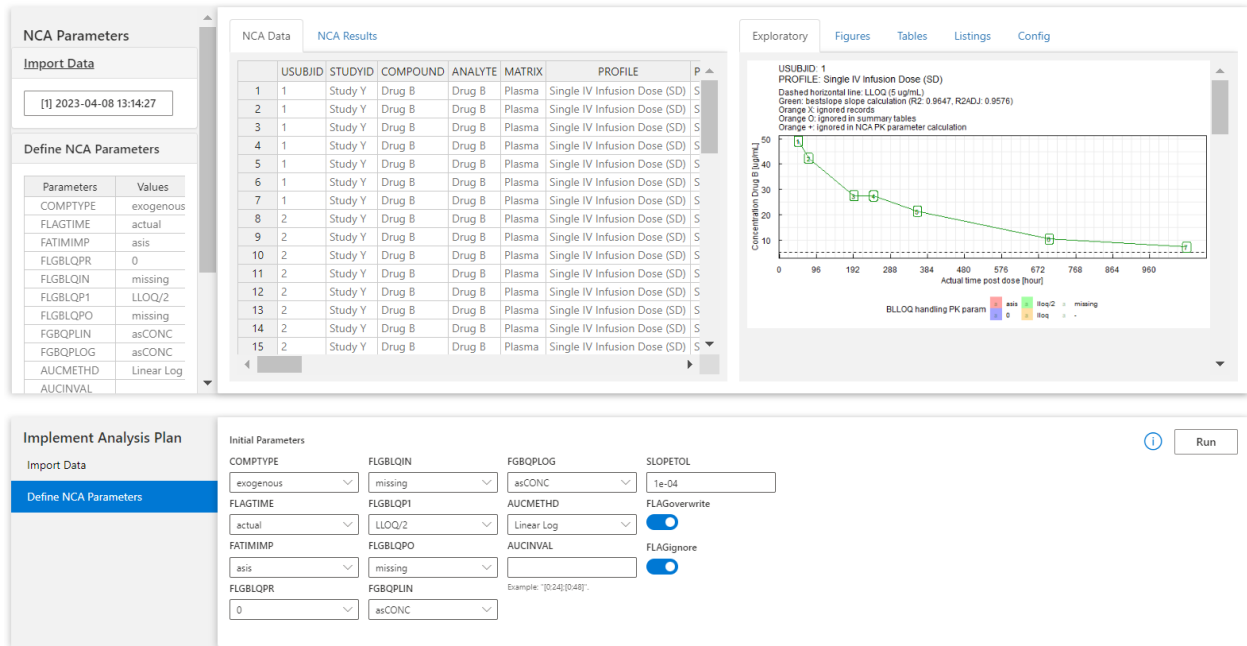


Figure 11: Picture of Define page

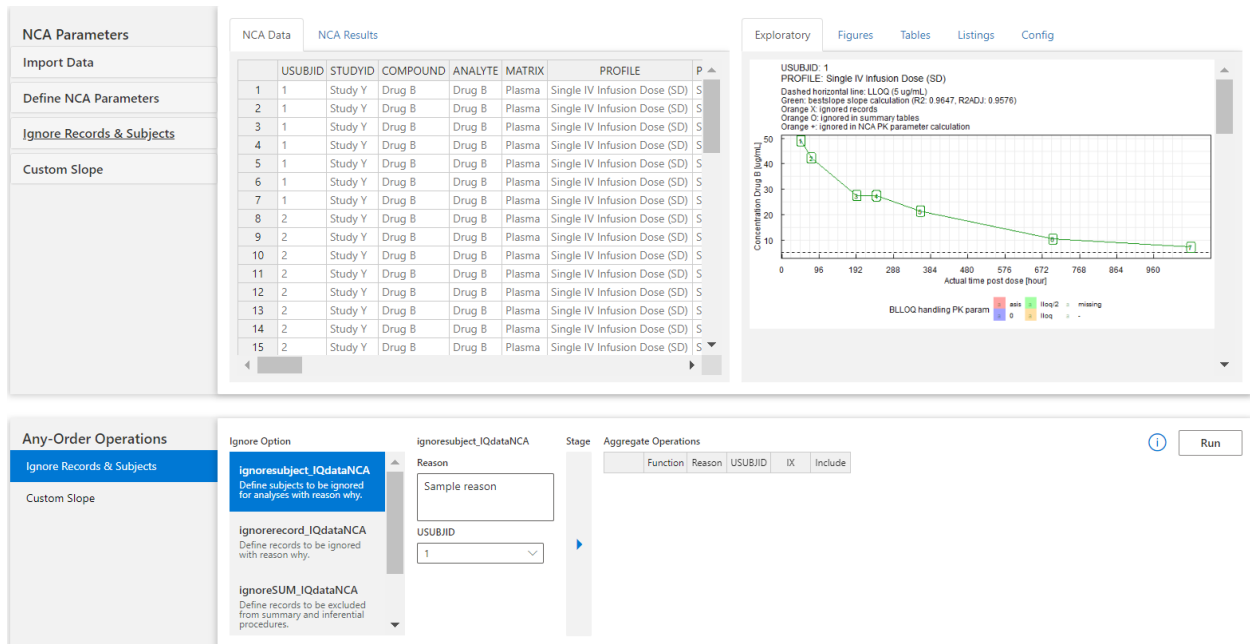


Figure 12: Picture of Ignore page

Any-Order Operations

These operations include ignore data functions and custom slope.

Ignore Records & Subjects

- Use this page to ignore records or subjects. Reference the IQnca documentation for more information on these functions.

1. Set the method of ignoring using the **Ignore Option** interface.
2. Fill out a reason, select an USUBJID, and if needed enter a IX Column value.
3. Stage the operation with the **Stage** button, and run using the **Run** button

- The operation will be reflected in the **NCA Data** tab and the **Exploratory** tab as seen below.

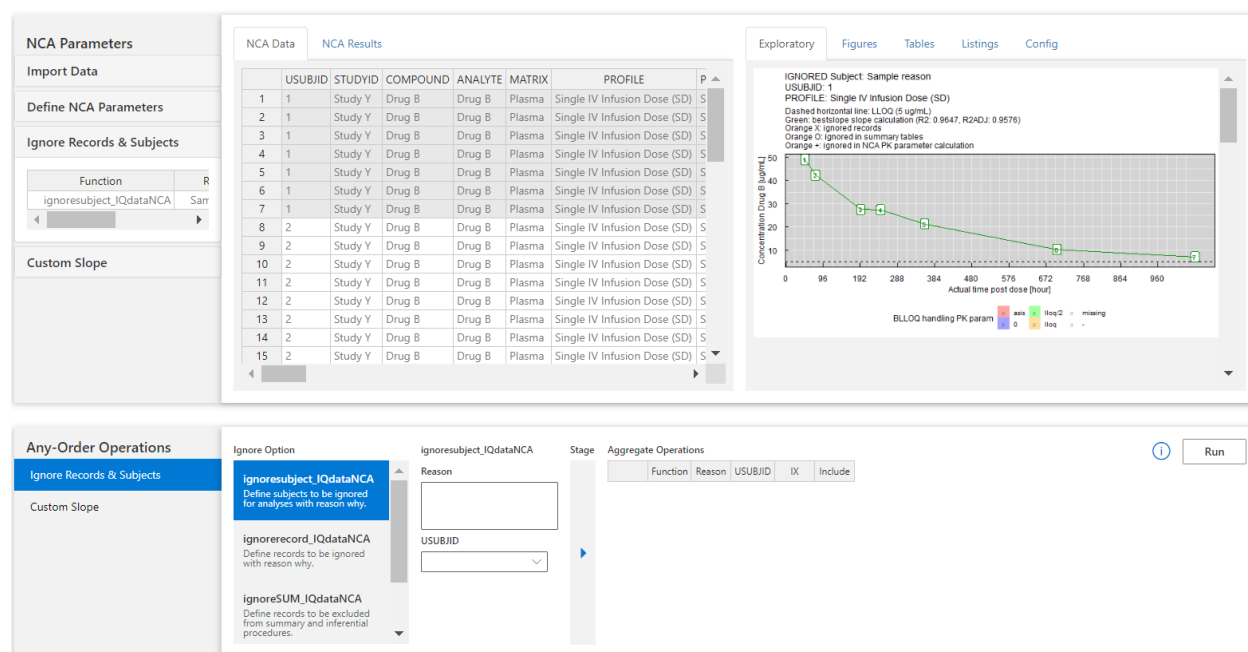


Figure 13: Picture of Ignore page

Custom Slope

- Uses IQnca's slope_IQdataNCA function to calculate a custom slope. Check the IQnca documentation for more information(https://iqnca.intiquan.com/book/reference/slope_IQdataNCA.html).

Calculate NCA

Hit Run to generate NCA results. The NCA results can be found on the **NCA Results** tab.

Figures

The figures tab is meant to be used after the user defines NCA parameters. At this point, the user can generate, preview, and add graphs to the report.

Summary Plots

Plots in this section are summarized off all non-ignored-USUBJID.

The general workflow of all the Summary Plots pages is as follows:

1. Navigate to the desired graph generation panel.
2. Adjust variables such as logY and strat as desired.
3. Hit the **Stage** button to view a preview of the plot.
4. Should the user wish to add the plot to their report, they may do so with the **Add to Report** button.

Dose Normalized

Figures in this section are dose normalized. See each section for details, and reference documentation for further information.

Spaghetti Plot Since dose-normalization is done, standard stratification is done by PROFILE. Additional stratification can be provided by the user and is shown in different colors. Default stratification is by GROUP (ordered by GROUPN). Ignored records (IGNORER) are excluded from these plots.

https://iqnca.intiquan.com/book/reference/figure_spaghetti_dosenorm_IQdataNCA.html

Geometric Mean Always only for nominal time (NTIME or NTAFD)! Since dose-normalization is done, standard stratification is done by PROFILE. Additional stratification can be provided by the user and is shown in different colors. Default stratification is by GROUP (ordered by GROUPN). Ignored subjects (IGNOREI) and ignored records (IGNORER and IGNORSUM) are excluded from these plots.

https://iqnca.intiquan.com/book/reference/figure_summary_geommean_dosenorm_IQdataNCA.html

Mean Always only for nominal time (NTIME or NTAFD)! Since dose-normalization is done, standard stratification is done by PROFILE. Additional stratification can be provided by the user and is shown in different colors. Default stratification is by GROUP (ordered by GROUPN). Ignored subjects (IGNOREI) and ignored records (IGNORER and IGNORSUM) are excluded from these plots.

https://iqnca.intiquan.com/book/reference/figure_summary_mean_dosenorm_IQdataNCA.html

Non-Dose Normalized

Figures in this section are non-dose normalized. See each section for details, and reference documentation for further information.

Spaghetti Plots Stratified by GROUP and PROFILE in the data. Ordered by GROUP(N) and then PROFILE. Default colored by USUBJID. Only ignored records (IQGNORER) are excluded from these plots. Stratification in terms of coloring by selected column can be done.

https://iqnca.intiquan.com/book/reference/figure_spaghetti_IQdataNCA.html

Geometric Mean Always only for nominal time (NTIME)! Stratified by PROFILE and GROUP (ordered by GROUPN). One plot per stratum. Ignored subjects (IGNOREI) and ignored records (IGNORER and IGNORSUM) are excluded from these plots.

https://iqnca.intiquan.com/book/reference/figure_summary_geomean_IQdataNCA.html

Mean Always only for nominal time (NTIME)! Stratified by PROFILE and GROUP (ordered by GROUPN). One plot per stratum. Ignored subjects (IGNOREI) and ignored records (IGNORER and IGNORSUM) are excluded from these plots.

https://iqnca.intiquan.com/book/reference/figure_summary_mean_IQdataNCA.html

Individual Plots

Plots in this section are per-USUBJID.

PK Concentrations

Ignored records (IGNORER) are removed from these plots. IGNORSUM and IGNORNCA records are included. Ignored subjects (IGNOREI) are included.

https://iqnca.intiquan.com/book/reference/figures_indiv_IQdataNCA.html

Listings

Users can generate listings in the **Listings** tab. Listings are a general collection of various summary information separated by subject.

Below is what the Listings tab view looks like.

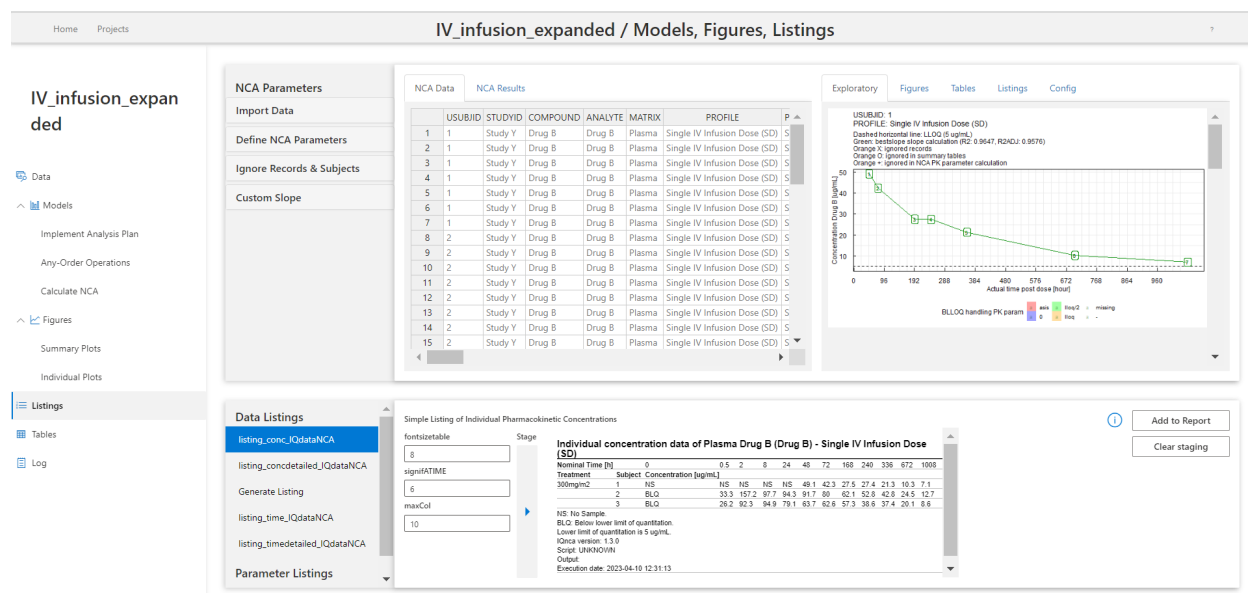


Figure 16: Picture of the listings tab

Data Listings

Data listings contain summary information for each subject. An example of a data listing is seen below.

Individual concentration data of Plasma Drug B (Drug B) - Single IV Infusion Dose (SD)												
Nominal Time [h]	0	0.5	2	8	24	48	72	168	240	336	672	1008
Treatment	Subject	Concentration [ug/mL]										
300mg/m2	1	NS	NS	NS	NS	49.1	42.3	27.5	27.4	21.3	10.3	7.1
	2	BLQ	33.3	157.2	97.7	94.3	91.7	80	62.1	52.8	42.8	24.5
	3	BLQ	26.2	92.3	94.9	79.1	63.7	62.6	57.3	38.6	37.4	20.1
NS: No Sample. BLQ: Below lower limit of quantitation. Lower limit of quantitation is 5 ug/mL. IQnca version: 1.3.0 Script: UNKNOWN Output: Execution date: 2023-04-10 12:31:13												

Figure 17: Picture of the data listing

To generate data listings, users must first import a dataset and define NCA parameters in **Models**. After doing so, the user may visit any of the **Data Listings** and generate listings.

After generating a listing, users may add the listing to the report using the **Add to Report** button.

For more information on each data listing, reference the IQnca documentation on data listings(<https://iqnca.intiquan.com/book/function-reference.html#nca-data-listings>).

Parameter Listings

Parameter listings are generated in the same way data listings are.

Below is an example of a parameter listing.

Individual pharmacokinetic parameters of Plasma Drug B (Drug B): USUBJID 1; Age 35; Gender Female - Single IV Infusion Dose (SD)					
Profile	Group	Dose [mg]	Description	Parameter (Unit)	Value
Single IV Infusion Dose (SD)	300mg/m2	540	Number of Points for Lambda z	LAMZNPT (-)	7
			R Squared Adjusted	R2ADJ (-)	0.957607
			Half-Life Lambda z	LAMZHL (h)	365.906
			Span	SPAN (-)	2.75027
			Time of CMAX	TMAX (h)	49.08
			Max Conc	CMAX (mg/L)	49.1
			Max Conc Norm by Dose	CMAXD (mg/L/mg)	0.0909259
			Time of CMIN Observation	TMIN (h)	1055.42
			Min Conc	CMIN (mg/L)	7.1
			Min Conc Norm by Dose	CMIND (mg/L/mg)	0.0131481
			Time of Last Nonzero Conc	TLST (h)	1055.42

Figure 18: Picture of the listings tab

https://iqnca.intiquan.com/book/reference/listing_pkparameter_IQnca.html

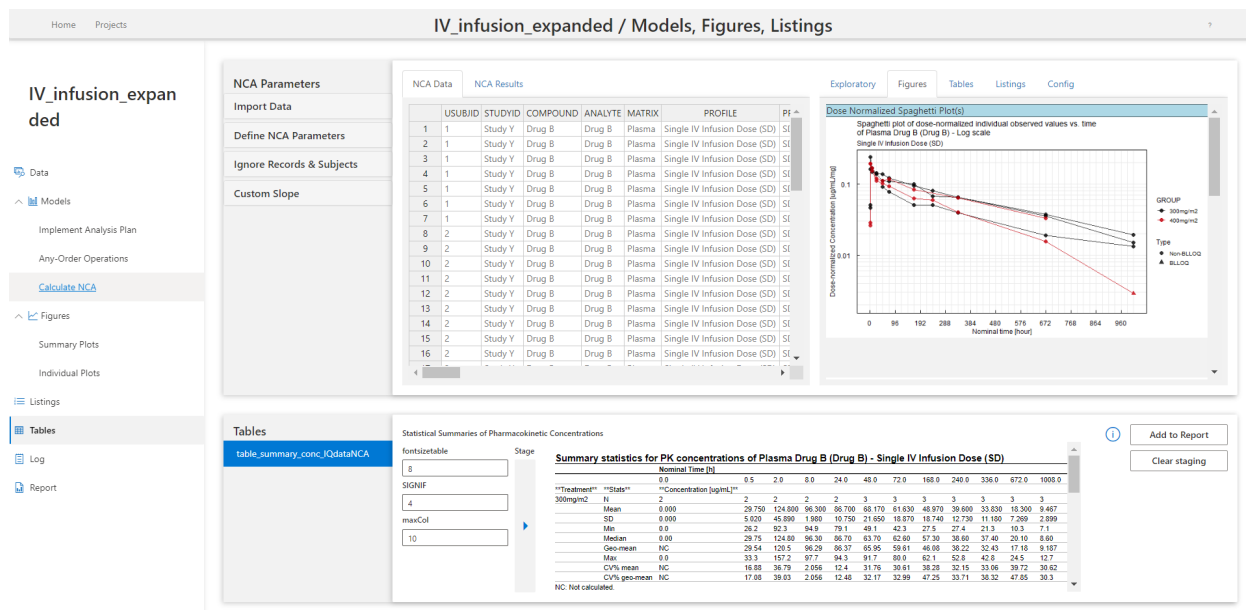
For more information on parameter listings, reference the IQnca documentation on parameter listing(https://iqnca.intiquan.com/book/reference/listing_pkparameter_IQnca.html).

Tables

With tables we can generate statistical summaries of pharmacokinetic concentrations.

1. First click on the **Stage** button. This will generate the summary statistics, and if you do not like the font size, significant figures, or how many columns feel free to change the values that are to the left of the side bar.

- Now that we have the summary statistics, we can either **Clear staging**, which just removes this table from being added to the report, or we can click **Add to Report**.



Log

The Log tab is a record of all the modifications that have been done to the imported data.

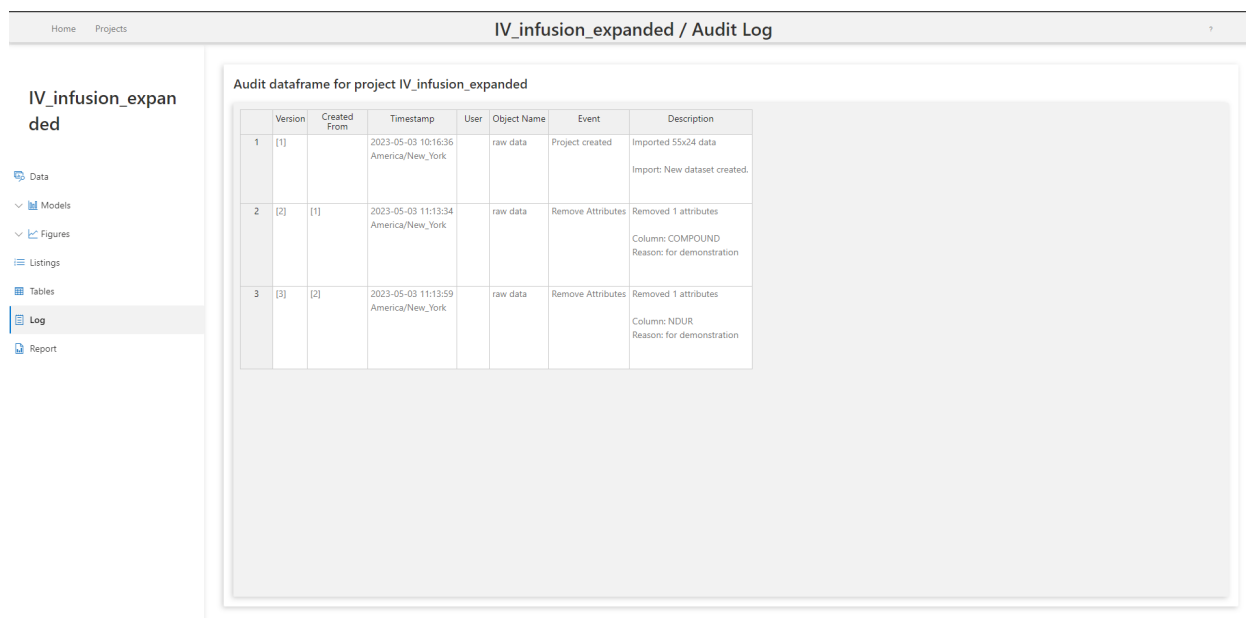


Figure 19: Example of Modifications to Data