PKPlus™ 2.5

‘Plug-n-Play’ PK Modeling

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simulations-plus.com/pkplus

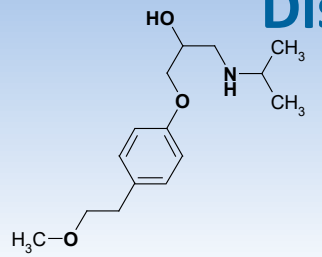
Simulations Plus (NASDAQ: SLP) (total employees ~100)

- **Simulations Plus, Inc.**
  - Incorporated in 1996
  - Software development, PBPK modeling & simulation, and QSAR modeling

- **Cognigen Corporation, a Simulations Plus company**
  - Incorporated in 1992
  - Software development, pharmacometric services, and population PK/PD data analyses

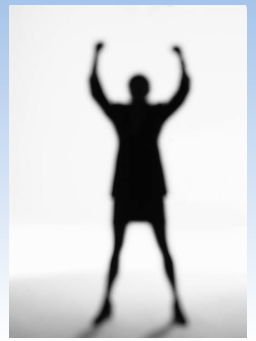
- **DILIsym Services, a Simulations Plus company**
  - Incorporated in 2015
  - Software development, systems pharmacology/toxicology modeling

Simulations Plus:
Your end-to-end M&S solutions provider



Discovery

Preclinical



Clinical

ADMET Predictor™ / ADMET Modeler™

GastroPlus™

MedChem Studio™
MedChem Designer™

DDDPlus™
MembranePlus™

PKPlus™

KIWI™

DILIsym™

NAFLDsym™

Consulting Services and Collaborations

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PKPlus™:

'Plug-n-Play' PK Modeling Platform That Combines…

✓ Sophistication	✓ Simplicity
• Powerful NCA options • Streamlined data visualization and review • Efficient compartmental analysis routines • NEW! Import of CDISC SEND packages with PC as the source data • NEW! Compatible with 64 bit windows operating systems	• Gives you what is needed for NCA/CA work • Database file format serves as repository • Point-and-click interface to minimize errors • Easy import of common data files • Smooth Exploratory Data Analysis features • NEW! Improved auto-reporting • NEW! Command line script options

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How Does This Benefit You?

✓ Industry

- **DMPK scientists/preclinical PK study managers:**
  - Generate quick, accurate PK study reports
  - Simulate single/multiple-dose regimens
- **Clinical pharmacologists:**
  - Store large data sets in secure file formats
  - Reuse custom variable/plot settings for quick analyses
- **Modelers:**
  - Easy setup of analysis datasets
  - Automate fitting different compartmental PK models

✓ Academia

- **Students:**
  - Learn fundamentals of PK modeling within intuitive interface
- **Professors:**
  - Teach students PK modeling principles in 'real-world' environment
- **Researchers on government/nonprofit grants:**
  - Perform PK data analyses and generate validated reports

- ✓ **EVERY PKPlus™ user license treated as 'floating seat', able to be shared across/within departments**
- ✓ **NO optional modules**
- ✓ **User licenses cost fraction of competing tools**
- ✓ **Dedicated development team providing rapid support**

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PKPLUS™ V2 – A REFRESHER…

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PKPlus™ v2 – Features

- **Microsoft® Windows program that provides:**
  - Point-and-click ease of use
    - Eliminate/minimize typing errors
    - Maximize productivity
  - Easy import of common data file formats (.csv, .xpt)
  - Easy **File Mapping** to internal **Display Names**
  - Easy **Data Preview**/Exploratory Data Analysis (EDA)
  - Easy set up of **Analysis Datasets**
    - **Filters**
    - **BLQs**
    - **Exclusions**
  - Easy **NCA** & compartmental analysis (**CA**)
  - Easy report-quality output of **Tables, Figures, and Lists**
  - Easy command line functionality for high throughput analysis

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Database Repository

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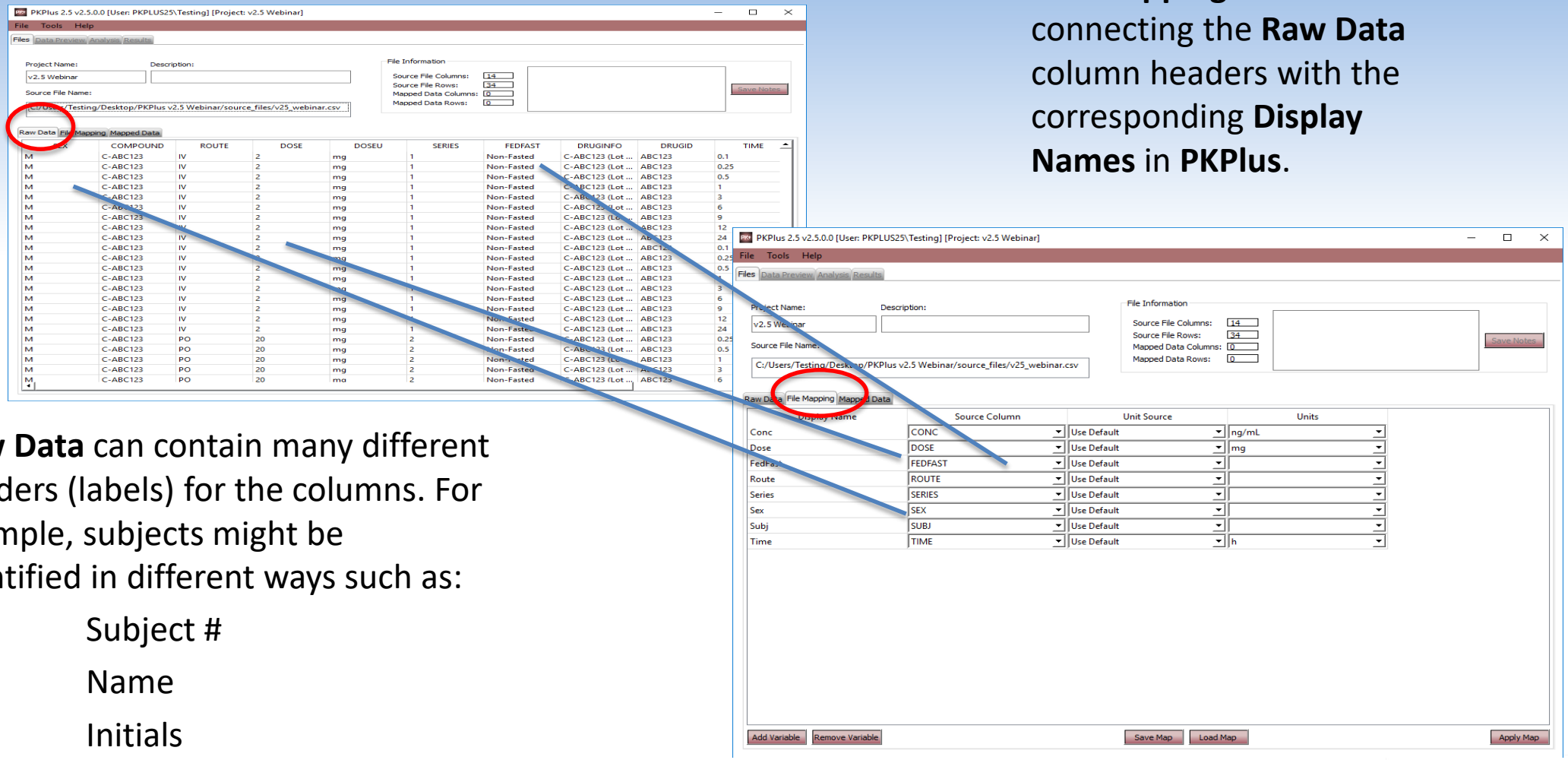
Mapping Raw Data Names to Display Names



File Mapping means connecting the **Raw Data** column headers with the corresponding **Display Names** in **PKPlus**.

Raw Data can contain many different headers (labels) for the columns. For example, subjects might be identified in different ways such as:

- Subject #
- Name
- Initials
- Alphanumeric code

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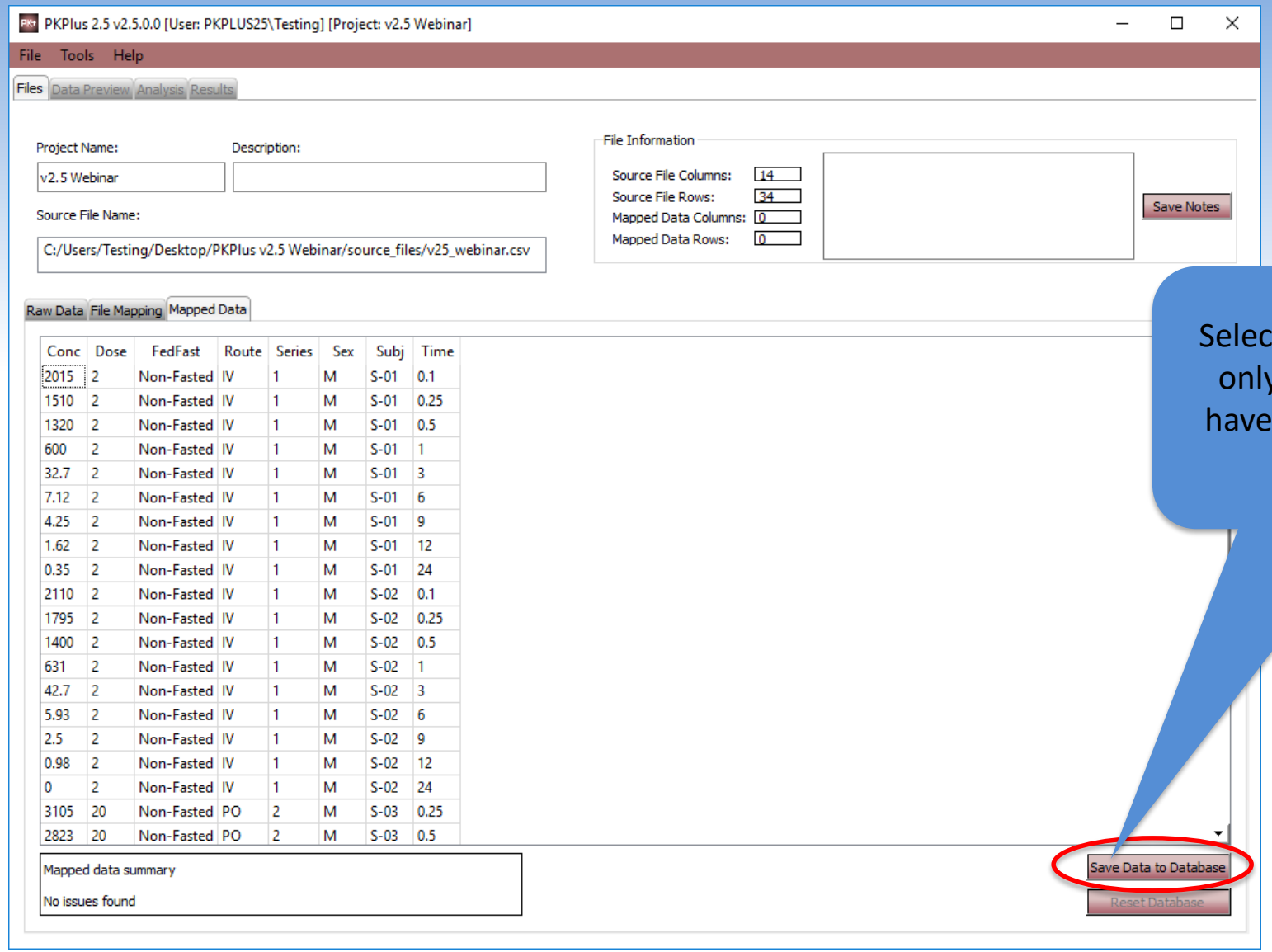
File Mapping – Saving to Database



Select **Save Data to Database** only after you are sure you have mapped everything the way you want

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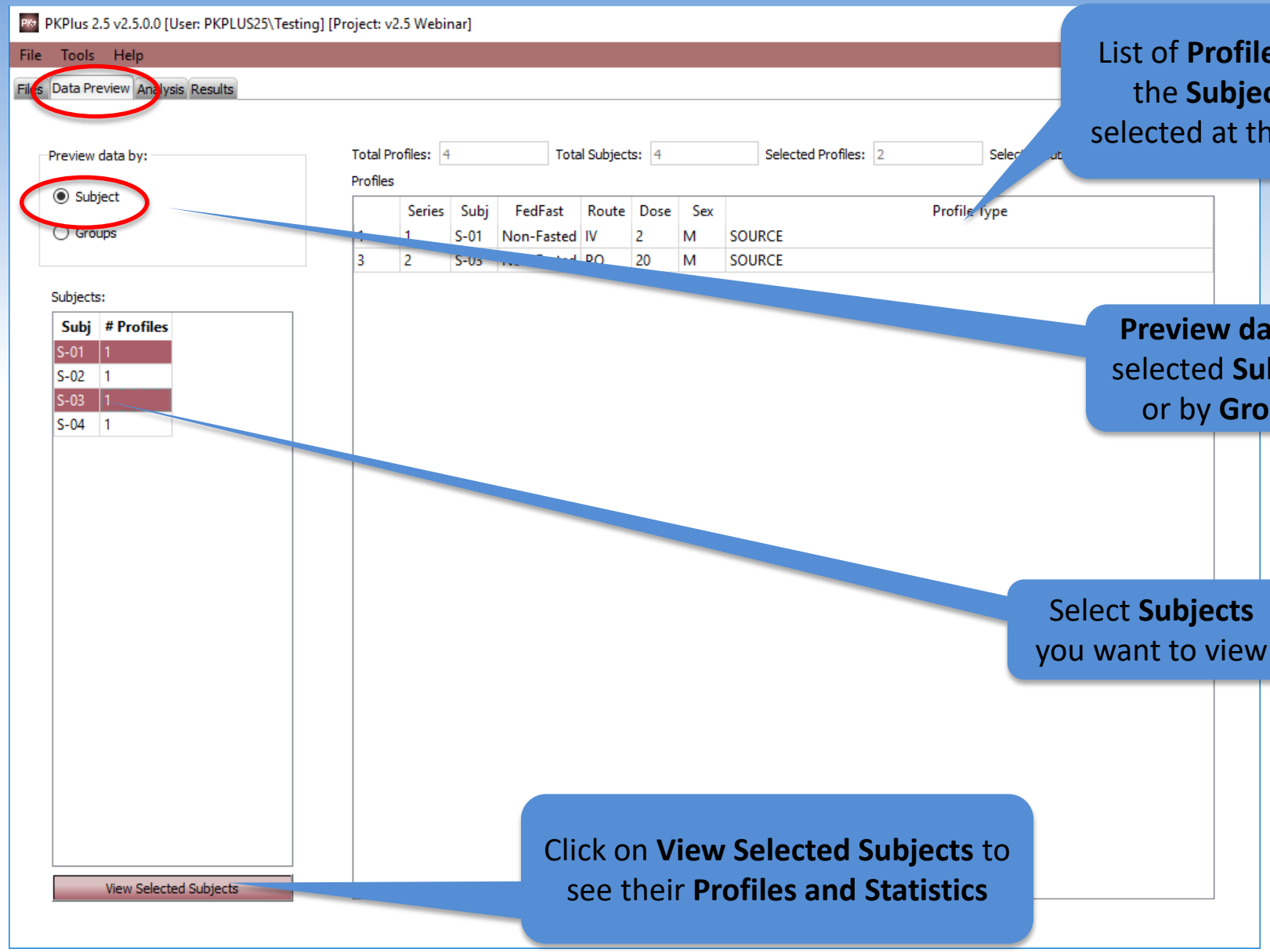
Data Preview – Preview data by: Subject



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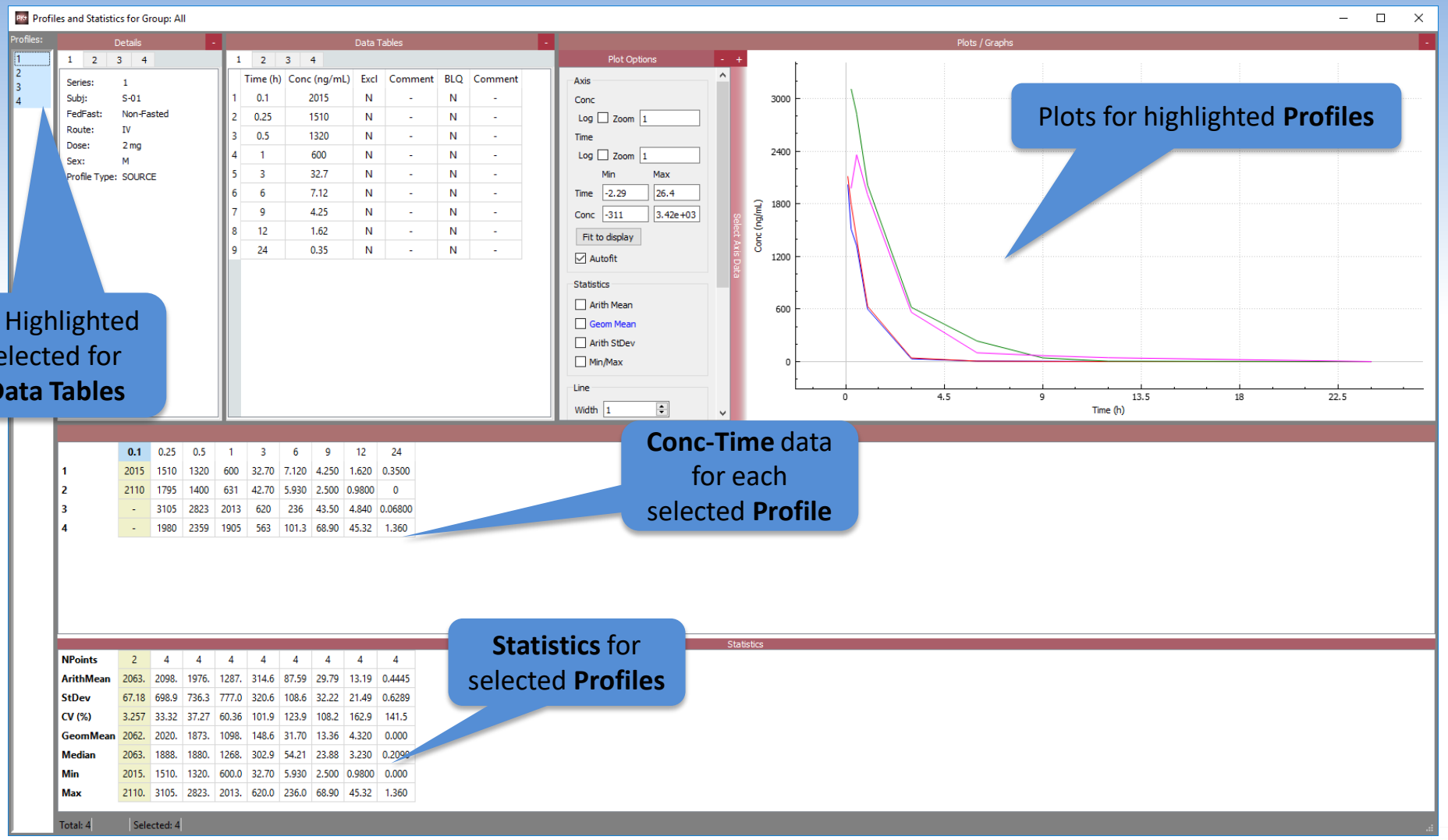
Data Preview – Profiles and Statistics



	0.1	0.25	0.5	1	3	6	9	12	24
1	2015	1510	1320	600	32.70	7.120	4.250	1.620	0.3500
2	2110	1795	1400	631	42.70	5.930	2.500	0.9800	0
3	-	3105	2823	2013	620	236	43.50	4.840	0.06800
4	-	1980	2359	1905	563	101.3	68.90	45.32	1.360

NPoints	2	4	4	4	4	4	4	4	4
ArithMean	2063.	2098.	1976.	1287.	314.6	87.59	29.79	13.19	0.4445
StDev	67.18	698.9	736.3	777.0	320.6	108.6	32.22	21.49	0.6289
CV (%)	3.257	33.32	37.27	60.36	101.9	123.9	108.2	162.9	141.5
GeomMean	2062.	2020.	1873.	1098.	148.6	31.70	13.36	4.320	0.000
Median	2063.	1888.	1880.	1268.	302.9	54.21	23.88	3.230	0.2099
Min	2015.	1510.	1320.	600.0	32.70	5.930	2.500	0.9800	0.000
Max	2110.	3105.	2823.	2013.	620.0	236.0	68.90	45.32	1.360

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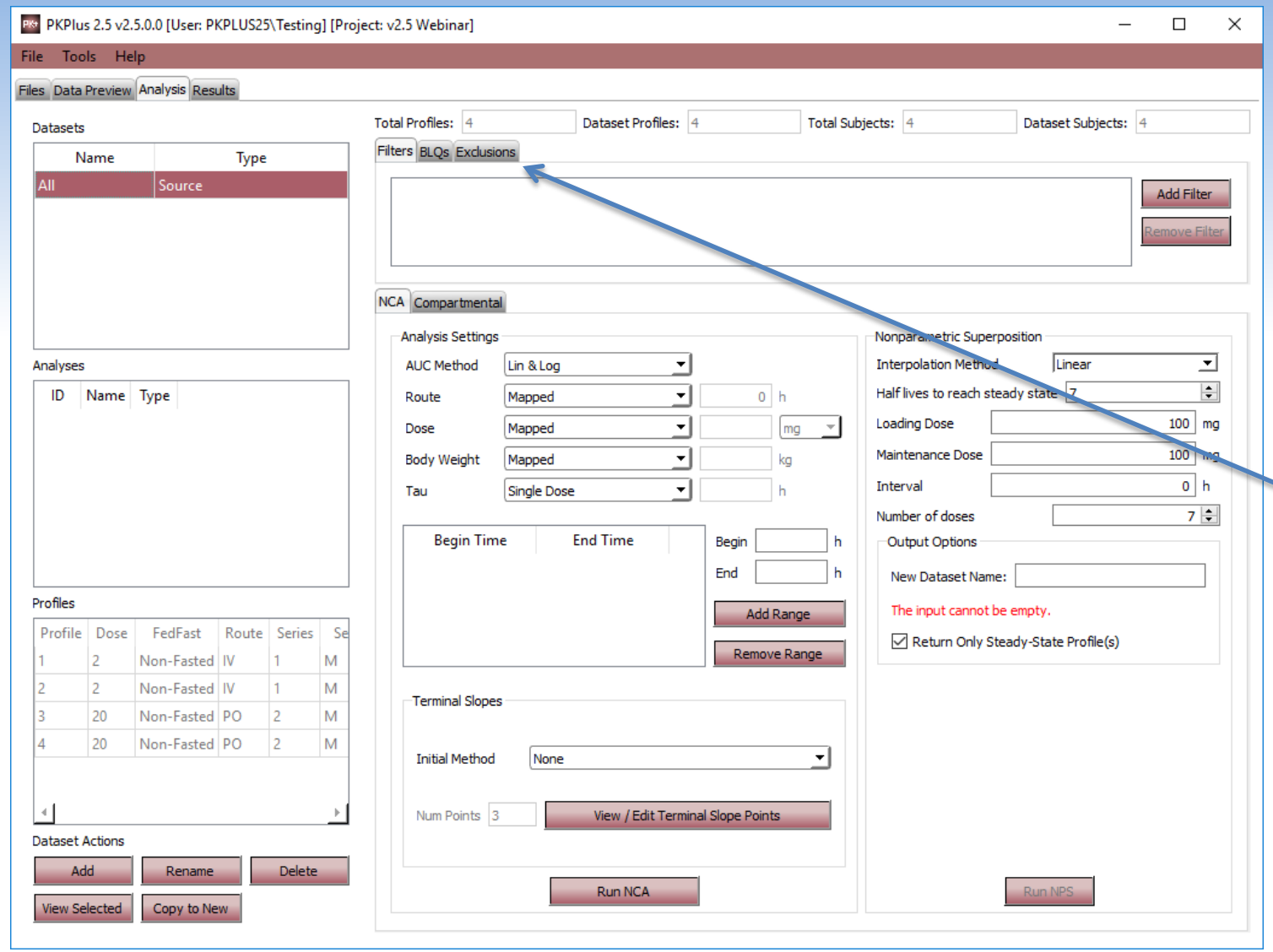
Analysis Tab – Analysis Datasets



Groups from the **Data Preview** tab can be pushed here as potential **Analysis Datasets**.

Different **Analysis Datasets** can have different treatments for **BLQs** and **Exclusions**.

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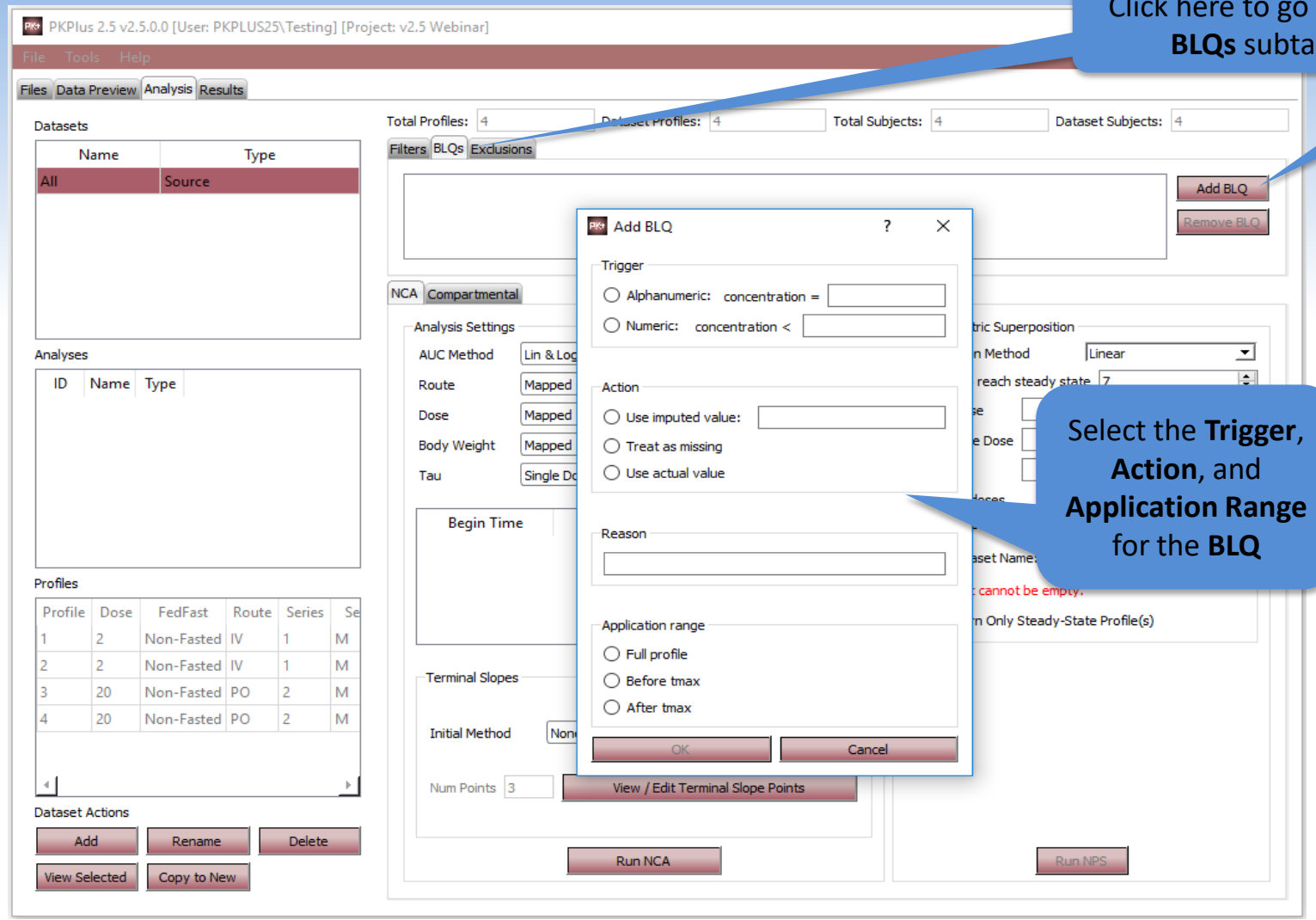
Adding BLQs:
works on Data Preview and Analysis tabs



BLQs and **Exclusions** are tied to each **Analysis Dataset**. If you copy a dataset, they are carried along (and then you can modify them for the copy).

If you create a **new dataset**, you **must set** the **BLQs** and **Exclusions** for it.

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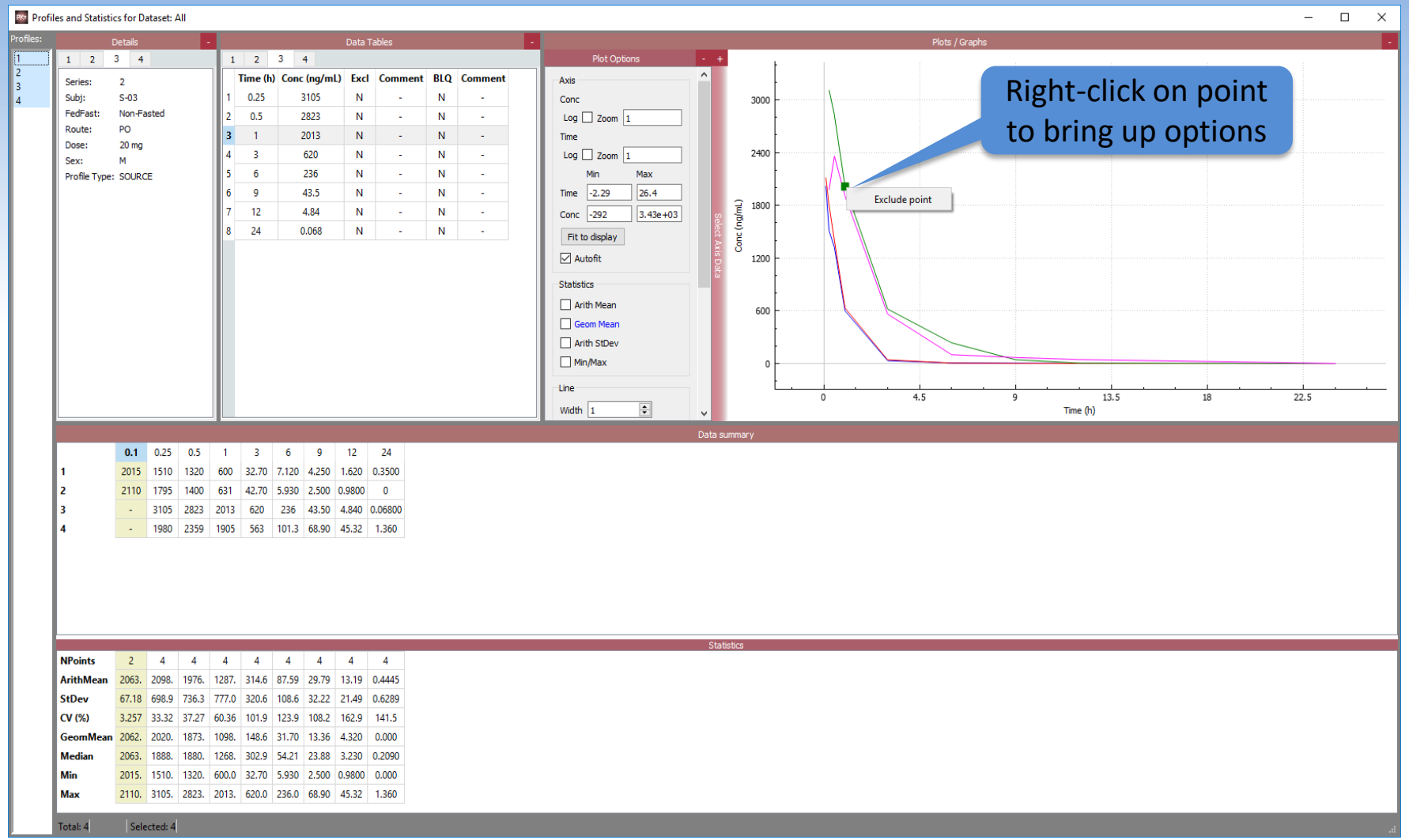
Excluding Data Points…



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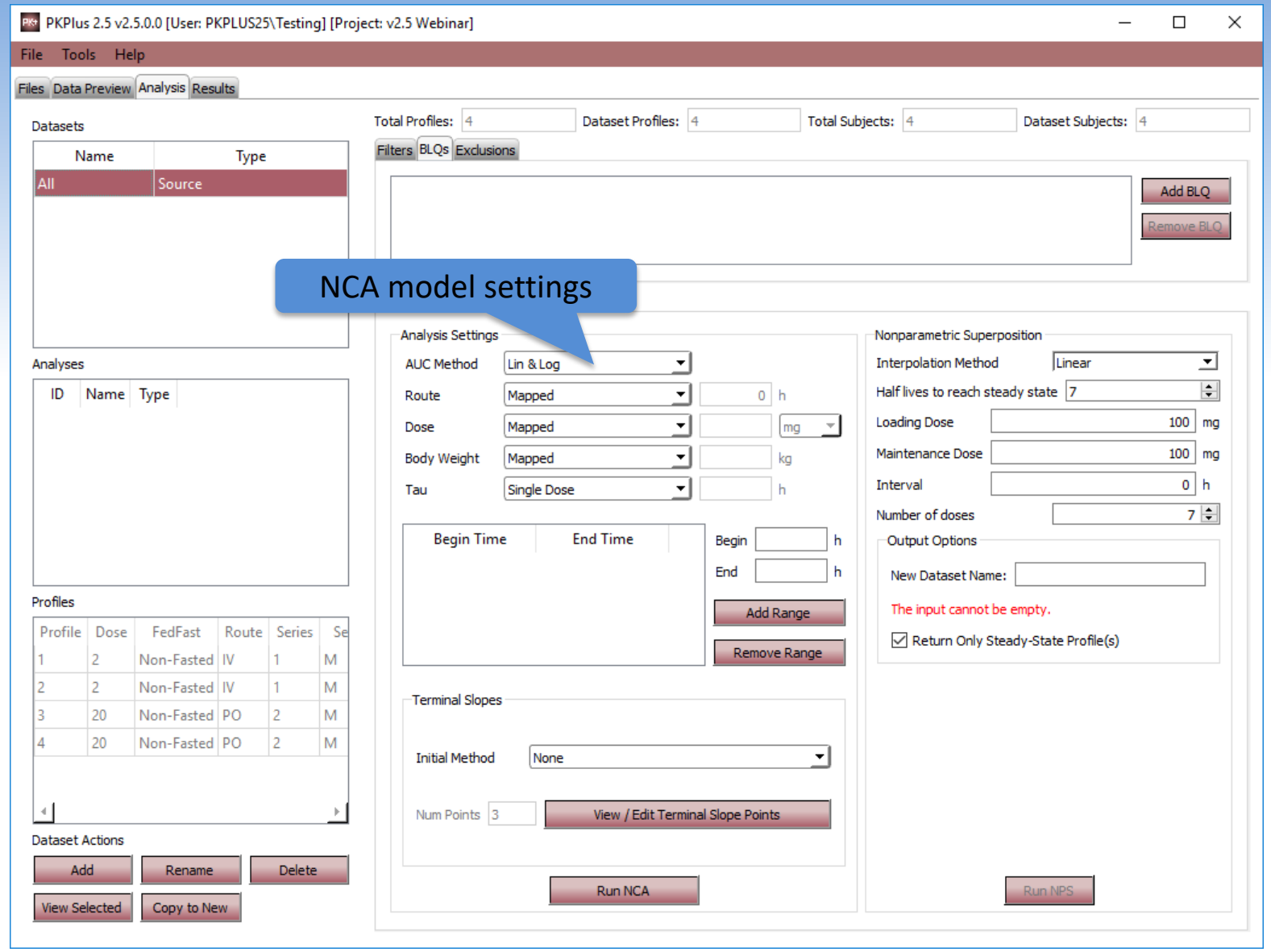
Analysis Tab – NCA Model Settings



To run an **NCA**:

(1) Select the **Analysis Dataset**
(2) Set terminal slopes
(3) Select the **NCA Model Settings**
(4) Click on **Run NCA**

When the **NCA** is complete, the **NCA Results** window will appear.

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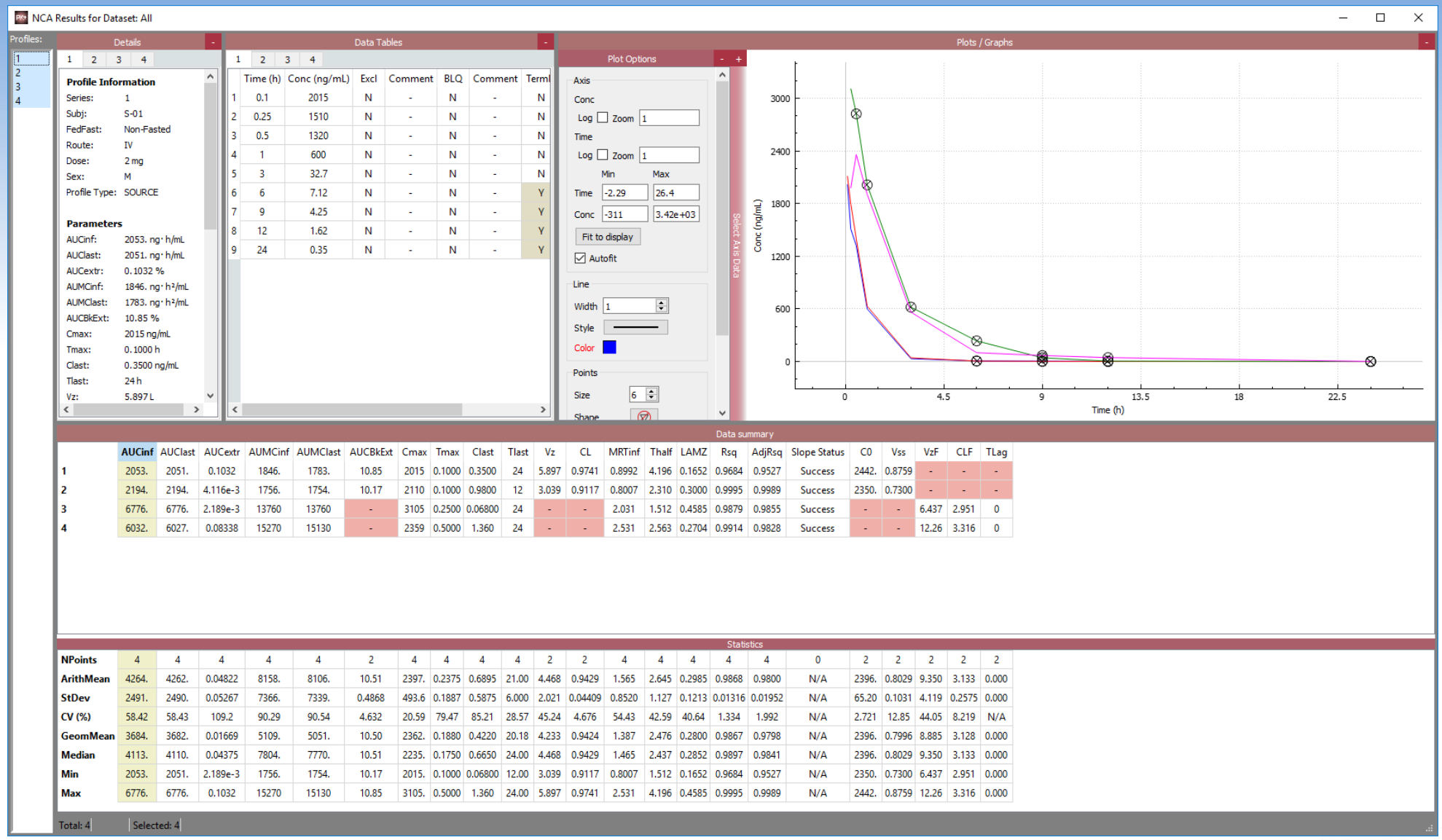
NCA Results Window



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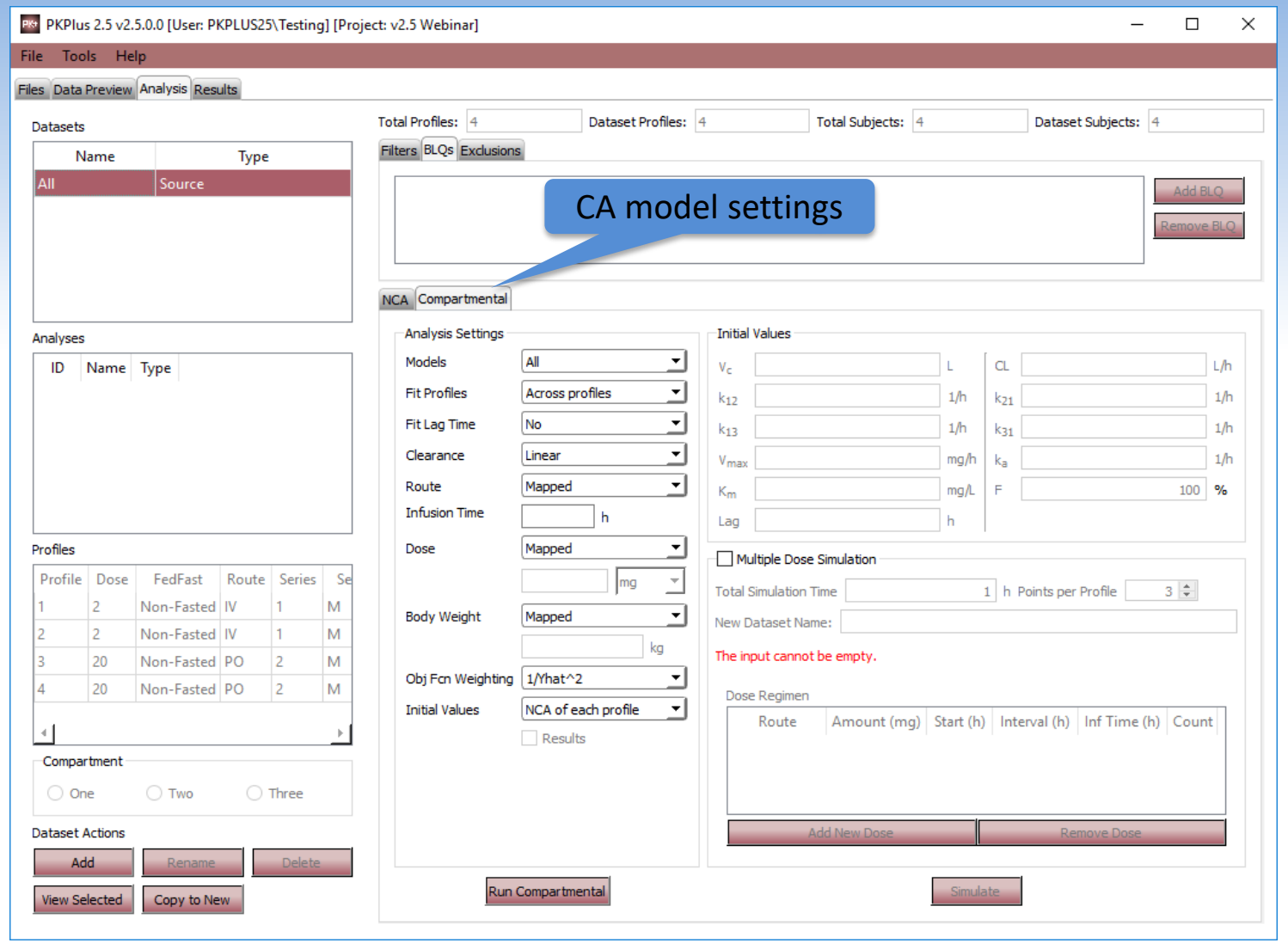
Compartmental PK Analysis



To run a **CA** on any **Analysis Dataset:**
(1) Select the dataset
(2) Set the **CA** settings
(3) Click on **Run Compartmental**

When the **CA** is complete, the **CA Results** window will appear

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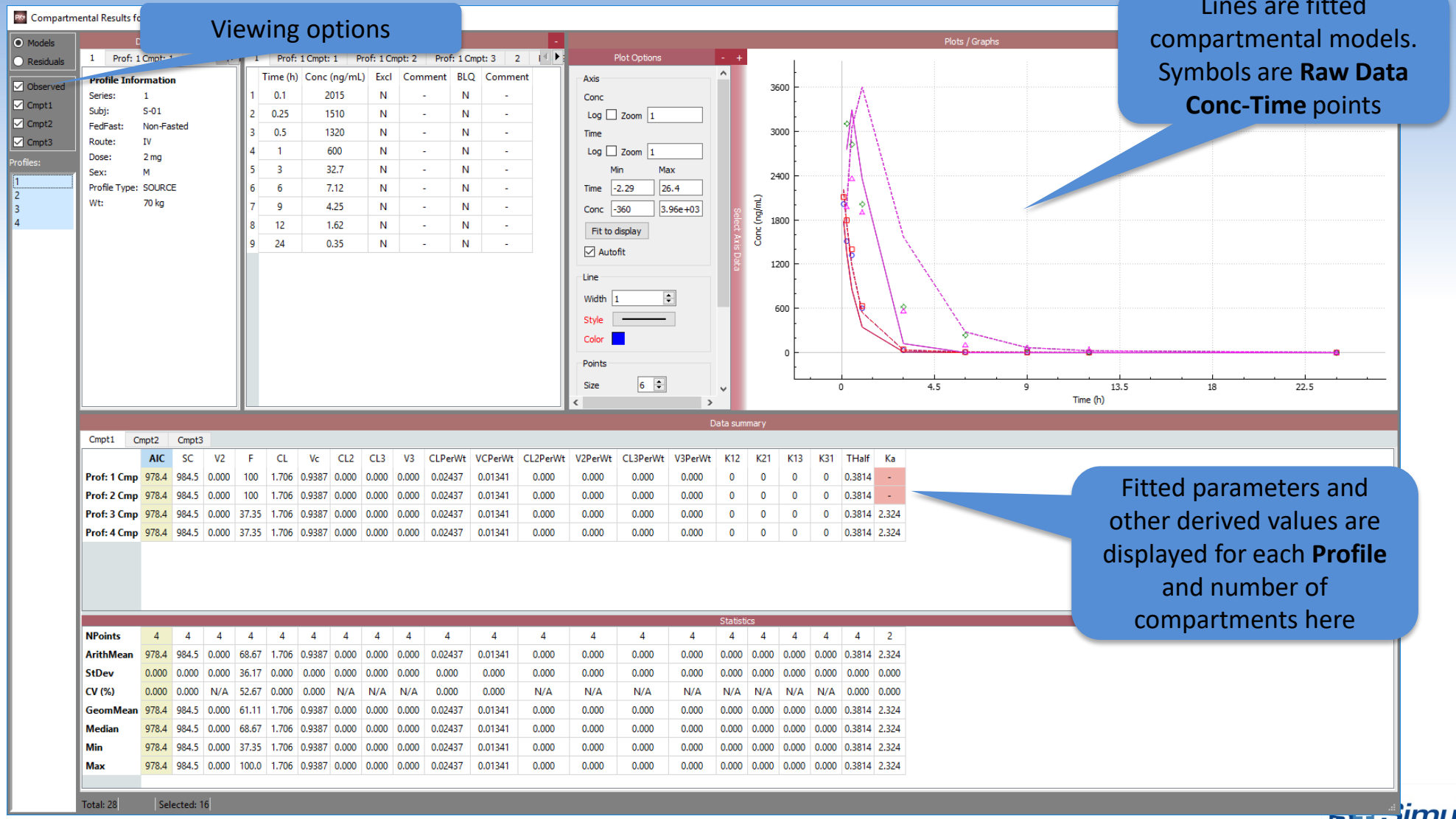
Compartmental PK Results Window



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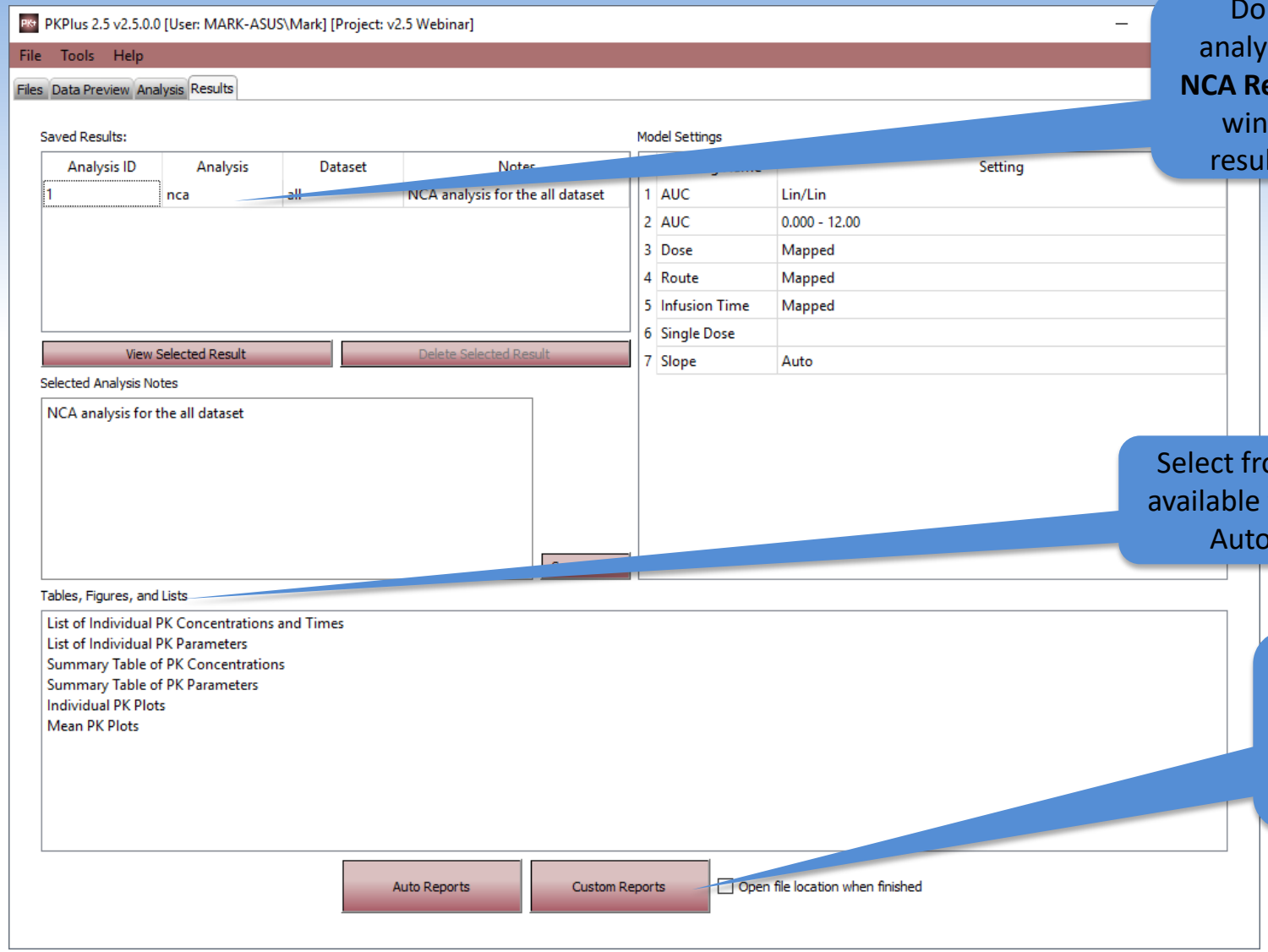
Results Tab



Double-click on an analysis to bring up the **NCA Results** or **CA Results** window to view the results of the analysis

Select from the list of available templates for Auto Reports

After selecting an analysis and the reports you want, click on **Auto or Custom Reports** to produce TFLs

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Example – Table of Individual PK Parameters (.docx file)

List of Individual PK Parameters

Dataset: All Username: Walt

Run date: 2016-04-29 04:00:45 Project: Example for manual

AUC Method	Slope Method	Dose	Route	Analysis ID	Slope Status												
Linear & Log Interpolation	Manually selected points	Mapped	Mapped	1	SUCCESS												
Profile ID	AUCinf	AUClast	AUMCinf	AUMClast	Num. Points	Cmax	LAMZ	MRTinf	Tmax	VzF	AUCextr	CLF	Clast	Tlast	Thalf	Rsq	AdjRsq
9	1.138	1.093	8.585	7.177	14	0.1546	0.1359	7.543	1.500	905.3	3.945	123.0	6.100e-3	24.00	5.101	0.9993	0.9991
10	0.8355	0.8237	4.684	4.332	14	0.1571	0.1734	5.606	1.500	966.5	1.415	167.6	2.050e-3	24.00	3.998	1.000	0.9999
11	0.7076	0.7071	2.470	2.456	14	0.1961	0.3003	3.490	1.000	658.9	0.07059	197.9	1.500e-4	24.00	2.308	0.9999	0.9999
12	1.094	1.065	7.718	6.859	14	0.1484	0.1586	7.056	1.500	806.8	2.593	128.0	4.500e-3	24.00	4.369	0.9994	0.9987
13	0.6053	0.6016	3.160	3.055	14	0.1087	0.2184	5.221	1.500	1.059e+3	0.6052	231.3	8.000e-4	24.00	3.174	1.000	0.9999
14	0.9283	0.9131	5.796	5.347	14	0.1388	0.1779	6.244	2.000	847.7	1.635	150.8	2.700e-3	24.00	3.896	0.9994	0.9993
15	0.9414	0.8979	7.687	6.309	14	0.1092	0.1308	8.166	1.500	1.137e+3	4.628	148.7	5.700e-3	24.00	5.298	0.9998	0.9998
16	0.7466	0.7321	4.762	4.327	14	0.1137	0.1657	6.378	2.000	1.132e+3	1.940	187.5	2.400e-3	24.00	4.183	0.9993	0.9991
17	0.8697	0.8475	5.902	5.226	14	0.1288	0.1535	6.787	1.500	1.049e+3	2.547	161.0	3.400e-3	24.00	4.516	0.9999	0.9997
18	0.7774	0.7706	4.344	4.147	14	0.1317	0.2056	5.587	1.500	876.0	0.8760	180.1	1.400e-3	24.00	3.372	1.000	0.9999
19	1.242	1.215	8.312	7.477	14	0.1731	0.1594	6.691	2.000	706.9	2.222	112.7	4.400e-3	24.00	4.348	0.9996	0.9994
20	0.9334	0.9304	3.889	3.804	14	0.2200	0.2326	4.167	1.000	644.8	0.3224	150.0	7.000e-4	24.00	2.980	0.9998	0.9997
21	1.204	1.132	10.67	8.360	14	0.1383	0.1218	8.865	2.000	954.5	5.966	116.3	8.750e-3	24.00	5.690	1.000	1.000
22	0.5786	0.5757	2.861	2.778	14	0.1107	0.2227	4.945	1.500	1.087e+3	0.5045	242.0	6.500e-4	24.00	3.113	0.9999	0.9998

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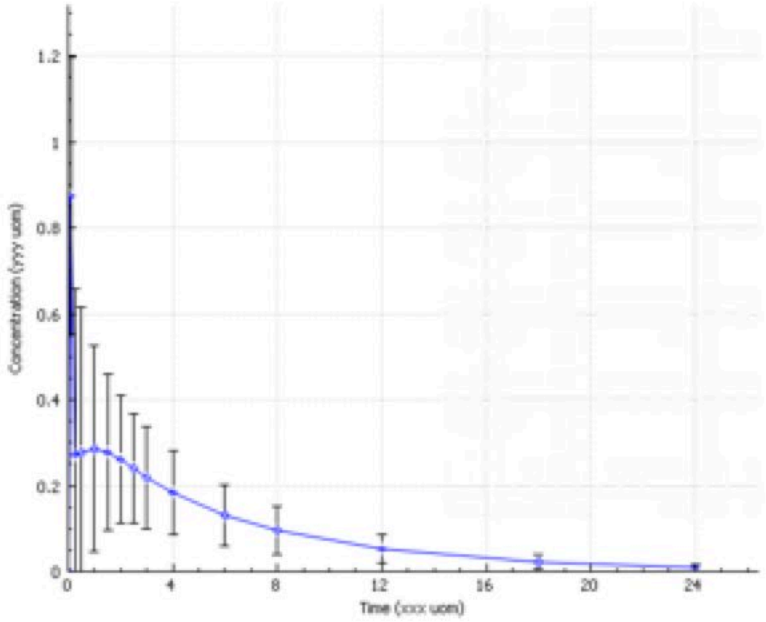
Example – Mean PK Plots (.docx file)

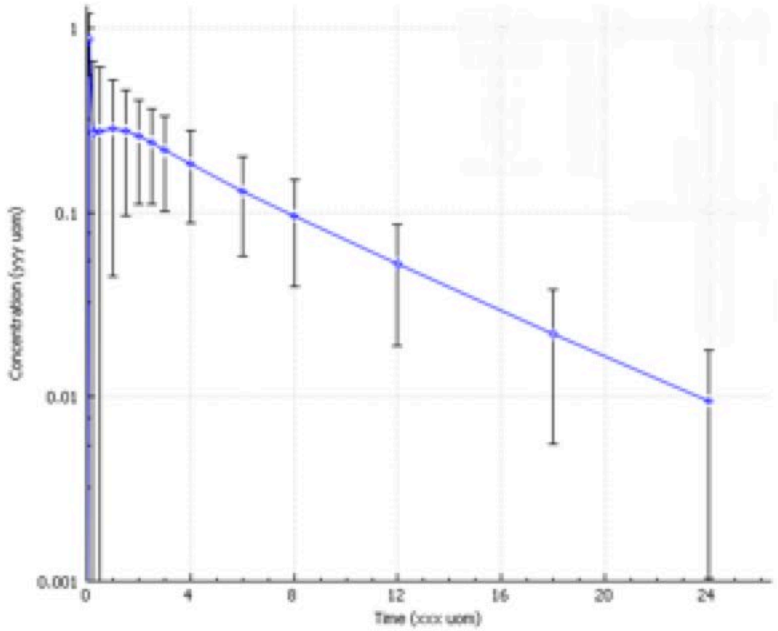
Mean PK Plots

Dataset: All
Username: Walt
Run date: 2016-04-29 04:00:45
Project: Example for manual

Linear View



Semilogarithmic View



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WHAT'S NEW IN PKPLUS™ V2.5?

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NEW Additions in PKPlus™ v2.5 – Highlights

- Now compatible with 64 bit windows operating systems
- Import of CDISC SEND packages with PC as the source file data
- Improvements to auto-reporting
- Improvements to command line processing
- Bug fixes

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PRODUCT DEMONSTRATION

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SUMMARY

SimulationsPlus
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PKPlus™ v2.5 Adds…

- Now compatible with 64 bit windows operating systems
- Import of CDISC SEND packages with PC as the source file data
- Improvements to auto-reporting
- Improvements to command line processing

PKPlus™ offers all necessary PK modeling & simulation functionality!

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Final Questions to Ask Yourself…

- **Competing tools offer more capabilities with:**
  - Higher prices
  - Restrictive licensing (e.g., standalone only)
- **Ask yourself these questions about competing tools:**
  - Is it easy to perform the basic PK operations I need?
  - How much of the functionality do I really use?
  - What am I paying for?
- **Honest answers will lead you to PKPlus™**

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