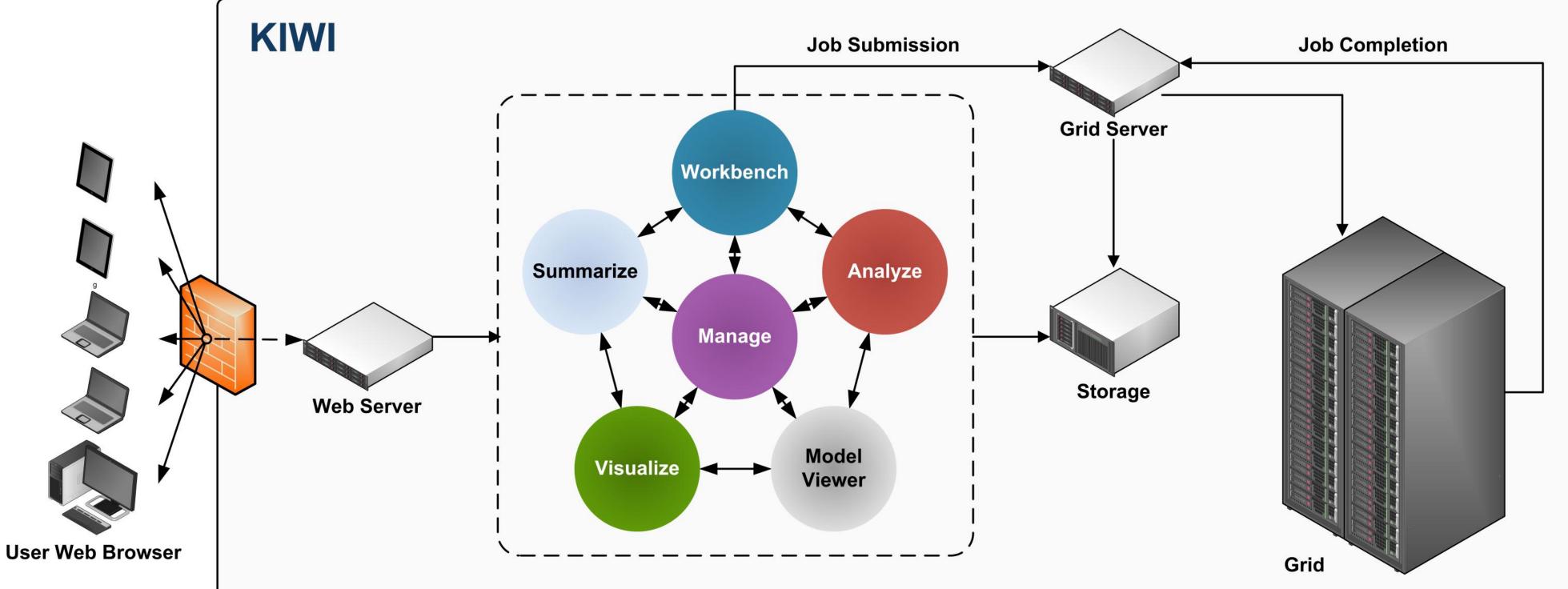


INTRODUCTION

Drug development programs rely increasingly on pharmacometric analysis to support decision-making and submissions to regulatory agencies.^{1,2} To ensure high quality analysis, organizations must apply state-of-the-art science and implement a comprehensive infrastructure of procedures, workflows, and informatics capable of efficiently organizing, maintaining, and communicating the volume of data and results generated by pharmacometric departments over the duration of a development program.^{3,4} KIWI is a novel platform designed to meet these challenges.





DESIGN CONCEPTS

KIWI was created as a general platform to efficiently and consistently organize, process, evaluate, and communicate results of pharmacometric analyses. The systematic analysis of requirements, constraints, and practice across pharmacometrics, data management, standard administrative support, and IT departments supported the formalization of data and scientific workflows within KIWI.

Collaborative work, scalability, and security

- Cloud-based design allows multiple users to simultaneously access data and analysis tools using a simple web browser
- Scaled for cooperative work across departments
- 24/7 secure system access
- Permission system restricts user access within the shared workspace
- Validation
- Full validation of workflows, front-end and back-end analysis tools, and exported reports, tables, and figures
- 21 CFR Part 11 compliant with implementation of local SOPs

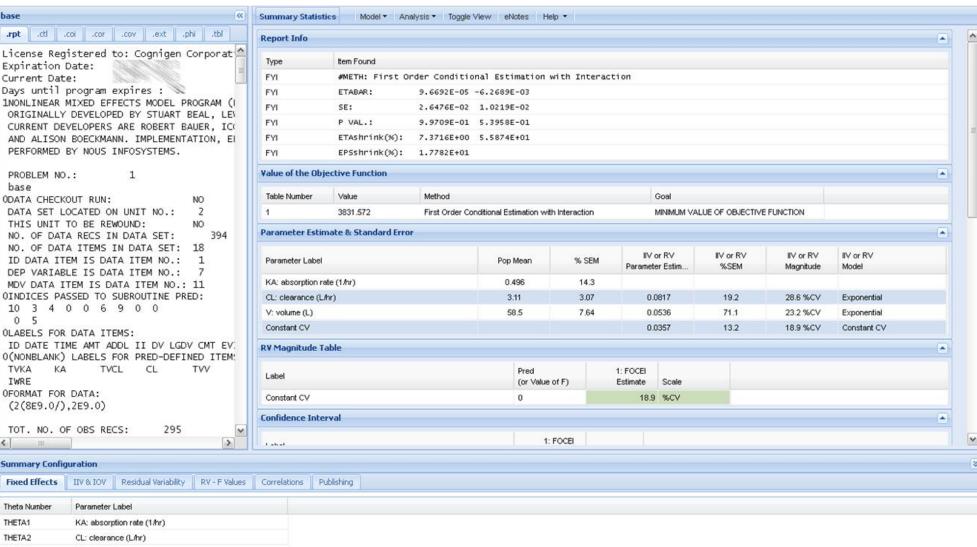
Performance

- Leverage the power of computational grid environments
- Facilitate the use of NONMEM, Perl-speaks-NONMEM, covariate search methods, and high-quality R-based diagnostic plotting
- Efficiency and consistency across modeling projects
- Systematic data organization
- Intuitive user interfaces with optimized display of data and access to analysis tools
- Automated analysis tools, such as computation of summary statistics and creation of diagnostic plots

SUMMARIZE

- Generate run-specific summary statistics automatically
- Extract NONMEM warning and error messages
- Extract parameter meta-information, such as parameter labels or variability models
- View formatted tables of summary statistics, including Parameter estimates
- Magnitude of interindividual and residual variability Confidence intervals
- Allow users to add electronic notes and flags

Export tables to formatted and validated HTML and Microsoft Word files



ANALYZE

- Provides organized and functional spaces to
- Generate summary statistics and tables for full stepwise covariate analyses to support the selection/elimination of covariates
- Perform and compare generalized additive model analyses
- Export reports to formatted and validated HTML and Microsoft Office Word files

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MODEL VIEWER

Combine summary statistics, diagnostic plots, and files in a single snapshot view

- Standardized table and plot styles and naming conventions
- Validated workflow and tools promote traceability and reproducibility of results and reduce data manipulation errors
- Enhanced communication
- Encourage a disciplined approach to model development, evaluation, and documentation of results
- Export validated tables and plots eliminating the need for quality checks Modularity
- Expandable to additional NONMEM-based or non-NONMEM-based analysis tools

WORKBENCH

- Organize projects and set access permissions for users
- Upload existing NONMEM-ready datasets and control streams
- Create and edit control streams using an embedded text editor with syntax highlighting
- Submit jobs
- View output files
- Archive or delete previously run control streams

KIWI WORKBENCH	MANAG	E SUMMARIZE ANALYZE	VISUALIZE			
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		near_boundary.cov	Covariance File	907	03/12/2013 11:17	
		near_boundary.ctl	Control Stream	1489	02/11/2013 09:17	
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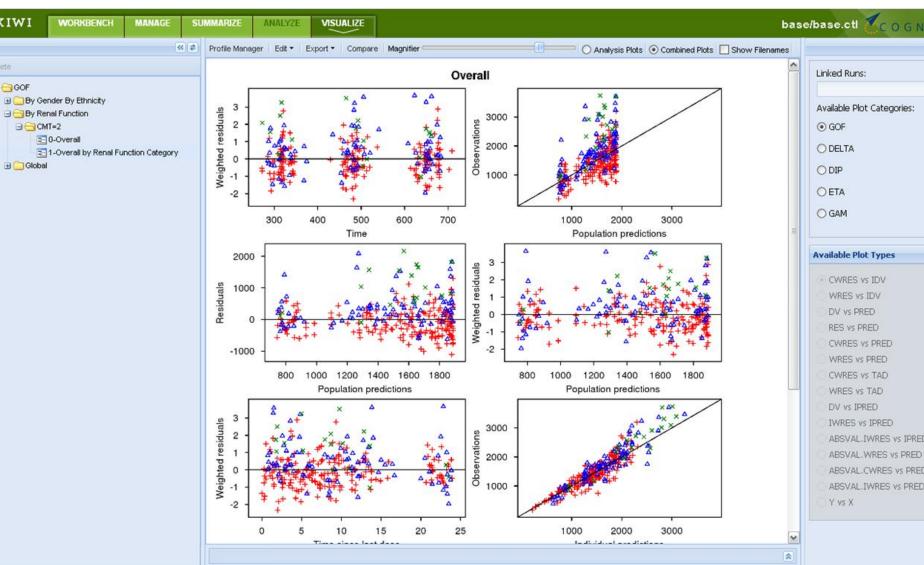
VISUALIZE

JAN C 🖃 😋 By Gender

🔁 1-Overall

🗄 🦲 Global

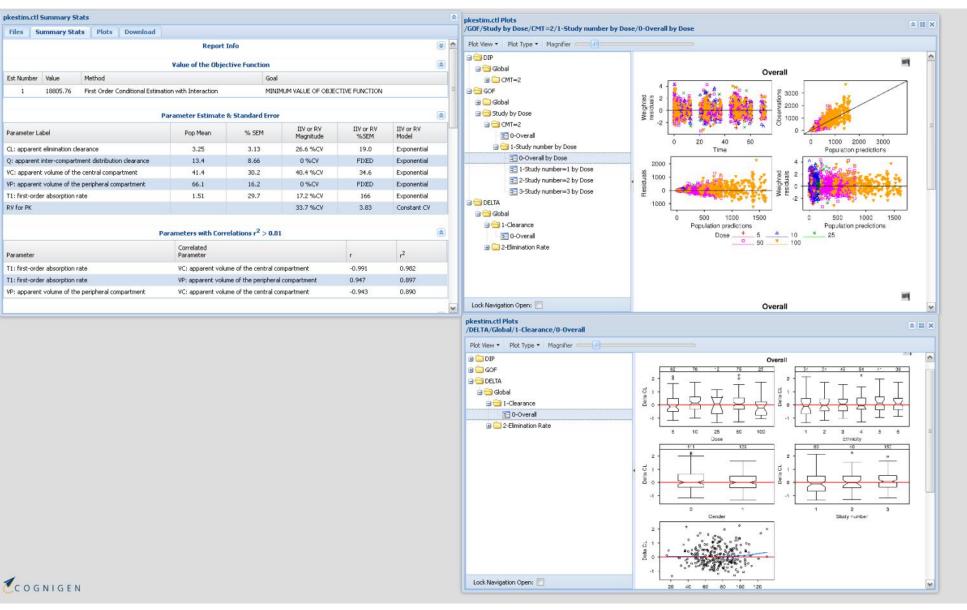
- Create, manage, view, store, and export diagnostic plots
- User interface facilitates the definition of custom settings for users with limited or no knowledge of R
- Several categories of plots are available, including
- Goodness-of-fit plots
- Individual overlays of observations, population, and individual predictions
- Delta-parameter versus covariate plots
- Random parameter (co-)distribution plots
- Diagnostic plots for GAM (generalized additive model) analyses
- Visual predictive check plots



6						
KIWI	WORKBENCH	MANAGE	SUMMARIZE	ANALYZE	VISUALIZE	validate/final_gender.ctl 💆 🕻 🛛 G N
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Allow comparison of plots

Export to formatted and validated HTML and Microsoft Word files



CONCLUSIONS

As an integral part of an ongoing effort to enhance cross-department team collaboration and systematize the modeling and simulation workflow, KIWI was developed as an intuitive cloud-based platform for pharmacometrics designed to meet the demands of global teams. The design of the KIWI platform directly reflects Cognigen's years of experience in analyzing data management, scientific, and project workflows.

ONGOING DEVELOPMENT

Presentation module

- Facilitate the automated integration of KIWI-based tables and plots into interactive and nonlinear presentation media



MANAGE

Cornerstone of the KIWI system allowing access to all other KIWI modules Provide an organized and functional space to

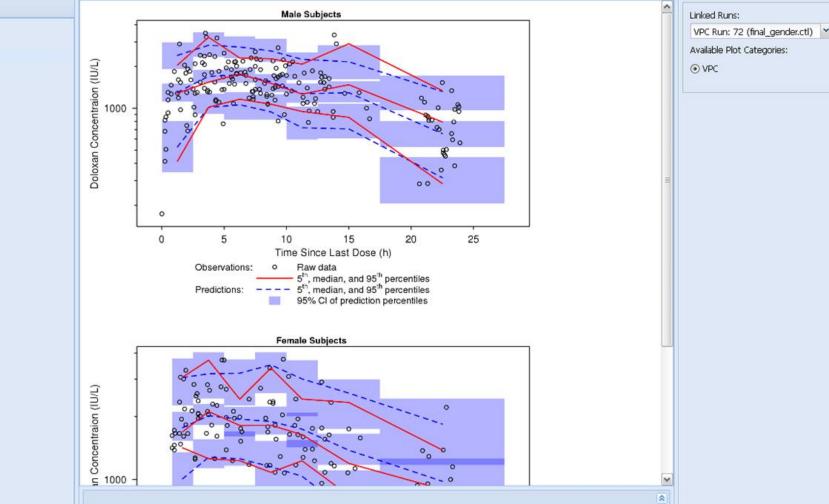
Review NONMEM run results

Compare results and parameter estimates across NONMEM runs

Annotate NONMEM runs using electronic notes and flags

Access run history when a control stream was submitted multiple times Export reports to formatted and validated HTML and Microsoft Word files

CIWI WORKBENCH	MANAG	SUM	IMARIZE	ANALY	ZE VISUALIZI						(
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Bihorel S, Fox D, Phillips L, Fiedler-Kelly J, Rokitka A, Walawander C, Grasela TH. KIWI: a collaborative platform for modeling and simulation. Poster presented at: Twenty-Third Meeting of the Population Approach Group in Europe (PAGE); June 10-13, 2014; Alicante, Spain.

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- Accelerate communication within global teams
- Analysis tools under consideration for further development
- Generic interface for Perl-speaks-NONMEM commands

Generic exploratory plot creator

Import of external files (that is, plots, tables, proprietary files) within KIWI

THREE-STEP IMPLEMENTATION

Purchase KIWI license

Procure NONMEM licenses

Point browser to your secure 24/7 private cloud

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- Grasela TH, Dement CW, Kolterman OG, et al. Pharmacometrics and the transition to model-based development. Clin Pharmacol Ther. 2007;82:137-142.
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- 4. Grasela TH, Fiedler-Kelly J, Cirincione BB, et al. Informatics: the fuel for pharmacometric analysis. AAPS J. 2007:9(5):Article 8. DOI: 10.1208/ aapsj0901008.