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## NCA examples

This section presents several examples of the NCA operational object usage within Phoenix. Knowledge of how to do basic tasks using the Phoenix interface, such as creating a project and importing data, is assumed.

The examples include:

- [Analysis of three profiles using NCA](#)
- [Exclusion and partial area NCA example](#)
- [Sparse sampling NCA example](#)
- [Urine study NCA example](#)
- [Drug effect NCA example](#)
- [Multiple profile analysis using NCA](#)

### ***Analysis of three profiles using NCA***

Suppose a researcher has obtained time and concentration data following oral administration of a test compound to three subjects, and wants to perform noncompartmental analysis and summarize the results.

The completed project (NCA.phxproj) is available for reference in ...  
\Examples\WinNonlin.

#### *Set up the project and data for the three profiles*

1. Create a new project named NCA.
2. Import the file ...\Examples\WinNonlin\Supporting files\Bguide1 single dose and steady state.dat.

**Note:** Units must be added to the time and concentration columns before the dataset can be used in a noncompartmental analysis.

3. With **Bguide1 single dose and steady state** selected in the Data folder, go to the Columns tab (lower part of the Phoenix window) and select the **Time** column header in the Columns box.
4. Clear the **Unit** field and type hr.
5. Select the **Conc** column header in the Columns box.
6. Clear the **Unit** field and type ng/mL.  
Or

**Note:** Units added to ASCII datasets can be preserved if the datasets are saved in .dat or .csv file format. Phoenix adds the units to a row below the column headers. To import a .dat or .csv file with units, select the **Has units row** option in the *File Import Wizard* dialog.

### *Set up the NCA object for analysis of the three profiles*

Noncompartmental analysis for extravascular dosing is available as Model 200 in the Phoenix model library. Phoenix displays the model type (Plasma, Urine, or Drug Effect) in the Options tab of an NCA object.

**Note:** The exact model used is determined by the dose type. Extravascular Input uses Model 200, IV-Bolus Input uses Model 201, and Constant Infusion uses Model 202.

1. Select **Workflow** in the Object Browser and then select **Insert > NonCompartmental Analysis > NCA**.
2. Drag the **Bguide1 single dose and steady state** worksheet from the Data folder to the NCA object's Main Mappings panel.
3. Map the data types as follows:  
**Day** to the **Sort** context (make sure to map **Day** first)  
**Subject** to the **Sort** context  
**Time** mapped to the **Time** context  
**Conc** to the **Concentration** context

### *Prepare the dosing information from the profiles*

1. Select **Dosing** in the NCA object's Setup list.
2. In the Dosing panel, select the **Use Internal Worksheet** checkbox.
3. Click **OK** in the *Select sorts* dialog to accept the default sort variables.
4. For each row:  
In the Time column, enter 0.  
In the Dose column, enter 55.  
In the Tau column, enter 24 for the three Day 14 rows (rows 4, 5, and 6).



	Day	Subject	Time	Dose (mg)	Tau
1	1	DW	0	55	
2	1	GS	0	55	
3	1	RH	0	55	
4	14	DW	0	55	24
5	14	GS	0	55	24
6	14	RH	0	55	24

- In the Dose Options area of the Options tab, type mg in the **Unit** field and press the **Enter** key.  
The units are immediately added to the column header.
- Extravascular** is selected by default in the **Type** menu. Do not change this setting.

### Set up the terminal elimination phase for the analysis

Phoenix attempts to estimate the rate constant Lambda Z, associated with the terminal elimination phase. Although Phoenix is capable of selecting the times to be used in the estimation of Lambda Z, this example provides Phoenix with the time range.

Specify the times to be included.

- Select **Slopes** in the Setup list.
- For each row:  
In the Start Time column, type 8.  
In the End Time column, type 24.  
Do not type any values into the **Exclusions** column.
- Select **Slopes Selector** in the Setup list.

The **Time Range** is selected in the **Lambda Z Calculation Method** menu. The **Start** and **End** times have been specified for each subject. A line is displayed on each graph that shows the Lambda Z time range.

In this example, no points are excluded from the specified Lambda Z time range. The example ["Exclusion and partial area NCA example"](#) demonstrates Lambda Z exclusions.

The next step is to define a target concentration range to enable calculation of the time and area located above, below, and within that range.

**Note:** See [“Exclusion and partial area NCA example”](#) for an NCA example that includes computation of partial areas under the curve.

1. Select **Therapeutic Response** in the Setup list.
2. Select the **Use Internal Worksheet** checkbox.
3. Click **OK** in the sorts dialog to accept the default sort variables.
4. For each row:  
Type 2 in the **Lower** column.  
Type 4 in the **Upper** column.

### *Set preferred units for the analysis*

The next step in setting options is to specify preferred output units. The independent variable, dependent variable, and dosing regimen must have units before preferred output units can be set.

1. Select **Units** in the Setup list.

The Units worksheet lists both the Default units and the Preferred units for each parameter. The new preferred volume unit needs to be set to L (liter).

2. Select the cell in the **Preferred** column for Volume ( $V_z$ ,  $V_z/F$ ,  $V_{ss}$ ).
3. Type L and press **ENTER**.

### *Specify NCA model options for the analysis*

Four methods are available for computing the area under the curve. The default method is the linear trapezoidal rule with linear interpolation. This example uses the **Linear Log Trapezoidal** method: linear trapezoidal rule up to  $T_{max}$ , and log trapezoidal rule for the remainder of the curve.

Use the Options tab to specify settings for the NCA model options. The Options tab is located underneath the Setup tab.

1. Select **Linear Log Trapezoidal** in the **Calculation Method** menu.
2. In the **Titles** field type Example of Noncompartmental Analysis.

### *Set an acceptance criteria rule*

Acceptance criteria for Lambda Z, which are applicable to both the **Best Fit** method and the **Time Range** method, can be specified on the Rules tab. These rules are

1. Select the **Rules** tab.
2. In the **Rsq\_adjusted** field, type 0.97 to flag any profile with an Rsq\_adjusted value greater than or equal to this value.

Profiles that break the rule are flagged in the output and can be quickly filtered out of the results. The process will be illustrated later in this example.

### *Execute and view the results of the analysis*

At this point, all of the necessary commands have been specified.

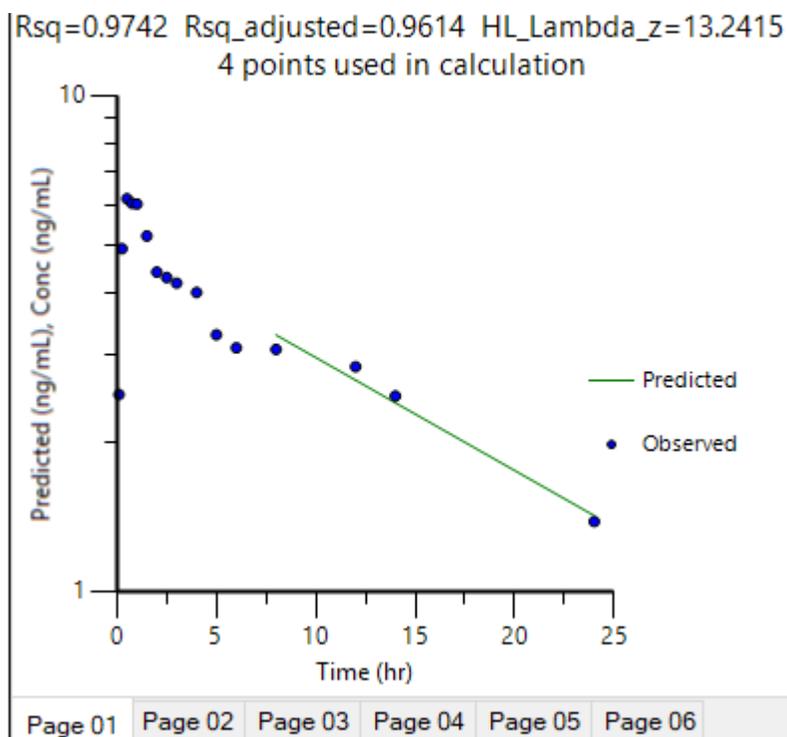
1. Click  (**Execute** icon) to execute the object.
2. In the Results tab, select **Final Parameters** in the list.

Subject DW's concentrations were within the theoretical therapeutic range for just over 13.8 hours, as reflected in the parameter TimeBetween.

	Day	Subject	Parameter	Units	Estimate
41	1	DW	MRTINF_pred	hr	19.187241
42	1	DW	TimeLow	hr	6.3652263
43	1	DW	TimeBetween	hr	13.811328
44	1	DW	TimeHigh	hr	3.8234453
45	1	DW	TimeInfBetween	hr	13.811328

3. In the Results tab, select **Observed Y and Predicted Y vs X** in the list.

The NCA object's plot output includes Observed Y and Predicted Y vs X graphs for each subject (switch between the plots using the tabs below the graph).



- In the Results tab, select **Core output** in the list.

The NCA object's Core Output text file contains user settings, a brief summary table, and final parameters output for each subject.

```

13 Settings
14 -----
15 Model: Plasma Data, Extravascular Administration
16 Number of nonmissing observations: 16
17 Dose time: 0.00
18 Dose amount: 55.00
19 Calculation method: Linear/Log Trapezoidal
20 Weighting for lambda_z calculations: Uniform weighting
21 Lambda_z method: User-specified lambda_z range, Log regression
22 User's lambda_z bounds: 8.00, 24.00
23 Lower bound for therapeutic window: 2.00
24 Upper bound for therapeutic window: 4.00
25 Lambda_z Acceptance Criterion, Min Rsq_Adjusted: 0.9700
  
```

*Settings portion of the Core Output*

*Filter out flagged profiles*

- In the Results tab, select **Final Parameters Pivoted** in the list.



1	2	3	4	5	6	7	8	9	10
2	1	GS	16	55	0.98383816	0.97575725	Accepted	-0.99188616	4
3	1	RH	16	55	0.99441626	0.9916244	Accepted	-0.99720422	4
4	14	DW	16	55	0.98659088	0.97988632	Accepted	-0.99327281	4
5	14	GS	16	55	0.99108753	0.98663129	Accepted	-0.99553379	4
6	14	RH	16	55	0.99666853	0.9950028	Accepted	-0.99833288	4

### *Part of the Final Parameters Pivoted worksheet*

For this example, a rule was set for the value of Rsq\_adjusted (see ["Set an acceptance criteria rule"](#)). The output indicates that the profile for DW broke this rule with a value of 'Accepted' in the Flag\_Rsq\_adjusted column.

To remove any profiles failing to meet acceptance criteria from the output, the Final Parameters Pivoted worksheet can be processed by the Data Wizard to delete these profiles. The worksheet is filtered on the flag values of 'Not Accepted' and identified rows are then excluded.

**Note:** The NCA.phxproj file does not include processing by the Data Wizard, but the information is included here as a reference.

- a) Insert a Data Wizard object.
- b) In the Options tab, set Action to **Filter** and click **Add**.
- c) Click the **Select Source** icon in the Mappings panel and select the NCA Final Parameter Pivoted worksheet.
- d) In the Options tab, click the **Add** button to the right of the **Specify Filter** field.
- e) In the *Filter Specification* dialog, define the filter to **Exclude** rows that have a value of **Not Accepted** in the **Flag\_Rsq\_adjusted** column (or other "Flag\_" column on which you want to filter profiles).  
Once the filter is defined, execute the Data Wizard object.

### *Summarize the analysis output with statistics*

At this point, it is convenient to summarize the results of the noncompartmental analysis using a Descriptive Statistics object. This example summarizes parameter estimates across subjects.

1. Select **Workflow** in the Object Browser and then select **Insert > Computation Tools > Descriptive Statistics**.
2. In the Descriptive Statistic's Main Mappings panel click the **Select Source** icon.
3. Under the **NCA** node, select the **Final Parameters** worksheet and click **OK**.
4. In the Main Mappings panel, map the data types to the following contexts:  
Map **Day** to the **Sort** context (make sure to map **Day** first).  
Leave **Subject** mapped to **None**.  
Map **Parameter** to the **Sort** context.

**Note:** Mapping Day and Parameter to Sort computes statistics on the parameter estimates for each day and mapping Estimate to Summary computes one statistic per parameter per day.

5. In the Options tab, check the **Confidence Intervals** and **Number of SD Statistics** checkboxes, but do not change the default values for these two items.
6. Execute the object.

The three subjects spent an average of 13.6 hours within the therapeutic concentration range on Day 1, as shown by the parameter TimeBetween.

41	Estimate	1	Rsq_adjusted	3	0	3	0.97624669
42	Estimate	1	Span	3	0	3	1.3132153
43	Estimate	1	TimeBetween	3	0	3	13.627457
44	Estimate	1	TimeHigh	3	0	3	3.4122411
45	Estimate	1	TimeInfBetween	3	0	3	13.627457

### Use ratios to compare data

The Ratios and Differences object can be used to quickly setup ratios and/or differences between parameter values in order to compare data. A description of the object can be found in ["Ratios and Differences"](#).

1. In the Object Browser, click the NCA object.
2. In the Results list, right-click **Final Parameters Pivoted** and select **Send To > Computation Tools > Ratios and Differences**.
3. In the Main Mappings panel of the Ratios and Differences object, map the data types to the following contexts:  
 Map **Day** to the **Filter** context.  
 Map **Subject** to the **Sort** context.  
 Map the rest of the data types to the **Carry** context by first mapping **N\_Samples** to **Carry** and then drag the corner of the selected cell all the way to the bottom of the grid. It may take a few seconds.
4. In the Options tab, set up two ratios as shown in the following image. Use the **Add** button to add the second row of options to the table.

	X			Y			
Comparison	Column	Filter Value	Column	Filter Value	New Column Name		
X/Y	Cmax	14	Cmax	1	Ratio_Cmax14_Cmax1		
X/Y	AUC_TAU	14	AUClast	1	Ratio_AUC_TAU14_AUClast1		



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6. In the RESULTS tab, select **RATIOS DIFFERENCES** and compare the ratios for each subject.

	Subject	Ratio_Cmax14 _Cmax1	Ratio_AUC_TAU14_ AUClast1
1	DW	1.2559716	1.2609336
2	GS	1.0863854	1.2330284
3	RH	1.2174045	1.2203516

This concludes the multiple profile example.

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