

Introducing the IVIVC Toolkit™ for WinNonlin®

Objectives for The IVIVC Toolkit

The latest version of Pharsight® WinNonlin™ nonlinear modeling software was released to introduce the optional IVIVC (In Vivo In Vitro Correlation) Toolkit™ for WinNonlin®. The IVIVC Toolkit is versioned with WinNonlin and future enhancements and bug fixes will coincide with the release of a new version of WinNonlin.

Key Features of the IVIVC Toolkit

➤ IVIVC Wizard

- The IVIVC Wizard provides an organized environment in which to build and manipulate in-vitro in-vivo correlation (IVIVC) models, plus a feature to automatically estimate the unit impulse response (UIR) for one or more profiles given an oral, IV or IR formulation. The Wizard supports setup and running of all or a subset of operations required to create an IVIVC, validate it and use it to make predictions. It provides workflow support for complete, two-stage IVIVC development. Any set of operations set up in the Wizard can be saved and reloaded as an IVIVC project (*.IVC), including the related data sets. See the WinNonlin Examples Guide for examples demonstrating a full IVIVC workflow.

IVIVC Wizard

In-Vitro | In-Vivo | **Correlation** | Prediction | Options

Correlation Model

- Fabs = AbsScale * Diss(Tscale * Tvivo)
- Fabs = AbsScale * Diss(Tscale * Tvivo - Tshift)
- Fabs = AbsScale * (Diss(Tscale * Tvivo - Tshift) - AbsBase)
- User Specified

Tcutoff
 * Diss stops increasing for Tvivo > Tcutoff

Plots

- Tivo vs. Tvitro (Levy)
- Fabs vs. Fdiss

Project Information

Project Name:

Project Status

- Specify in-vitro data
- Fit in-vitro models
- Specify in-vivo data
- Generate UIR
- Deconvolve
- Build correlation
- Validate correlation
- Prediction

Validation

AUC: Calculation Method: Averaging:

Formulation	Parameter	Predicted	Observed	% PE	Ratio
CR1 Internal	AUClast	7502.22385	7545.57500	-0.6	0.99
	Cmax	588.57213	617.75000	-4.7	0.95
CR2 External	AUClast	7076.96744	6652.73750	6.4	1.06
	Cmax	458.29968	474.17000	-3.3	0.97
CR3 Internal	AUClast	7324.32407	7935.43500	-7.7	0.92
	Cmax	625.03927	684.08000	-8.6	0.91
CR4 External	AUClast	5614.85402	5550.25500	1.2	1.01
	Cmax	414.14283	435.13000	-4.8	0.95

➤ Deconvolution

- In addition to the numerical deconvolution (deconvolution through convolution) tool available with WinNonlin, the IVIVC Toolkit makes available tools for Wagner-Nelson and Loo-Riegelman (two compartment) deconvolution methods.

➤ Convolution

- Convolution of pairs of profiles/curves is now possible in WinNonlin (with the IVIVC Toolkit). The profiles can both be either a: polyexponential function (like a pharmacokinetic disposition function) defined by coefficients and exponents; or a series of points (like an absorption profile). The convolution tool is aware of sort keys, and can perform “smart” matching of sort keys to select which profiles to convolve with one another.

➤ Levy Plots

- Levy plots enable a user to compare in vivo absorption versus in-vitro dissolution data visually, as time-versus-time plots at matched values for absorption and dissolution. The plots include a linear fit of the data points with intersection at origin, and the correlation (R2) value and the slope for the model line, as well as a line at unity. The capabilities of the Levy Plot can be extended to ANY two datasets that can be joined on a continuous variable.

