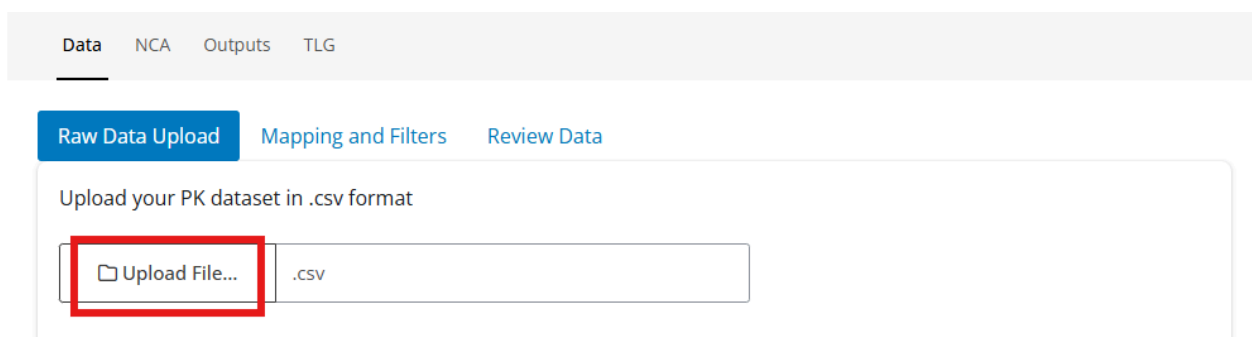


aNCA Shiny App User Guide

This guide will provide users with information on how to get started with the aNCA app.

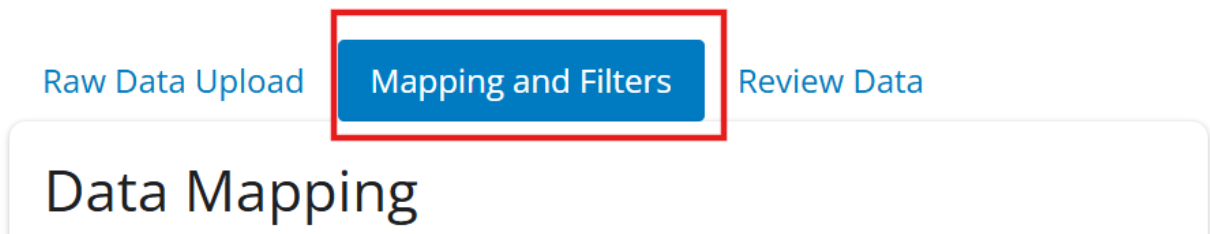
Step 1: Prepare Dataset

1. Click “Upload File” and select the dataset you would like to use. The data must be in .csv or .rds format. The best input for the app is data that follows the ADNCA format. Other formats of data will also work.



The screenshot shows the top navigation bar with tabs: Data, NCA, Outputs, and TLG. Below this is a sub-navigation bar with three buttons: 'Raw Data Upload' (highlighted in blue), 'Mapping and Filters', and 'Review Data'. The main content area under 'Raw Data Upload' says 'Upload your PK dataset in .csv format'. Below this text is a file upload interface with a button labeled 'Upload File...' (highlighted with a red box) and a text input field with '.csv' entered.

2. Once the dataset has been uploaded, you can check that the data is as expected, and then click on the “Mapping and Filters” tab.
 - a. Map the correct columns in your dataset to the corresponding label. For more information on what the column requires, hover over the input boxes.
 - b. For Unit Variables, if your dataset has a defined column for units, select it, otherwise manually input the units for the corresponding columns.
 - c. Click “Submit Mapping”. You will automatically be directed to the next tab.



The screenshot shows the sub-navigation bar with three buttons: 'Raw Data Upload', 'Mapping and Filters' (highlighted in blue and with a red box), and 'Review Data'. Below this bar, the main content area displays the heading 'Data Mapping'.

Time Variables

AFRLT	▼	AFRLT: Act. Rel. Time from Analyte First Dose
ARRLT	▼	ARRLT: Actual Rel. Time from Ref. Dose
NFRLT	▼	NFRLT: Nom. Rel. Time from Analyte First Dose
NRRLT	▼	NRRLT: Nominal Rel. Time from Ref. Dose

Unit Variables

µg/mL	▼	Character format. Value Unit
DOSEU	▼	DOSEU: Treatment Dose Units
RRLTU	▼	RRLTU: Rel. Time from Ref. Dose Unit

Submit Mapping

3. Review Data: Check that the data contains all the information you were expecting and is mapped correctly. If you want to change the data by adding filters, return to the “Mapping and Filters” page, and scroll down to add filters.

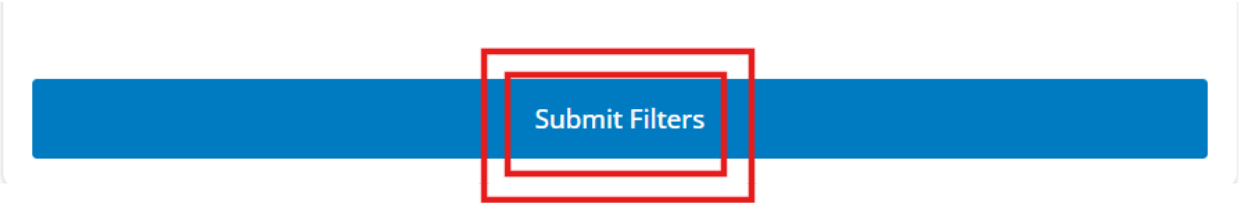
Filters

Click the 'Add Filters' button to add filters to your data. Be sure to click 'Submit' in order to apply the changes. Any filters added here will be applied across the whole analysis.

Add Filter

X

Don't forget to scroll down and click submit!



Step 2: Run NCA

Click on the “NCA” Tab at the top of the screen to switch to the next section.

1. Data Selection: Choose the analyte you would like to run the NCA on (it is currently only possible to analyse one analyte at a time).
2. Click ‘Submit’ and check that the data is as expected.

Note: the current version of the app only works with **one matrix (PCSPEC)** at a time. If you are having problems when clicking “Submit”, ensure that your data has been filtered to fit these specifications. You can return to the “Mapping and Filtering” tab in Data to do this.

Data

NCA

Outputs

TLG

Setup

Results

Run NCA

Data Selection

Settings

Slope Selector

Upload Settings

Browse

No file selected

Choose the analyte :

Analyte01

Submit

Show 10 entries

Search:

	STUDYID	USUBJID	ANALYTE	PCSPEC	AVAL	AVALU	AFRLT	ARRLT	NRI
1	XX01	11101	Analyte01	SERUM	7.58	ug/mL	1.5	1.5	
2	XX01	11101	Analyte01	SERUM	8.5	ug/mL	5	5	
3	XX01	11101	Analyte01	SERUM	8.66	ug/mL	7.5	7.5	
4	XX01	11101	Analyte01	SERUM	7.03	ug/mL	27.25	27.25	
5	XX01	11101	Analyte01	SERUM	3.78	ug/mL	73.08	73.08	

3. Move to “Settings” in the menu on the left hand side. Choose the Dose Number(s) you would like to run the NCA on, and the extrapolation method. Select additional options including partial AUCs, or rule sets to Flag the data.

Data **NCA** Outputs TLG

Setup Results Run NCA

Data Selection

Settings

Slope Selector

Choose the Dose Number:

1 5

Extrapolation Method:

lin up/log down

☒ Select Partial AUC

☒ + ☐ -

Min: 0 Max: 24

Flag Rule Sets:

☒ RSQADJ: \geq 0.7

☒ AUCPEO (% ext. observed): \geq 20

☐ AUCPEP (% ext. predicted):

☒ SPAN: \geq 2

4. Click “Run NCA”. You will automatically be redirected to the Results tab.

Data
NCA
Outputs
TLG

Setup

Results

Data Selection

Settings

Slope Selector

Choose the Dose Number:

1 5

Extrapolation Method:

lin up/log down

☒ Select Partial AUC

+

-

Min:

0

Max:

24

Flag Rule Sets:

☒ RSQADJ:

>=

0.7

☒ AUCPEO (% ext. observed):

>=

20

☐ AUCPEP (% ext. predicted):

☒ SPAN:

>=

2

Run NCA

Step 3: NCA Results

3.1 Main Results

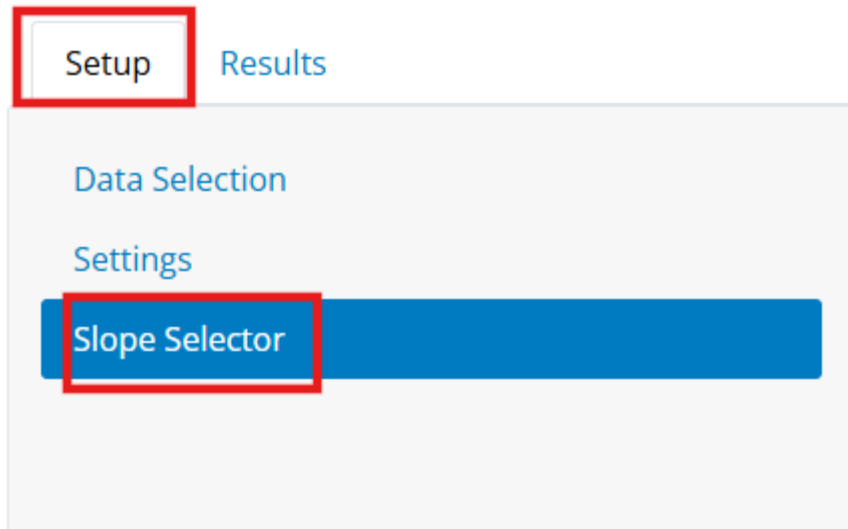
The NCA results tab shows the individual results of the NCA. You can select which parameters you would like to view. Results in red have been flagged as “False” for the rule sets selected, results in purple are flagged as “Missing”, and results in white are not flagged.

Click on the Slopes Tab to view more detailed information about the slopes selected in the NCA.

In Parameter datasets you can see and export the ADPP and PP datasets.

3.2 Exclusions and Manual Slopes

To add exclusions or manual slope selections, redirect to the Slope Selector tab in the Setup Page.



There are two different ways to add exclusions/selections to the slopes:

1. Via the Buttons.
 - a. Click “+ Exclusion/Selection”
 - b. Input the information: Type, Patient, Profile, Range, Reason. IXrange is the Data Point number in the slope, which can be seen by hovering over the points in the plots below.

	TYPE	PATIENT	PROFILE	IXrange	REASON
<input type="checkbox"/>	Exclusion	11103	1	1:3	incorrect sample

- c. To remove, select the sample row and click “-Remove selected rows”

+ Exclusion/Selection

- Remove selected rows

Apply



<input checked="" type="checkbox"/>	TYPE	PATIENT	PROFILE	IXrange	REASON
		T	E	e	
<input checked="" type="checkbox"/>	Exclusion	11103	1	1:3	incorrect sample

2. Via the Plots (Click the ? Button for guidance)

- For selection, click the first point and then the last point you want included in the slope. The plot should then update and a row should be added to the table. There you can add your reason for selection.
- For exclusion, double click the point you want to exclude. The plot should update along with the table.
- To remove, either remove via the table selection, or repeat the same action (ie select a new slope, double click the same point).

?

☐ TYPE

☐ Exclusion

☐ Exclusion

Plots per page: 1

Search Patient

Nothing selected

Previous Page

Slope selector guide

Upon initial NCA run, the plots will display the optimal slope selection. However, you have the flexibility to change it. Remember to apply your changes once you are done!

Check

Zoom

Select

Exclude

Once the exclusions/selections have been added, click "Apply" to apply them.

+ Exclusion/Selection

- Remove selected rows

Apply

You can check if they have been applied in the Results -> Exclusions Tab.

Setup	Results
NCA Results	
Slopes	
Exclusions	

TYPE	PATIENT	PROFILE	IXrange	REASON
Exclusion	11103	1	1:3	incorrect sample
Exclusion	11101	1	5:5	because

!!! If you don't click "Apply", the manual slopes will not be added !!!

3.3 Saving Settings

After completing an NCA and creating manual slopes, you may want to save these for next time. This is very easy:

1. Click Results -> NCA Results -> Save Project Settings. This will download a .csv file.

aNCA Data **NCA** Visualisation TLG

Setup Results

Run NCA

Save Project Settings

Select Parameters :
adj.r.squared[unitless], ANALYTE

Show 10 entries Search:

	STUDYID	PCSPEC	ANALYTE	USUBJID	DOSNO	start	end	adj.r.squared[unitless]	aucinf.c
1	XX01	SERUM	Analyte01	11101	1	1.5		0.997	
2	XX01	SERUM	Analyte01	11102	1	170.25		0.999	
3	XX01	SERUM	Analyte01	11103	1	1.63		1	
4	XX01	SERUM	Analyte01	11104	1	1.5		0.9	
5	XX01	SERUM	Analyte01	11105	1	2.968		0.994	
6	XX01	SERUM	Analyte01	11106	1	1.55		0.952	
7	XX01	SERUM	Analyte01	11107	1	1.802		0.968	
8	XX01	SERUM	Analyte01	11108	1	1.85		0.976	
9	XX01	SERUM	Analyte01	11109	1	1.602		0.992	
10	XX01	SERUM	Analyte01	11110	1	1.604		0.958	

Download the NCA data

Download locally the NCA data

Showing 1 to 10 of 23 entries Previous 1 2 3 Next

2. To upload settings next time, **after column mapping**, Setup -> Data Selection -> Upload settings. The inclusions and exclusions will be automatically added to the data.

Setup Results

Data Selection

Settings

Slope Selector

Upload Settings

Browse No file selected

Choose the analyte :

Analyte01

Run NCA

Step 4: Visualisation

In the “Visualisation” tab, you will find the different visualisation options, including individual plots, mean plots, descriptive statistics, and boxplots.

Step 5: TLG

Currently Unavailable/ Work in Progress