# Benefits of Upgrading to Phoenix™ WinNonlin® 6.1

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## Contents

## Introduction

Phoenix is Pharsight's® new desktop software platform that provides a cohesive environment for data analysis, modeling, and simulation enabling improved drug development.

Phoenix™ WinNonlin® 6.1 is the next generation of the industry standard for PK and PD modeling and noncompartmental and compartmental analysis.

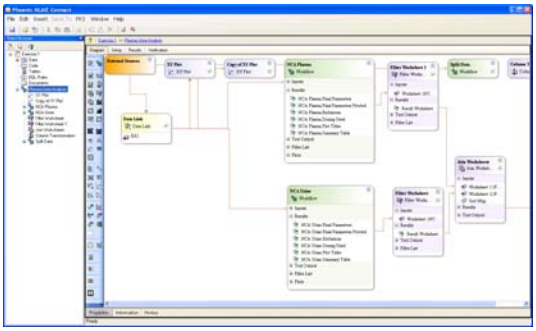
Phoenix WinNonlin 6.1 improves the scientific productivity of critical drug development tasks by providing a comprehensive analysis environment that implements efficient, reusable, and compliant workflows and powerful native graphics to reduce barriers to learning and collaboration and enable more impactful quantitative decision making.

Phoenix WinNonlin 6.1 is implemented as a set of tools within the Phoenix platform. This new platform takes advantage of state of the art graphics and interaction capabilities. Phoenix WinNonlin provides the same capabilities as previous versions of WinNonlin in addition to some new enhancements to improve ease of use, flexibility, and repeatability of processes. In the future, users will be able to leverage and extend the Phoenix platform by adding applications that perform analyses for population PK/PD modeling as well as vitro/in vivo correlation, safety analysis, and trial simulation.

This paper summarizes the benefits of upgrading to Phoenix WinNonlin 6.1 for current WinNonlin users with previous versions (version 5.x or earlier).

## Workflows: Your Key to Better Organization and Reusability of Analyses

In PK/PD work and most often in non-compartmental analysis, the steps to prepare, analyze, and report on drug study data are often similar. The analysis workflow followed for one study is often applicable to other studies with similar designs. Homogeneity of drug study data input formats and structures (such as using CDISC conventions) has further facilitated standardization of analyses.



Phoenix WinNonlin 6.1 implements the concept of *workflows* as a powerful software feature enabling you to easily organize and display various study components and their relationships (inputs, analyses, outputs, etc.), as well as copy and reuse workflows as templates in order to automate routine analyses. Workflows are a new concept in Phoenix WinNonlin 6.1, where your data manipulation and analysis steps are recorded graphically (in a menu listing and as a diagram).

Workflows make it possible to see a complex analysis you have performed in a map-like view. You can copy parts of a workflow and reuse them with new data. You can find a mistake and fix it, then refresh the workflow. You can find an output worksheet or chart by looking for the operation that generated it. No more shuffling through a long list of windows. Your Quality Assurance team members can see your workflow and settings to easily double-check your output.

Phoenix enables you to turn workflows that you plan to reuse into *templates*. Perform an analysis, save it as a template, and reuse the template again and again with different data. Templates can be complete workflows, partial workflows, or just individual operational objects. All templates are reusable. They can be rerun with a single click for datasets that contain the same structure (e.g., same study design), or with a quick remapping of the data for datasets with different fields and naming conventions. Where WinNonlin 5 provided wizards, Phoenix WinNonlin 6 now allows you to create and share your own wizards in the form of templates. Pharsight will provide templates to handle the most common workflows users typically use. These templates can be used as a starting point and edited to fit the specific needs of each organization.

The integrated, visual environment of Phoenix WinNonlin 6.1 shortens the learning curve. As Pharsight adds more applications to the Phoenix platform in the future, Phoenix WinNonlin users will easily be able to transition from performing NCA and fixed effects modeling to undertaking more complex and impactful modeling tasks. This will open up the benefits of modeling and make it accessible to more staff.

## Data Visualization (Graphics)

Graphics in WinNonlin 5 have been completely redesigned for Phoenix WinNonlin 6.1. The new data visualization tools in Phoenix WinNonlin 6.1 provide advanced, feature rich, visually appealing, and high quality graphics. The changes are too long to enumerate here but many of the enhancements that WinNonlin users have requested in the past are now available. Some of these new features include:

- Latticing (trellis) plots,
- Plot overlays,
- Double y-axis feature,
- Editable legends,
- Regression and reference lines,
- Intuitive format changes,
- Support for symbols and subscripts in text titles, and
- Easy export of plots of high quality to multiple file formats.

Several additional graph types are also available such as:

- Box and Whisker,
- Quantile-Quantile,
- Histogram,
- Bar and column plots.

Graphics are also one of the many components of workflows and can, therefore, enable you to reuse your favorite plots with new datasets.

## Data Management

Preparation of data for analysis can be time-consuming and resource-intensive. Phoenix WinNonlin 6.1 has addressed some common PK/PD data management steps by providing new tools. First, Phoenix WinNonlin offers improved flexibility for importing data (i.e., selecting columns of headers and units in preview panels), and for editing imported data using Excel directly from within the Phoenix user interface. Second, several data transformations have been added to Phoenix WinNonlin 6.1. These include new features to:

- Split worksheets into multiple worksheets based on sort criteria (e.g. Matrix, Treatment),
- Pivot worksheets,
- Stack data in one step,
- Build several functions based on worksheet column names and to calculate "Relative Time" based on a first dose by profile.

The data management functions found in previous versions of WinNonlin are still available. All data management steps are part of Phoenix workflows and can be easily visualized and reused.

## Non-Compartmental and Compartmental Modeling

The capabilities of WinNonlin's Non-Compartmental model engine (NCA) have been notably enhanced in Phoenix WinNonlin 6.1. NCA now allows simultaneous execution of multiple models. Data from several routes or days no longer require separate models. Using the workflow engine, many models of all types (different engines) can also be executed in one single click – the data, models, and results contained in within a single Phoenix Project File.

Additionally, NCA has been enhanced to allow previewing Lambda_z ranges selected by the default WinNonlin algorithm (i.e., best fit). This default algorithm no longer allows $C_{max}$ to be included in the apparent terminal slope. Additional output is provided which lists excluded time points from Lambda_z ranges. Partial areas can be labeled according to user preferences. For example, partial areas done on actual times can be grouped under AUC_24 representing a nominal time.

Compartmental model output from classical WinNonlin 5 engines have been modified to include units for initial estimates and dosing. In addition, the unbounded condition number is also included in result worksheets rather than just in plain text.

Phoenix WinNonlin 6.1 provides a new Maximum Likelihood Estimation (MLE) engine that can be applied to individual or naïve, pooled analysis, easing the transition to population modeling. This engine, as well as others, is accessible from a new interface,

where the user can select library models or build models graphically with a patented Drug Model Editor (DME) interface. The DME makes model building easy to use and more powerful. This new engine can be applied to individuals or to a population, making the transition to population modeling easier when Pharsight releases future population modeling tools.

Finally, comparisons of results from several model executions are more readily available in Phoenix WinNonlin 6.1, since the model runs are all contained within the same project. A single project (i.e., one file) has all the information (input, models, settings, results, etc.) necessary to understand the complete analysis performed and can be shared for easy collaboration.

## Toolbox

All previous WinNonlin Toolbox objects are present in Phoenix WinNonlin 6.1. Some minor maintenance upgrades have been implemented as needed. The most noteworthy is for the toolbox option of nonparametric superposition. Nonparametric superposition now has the ability to enter original dose administered and simulate a different dose without having to modify the data *a priori*.

## Tables

WinNonlin tables have always provided a quick and easy way to tabulate data. In previous versions there were nine available templates for tables. In Phoenix WinNonlin 6.1 the table templates have been expanded to include an additional 'Default' template that allows the user flexibly to design different tabulations of data. The new table module also has the ability to create static table templates that can be customized for specific output and reused.

Both WinNonlin versions 5.x and 6.1 allow for the creation of tables that are not editable – a feature that allows them to be refreshed if the source changes. However, Phoenix WinNonlin 6.1 adds the capability to make a copy of the table output, which allows tables to be edited in Excel and still remain part of the project.

## Plug-Ins and Performance

The Phoenix platform approach to application development allows users of Phoenix WinNonlin 6.1 to reap the benefits of adding future applications, toolkits, and plugins to their repertoire of tools without learning a whole new interface or supporting separate non-interoperable systems. Phoenix's plug-in approach to software architecture enables seamless integration of additional tools. The Enterprise edition of Phoenix WinNonlin comes with plugins that work with industry standard 3rd party tools including S-PLUS®, SigmaPlot®, SAS® and NONMEM® 6.

## Compatibility

New installations of Phoenix WinNonlin 6.1 on computers that currently have node licenses of WinNonlin 5.x installed will be able to use *both* software packages on the same computer but not at the same time (concurrently). On networks where WinNonlin 5.x uses floating licenses, both software packages can be used simultaneously as long as two licenses are available from the floating license server because each application will tie up one license each.

Phoenix WinNonlin 6.1 has limited backward compatibility with files from earlier versions of WinNonlin. Data and models may be accessed but not outputs. However, once loaded into Phoenix WinNonlin 6.1, these models may be re-run to obtain outputs.

## Summary

The benefits of upgrading to Phoenix WinNonlin 6.1 are substantial. Comprehensive analyses, reusable workflows, more powerful graphics, better data management tools, improvements in the analysis engines, and the tools for building a compliant PK/PD environment will improve the efficiency and productivity of any DMPK or clinical pharmacology organization.

Organizations that own previous versions of WinNonlin and are currently covered under a maintenance and support agreement will be able to upgrade to Phoenix WinNonlin 6.1 at no additional charge.

Phoenix WinNonlin will create new opportunities for existing NCA modelers to easily expand their modeling skills to include population PK modeling, *in vitro / in vivo* correlation, and/or trial simulation with the addition of future applications currently being designed and developed by Pharsight.

For more information, go to www.pharsight.com or contact sales via email at Sales@Pharsight.com; or via phone in the U.S at +1 919-852-4685; in the E.U. or India at +49 89 451 03036; or in Japan at +81 471-74-9918.