CERTARA

Phoenix NLME

The Modern PK/PD Modeling Software for Today's Scientists

Phoenix® NLME™ is the PK/PD modeling software that is user-friendly and easy-to-learn. Built from the ground up on the Phoenix workbench architecture, Phoenix NLME enables users to focus on modeling, and not on the tools or coding required to implement the modeling. The result is more time for analysis and strategic decision-making. Phoenix NLME is the most powerful non-linear mixed effect modeling engine available to scientists today and is used by 1,400 scientists, 18 of the top 20 pharmaceutical companies in the world, renowned academic institutes and multiple regulatory agencies, including the US Food and Drug Administration (FDA). Plus, Phoenix NLME is the first PK/PD modeling software to be out-of-the-box grid-enabled, supporting remote parallel execution on multiple compute platforms.

Most user-friendly PK/PD software available

Phoenix NLME uses a modern, intuitive graphical user interface (GUI) that provides a seamless transition between modeling ideas and modeling execution.

- Select from a complete library of built-in models, or use the graphical model editor for quick customizations. In either case, the full model code is available using Pharsight Modeling Language (PML), a modern modeling language that is easy to read and understand.
- Informative diagnostic messages are provided during model building and execution to quickly and easily identify and remedy errors in a model. Phoenix NLME automatically produces the required diagnostic tables and plots enabling instant evaluation of model results.
- Comparing two versions of a PK/PD model is easy with Phoenix NLME by using 'copy-paste' like you would in a word processing application to create a second model with all of the data inputs and settings - simply make your adjustments and then view the results of the models side-by-side.

Phoenix NLME is the all-in-one PK/PD modeling tool. It enables users to perform exploratory analyses; develop, evaluate and compare multiple models; and create a library of models using templates.

Combining these innovative features for modeling with data preparation, data formatting, statistics, table, and plotting tools built into the Phoenix workbench makes Phoenix NLME a modern tool for today's PK/PD modeling scientist.

Leverage your experience with Phoenix WinNonlin®

Since it is built on the Phoenix workbench, Phoenix NLME leverages the same GUI that you rely on when using WinNonlin. Combining Phoenix NLME with WinNonlin creates a comprehensive analysis package that can be used for optimal PK/PD modeling and simulation through all stages of drug development, including regulatory submission. The integrated tools for data processing, PK/PD modeling, post analysis statistics, table creation, and an integrated graphics engine create a single all-in-one collaboration workbench for scientists, reviewers, medical writers and quality assurance team members.

Powerful and widely used for regulatory PK/PD submissions

Phoenix NLME was developed for optimal performance and maximum flexibility. Both beginners and advanced users can leverage the power of NLME for PK/PD analysis. Phoenix NLME includes a full suite of algorithms for non-linear mixed effects models including QRPEM[1], the most advanced expectation maximization algorithm available anywhere. Integrated support for parameter estimation, simulation, automated covariate searches, bootstrap parameter estimation, and visual predictive checks give a user the flexibility to conduct all phases of a PK/PD analysis with a single intuitive tool.

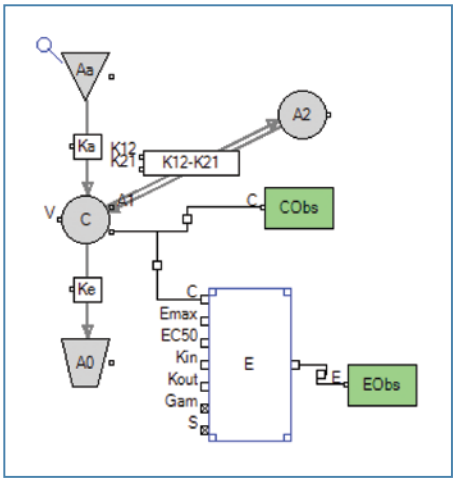
Phoenix NLME software meets all scientific, technical and regulatory requirements for PK/PD studies. NLME has been used for PK/PD modeling in support of numerous global marketing authorization applications by Certara Strategic Consulting as well as other pharmaceutical companies. Because of its flexibility and power, Phoenix NLME is increasingly used in multiple applications including:

- Translational modeling
- Extrapolating PK data from animals to humans
- Enabling sparse sampling strategies
- Predicting the pharmacodynamics in humans based on *in vitro* models
- Combining PK and PD data from multiple studies
- Enhancing study designs to minimize animal use

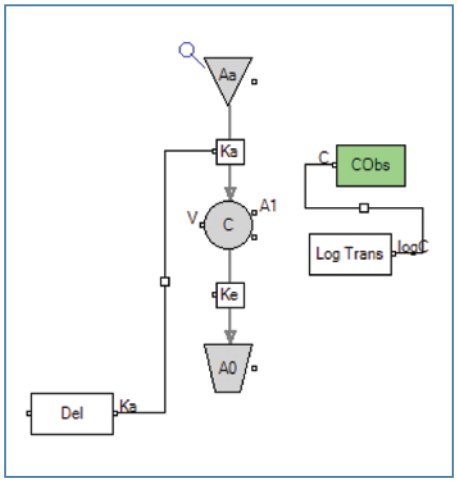
Guided model development

Phoenix NLME provides full 1-to-1 mapping between the development of an optimal modeling strategy and corresponding tools required to perform the analysis. Often the most difficult part of PK/PD modeling is building the right model for your study. Phoenix NLME makes that easy with a graphical model building interface called the Drug Model Explorer (DME) that can easily create custom models including multiple absorption or clearance pathways, parent-metabolite models, and complex exposure-response models. The DME also writes PML code for you, helping new users learn model coding. Combining these innovative features of the software with step-by-step examples and classroom/online training courses at Certara University make Phoenix NLME easy to learn for beginners, self-guiding for novice modelers and optimized for advanced users.

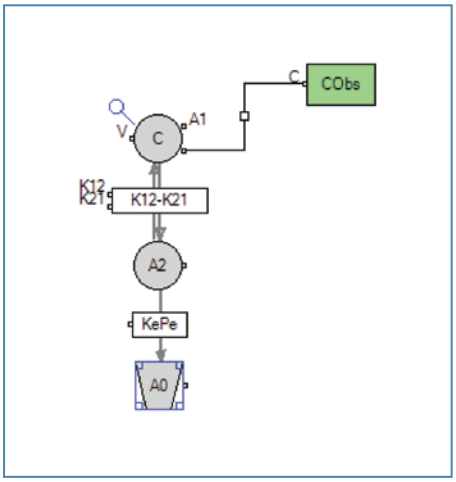
Custom Models Created by Drug Model Explorer



PK/PD Model with Emax Pharmacodynamics Response



PK Model with Modified Ka and Log-transformed Concentration Data



2-Compartment PK Model with Elimination from the Peripheral Compartment

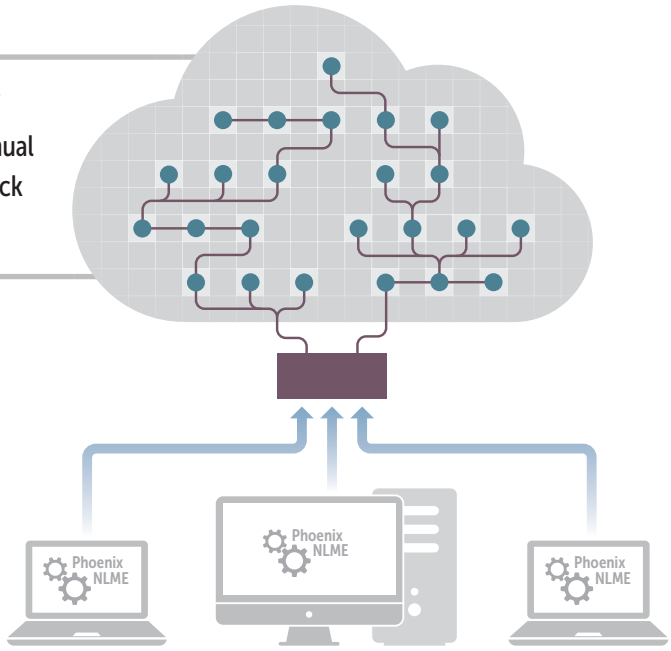
Included Algorithms

Exact Likelihood	Approximate Likelihood	Linearization	Laplacian	Single Subject
• QRPEM • Non-parametric	• IT2S-EM	• FO • FOCE-ELS • FOCE-LB	• Laplacian • AGQ	• Naïve Pooled

Out-of-the-box grid-enabled

Phoenix NLME supports execution of NLME jobs on remote compute platforms right out of the box, versus command line and manual execution. Cloud computing platforms, such as a linux grid or an MPI cluster, provide compute power that can significantly reduce model fitting time. For example, a standard laptop computer has 4 CPU cores available for model fitting, but a Linux grid configured with 100 cores will run a NLME job 25 times faster than the laptop computer. After sending a NLME job to a Linux grid, users can close the Phoenix application, and the results are automatically downloaded to the project file when the job is finished. Phoenix NLME also enables a user to initiate a NLME job on a remote/parallel compute platform directly from the desktop application without the need to install Phoenix NLME on the remote computer.

Phoenix NLME licenses have access to unlimited cores/nodes on any remote/ parallel compute platform. Phoenix NLME eliminates complicated setup, manual data transfers, and command-line execution. The result? With a point-and-click users have the power of grid computing when they need it.



Cutting-edge science

NLME is the first PK/PD modeling engine to offer integration of a model delay function eliminating the need to add complex lines of code for each delay differential equation (DDE). The new delay function greatly simplifies modeling delayed outcomes, an important function in several therapeutic areas such as oncology, diabetes and arthritis. In Phoenix 7.0 you can add a delay function with a single Pharsight Modeling Language (PML) command avoiding inefficient workarounds and approximations.

Interoperability

Phoenix NLME is interoperable with any PK/PD modeling paradigm. The Phoenix Connect tool also provides interoperability with software packages such as SAS®, R, TIBCO™ Spotfire® S+, SigmaPlot®, NONMEM®, PSN, Watson LIMS™ and more. This allows users to integrate specialized software tools into a Phoenix workflow to ensure compliance and data traceability. Phoenix NLME is designed to easily export analysis results for incorporation into PK/PD reports. Any plot, figure, or table can be exported to a Microsoft® Word document with a single click. Using the Phoenix Connect Reporter tool users can compile a series of plots, figures and tables into a single Microsoft® Word file with customized numbering and headers. This output can then be quickly and easily attached to a PK/PD report for communicating results internally and to regulatory agencies.

Compliance

PK/PD modeling requires users to follow regulations to ensure compliance with regulatory agencies around the world. Phoenix NLME does the compliance work for you. Each object includes a validation tab to confirm proper operation, a history tab that keeps an audit trail of any changes, and a settings output that records the settings used for analysis. And 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).

Are you ready to experience the power of Phoenix NLME?

Contact us at sales@certara.com to learn how you can join other modelers and start using NLME today.

References

1. Liu, Xiaoxi and Wang, Yuhuan. Comparing the performance of FOCE and different expectation-maximization methods in handling complex population physiologically-based pharmacokinetic models. *J. Pharmacokinetics and Pharmacodynamics* (2016). 43:359-370.

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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