

Phoenix[®] 8.3.5

Release Notes

March 2022

March 2022: Phoenix 8.3.5, added entries for QC 16931, QC 18108, QC 18125, QC 18126, QC 18152, QC 18155, QC 18159, and QC 18172 November 2021: Phoenix 8.3.4, added entries for QC 18053, QC 18110, QC 18111, and QC 18119 April 2021: Phoenix 8.3.3, added entries for QC 18081 and 18082, updated entry for 18061 January 2021: Phoenix 8.3.2, added entries for QC 18054, 18060, 18061, 18062 End of June 2020: Phoenix 8.3.1, added entry for QC 18043 Mid June 2020: Phoenix 8.3 release

Contents

Installing Phoenix 8.3.5	2
Phoenix Product Interoperability	2
Certara® Contact Information.	3
Phoenix 8.3.5 Updates	3
Phoenix 8.3.4 Updates	4
Phoenix 8.3.3 Updates	4
Phoenix 8.3.2 Updates	5
Phoenix 8.3.1 Updates	5
Phoenix 8.3.	5



Installing Phoenix 8.3.5

To install Phoenix 8.3.5:

- 1. Manually uninstall any previous version of Phoenix using Windows > Settings > Apps & features.
- 2. Manually uninstall any plugins that were installed separately from Phoenix using **Windows > Settings > Apps & features**.

Folders for these separately installed plugins will remain in C:\Program Files (x86)\Certara\Phoenix\application\Plugins after uninstalling Phoenix. Such plugins include: Phoenix Integral Plugin, PKAssist, and PKSubmit.

- Copy the license file (lservrc) from C:\Program Files (x86)\Certara\Phoenix\application\Services\Licensing to a temporary location.
- 4. Remove all remaining folders and files under C:\Program Files (x86)\Certara.
- 5. Run the Phoenix 8.3.5 installer.
- 6. Copy your license file back to C:\Program Files (x86)\Certara\Phoenix\application\Services\Licensing.
- Reinstall the plugins that you uninstalled. For PK Assist customers using Integral, the Phoenix Integral Plugin must be reinstalled before PK Assist is reinstalled.

If you encounter any difficulties with these steps, please contact Certara Support.

Note: The above instructions assume that the license is installed on the end user's local machine. If Server license(s) are being used, Phoenix will need to be configured to use the Server license(s) after installation of this maintenance release. For instructions, please refer to the "Licensing of Phoenix software" section of the Getting Started Guide.pdf that was downloaded with the Phoenix installer.

Phoenix Product Interoperability

Phoenix 8.3.5 is compatible with the Integral 22.4.1 repository, which utilizes the 22.4.1 version of the Phoenix Integral Plugin. Phoenix 8.3.5 is also compatible with PKS 4.0.4.

Phoenix can co-exist on the same workstation and run independently with Trial Simulator 2.3.



Certara[®] Contact Information

Technical support

Consult the software documentation to address questions. If further assistance is needed, contact Certara Support through e-mail or our support portal.

 E-mail:
 support@certara.com

 Web:
 https://certaracommunity.force.com/support/s/

For the most efficient service, e-mail a complete description of the problem, including copies of the input data.

User forum.

Get tips and discuss Certara software with other users: <u>https://support.certara.com/forums</u>

Phoenix 8.3.5 Updates

A checksum and a test unzip are now done when Phoenix projects are saved as zip files (QC 16931): If the checksum or the test unzip fails, the projects are resaved. This may prevent some cases of project files becoming corrupted.

Autoback up feature implemented to aid in recovering from corrupt projects (QC 18108): When saving a project, Phoenix now creates a backup project file (with an extension of .phxbackup) in the same directory. This provides a recent "checkpoint" from which most of the work can be recovered in the event that a project becomes corrupt. Note that there is only one backup file maintained for a project, i.e., subsequent save operations overwrite the project's backup file.

R script changes are now retained when using "Start Development Environment" within the **R** Shell object (QC 18125): When using Phoenix 8.3.3, once changes to the script were made, saved back to disc, and R-Studio was exited, re-loading the script in Phoenix showed none of the changes. With Phoenix 8.3.5, the edits are now visible upon re-loading in Phoenix.

Saving an un-executed NCA object created with Phoenix 8.3.x outside of Phoenix, then reloading the project and executing it, no longer generates an error (QC 18126)

An issue where using Phoenix 8.3 to execute an NCA with a large number of profiles resulted in a "Phoenix has stopped working" error due to a stack overflow has been fixed (QC 18152/CRM 215821).

Reporter object no longer wraps data in Table cells differently than Phoenix 8.1 (QC 18155): A different padding constant was implemented in Phoenix 8.3 but has been reverted to the 0.38 inches padding width value that was used in Phoenix 8.1.



An NCA with many profiles no longer fails to run when executed while viewing a panel with mapped data (QC 18159).

IWRES and epsilon shrinkage are now calculated correctly for all observe() statements in a model (QC 18172): Previously, the IWRES and epsilon shrinkage calculation was only correct for the first observed() variable listed in the model. Now, calculations are correct for all observe() variables that appear after the first observe() statement in the PML model.

Phoenix 8.3.4 Updates

Installation of this maintenance release (Phoenix 8.3.4) is necessary to prevent erroneous detection of Certara executables as "unsigned" after certificate replacement, and is mandatory for all Phoenix NLME and Phoenix WinNonlin customers.

Phoenix Installation test case in Validation Suite runs successfully with installation of PKSubmit 1.1 plugin is installed (QC 18053): Failure of the Phoenix Installation test case was actually fixed in the Phoenix 8.3.2 release, but inadvertently remained listed as a Known Issue.

NCA no longer omits profile from execution with incorrect dosing warning (QC 18110): Previously, when using an external Dosing worksheet and the Dosing Defined option, with multiple doing routes in the same dataset, it was possible for one or more profiles to be incorrectly missing from NCA results, with a warning message "Dosing Type not Defined." This issue is resolved in Phoenix 8.3.4.

An issue where NCA would fail to execute and give a pop-up message "one or more errors" or unhandled error has been resolved (QC 18111).

An issue where Phoenix 8.3.x freezes has been resolved (QC 18119): In varying circumstances, freezes were reported to occur when using Phoenix 8.3, 8.3.1, 8.3.2, or 8.3.3. The problem was related to the Rich Text control being created in the non-GUI thread, which caused a deadlock.

Phoenix 8.3.3 Updates

Phoenix installer now supports SCCM (QC 18082): Phoenix 8.3.3 has been tested using Certara's internal SCCM system and several customers' SCCM system.

An issue where Phoenix would freeze up when idle and needed to be closed from the Task Manager has been fixed (QC 18081): There was a rare condition involving the memory manager tool that, in certain circumstances, caused Phoenix to freeze. This issue has been resolved in Phoenix 8.3.3.



Phoenix 8.3.2 Updates

Work flow execution speed no longer slower than 8.2 or 8.1 (QC 18054): In Phoenix 8.3, a change was made to update the icon of a workflow item when its parent was being executed; this change caused a slower execution speed while providing little information. The Phoenix 8.2 behavior has been restored.

The Certara Integral 1.1.1 Plugin no longer breaks ggquickeda (QC 18060): Installing the Certara Integral 1.1.1 Plugin for Phoenix laid down a new version of the DotNetBrowser control, as required by the Integral plugin. This version of the DotNetBrowser, however, was not compatible with the plugin used for ggquickeda. In Phoenix 8.3.2, the ggquickeda plugin has been updated to use the newer version of the DotNetBrowser control in order to fix this issue.

Issue with Validation Suite failing due to projects sometimes not loading has been fixed (QC 18061).

Objects can now be renamed after JMS execution (QC 18062): JMS (Job Management System) enables users to execute Phoenix jobs in the background of the local machine or remotely on another machine. A change was introduced in Phoenix 8.0 that prohibited renaming a project after it had been executed using JMS. In Phoenix 8.3.2, users are able to rename the project, restoring the behavior prior to Phoenix 8.0. Note that this change only impacts the ability to rename the project and not the execution or results of the project.

Phoenix 8.3.1 Updates

An issue reported for Phoenix 8.3, where running the Data Wizard's Filter function in a native Chinese environment generated errors, has been fixed in Phoenix 8.3.1 (QC 18043).

Phoenix 8.3

What's New

Data Tools and Plots Framework IVIVC NLME PML Reporter Tools



Data Tools and Plots

Charting

Add annotations to plots (QC 1648): Add one or more annotations to a plot using the Annotations tab. Drag and drop the annotation anywhere within the graph area.

New "Start axis at 0" option (QC 2974): A new Start axis at 0 option is now available on the Axis Options – Content tab. When checked, this option forces the axis numbering to start at zero, regardless of the data values. The option is available for a linearly scaled, continuous axis, with either auto-scale option selected.

Display individual data points on a Box plot (QC 11454): A Show All Data Points checkbox is now available in the Graph Content tab of a Box plot.

Control the appearance of error bars in XY Plots (QC 12844): The following options are now available on the Appearance tab for error bars:

Center Marker Size: Sets the size of the marker used to indicate the center point of the error bar

Cap Width: Changes the width of the top and bottom bars

Line Weight: Controls the thickness of the error bar lines.

Color	Black	Use Group Color
Center Marker Shape	None	~
Center Marker Size	5	* *
Cap Width	15	* *
Line Weight	1	•
	Increased CapWidth	
	Increased Line Width	T

Group names now appear as the X-axis label (QC 16303): As a result, the Include Column Names in Tick Labels when Grouping checkbox is no longer needed and has been removed.

"Collapse Sparse Latticing" option is now on by default for NLME plots "Ind DV, IPRED vs IVAR Lattice" and "Ind DV, IPRED vs TAD Lattice" in order to remove empty plots (QC 16377).

Modify the font of diagonal labels in a Scatter Plot Matrix (QC 17678): A Display Diagonal Labels checkbox is available in the Graphs Options – Appearance tab for Scatter Plot Matrices. Checking this box adds a **Change Font** button to the tab for adjusting the font properties of the diagonal labels.



"Bring to Front" option for regression lines is now functioning properly (QC 17938): In Phoenix 8.2, the regression line would not display in front of the points, even when the Bring to Front checkbox was turned on. This issue is fixed in Phoenix 8.3.

A blank cell in a data label column now results in a blank label for the associated observation (QC 17961): If a column mapped for use as the data labels has blank cells, the data label for the associated observation is also blank. Previously, Phoenix would substitute the y-value if the data label was blank.

Colors can now be set for "Each Group by Color" option (QC 17962): In Phoenix 8.3, changing the marker or line color of an individual member of a group applies the color change to all individual members of the same group when the **Each Group by Color** option is checked.

Data Wizard

F distribution function added in Data Wizard Transformations Custom Functions (QC 13434): The Finv custom function is now available in the Data Wizard and calculates the quantile of F-distribution, returning the absolute value in the output. The format is: Finv (p, df1, df2).

ggquic keda

Phoenix 8.3 now provides access to the open-source plotting tool ggquickeda (QC 17971): The new ggquickeda object (**New > External Software > ggquickeda**) provides access to the ggquickeda R shiny application, which is an interface to ggplot2/table1. The application enables quick exploration of data to detect trends on the fly. This tool creates scatter, dot, box, and bar plots, as well as histograms, densities, and summary statistics tables.

Framework

Menus

Insert menu redesigned (QC 17036): Phoenix 8.3 includes a reorganized operational object list on the **Insert** menu and right-click menu to facilitate locating a desired object. Below is a list of changes.

Phoenix 8.2	Phoenix 8.3
Data	Renamed Data Management
NCA and Toolbox	Removed and content split into two menus:
	NonCompartmental Analysis >
	Contains NCA, Nonparametric Superposition, and Semicompartmental Modeling
	Computational Tools >
	Contains Bioequivalence , Convolution , Crossover , Deconvolution , Descriptive Statistics , and Linear Mixed Effects
Phoenix Modeling	Renamed Modeling

Phoenix Model	Moved under Modeling > Renamed Maximum Likelihood Models
Phoenix Model Comparer	Moved under Modeling > Renamed Maximum Likelihood Model Comparer
WNL5 Classic Modeling	Moved under Modeling > Renamed Least-Squares Regression Models
WNL ASCII Model	Renamed User ASCII Model
Reporter	Moved under Reporting >
Table	Moved under Reporting >
NONMEM Shell, NONMEM Comparer, PsN Shell, R Script, SAS Shell, SigmaPlot Shell	Moved under External Software >

IVIVC

Data Labels are off by default in IVIVC Levy Plots (QC 18024).

NLME

View PRED values in tables and at any time point (QC 16879): To obtain population predicted values, type the following in the **Variables** field on the Run Options tab, Simple mode, Tables section:

Pred (name of observed variable)

Binning is now available in Predictive Check for X-variable data when Y is categorical or count (QC 17488).

Grouping dependent (Y) values is now possible for categorical or count observations in Predicted Check (QC 17554): Choose the Right boundaries option from the new Grouping Y values menu in the tabs corresponding to a categorical/count observed variable to specify how values are grouped. When this option is chosen, a **Boundaries** field is available for entering a list of Y values to define the right boundaries of grouping intervals.

Select categorical covariates for stratification for each dependent variable (QC 17559): Menus for selecting up to three categorical covariates for stratification of a specific dependent variable are available in the "Predictive Check Options" section in the Run Options tab.

Initial estimates graph is no longer blank for non-time-varying parameters (QC 17964): In Phoenix 8.3, the graph is a horizontal line for the value of the parameter/covariate vs. time for non-time-varying parameters/covariates.

Engines

New ODE solver for non-stiff cases (QC 15778): The Max ODE selection now includes the option **non-stiff DOPRI5**. The **non-stiff** option, available in prior versions, is now referred to as **non-stiff DVERK**. The new DOPRI5 option has the conventional RTOL – ATOL (relative



and absolute tolerances) inputs found in all of the other solvers except the DVERK solver, which, on the other hand, only has a single combined tolerance.

Steady state analysis capability is added for models involving the delayInfCpt statements (QC 17371).

New algorithm implemented for the gamma distributed delay function is able to handle more complex problems and with increased speed (QC 17372).

A new "Output PRED" checkbox is available when prediction correction is applied (QC 17474): When checked, the population prediction results are included in the PredCheckAll worksheet as a replicate "-1". When unchecked, the output worksheet starts with the results of replicate zero.

User Interface

New columns in Predictive Check output work sheets report bin boundaries (QC 16216): The new Bin_Min and Bin_Max columns provide the minimum and maximum bin boundaries, respectively. These new columns are now available in the PredCheck_BQLFraction, PredCheck_Cat_ObsQ, PredCheck_Cat_SimQ, PredCheck_ObsQ_SimQCI and PredCheck_SimQ worksheets.

Simulation mode now has additional table options (QC 17412): Additional table options are now available when setting up a simulation run. These new options are include:

Keep source structure to keep the number of rows appearing in the simulation table for each replicate to be the same as the number of rows in the input datasets.

When covr set to specify any covariates to include

When dose to specify a dose point to include (e.g., Aa or A1)

When observe to specify any observed variable to include (e.g., CObs or EObs)

Separate results work sheets and plots are now available for Predictive Check categorical/count data (QC 17524): Worksheets and plots that contain the categorical or count data results will have "Cat" or "Categorical" in the name. For example, Observations_Categorical, PredCheck_Cat_ObsQ, PredCheck_Cat_SimQ, and Pop PredCheckCat ObsQ_SimQ.

New BQL fraction work sheet and plot output when BQL Fraction mode is used (QC 17525): The PredCheck_BQLFraction worksheet reports the stratum-bins, minimum and maximum of the bin boundaries, IVAR values, observed and predicted fractions, observation name, and observed quantile levels. The "PredCheck BQLFraction" plot data comes from this worksheet.

Simulation Table option is available in Predictive Check mode (QC 17736).

For Bootstrap, the initial estimates run is no longer performed by default, but is available as a new option (QC 17665): To preserve any setup work done by the user, the default mode for Bootstrap no longer performs an initial estimates run. When Bootstrap is selected as the Run Mode, a new Estimate initial model parameters? checkbox becomes available to allow users to choose if they want to perform this initial estimates run.



PML

The delayInfCpt statement and delay function are extended to include Weibull and Inverse Gaussian distributions (QC 17355): Use the new dist option in the delayInfCpt statement or the delay function to specify the distribution of the delay time as either Gamma, Weibull, or InverseGaussian.

Reporter

Number of levels for caption numbering increased to permit multiple levels (QC 12750): Previously, the **Major Index** field only allowed entry of a single digit. Phoenix 8.3 allows entering multiple numbers, separated by periods, to increase the level of the headings shown in the report. For example, if the user enters "16.2" in the **Major Index** field, then the table and figure caption numbers will be 16.2.1, 16.2.2, 16.2.3, etc.

Reporter supports importing of Word template files loaded from PKS (QC 16222).

Date and time stamp available for tables and figures as a global footnote (QC 17941): Options for adding global footnotes for **Source**, **Object Name**, and **Date and Time** to Worksheets/Tables, Figures, and Text results in the report are on the Options tab. The **Date and Time** option adds the date and time of the object execution that generated the result to the footnote. For objects that are not the result of an execution, such as data in the Data folder, the "last saved" date and time of the worksheet (such as what is shown on the Information tab) is included in the footnote. (Note that the **Source** and **Object Name** checkboxes located in the Footer settings dialogs for Tables, Figures, and Text objects have been removed since they are now available in the Options tab.)

New "Disable all automatic numbering of Tables, Figures, and Listings" checkbox on the Options tab allows turning on/off automatic numbering with a single click (QC 17942).

Control the number of lattice rows on a page (QC 17943): A new **Rows per page** option for controlling the number of rows on a page for a lattice of figures is available in the Figure tab of the options dialog. Select the number of desired rows to display on the page or select **To fit** to display as many rows as possible on the page (this is the Phoenix 8.2 behavior).

Subscripts, superscripts, and symbols such as "<" are now retained in the report (QC 17944, QC 17945).

Contextual footnotes list has a new Match column indicating the search type to perform when looking for the abbreviation: Entire or Partial (QC 17954).

Tools

NCA

Log trapezoidal methods calculating the AUC are now available for selection in Sparse Sampling (QC 17931): Previously, only the two linear methods of computing the AUC were available for selection with the Sparse Sampling option. The log methods were excluded because SE for AUC computations depend on AUC being a linear combination of the mean concentrations. In Phoenix 8.3, the two log methods are available for selection to allow users



to get all the parameters for the mean concentration curve. However, selecting either log method does not output the SE_AUClast and SE_AUCall parameters, but does output SE_Cmax.

Tables

Editing option for titles, column headers, table body, statistics, and footers is available, in addition to adding and removing (QC 11607).

Issues Corrected

Data Tools and Plots External Software Framework IVIVC NLME Reporter Tools Validation Suite

Data Tools and Plots

Charting

An issue involving an unhandled exception occurring when trying to edit the legend of a plot involving group variables is fixed in Phoenix 8.3 (QC 17804).

An issue where attributes (graph names, marker/line styles and colors) of two graphs switched in a copy of the plot or when using object settings is fixed (QC 17829).

In an XY Plot with zero or negative values and a y-axis that is log-scaled, only the upper error bars are shown now so that the lower error bars are not clipped at the x-axis (QC 17833/CRM 169645): This issue was actually fixed in Phoenix 8.2, however it inadvertently remained listed in the release notes as a Known Issue.

An issue where a custom ordering of columns for a box plot was ignored is resolved in Phoenix 8.3 (QC 17939).

Regression lines are drawn on the correct plot when "Collapsed Chart Latticing" option is used (QC 17957): In Phoenix 8.2, when the **Collapsed Chart Latticing** option was on, the program did not take into account the removal of empty plots. As a result, the regression line calculated for one plot could appear on a different plot or be missing because an empty plot was at that position originally. This issue is resolved in Phoenix 8.3.

An issue involving a missing overlaid plot title in the Table layout options is resolved (QC 17969).



Column Transformation

Custom column transformation Adjacent option now functions as expected (QC 11728): For custom transformations, the **Adjacent** option placed the new column at the end of the worksheet. This issue is fixed in Phoenix 8.3.

When a DF value for the Column Transformation tinv is negative or zero, the output is now null (QC 13876): Previously, when an invalid DF (i.e., a negative or zero DF) was entered for the custom function tinv (t-inverse), the output was incorrectly reported as one.

Data Wizard

A reported issue where unexpected spaces in Custom Transformation formulas caused the mapping panel to display improperly is obsolete (QC 14167): Spaces are still not permitted between the function name and the left parenthesis, but there is a clear error message displayed.

An unhandled exception when using the Data Wizard to create an empty column with no column header and then selecting it is fixed in Phoenix 8.3 (QC 17922).

Descriptive Stats

A reported issue where the statistic name change from "CV% Geometric Mean" to "Geometric CV%" caused back ward compatibility to not be maintained and the column became unmapped in referencing objects is obsolete (QC 17436): This issue applies to versions of Phoenix that are no longer supported.

External Software

SAS

Reordering of columns no longer causes mismatch of data upon export (QC 17921): This issue occurred when the dataset being exported using SAS had originated from the Data Wizard and had Sort Keys. When SAS column reorder settings were then applied, the exported results would contain mismatched data. In Phoenix 8.3, the original order of a dataset will be overridden by any SAS column reorder settings.

Framework

Data

After pasting data into a Phoenix work sheet (or deleting rows), the focus remains at the end of the pasted data (QC 16340/CRM 159195): Previously, the focus jumped to the top of the worksheet and the user would then have to scroll down to the bottom to paste more data.

File I/O - Excel

Data imported from Excel work books is now imported/displayed correctly (QC 17970): An issue was reported where Excel sheets (.xls, .xlsx) having columns with both text and numeric data were not imported correctly as a Phoenix worksheet. This was due to the program not looking at enough rows in Excel files to determine the column type. Phoenix 8.3 now uses the first 100 rows of an Excel file to determine the column type.



Object Browser

Upstream Data Wizards can no longer be deleted while executing Phoenix (QC 17819).

Plugins

Error when adding a default save option in PKS preferences is fixed (QC 17914): This issue was caused by the presence of duplicate Plotting objects and Next Generation Plot objects in Phoenix 8.2. With the removal of the Next Generation Plot objects in Phoenix 8.3, the error no longer occurs.

Printing

An issue where a wide Table becomes truncated is due to an IE print limitation (QC 5432): Printing tables comprised of wide data directly from Phoenix can result in truncated tables in the printed output. This is an Internet Explorer print limitation, not a defect within Phoenix, so this issue has been closed as "Not a bug." Users can copy the table from the Results tab to the Tables folder and use **Edit in Excel** to format the table as desired.

R

An issue where data source inputs remained when data source inputs were published using decorated attach statements that were later removed is not reproducible (QC 11839): This issue was reported as a Known Issue in Phoenix 8.2, but could not be reproduced in Phoenix 8.3 and has been closed.

IVIVC

Correct version of IVIVC is reported in the Core Output in Phoenix 8.3 (QC 18007): In Phoenix 8.1 and 8.2, the IVIVC Core Output reported the version as "IVIVC Toolkit 8.0".

Convolution

Convolution now generates results even if the source data set includes blank or text values (QC 10523): Previously, Convolution would not generate results for profiles that had any non-numeric Cumulative_Input values. This issue is resolved in Phoenix 8.3.

Convolution no longer fails execution when Time column is declared as type Text (QC 17732): The input data column mapped as Time is now sorted numerically, even if the type is set as Text.

Deconvolution

In Deconvolution, Cumulative Rates Plot is renamed to Cumulative Input Plot (QC 2441): When using an existing project from Phoenix 8.2 or earlier, select **Reset Existing Plots** on the Plots tab for plot names to update on re-execution in Phoenix 8.3.

Levy Plot

Levy Plot – The IVIVC output sometimes appeared out-of-date after executing (QC 11609): This issue is not reproducible in Phoenix 8.3 and has been closed.



Phoenix 8.3

Wagner-Nelson & Loo-Riegelman

Settings are now included in Settings text output and in History (QC 10348).

Workflow

Prediction and Validation Errors now match the Reference output (QC 14353): If columns mapped to IVIVC time mappings (i.e., InVitro Time, InVivo Independent, and Prediction Time) had type Text, these columns were being sorted as text rather than numerically when performing Validation and Prediction, which then caused errors in the internal interpolation routine. Input data columns mapped to IVIVC time mappings are now sorted numerically, even if the type is set as Text.

IVIVC Correlation and Pred Corr Sim Observed Y and Predicted Y vs X plots now have the correct Y-axis label of Fabs (QC 17826/CRM 00169719): An issue was reported where the Y-axis was labeled Cp when the buttons on the Options tabs of the IVIVC Workflow (**Build Correlation, Validate Correlation**, and **Predict PK**) were used, but was correctly labeled Fabs when the **Execute** icon in the Phoenix toolbar was used. In Phoenix 8.3, the Y axis is labeled "Fabs" for **Build Correlation** and **Predict PK**, regardless of the method of execution. The issue remains for **Validate Correlation**, however, and is included in the list of Known Issues.

NLME

If a dose and a categorical observation of zero appear together on the same line in the input dataset, then the observation is treated as real data and is not ignored (unless there is an explicit MDV entry of one on the line, in which case the observation is always ignored) (QC 17717): Previously, in such case, the observation was ignored unless there was an explicit MDV entry of zero on the line.

NLME temp file location can now be specified to avoid Anti-Virus applications problems (**QC 17818**): An issue was reported that the default temporary file location for NLME runs caused problems with Anti-Virus applications and the location could not be changed by the user. In Phoenix 8.3, the *Preferences* dialog includes an NLME page in which the user can set the temporary file location.

Multicore Bootstrap – Core Output tab information now contains information for all replicates (QC 17926): Previously, the multicore mode only output the results obtained for the last bootstrapping sample with "No output found" appearing at the very beginning. In Phoenix 8.3, results for all the bootstrapping samples are reported, which is consistent with the output when using local, and local MPI modes.

NLME no longer freezes on the grid with bootstrap run mode (QC 17983).

Engines

An issue where different -2LL values for the QRPEM engine were being reported in the Job Viewer and in the Overall results work sheet has been fixed (QC 17968): With some models, the Overall results worksheet would have an incorrect value for -2LL when the optimization was performed using the QRPEM engine. However, the Job Viewer would display the correct value. In Phoenix 8.3, the correct value is now reported in both locations.

Intermediate file no longer remains locked during Stepwise covariate search + MPI for the QRPEM engine (QC 17987): In a Covariate Search run, if the QRPEM engine is used, some temporary files could remain locked after the previous run completed and not be deleted. The issue was observed for MPI runs on Windows only. It is fixed in Phoenix 8.3.

Grid Computing

NLME license no longer fails on grid (QC 17982): When a job was sent from a Windows client to a remote host, NLME could not generate the model and start due to time out of sync. This issue is fixed in Phoenix 8.3.

User Interface

The maximum number of Sort and ID columns, which is five, is now checked in the user interface, thereby preventing missing columns in the output (QC 7905).

If SS or ADDL input is specified, and if input column names are given, verification now checks if the column names match those in the input data set (QC 8805): If column names do not match, verification now fails. Previously, there was no warning, resulting in potentially undefined behavior as NA values are used.

An issue where opening a Phoenix 8.1 model simulation project with zeroed random effects in Phoenix 8.2 led to an unusable NLME object has been resolved (QC 17948): In Phoenix 8.1 and earlier, zeroed random effects were treated as "1" in built-in and graphical mode. In Phoenix 8.2, this behavior was changed such that a diagonal random effect found to be "0" was excluded from any estimation/simulation (zero rule). A case was reported where a user zeroed the random effects and then excluded them by freezing the fixed effects (which is an unusual method). Since the random effects are excluded when fixed effects are frozen in built-in mode but the random effects are still present inside the structure, NLME would try to exclude them again according to the zero rule, causing an unusable NLME object. This issue has been resolved such that an NLME object with zeroed random effects that are excluded with frozen thetas works without error.

Column existence is now checked in the Dosing work sheet as well as in the Main work sheet when a column is selected in ADDL input options (QC 17949): In Phoenix 8.2, when an amount column was specified, only the main worksheet was being checked for the existence of that column. In Phoenix 8.3, both worksheets are checked to determine if the column exists.

Reporter

Subject tags in captions are now working correctly for NCA Plots (QC 17946): In Phoenix 8.2, the #formulation# and #subject# tags did not appear separately for each subject and formulation, as they had in the prior release. Instead, all subjects were listed in the caption. In Phoenix 8.3, only the subject that corresponds to a particular page in the plot is shown in the caption on that page.

An issue where not all of the partial-match footnotes were being added to the table is fixed in Phoenix 8.3 (QC 17953).



Phoenix 8.3

Tools

Bioequivalence

Table or other object using Bioequivalence output as the source is now updated correctly when the Bioequivalence object is re-executed (QC 7724): Previously, re-executing a Bioequivalence object created new instances of the Ratio output worksheets, rather than simply updating the existing instances. In Phoenix 8.3, re-execution of the Bioequivalence object updates the existing worksheets.

In a Bioequivalence Object, copy/paste, move-to-new-workflow, or use a template, and then map source will reset the Fixed model to the default (QC 9641): In earlier releases, mapping a new input dataset to a Bioequivalence object, a copy of a Bioequivalence object, or a Bioequivalence object loaded from a template, would cause the model specification to be reset to the default model, even if the mapped columns were identical for the new data. Any model specifications made by the user to the default model were lost. In Phoenix 8.3, if the mappings are identical for the new mapped dataset, then the model is not updated. If the user makes any mapping changes other than mapping an additional dependent variable, or if automatic mappings occur due to different column names in the dataset matching the mapping contexts, then the model is rebuilt to the default model since the existing model will not be valid anymore. (TIP: Note that therefore the user can reset to the default model at any time by unmapping and remapping a column.)

BQL

The "Carry over concentration column" checkbox is now checked by default (QC 7624).

NCA

Performance issues when navigating between profiles in the Slopes tab are resolved (QC 17438/CRM 00164916, 00168442).

NCA object settings created in Phoenix 8.1 or older versions are fully supported in 8.3 (QC 17933): In Phoenix 8.2, when setting up the dosing for NCA using an internal worksheet, if object settings created in Phoenix 8.1 or older were applied or if a default object settings file was in use, the error "Unable to construct internal source" was displayed. This issue is fixed in Phoenix 8.3.

An issue where the format of the Final Parameters work sheet could not be changed is resolved (QC 17975).

Correct Tau value is used in NCA user-defined parameter calculation (QC 17985): In Phoenix 8.0 or later, a user-defined parameter can be defined in NCA and dosing variables such as Dose or Tau can be used in its expression. Due to incorrect merging of the worksheets, the wrong value for Tau was used in the calculation. The merging issue is fixed in Phoenix 8.3 and the correct Tau value is now used in NCA user-defined parameter calculations.

Tables

An issue with empty cells not being handled properly in French Operating Systems is resolved (QC 17464): On English Operating Systems, Phoenix automatically replaces 'NaN'



(Not a Number) with a blank cell. This was not happening for other languages, which led to an inability to identify and remove empty cells. Phoenix 8.3 properly handles empty cells in all supported languages.

Validation Suite

Phoenix Model validation tests no longer fail when Phoenix is installed on a volume with 8dot3 policy disabled (QC 17958).