CERTARA

Phoenix Workflow Templates

Automate and Standardize Non-clinical and Clinical Data Preparation

Escalating drug development costs combined with the ever-increasing complexity in bringing novel drugs to market have challenged the biopharmaceutical industry to develop and adopt methods that boost efficiency and productivity. Tools to validate safety and conduct efficacy analyses faster, or help achieve regulatory compliance, can result in significant time and cost savings.

At Certara we are focused and committed to developing modeling and simulation technologies and solutions that will streamline and accelerate your R&D productivity to achieve your goals faster.

Establish Best Practices

- Standardize outputs, business rules and comparison parameters
- Increase data consistency and make better decisions with post-analysis calculation of ratios
- Prepare CDISC STDM and SEND data earlier and closer to the source
- Achieve regulatory compliance

Phoenix WinNonlin Workflow Templates

Phoenix® WinNonlin® is the trusted industry standard biosimulation software tool for pharmacokinetic and pharmacodynamic (PK/PD) modeling, non-compartmental and compartmental analysis. Over 6,000 researchers at 1,500 global biopharmaceutical companies, academic institutes and regulatory agencies rely on WinNonlin for their biosimulation studies.

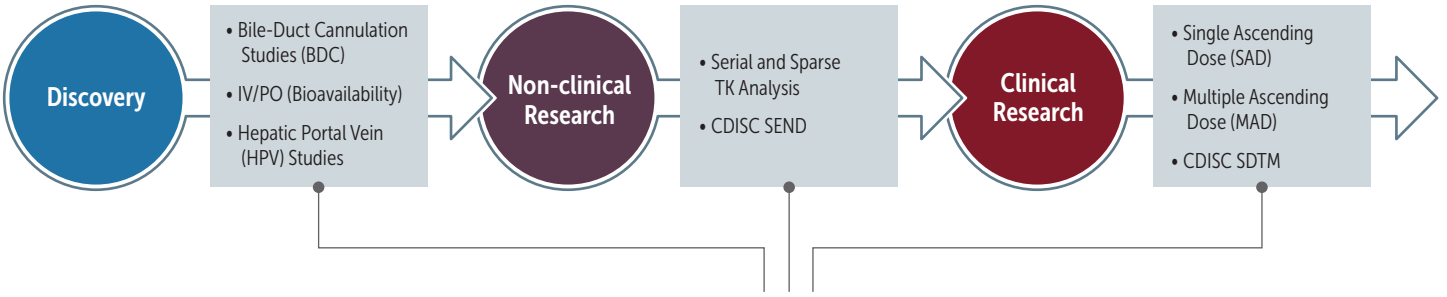
As experts in the modeling and simulation field, our Phoenix Technology Services team has designed pre-defined Phoenix WinNonlin Workflow templates that will increase output and efficiency, establish best practices and systematize quality control. Although any Phoenix WinNonlin workflow can be saved as a template, creating templates that are reusable across different studies with varying numbers of parameters, such as treatments, analytes, matrices, and doses, requires expertise and significant development time.

Certara's Phoenix Technology Services team has developed workflow templates for CDISC SDTM and SEND data submissions, Non-clinical Toxicokinetic (TK) Studies, Clinical Pharmacokinetic (PK), and Discovery PK studies to streamline routine tasks, reduce QC efforts, and optimize R&D productivity.

In addition to the Phoenix WinNonlin workflow templates used in routine analyses, our team will work with you to develop tailored templates for specific workflows and parameters.

Workflow Template Services for Discovery, Non-clinical, and Clinical Phase Drug Development Studies

Phoenix Technology Services will assist with the integration of Phoenix WinNonlin workflow templates or customized templates that have been developed for common analyses used in discovery, non-clinical and clinical pharmacokinetic research studies.



Increase Output and Efficiency

- Increase the number of studies with faster analysis times
- Achieve greater efficiencies through simultaneous execution of multiple non-compartmental analysis (NCA) models in a single object
- Devote more time to interpretation of data versus time spent developing workflows for routine analysis
- Reduce labor input and increase profit per report

Phoenix Workflow Templates for Drug Development Modeling and Simulation Studies

Backed by years of knowledge developing and supporting modeling and simulation solutions for major biopharmaceutical companies, Certara's Phoenix Technology Services team has developed reusable validated WinNonlin workflow templates for routine drug development studies.

Workflow Templates for Tokicokinetic Analysis and CDISC Electronic Data Submission

Toxicokinetics (TK): The Serial and Sparse workflow template is designed for TK analysis in non-clinical studies. TK is a standard non-clinical study where groups of animals are given a compound for a period of time to confirm safety and tolerability. In addition, PK Parameters, such as Area Under the Curve (AUC), Maximum Concentration (C_{max}) and Time to Reach Maximum Concentration (T_{max}) are calculated from a test subject's biological fluids (ie, plasma) to provide exposure data related to the compound and information for selecting an initial dose in human trials. Sampling of the biological fluids can be conducted as either Serial (full profile) for larger animals or as Sparse (partial profile) for smaller animals where the partial profiles are subsequently combined in order to create a composite profile.

CDISC SDTM and SEND: The Clinical Data Interchange Standards Consortium (CDISC) has developed models for the submission of non-clinical and clinical data to regulatory agencies. Since the end of 2016, numerous agencies have required mandatory submissions of electronic non-clinical and clinical data using CDISC standard formats. Standard Data Tabulation Model (SDTM) is a fundamental model for organizing data collected in clinical trials and Standard Exchange of Non-clinical Data (SEND) is an implementation of the SDTM model for non-clinical studies. The CDISC workflow templates will complete specific data transformation, analysis, and data preparation tasks to streamline routine analysis, maximize quality control output, and package data for SDTM and SEND regulatory submissions.

Pharmacokinetic Workflow Templates for Clinical Safety and Tolerability Studies

Single Ascending Dose (SAD): SAD is a common PK study where small groups of subjects are given a single dose of the drug while they are observed and tested for a period of time to confirm safety. If they do not exhibit any adverse effects, and the pharmacokinetic data are roughly in line with predicted safe values, the dose is escalated, a new group of subjects is given a higher dose, and dose proportionality is calculated.

Multiple Ascending Dose (MAD): MAD PK studies examine the pharmacokinetics of multiple doses of the drug to determine safety and tolerability. In this study, a group of subjects receives multiple low doses of the drug to acquire information on how the drug is processed within the body Accumulation (Rac) is often calculated comparing the single-dose (first dose) with dosing once steady-state has been achieved.

Workflow Templates for Discovery Research

Bile-Duct Cannulation (BDC): BDC is used in non-clinical studies to calculate the amount and rate of biliary drug excretion of a compound and also assist in determining the clearance route of a compound.

IV/PO (Bioavailability): Bioavailability studies provide an understanding of how readily absorbed a compound is when administered orally. Absolute bioavailability, F_{abs}, compares the bioavailability of the active drug in systemic circulation following non-intravenous administration (ie, oral, subcutaneous, etc.), with the bioavailability of the same drug following intravenous administration where the fraction of the drug absorbed through non-intravenous administration compared with the corresponding intravenous administration.

Hepatic Portal Vein (HPV): HPV cannulated models are used in non-clinical studies to understand how orally administered drugs are absorbed and metabolized. Compound concentrations in the hepatic portal vein blood and in systemic circulation are measured at various time points for comparison.

Leverage the Full Power of Phoenix

Implementing pre-defined or custom-designed WinNonlin workflow templates will increase productivity and standardize data preparation analysis and output presentation across large data sets for PK and TK studies.

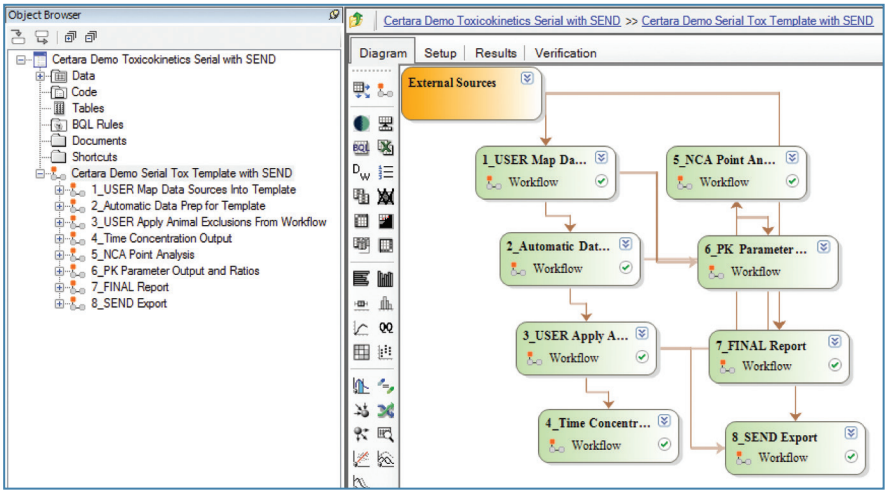
Phoenix workflow templates can be reused across different studies reducing the need to recreate transformations, analyses and outputs for routine non-compartmental analysis (NCA).

CDISC Registered Solutions Provider

Certara is a CDISC Registered Solutions Provider

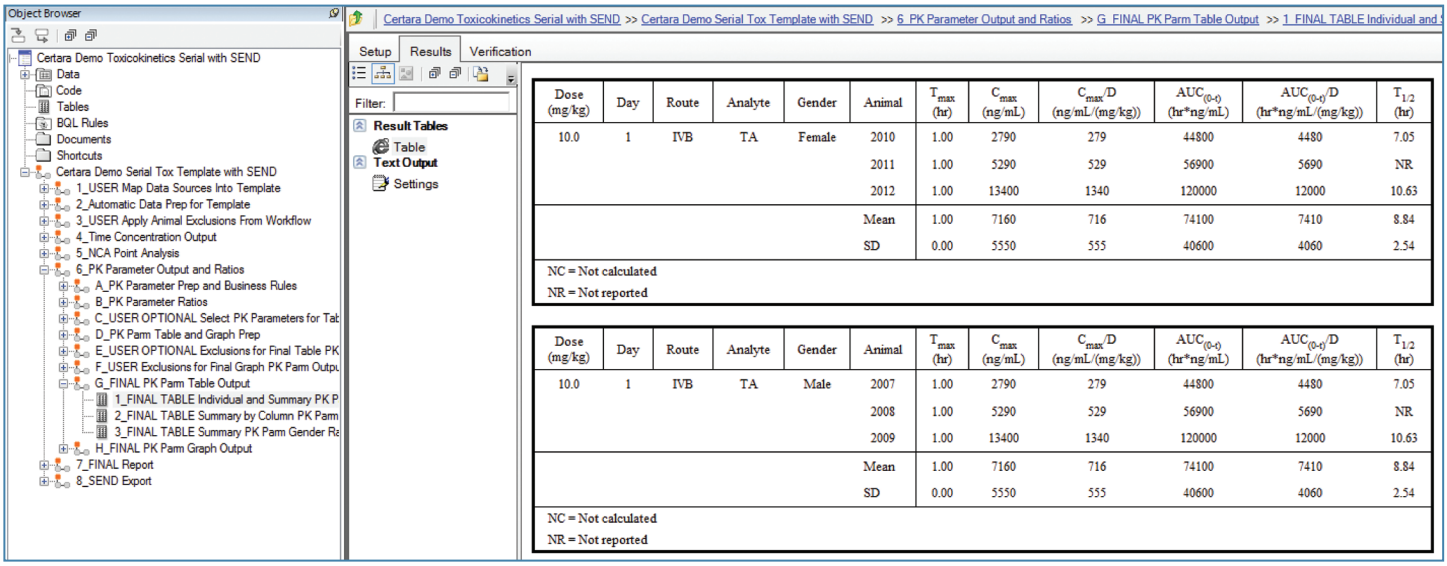
Systematize Quality Control

- Reduce QC in data hand-offs and output review
- Minimize the need for QC checks with validated templates
- Easily track data set changes and auditable activities
- Eliminate errors associated with manual entries
- Report quality outputs



Phoenix Workflow Illustrating End-to-End Toxicokinetic PK Analysis with Pre-defined Serial and SEND Templates

Contact us at sales@certara.com to discuss how Phoenix Technology Services can create workflow templates to increase efficiency and productivity.



Dose (mg/kg)	Day	Route	Analyte	Gender	Animal	T_{max} (hr)	C_{max} (ng/mL)	C_{max}/D (ng/mL/(mg/kg))	$AUC_{(0-t)}$ (hr*ng/mL)	$AUC_{(0-t)}/D$ (hr*ng/mL/(mg/kg))	$T_{1/2}$ (hr)
10.0	1	IVB	TA	Female	2010	1.00	2790	279	44800	4480	7.05
					2011	1.00	5290	529	56900	5690	NR
					2012	1.00	13400	1340	120000	12000	10.63
					Mean	1.00	7160	716	74100	7410	8.84
					SD	0.00	5550	555	40600	4060	2.54

NC = Not calculated
NR = Not reported

Dose (mg/kg)	Day	Route	Analyte	Gender	Animal	T_{max} (hr)	C_{max} (ng/mL)	C_{max}/D (ng/mL/(mg/kg))	$AUC_{(0-t)}$ (hr*ng/mL)	$AUC_{(0-t)}/D$ (hr*ng/mL/(mg/kg))	$T_{1/2}$ (hr)
10.0	1	IVB	TA	Male	2007	1.00	2790	279	44800	4480	7.05
					2008	1.00	5290	529	56900	5690	NR
					2009	1.00	13400	1340	120000	12000	10.63
					Mean	1.00	7160	716	74100	7410	8.84
					SD	0.00	5550	555	40600	4060	2.54

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Summary

Pre-defined or customized Phoenix Workflow Templates, when implemented into WinNonlin, will become valuable time-saving assets for Drug Development organizations. Whether you are a discovery, pre-clinical or clinical scientist, pharmacometrician, clinical pharmacologist, biostatistician, or responsible for preparing CDISC data for regulatory submissions, these tools will improve your efficiency and productivity, reduce QC efforts, and provide greater standardization.

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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