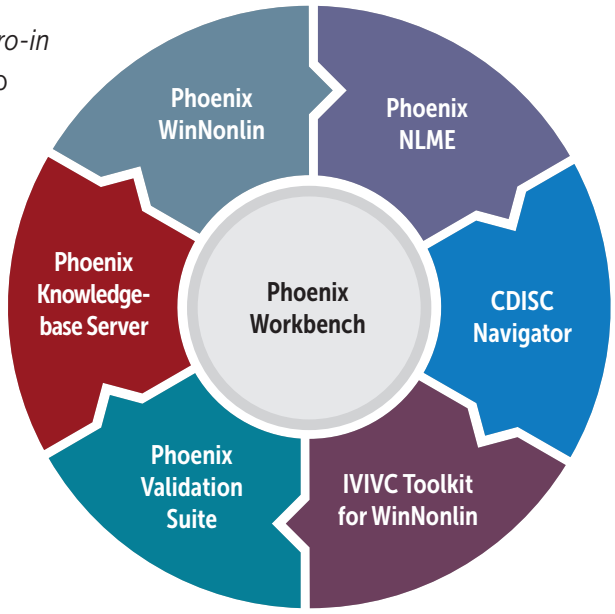
CERTARA

# Phoenix IVIVC Toolkit

## The Clear Choice in Drug Development and Formulations for Obtaining Biowaivers

*In Vitro-In Vivo* Correlation (IVIVC) is a predictive mathematical tool that describes the relationship between the *in vitro* property of a drug dosage form and an *in vivo* pharmacokinetic (PK) response. Developing IVIVCs for solid dosage forms, especially for extended release formulations, is encouraged by the US FDA[1], EMA, PMDA and other regulatory agencies. It is considered an important tool for supporting biowaivers and has become a surrogate for *in vivo* human bioequivalence (BE) studies.[2]

The Phoenix® IVIVC Toolkit™ from Certara provides enhanced tools for *in vitro-in vivo* correlation studies used by formulation and pharmaceutical scientists to improve the success of BE studies. The IVIVC Toolkit approach requires less assumptions, as compared to other methods, and helps the user define the correlation observed from real *in vivo* profiles as compared to the dissolution profiles.




### Streamline development time, standardize the process, and reduce costs of expensive bioavailability/ bioequivalence (BA/BE) studies

In most cases, a large amount of available dissolution and PK data will be used to develop and test a robust and predictive IVIVC. By using the IVIVC Toolkit, scientists can accelerate the analysis and documentation of IVIVC to support regulatory filings.

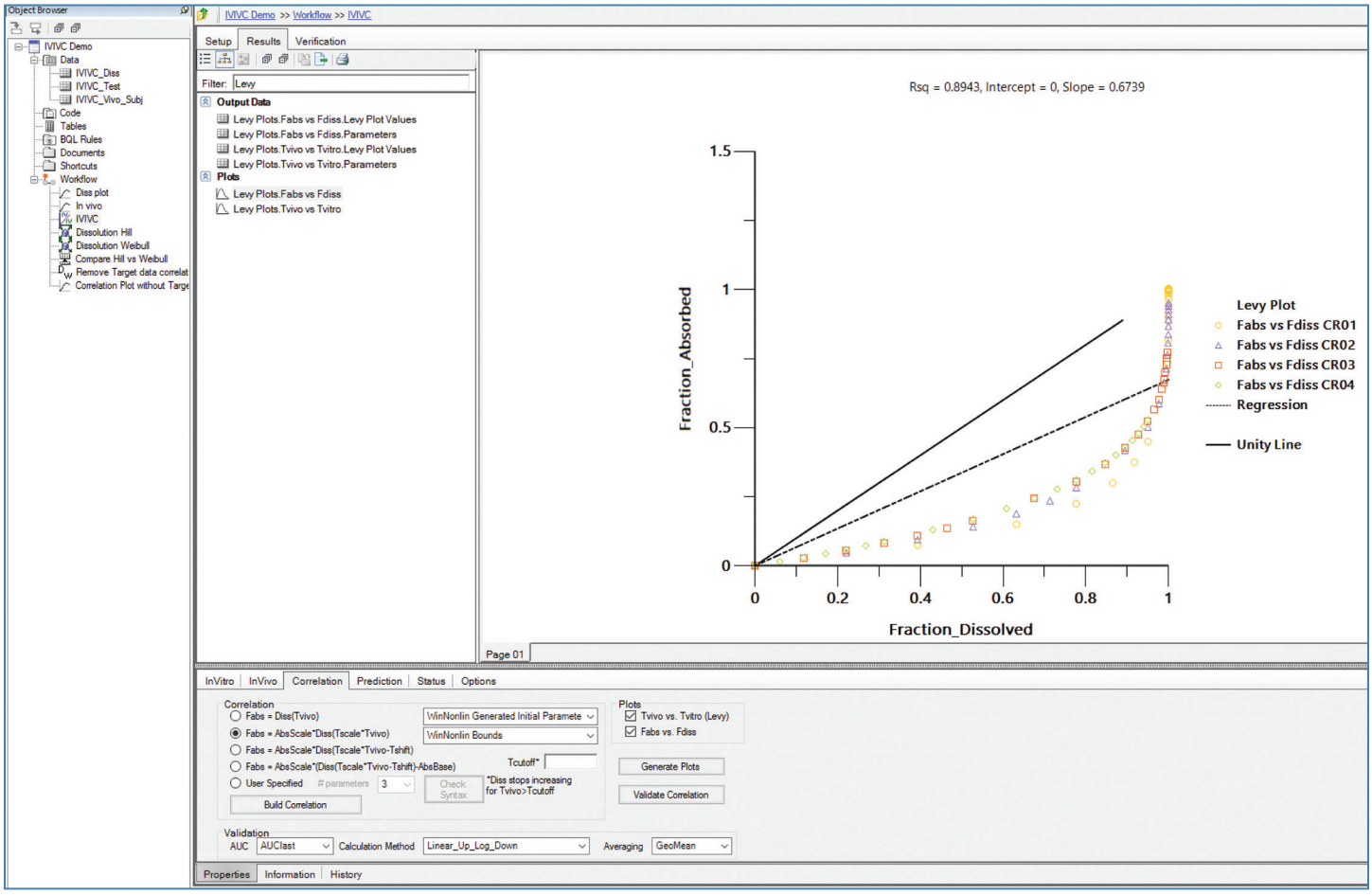
- Decreases the number of costly BA/BE studies by quickly generating IVIVC results using workflows and high quality outputs
- Organizes and simplifies the process, saving time and reducing error every time an IVIVC is needed
- Shortens the typical IVIVC development effort from weeks to days, dramatically lowering cost and bringing the drug to market quicker
- Facilitates collaborations—entire projects can be stored in a single file that can be easily shared internally or with external partners

## Standardize and simplify the IVIVC workflow: Advantages of using the IVIVC Toolkit over Microsoft® Excel®

Although Excel can be used as a manual method to generate IVIVC results, it is simply not geared to efficiently manage this highly specialized workflow. Many users of IVIVC Toolkit find they benefit from many features that Excel does not provide.

- Dialog-guided wizards and tools to streamline the IVIVC workflow processes
- Automatic estimation of Unit Impulse Response (UIR)
- Workflow support for a complete, 2-stage IVIVC with the ability to extend to a 1-stage IVIVC using the Phoenix model engine
- Levy Plots to assess time-scale of dissolution experiments
- Wide range of programmed and validated tools, including NCA, interpolation, deconvolution, convolution, PK modeling, model selection criteria (AIC), data merge and join
- History and Settings information for each workbook preserves auditability
- Access to continuing education and domain support

Example of a Levy Plot Generated in the Phoenix IVIVC Toolkit



## Phoenix IVIVC Toolkit

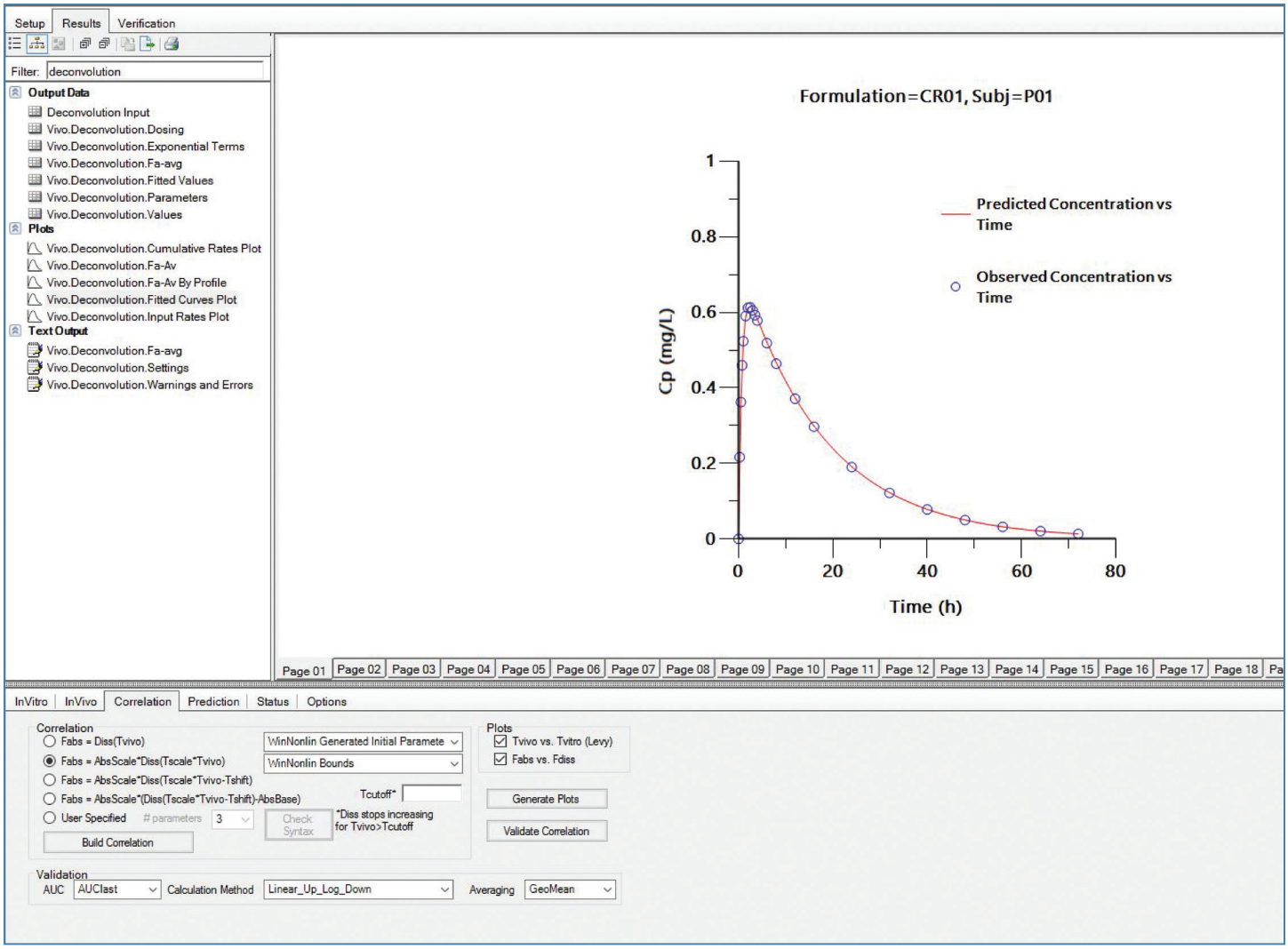
| Modeling Capabilities | Workflow Management | Reusable Workflow Templates | High Quality Outputs | Compliance and Validation |
|---|---|---|---|---|
| • Deconvolution<br>– Wagner-Nelson<br>– Loo-Riegelman<br>– Numerical<br>• Convolution<br>• IVIVC Wizard | • Visualize data flow and analysis pathways<br>• Store analysis steps and documentation in a single project<br>• Simplify QA | • Save up to 75% of time spent on routine analysis with templates<br>• Make changes without rebuilding the whole analysis project<br>• Create a corporate library of workflows and templates for standardization and training | • Create report- and publication-quality tables, listings and figures<br>• Assess the time-scale of dissolution experiments with Levy Plots<br>• Reuse favorite plots with new datasets<br>• Utilize export and overlay features | • Verification tab indicates status of object execution and errors<br>• Settings output indicates which options were selected<br>• History output shows when objects were executed<br>• Toolkit was built in accordance to software development lifecycle (SDLC) |

## The Phoenix IVIVC Toolkit is differentiated from other commercial software for *in vitro-in vivo* correlation studies

- **Affordability**—Low start-up expense and add-on costs make Phoenix IVIVC Toolkit an affordable choice
- **User Interface**—Dialog-guided tools and wizard provide unique time savings
- **Quick Learning Curve**—The easy-to-learn Phoenix interface includes examples to get users up to speed quickly
- **Navigation**—IVIVC wizard provides an easily navigable interface that walks users through the process of creating a Level A IVIVC; informative status indicators signal completion, missing information or out-of-date steps
- **Deconvolution Methods**—Numerical deconvolution is a documented method known for its stability and accuracy, and overall is less susceptible to study design variations
- **Fitting the Correlation**—IVIVC Toolkit provides Level A correlation; unlike other software packages, Level B and C can be done using regular WinNonlin
- **Custom Models**—Unlike other IVIVIC software, the Toolkit provides the flexibility to use built-in correlations or the ability to develop a custom correlation model
- **Dissolution Modeling**—Built-in models better interpolate dissolution data, resulting in accurate interpolation that can make the difference between failure and success
- **Proven Phoenix Workbench**—Trusted powerful workbench can easily handle the large amount of data that an IVIVC can generate

## Start Using the Phoenix IVIVC Toolkit Today

Contact us at sales@certara.com to find out how the comprehensive IVIVC Toolkit can be used to demonstrate virtual bioequivalence, streamline drug development and formulations, reduce costs and support attaining regulatory biowaivers.




Numerical Deconvolution Setup Tab and Outputs from the Phoenix IVIVC Toolkit

## References


1. US Department of Health and Human Services, Food and Drug Administration, and Center for Drug Evaluation and Research (CDER). Guidance for the Industry. Extended Release Oral Dosage Forms: Development, Evaluation, and Application of *In Vitro/In Vivo* Correlations. September 1997.

2. S. Suarez-Sharpe, M. Li, J. Duan, H. Shah, and P. Sen. Regulatory Experience with *In Vivo In Vitro* Correlations (IVIVC) in New Drug Applications. *The AAPS Journal* (2016). 18 (6):1379-1390.


## 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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