



# MonolixSuite™

A fast, easy-to-use, and powerful suite of applications for pharmacometrics analysis, modeling and simulation

## Easy-to-use

Designed for ease of use –via a modern and user-friendly graphical interface, or command line for powerful scripting. Simple and intuitive workflow means less programming for you and more time to focus on analysis.

## Powerful

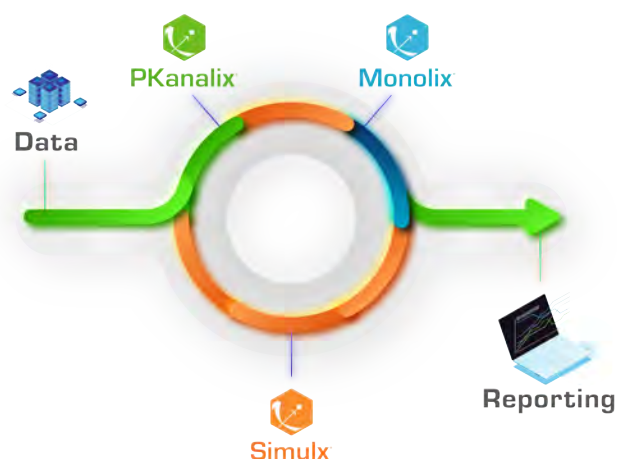
Efficient C++ solver package with pioneered implementation of the SAEM algorithm, standardized model language, model libraries and automatically generated out-of-the-box diagnostic plots. All contribute to better productivity and quality.

## Interoperable

Fully interconnected applications in the suite cover the complete modeling and simulation workflow. In one click, go from NCA, to population model development and simulations - without rewriting any dataset, models or parameters.

## Expert support

Behind MonolixSuite is a dedicated developer and expert team you can contact for technical questions. Extensive and tailored support is available on request. Comprehensive documentation with software manuals and tutorials is online.



Fully interoperable applications give you a complete modeling and simulation workflow from data visualization and non-compartmental analysis to population modeling and simulations. Intuitive, effective, and offering the most advanced calculation capabilities.

The Monolix Suite was developed in view of the increasing importance of pharmacometric experts in drug development. This key role requires integrated software tools with the most rigorous statistical methodologies to deliver high quality modeling results in time.

Experience the right tools for model-based drug development. All integrated for modeling in one go – without rewriting any data set, models or parameters:



**PKanalix** - User-friendly and fast non-compartmental, bioequivalence and compartmental analysis.



**Monolix** - The most advanced solution for NLME modeling with the SAEM algorithm for robust parameter estimation and built-in diagnostic plots.



**Simulx** - High performance simulation of new scenarios, including clinical trials.



## The best solution for Model Based Drug Development

Monolix is the most advanced and simple solution for non-linear mixed effects (NLME) modeling for pharmacometrics. It is based on the SAEM algorithm to provide robust, global convergence even for complex models, and is equipped with a user-friendly interface to ensure a simple and fast workflow - from preclinical and clinical population PK/PD modeling to Systems Pharmacology.

### Key features

**Support of all relevant data types and statistical features for population PK/PD modeling.**

Monolix covers:

- continuous, categorical, count and time to event data (or any combination);
- inter-individual and inter-occasion variability (with any number of level);
- automatic handling of BLQ data;
- normal, lognormal, logit, probit and user defined distributions for individual parameters;
- effect of covariates and correlations.

#### **Mlxtran and model libraries.**

Monolix provides a fully documented, open source, built-in model's library with more than 30000 models. Mlxtran, language for library and custom-built models, is a simple, yet powerful, human readable language suitable for simple as well as complex models.

#### **Automatically generated results and out-of-the-box diagnostic plots.**

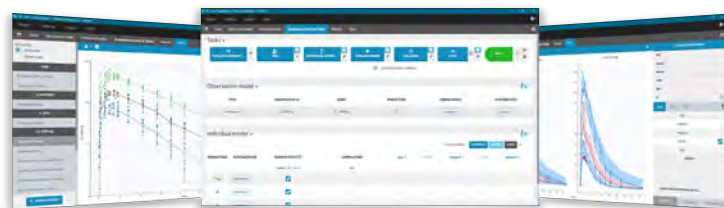
All results are displayed in formatted tables easy to copy in any document and are exported in the result folder in an R-compatible format. Full set of interactive diagnostic plots is also automatically generated for straightforward interpretation of the results.

#### **Comprehensive documentation and tutorial materials.**

We provide a comprehensive online documentation that includes methodology, software manuals and tutorials. A wide collection of examples can be used as templates to start your own project. Regular online courses and webinars build a large user community.



A fast, easy-to-use and powerful application for data visualization, parameter estimation in NLME models, model diagnosis and assessment with advanced graphical interface.



## Why Monolix?

- ✓ **Regulatory compliance**  
Accepted by regulatory agencies for submissions. It assures data integrity and reproducibility of results and includes integrated validation suite.
- ✓ **Easy-to-use interface**  
Can be used via a modern, user-friendly graphical interface. The workflow is simple and intuitive, with guided steps to go through all your project.
- ✓ **Efficient model building**  
Provides fast and robust model development with built-in libraries for structural model and interactive settings in the GUI for the statistical model.
- ✓ **Advanced Statistical Methodologies**  
Assures proper handling of modeling and reliable convergence for all type of data thanks to pioneered implementation of the SAEM algorithm.
- ✓ **Out-of-the-box diagnostic plots**  
Generates automatically a full set of diagnostic plots ready for analysis. You can instantaneously create VPC plot and split it by any patient subgroups.
- ✓ **Powerful computing**  
Includes efficient C++ solver packages, and possibility to script complex workflows in R using a dedicated R-API.
- ✓ **Interoperability**  
Allows for non-compartmental analysis and simulations via the built-in integration with PKanalix and Simulx.





## Intuitive, efficient and integrated in MIDD workflow

PKanalix calculates NCA parameters with industry-standard methods, and automatically generates a full set of plots and results tables. Reproducibility of results is guaranteed by saving settings in the project, while integrated validation suite ensures correct installation and calculations. And thanks to a direct link to Monolix and Simulx, you can extend analysis to population modeling and explore new scenarios in simulations.

### Key features

#### Non Compartmental Analysis

The main feature of PKanalix is the calculation of the parameters in the NCA framework. It includes:

- specification of calculation methods and acceptance criteria with intuitive settings;
- definition of rules for the calculation of the  $\lambda_z$  – slope of the terminal elimination phase – that can be done via global rules or customized on each individual;
- selection of NCA metrics, their ratios and custom parameters to be computed.

#### Compartmental Analysis

The second feature of PKanalix is the calculation of the parameters in the CA framework. It includes:

- selection of a compartmental model using built-in libraries or user-defined custom models;
- initialization (with the help of automatic algorithms) of parameters for a better convergence;
- specification of calculation methods such as objective function or pool fit option.

#### Bioequivalence Analysis

The next task in PKanalix compares the average NCA parameters obtained for different groups, e.g. a test and a reference formulations. It includes linear model definition with one or several fixed effects selected in an integrated module. And allows to obtain a confidence interval compared to the predefined BE limits.

#### Outputs and plots

All NCA, CA and Bioequivalence outputs are displayed in sortable tables and exported in the result folder in a R-compatible format. Interactive plots are also proposed for straightforward interpretation of the results.



PKanalix is a user-friendly and fast application for non-compartmental (NCA), bioequivalence (BE) and compartmental (CA) analysis.



## Why PKanalix?



#### Very intuitive interface

Intuitive settings panels, clear definitions of methods, visual tools to check the calculations and personalized display of results – all contribute to a better productivity.



#### Straightforward NCA & Bioequivalence Studies

Complete workflow - integrated calculation of NCA parameters with industry standard methods and bioequivalence study as recommended by regulatory agencies - is done in a few clicks. NCA analysis has never been so simple.



#### Reliable and clear results

Publication quality customizable plots, intuitive tables and sortable summaries provide a powerful environment for analysis of results. Includes integrated reporting with customized templates.



#### Seamless integration for simulations and population modeling

Use the same data and model for all your analysis. Export project in one-click to Monolix for population modeling or to Simulx for simulations of a new dosing regimen.

#### Reporting

Built-in generation of a report with result tables and plots. Create customized templates and use them in your company for different projects.

## Documentation

Great care has been taken to provide the user with a comprehensive PKanalix documentation that includes methodology, software manuals and tutorials. A wide collection of examples that include models and data can be used as templates to start your own project.



# Simulx®

## Simulations in a user-friendly and fast environment

Simulx is an advanced clinical trial simulation software to build and simulate user-designed scenarios. It combines a user-friendly interface with the highest computational capabilities to quickly answer your questions and find optimal solutions.



**Simulx** is an easy, efficient and flexible application for clinical trial simulations



## Why Simulx?

- ✓ **To gain new insights**  
using an interactive exploration of effects of dosing regimens and model parameters with real-time predictions.
- ✓ **To anticipate clinical trials**  
by simulating new scenarios using your estimated model and analysing results with dedicated plots.
- ✓ **To justify**  
dose and dosing regimens using built-in post-processing into outcomes & endpoints and statistical tools for comparison between groups.
- ✓ **To focus**  
on analysis and answering precise questions instead of implementation details thanks to a modern and intuitive graphical interface with easy simulation setup.
- ✓ **To save time**  
by working in a simple and efficient environment interconnected with Monolix and PKanalix.

## Documentation

Great care has been taken to provide the user with a comprehensive Simulx documentation that includes methodology, software manuals and tutorials. A wide collection of examples that include models and simulation setups can be used as templates to start your own project.

### Optimal environment to build and analyze simulation scenarios

**Definition** – create easily new exploration and simulation elements (parameters, treatments, outputs, covariates, etc.) of different types using built-in methods or external tables.

**Exploration** – analyze in real time different treatments and effects of model parameters by simulating a typical individual; create several exploration groups, overlay experimental data and send a scenario in a single click to a clinical trial simulation.

**Simulation** – simulate original individuals or virtual patients in one or several groups with specific treatment, individual characteristic or measurements times; use a previously developed population model in Monolix or write a new one.

**Outcomes & endpoints** – analyse efficacy and safety targets with built-in tools for post-processing of simulations outputs and compare results in different groups using statistical tests.

**R-API to automate workflows** – build and run scenario directly from R using the lixoftConnectors package. What you have done once intuitively in the interface, can be generalized to a script automating the process for any other scenario.

### Outputs and plots

All simulation outputs are displayed in sortable and formatted tables easy to copy in any document and are exported in the result folder in an R-compatible format. Interactive plots are also automatically generated for straightforward interpretation of the results.