

Phoenix WinNonlin

The Gold-Standard in Pharmacokinetic, Pharmacodynamic and Non-compartmental Analysis

Phoenix® WinNonlin® is the industry standard for the analysis of pharmacokinetic and pharmacodynamics data. The integrated tools for data processing, non-compartmental analysis (NCA), PK/PD modeling, post-analysis statistics, table creation, and graphics create an all-in-one collaboration workbench for analysts, reviewers, medical writers, and quality assurance team members. The intuitive graphical user interface allows users to spend less time learning the software and managing data and more time to model, interpret, and understand the data. The result? Efficient drug development decisions with more confidence.

Proven Software with a Vast Global Footprint

Phoenix WinNonlin has a proven 30-year history of providing trusted PK/PD analysis results. It is used by over 6,000 scientists in 60 countries at nearly 2,000 institutions, including the top 50 global pharmaceutical companies. Regulatory agencies, including 11 divisions of the US Food and Drug Administration (FDA), Japan Pharmaceutical and Medical Device Agency (PMDA), China Food and Drug Administration (CFDA), and the UK Medicines and Healthcare Products Regulatory Agency (MHRA), use Phoenix WinNonlin for analysis and to evaluate drug submissions.

The WinNonlin NCA Engine Can Do It All

The Most Comprehensive Set of Analysis Tools for any Non-clinical or Clinical PK/PD Study

From early non-clinical research to large clinical trials, the NCA engine, individual PK/PD modeling engine, and statistical analysis tools can be used for a wide-range of studies and analyses:

- Single, multiple or steady-state dosing
- Sparse sampling studies
- Drug concentration data in plasma or urine, or pharmacodynamics data
- Formulation comparison
- Toxicokinetics
- First-in-human
- Single and multiple ascending dose
- Drug-drug interaction
- Bioequivalence
- Mass balance

New in Phoenix WinNonlin

- New Ratios and Differences tool provides automated calculation of NCA ratios
- Additional descriptive statistics
- More flexible charting and plotting capabilities
- Additional new NCA parameters for plasma and urine
- User-defined NCA parameters
- Setting of criteria for the terminal slope calculation in NCA
- Enhanced fully-integrated Phoenix WinNonlin Validation Suite for fast automated software validation in under 30 minutes

Workflows are the key to consistency across an organization:

- Increase productivity by reusing workflows across multiple projects and analyses
- Output with the click of a button—data processing/formatting, analysis, figure, plots, and tables
- Drag and drop new data into an existing workflow to generate updated results effortlessly
- Eliminate time-consuming analyst work or the need for a separate data programmer

Statistical Tools Help Answer Critical Questions

Did the new formulation meet bioequivalence criteria? Is the exposure dose proportional? Did the drug cause an increase in a biomarker? Use statistical tools in WinNonlin to integrate and report inferential analysis of study results. New descriptive statistics have been added, including 2.5% and 97.5% percentiles, user-specified percentiles, sample and population statistics for skewness and kurtosis, and range, min and max when weighting is used.



Bioequivalence



Superposition



Analysis of variance/General linear models



Semi-compartment modeling



Deconvolution



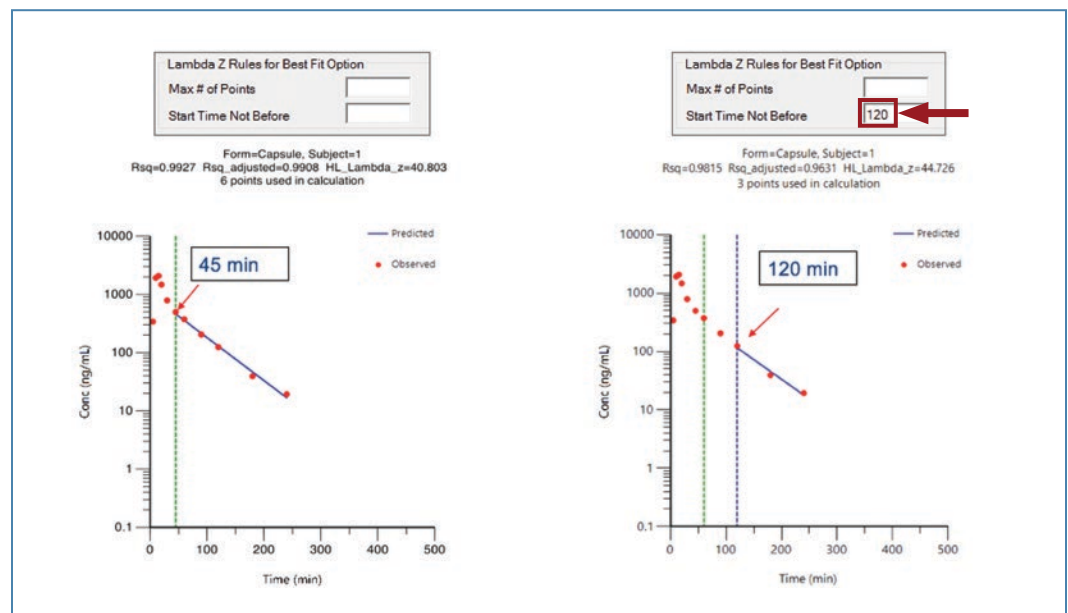
Descriptive statistics

Phoenix WinNonlin takes non-compartmental analysis (NCA) to a new level by adding many commonly calculated NCA parameters to the standard output, providing the ability to define custom NCA parameters, business rules for calculating the terminal slope, and acceptance flags based on terminal slope quality assessments. These new features minimize post-processing work and increase transparency with analysis.

Business Rules for Terminal Slope Calculation

Organizations can set strict criteria for the calculation of the terminal slope in NCA. Those rules can be implemented directly in Phoenix's updated NCA tool. Users can specify the maximum number of points to be included in the regression or the earliest time to be used (see figure below). The settings are retained and can be reviewed for compliance with organization policies and procedures.

Example of Lambda Z Rules for Best Fit Option: Before and After Setting "Start Time Not Before"



In addition, users can define acceptance criteria for adjusted r^2 , % extrapolated AUC, or Span (lambda z sampling interval/ $t_{1/2}$). All calculated values will be marked as meeting the criteria, not meeting the criteria, or missing. This permits easy post-processing of results based on quality standards for lambda z.

New Parameters for Non-compartmental Analysis

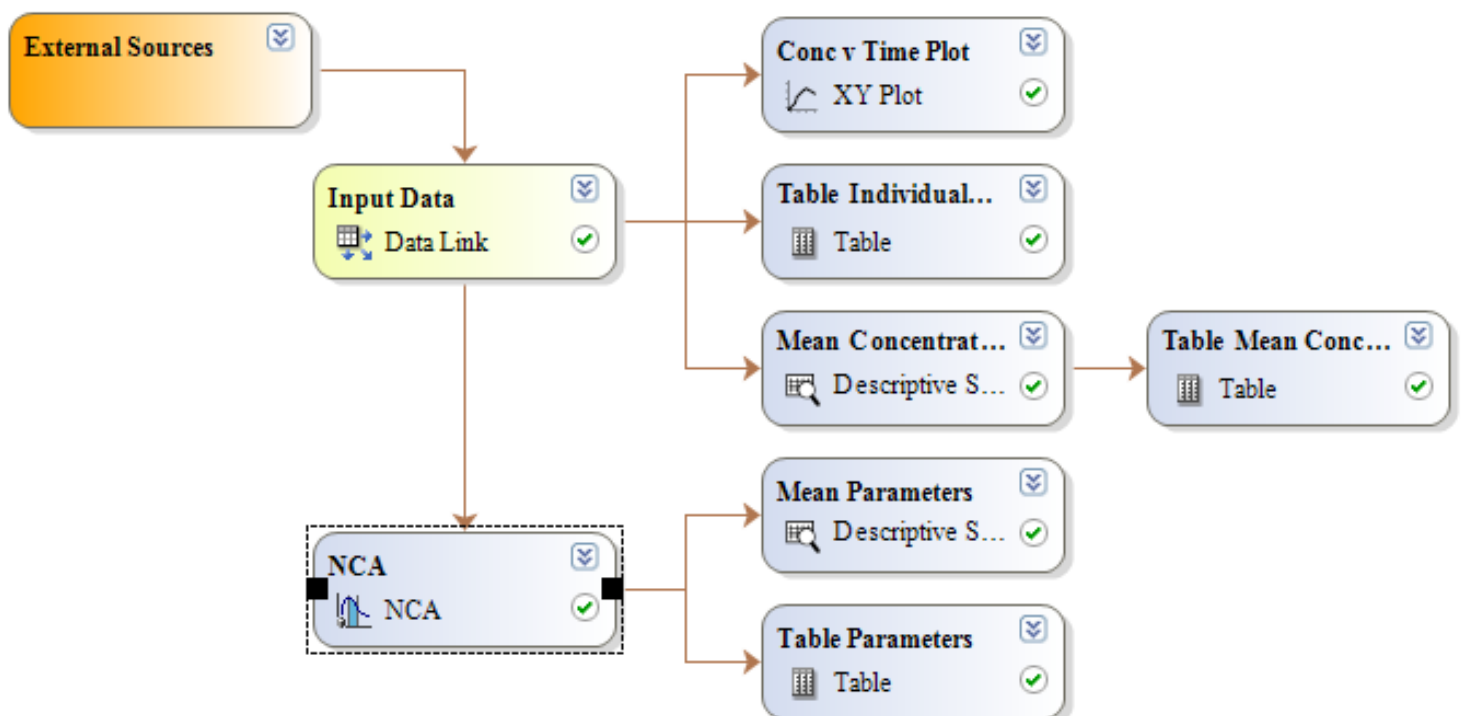
The automated calculation of over a dozen of parameters for plasma and urine will save time by reducing manual work and reduce errors with non-compartmental analysis in Phoenix WinNonlin.

- Plasma parameters
 - Swing (single dose and steady-state)
 - %Fluctuation (single dose and steady)
 - C_{last} (predicted)
 - C_{tau} (observed and predicted)
 - Span
 - $AUC_{last}/Dose$
 - $AUC_{Tau}/Dose$
 - $AUC_{Tau} \%Extrap$
 - $\lambda_{z_intercept}$
 - $N_{samples}$
 - Dose
- Urine parameters
 - $Rate_{last}$ (predicted)
 - $AURC_{last}/Dose$
 - $N_{samples}$
 - Dose
- User-defined parameters
 - Computed concentrations at any time point (uses AUC calculation interpolation)
 - Arithmetic combinations of any NCA parameter (eg, partial AUC/Dose)

An Intuitive Graphical User Interface

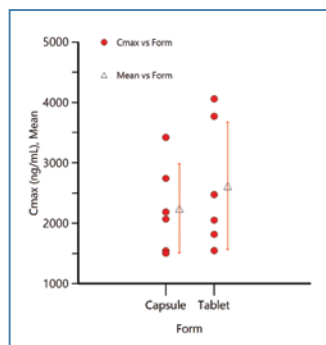
Phoenix WinNonlin was designed to help users efficiently move from data to reporting results using a graphical workflow designed to visualize data flow and analysis pathways. Each workflow contains separate objects for each action—eg, data processing, NCA, PK/PD models, table creation, figures and plot creation, and reporting—which are linked together within an intuitive graphical user interface. Locking the workflow provides consistent results and eliminates QC checks for approved workflows. Traceable workflows increase productivity by nearly 2-fold.

Workflows enable users to spend less time preparing and manipulating data and results. Scientific and QA reviewers can use tools for rapid error identification to reduce review time.

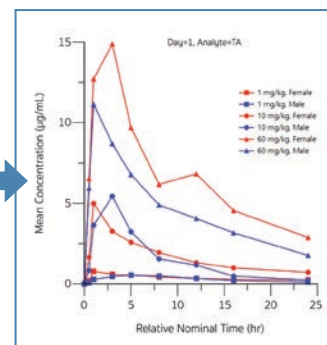
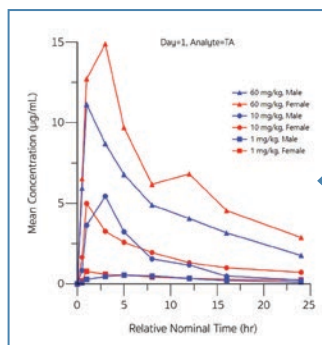


Powerful Integrated Graphics Engine and Table Generator

The integrated graphics engine in Phoenix WinNonlin automatically creates publication-quality plots and figures and well-organized tables to help create standardized PK/PD reports more efficiently. More flexible charting and plotting tools have been added, including ordering the presentation of categorical axes, allowing for offsets, changing font style and size, customizable legend placement, and more. High native resolution plots and figures can be easily customized to meet user specifications without the need for third party software packages. Do you have standard plots and figures in your organization? Custom plot templates can be shared by everyone and loaded with one command.



X-Categorical Plot with Error Bars and Offsets



Group Label Order Change

Tools for Data Processing and Preparation

Analysis dataset preparation is a breeze with Phoenix WinNonlin's data processing tools. The Phoenix workflow traces data from the moment it is imported through the final analysis, preventing data loss and costly re-analysis.

Integrated data processing functions—sorting, splitting, filtering, transforming, merging, appending, stacking, pivoting, joining, and more—provide full visibility into the incoming data and the results of each data set.



CDISC Data Preparer



Merge Worksheets



Append Worksheets



Pivot Worksheet



BQL



Rank Worksheet



Crossproduct Worksheets



Ratios and Differences



Data Wizard



Split Worksheet



Enumerate Worksheets



Stacker

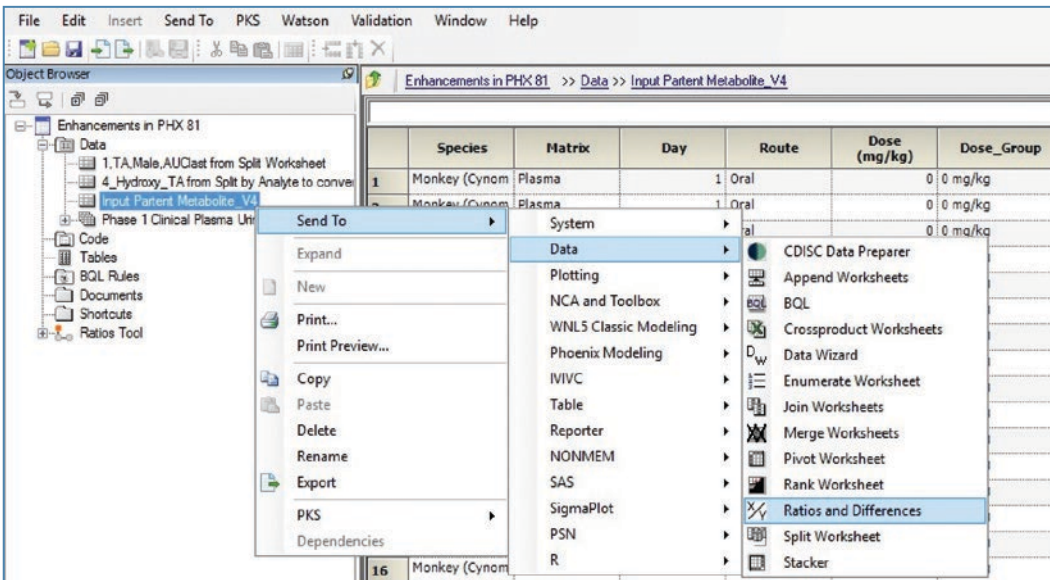


Join Worksheets

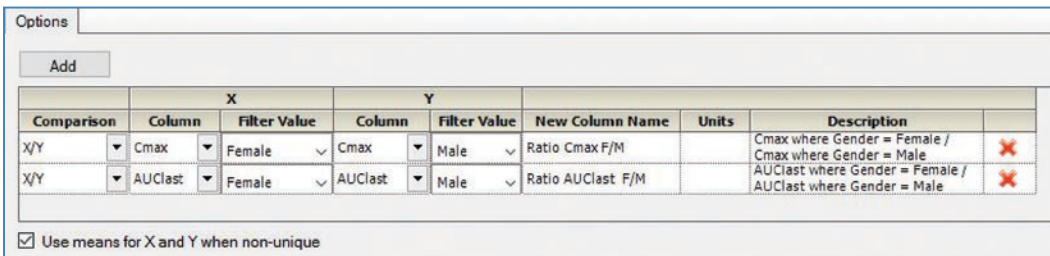
Ratios and Differences Tool

The new Ratios and Differences tool automatically calculates NCA ratios, including renal clearance, accumulation ratio, linearity index, parent to metabolite exposure ratios, and more.

Step 1. Select Data



Step 2. Map Data and Add Options



Step 3. Obtain Results

The 'Results' tab displays a table with the following columns: Day, Dose_Group, Analyte, Gender, Cmax (ug/mL), AUClast (hr*ug/mL), Ratio_Cmax_F_M, Ratio_AUClast_F_M, and Treatment. The table contains 24 rows of data, showing results for various days and doses of 4-Hydroxy-TA in both Female and Male subjects.

Day	Dose_Group	Analyte	Gender	Cmax (ug/mL)	AUClast (hr*ug/mL)	Ratio_Cmax_F_M	Ratio_AUClast_F_M	Treatment
1	1 mg/kg	4-Hydroxy-TA	Female	0.2090437	2.936282	1.8510752	1.6672423	TA
2	1 mg/kg	4-Hydroxy-TA	Male	0.11291511	1.7415755			TA
3	1 mg/kg	TA	Female	0.83465291	9.1618096	1.4765833	1.2342322	TA
4	1 mg/kg	TA	Male	0.56525962	7.4230843			TA
5	10 mg/kg	4-Hydroxy-TA	Female	1.0624565	11.838327	4.6513039	5.0796955	TA
6	10 mg/kg	4-Hydroxy-TA	Male	0.22842122	2.3305191			TA
7	10 mg/kg	TA	Female	5.308485	40.996543	0.9762894	1.0825018	TA
8	10 mg/kg	TA	Male	5.4374063	37.872032			TA
9	60 mg/kg	4-Hydroxy-TA	Female	10.120435	112.16525	6.439756	10.292551	TA
10	60 mg/kg	4-Hydroxy-TA	Male	1.1991384	10.897711			TA
11	60 mg/kg	TA	Female	17.07328	166.89073	1.534125	1.4538612	TA
12	60 mg/kg	TA	Male	11.129002	110.66443			TA
13	14 mg/kg	4-Hydroxy-TA	Female	0.36507452	2.7889805	0.82251062	0.76783037	TA
14	14 mg/kg	4-Hydroxy-TA	Male	0.44385387	3.6322873			TA
15	14 mg/kg	TA	Female	3.2763012	35.291575	1.325344	1.8659947	TA
16	14 mg/kg	TA	Male	2.4720383	18.91301			TA
17	10 mg/kg	4-Hydroxy-TA	Female	4.7414357	25.242751	1.696608	1.5241737	TA
18	10 mg/kg	4-Hydroxy-TA	Male	2.7897231	19.185971			TA
19	10 mg/kg	TA	Female	22.110346	191.55611	1.1326991	1.2023485	TA
20	10 mg/kg	TA	Male	19.520052	159.31829			TA
21	60 mg/kg	4-Hydroxy-TA	Female	20.199662	190.17738	1.6886325	1.7536353	TA
22	60 mg/kg	4-Hydroxy-TA	Male	11.962142	108.44751			TA
23	60 mg/kg	TA	Female	103.40416	1236.6579	1.6995564	2.3777473	TA
24	60 mg/kg	TA	Male	60.841853	520.09644			TA

Phoenix WinNonlin Makes Compliance Work Much Easier

The analysis of PK, PD, and TK data requires users to follow regulations to ensure compliance with regulatory agencies around the world. Each object includes a validation tab to confirm proper operation, a history tab that keeps an audit trail of changes, and a settings output that records the settings used for analysis.

Validation Suite, now fully integrated into Phoenix WinNonlin, eliminates the need to install a separate application. Automatic execution of detailed test scripts completes the validation of WinNonlin in minutes, not days. Validation is completed in less than 30 minutes with locked PDF reports containing links to saved reference files, user output files, and difference files. Updated validation template documents are aligned with the latest regulatory guidance computer system validation such as ICH E6 Good Clinical Practice (GCP) R2.

Full integration of Phoenix WinNonlin with the Phoenix Knowledgebase Server (PKS) enables the management of clinical and non-clinical PK and PD data and analyses in compliance with the US FDA electronic records and signatures regulation (21 CFR Part 11).

The Phoenix workbench provides an integrated solution to efficiently share pre-clinical and clinical knowledge throughout an organization and track a drug through the development lifecycle via a secure and consistent workflow.

Flexible and Powerful Compartmental Modeling Tools

WNL 5 Classic Modeling and Phoenix Modeling tools provide beginner to advanced users with suitable options. WNL 5 Classic Modeling has several built-in models including Dissolution, Indirect Response, Linear, Michaelis Menten, PD, PK, and PKPD models, and an option for user-defined models in ASCII format. Built-in, Graphical Editor and Textual editor options are available for Phoenix Modeling.

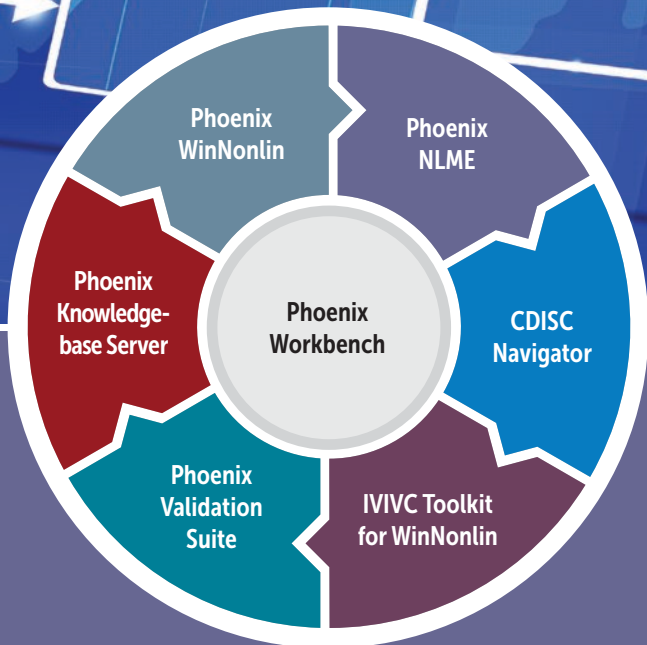
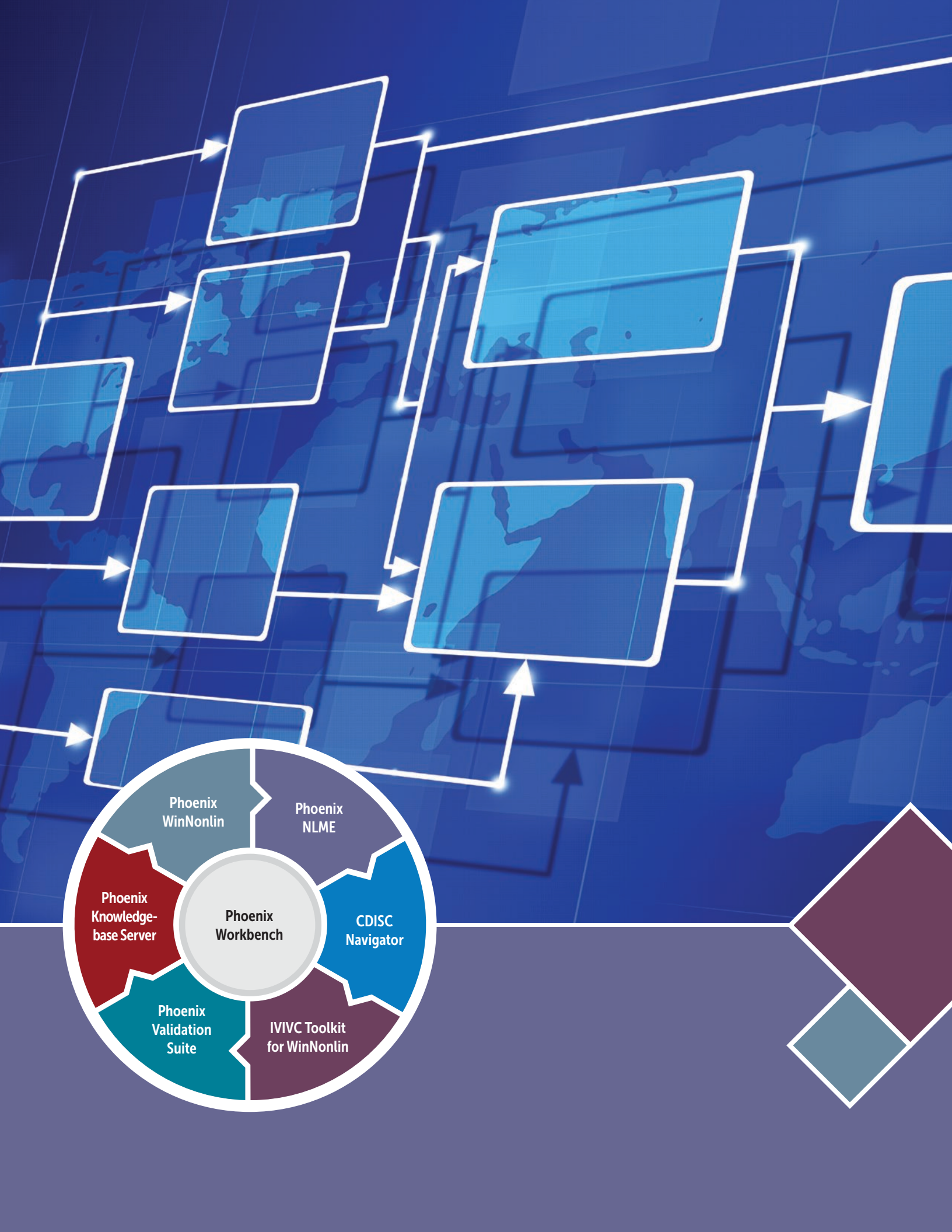
Access to Continuing Education and Support

Coming up to speed on WinNonlin is simple and easy with the graphical user interface. We provide a wide range of education and support tools to get users started and up to date with the most important advancements in modeling:

- Step-by-step user guide and examples
- Classroom and on-demand e-learning training courses available through Certara University (www.certarauniversity.com)
- The new Certara Professional Certification program offers online accreditation of user competency and proficiency analysis of PK/PD data using Phoenix WinNonlin 8.0 and 8.1 (www.certara.com/cpc)
- Webinars from world-renowned investigators and modelers
- White papers, educational blog posts, and access to an active user forum community (support.certara.com/forums)

Discover Why WinNonlin is the Industry Gold Standard for NCA, TK, and PK/PD Modeling and Simulation

Contact us at sales@certara.com to start using WinNonlin today.





About Certara

Certara is a leading provider of decision support technology and consulting services for optimizing drug development and improving health outcomes. Certara's solutions, which span the drug development and patient care lifecycle, help increase the probability of regulatory and commercial success by using the most scientifically advanced modeling and simulation technologies and regulatory strategies. Its clients include hundreds of global biopharmaceutical companies, leading academic institutions and key regulatory agencies.

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