CERTARA

Phoenix Platform Overview

Phoenix

Phoenix is the premier software platform focused on the management, analysis and reporting of pharmacokinetic (PK), pharmacodynamic (PD) and toxicokinetic (TK) data.

It is used by over 5,000 biopharmaceutical, veterinary and academic researchers, along with the FDA and other global regulatory agencies, to understand the safety and efficacy profile of drugs in development. Phoenix supports the concepts set forth in the Critical Path, an FDA program focused on the development of new tools to streamline drug development.

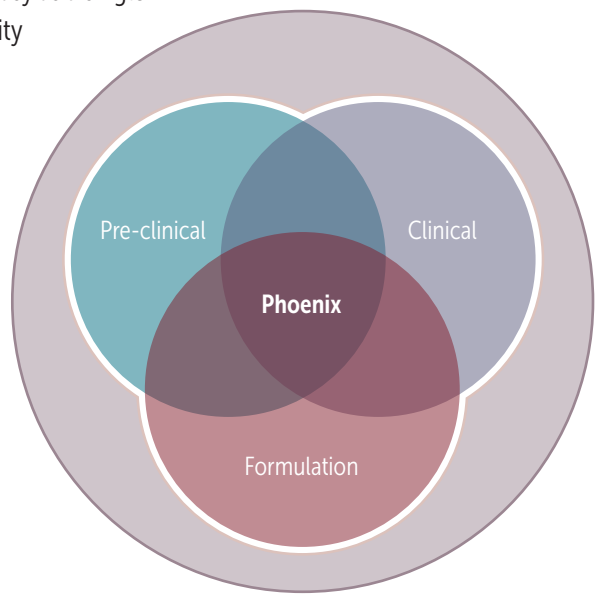
Phoenix was designed to build on the popularity of the original WinNonlin software package by improving ease-of-use and adding new analysis capabilities. It extends the winning formula of WinNonlin by combining its trusted algorithms with an easy-to-use graphical user interface and the additional tools needed to support more advanced analysis, such as population PK/PD modeling, in *vitro-in vivo* correlation (IVIVC) and cardiac safety analysis.

Phoenix is based on the concept of using visual workflows to vastly increase the efficiency of analysis and reporting. Once a Phoenix workflow is developed and customized to the user's needs, it can easily be reused. For example, if the underlying data to support an analysis has been updated, re-executing a complete workflow, including the generation of a report, can be as easy as a single click. Phoenix also includes tools for sophisticated data management, high quality table and figure generation, and a project centric design to easily store, share and reuse complete Phoenix projects.

> "Pharmacometrics is disruptive innovation. Phoenix allows scientists to focus on strategy by taking the burden off the tools."
>
> – Joga Gobburu, Professor
> Schools of Pharmacy
> and Medicine,
> University of Maryland

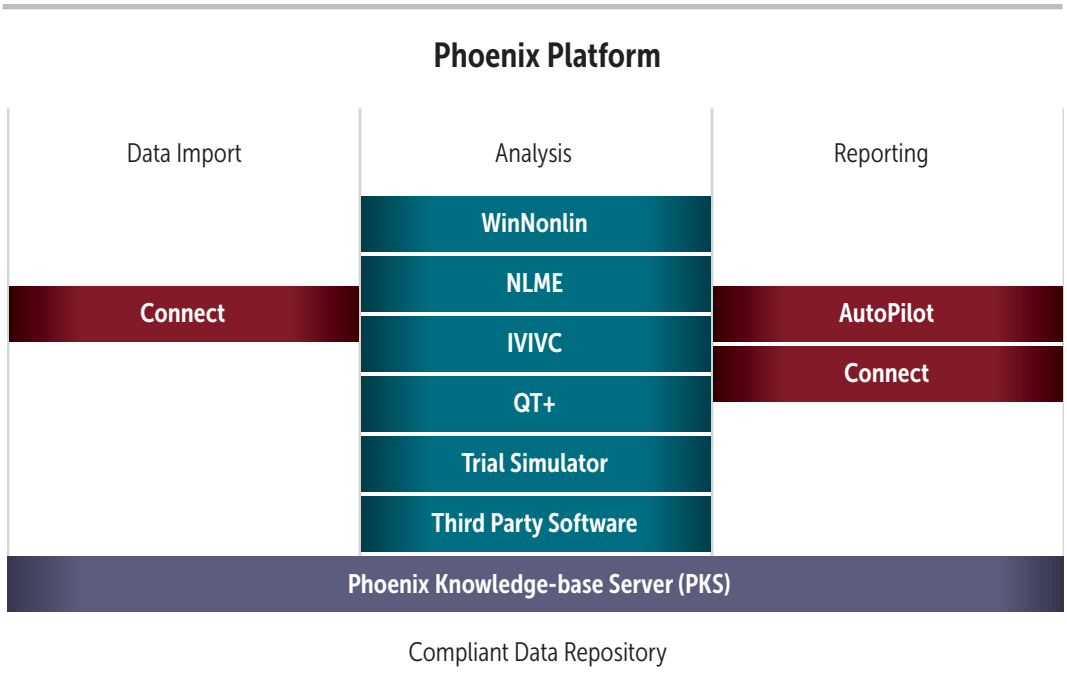
Phoenix Platform

Manage, analyze and report on pharmacokinetic (PK), pharmacodynamic (PD) and toxicokinetic (TK) data in a secure, validation-ready environment. By adopting one common platform, the Phoenix user community is able to efficiently share pre-clinical and clinical knowledge throughout the organization and track a drug through the development life cycle via a secure and consistent workflow.



Drug Development Science

> Model-based drug development is allowing pharmaceutical and biotechnology companies to adopt a more rigorous, quantitative approach to drug development, allowing more informed decisions to be made about drug candidates.
>
> – Dr. James Rothman
> Noble Prize Recipient in
> Physiology or Medicine



> Gone are the days when modelers are required to master a different user interface and program to perform several modeling and simulation tasks. Phoenix offers users the ability to do such work in an integrated and seamless fashion, flattening the learning curve and accelerating industry adoption.
>
> – Daniel Weiner, SVP
> of Certara and Original
> Developer of WinNonlin

WinNonlin

Non-compartmental analysis (NCA) and PK/PD modeling and simulation

Phoenix WinNonlin is the latest implementation of the industry standard WinNonlin, in use since 1984, for NCA, individual compartmental PK/PD modeling and bioequivalence analysis. Phoenix WinNonlin makes it easier to create modeling ready datasets, generate reports and manage projects.

Of course, Phoenix WinNonlin can easily calculate all of the required TK and PK parameters for a regulatory submission. But it also supports more advanced features such as creation of a simulation of multiple doses from single-dose data to understand the impact of the dosing regimen on the PK profile; or building a single workflow that includes multiple models, such as IV and PO or multiple NCA models, to simplify analysis. Other key features include a library of built-in PK/PD models, the ability to code custom models and support for bioequivalence analysis and non-parametric superposition modeling.

NLME

Population PK/PD modeling and simulation

Phoenix NLME (Non-Linear Mixed Effects) was designed to make it easy to perform population PK/PD modeling and simulation. It shortens the learning curve for those new to the science of population modeling, while including cutting-edge tools required by advanced modelers, such as automated covariate searching and bootstrapping. It was developed to support parallel execution on multiple processors, significantly reducing computation times by leveraging standard multiple core Intel® processors within a single computer or on remote high-performance compute systems.

Phoenix NLME gives researchers access to sophisticated tools for creating preliminary plots, determining a base model, doing covariate analysis, developing a final model and evaluating it, all within a single workflow. In addition, researchers can post-process results for reporting, run simulations on

new datasets and communicate the results of the analysis through automated summaries and figure generation. Users can choose a model in Phoenix NLME's built-in library, create their own model using a graphical model editor, or code one using the Pharsight Modeling Language.

IVIVC

In Vitro-In Vivo Correlation (IVIVC) Toolkit for Phoenix WinNonlin

The IVIVC Toolkit for Phoenix WinNonlin offers the ability to use the Level A correlation outlined in the FDA guidance to correlate the in vitro dissolution profile of a dosage form with the *in vivo* PK profile. It can be used to predict the impact a change in formulation will have or to predict the dissolution rate that is necessary to achieve a desired PK profile. The Level A IVIVC can support biowaver for changes in manufacturing site, raw material suppliers and minor changes in formulation.

Using the IVIVC Toolkit has been shown to reduce by days the time necessary to build, validate and use an IVIVC model by having the entire guided workflow available within Phoenix. It includes advanced time saving features such as the support for several deconvolution and convolution methods, Levy Plots and 2-stage IVIVC models. Seamless transfer of the PK and IVIVC parameters within Phoenix also provides a common collaboration platform for the formulation development and the pharmacology teams, making it easier to support critical drug development decisions.

Trial Simulator

Clinical trial simulation

The Trial Simulator allows drug development teams to test proposed clinical trials in a series of "what if" scenarios. It helps minimize risks and guide decision-making by formalizing assumptions and quantifying uncertainties about the drug being investigated in the context of upcoming trials. It is possible to conduct a series of simulations comparing different trial designs, dosing regimens, patient demographics and inclusion/exclusion criteria to optimize the probability of a successful trial. The Trial Simulator is the only tool of its kind that links population PK/PD models with clinical trial models to connect drug concentration and exposure with predicted trial outcomes. It also includes a graphical editor to easily build complex trial models.

The Trial Simulator helps to anticipate risks and preview the range of expected results before R&D dollars are committed to further development of a drug and human subjects are exposed to experimental therapies. Trial Simulator helps to address questions such as:

- How likely is trial success?
- What is the optimal treatment schedule for a particular indication?
- What is the expected range of responses across doses?
- How will a change in inclusion/exclusion criteria affect outcomes?
- How frequently should the response be measured?
- What is the impact of poor compliance or concomitant medication?

Connect

Data import, integration with third-party software and automated report generation

Phoenix Connect offers three major productivity enhancements that make it a must-have tool for any Phoenix user: simplified data import from several common sources; seamless integration of common third-party tools into Phoenix workflows; and automated export of tables, figures and listings directly to a Microsoft® Word® report.

Phoenix Connect can be used to import and export data in the Clinical Data Interchange Standards Consortium, Study Data Tabulation Model and Standard for Exchange of Non-clinical Data formats; it can be used to import data directly from third-party systems such as LabLogic's Debra™ LIMS and Watson LIMS™. It can also be used to import data from any Microsoft Open Database Connectivity (ODBC) driver.

Phoenix Connect also allows scientists to create workflows that include other commonly used tools such as NONMEM®, R, SAS®, and PsN©, directly within Phoenix. This enables the use of a native Phoenix algorithm and a third-party algorithm in the same workflow.

And finally, Phoenix Connect can generate a Word document with user-selected tables, listing and figures from any Phoenix object in the workflow and can add auto-numbered context sensitive captions and footnotes to each object, saving hours of time for each report.

PKS

Secure, regulatory-compliant PK/PD data management

The PKS (Phoenix Knowledgebase Server) is an Oracle®-based data repository that is tightly integrated with Phoenix. It was developed to help pharmaceutical and biotechnology companies meet 21 CFR Part 11 compliance requirements by providing full audit trail and version control for all analyses performed within any Phoenix application. This can be invaluable when it comes time to submit the drug for approval, out-license to a partner or respond to regulatory inquiries.

PKS enhances productivity by managing the complex time-based data that is the foundation of all PK/PD modeling. Since PKS monitors each individual cell in the database, the user will be notified if any of the underlying data has been modified prior to running a new Phoenix analysis. If the data has been updated, executing a new analysis and exporting all of the output to a new report can be performed in a single click.

PKS is available as an on-site solution or as PKS Online, an internet-accessible, pre-validated version. With PKS Online, it is now possible to implement a validated system in only a matter of weeks, ensuring that all Phoenix projects are stored in a completely secure environment with global access. PKS Online also supports collaboration with clinical research organizations or development partners by providing all researchers real time access to the latest results.

Validation Suite

Supports the validation of Phoenix WinNonlin, NLME, Connect and PKS

The Phoenix Validation Suite compares the calculated results of your system to verified reference output and reports the outcome in Microsoft Word. The Phoenix Validation Suite has been shown to reduce the amount of time required for validation by weeks or months by including the test datasets, reference output, editable automated test scripts and common validation life cycle document templates necessary for regulatory requirement.

Hundreds of Phoenix customers have accelerated their validation through use of the Phoenix Validations Suites and continue to benefit with each version upgrade.

Services

Phoenix training, validation services, and workflow consulting

Phoenix includes a full help manual and tutorials, but users can also benefit from certified training. An up-to-date list of beginner, intermediate and advanced courses with full descriptions can be found at www.certara.com/training. Users can either attend a public course or the training can be performed on-site for multiple users.

Certara also offers best practice services based on many years of experience to support such needs as the development of customized workflows, validation and regulatory compliance.

Certara also offers enterprise level support services for the installation of global Phoenix-based solutions, including the implementation of business rules, connection to data sources and export to downstream systems.

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.

For more information visit www.certara.com or email sales@certara.com.

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