



## Phoenix WinNonlin® Validation Suite™

### Frequently Asked Questions (FAQ)

**Q: What is the Phoenix WinNonlin Validation Suite?**

A: The Phoenix WinNonlin Validation Suite provides objective evidence of the testing of Phoenix WinNonlin's functionality required for validation using automated test scripts accessed through a graphical user interface.

**Q: How critical is the validation of the Phoenix WinNonlin software for regulatory submissions?**

A: If you include any output from Phoenix WinNonlin in a regulatory submission, you will likely need to prove that it was generated using a validated computer system. Your company Quality Assurance policies/SOPs will determine if Phoenix WinNonlin should be validated. Many regulations and guidelines require computer system validation. For example, *21 CFR Part 11 - Electronic records, electronic signatures regulation effective 20 March 1997*: 11.10(a) - Computer systems used to create, modify, and maintain electronic records and to manage electronic signatures must be "validated to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records."

**Q: Do CROs have to validate Phoenix WinNonlin?**

A: If you include any output from Phoenix WinNonlin in a regulatory submission, you will likely need to prove that it was generated using a validated computer system, although your company's Quality Assurance policies/SOPs will determine if Phoenix WinNonlin should be validated.

Many regulations and guidelines require computer system validation. For example, *Guidance for Industry: Computerized Systems Used in Clinical Trials - effective April 1999*: VIII.B.1. - "The sponsor or contract research organization should have documentation (either original validation documents or on-site vendor audit documents) of this design level validation by the vendor, and should have itself performed functional testing (e.g., by use of test data sets) and researched known software limitations, problems, and defect corrections."

**Q: Does Pharsight validate Phoenix WinNonlin?**

A: No, as a provider of software that is used by FDA-regulated customers, Pharsight Corporation develops software products in accordance with a documented software development life cycle (SDLC). In each of the phases of this life cycle, documentation deliverables are created, including Software Requirements Specifications, Design Specifications, Test Plans, Test Cases, and Traceability Matrices. These documents serve to document the development and testing of individual software products and contain proprietary information. At the end of the SDLC, Quality Assurance approval of the Release Approval/Validation Completion form completes Pharsight's validation of the software product.

Pharsight customers use Pharsight software products in the implementation of computer systems in FDA-regulated environments. To be compliant with FDA expectations, customers must validate the computer system, of which the software is but one component, along with the hardware (servers and workstations), network and operating systems environment, interfaces with other computer systems, and policies/standard operating procedures. Validation of the computer system must occur in the user's environment and must account for the user's unique set of user and functional requirements.

**Q: Does the Phoenix WinNonlin Validation Suite do the IQ, OQ, & PQ?**

A: The terms IQ, OQ, and PQ have come under some scrutiny from FDA as can be seen in these quotes from its *General Principles of Software Validation* guidance document: "For many years, both FDA and regulated industry have attempted to understand and define software validation within the context of process validation terminology. For example, industry documents and other FDA validation guidance sometimes describe user site software validation in terms of installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ)." "While IQ/OQ/PQ terminology has served its purpose well and is one of many legitimate ways to organize software validation tasks at the user site, this terminology may not be well understood among many software professionals, and it is not used in the guidance document. However, both FDA personnel and device[software] manufacturers need to be aware of these differences in terminology as they ask for and provide information regarding software validation." The FDA's guidance document uses the term "user site testing", and that type of testing is facilitated by the Validation Suite.

**Q: How have the test data and corresponding reference results been generated; in other words, are they independent?**

A: Test data have been obtained from different sources, e.g. NIST, PK textbooks. An explanation of the sources of test data and results from independent methods is explained in a document that comes with the Validation Suite (Computational Models Validation Report). The reference files have been generated at Pharsight and verified to be numerically and technologically correct. The results that you generate in your environment will be compared to the reference files generated in Pharsight's environment.

**Q: How is the IQ performed, i.e., does the Validation Suite check if all files have been correctly installed and correct?**

A: The Validation Suite automatically compares the list of files that should be installed with the files that are actually installed on the machine to be qualified to identify any differences.

**Q: Can we access the test data to check a sample of the outcomes with, for instance, SAS?**

A: The Computational Models Validation Report included with the Validation Suite summarizes the results for comparisons of output produced by Phoenix WinNonlin to output produced by independent methods (e.g., using SAS). Also you may perform your own additional independent verification of Phoenix WinNonlin's results by comparing the output in the Validation Suite reference files with your own output.

**Q: Can customers manually spot check the output generated by Phoenix WinNonlin using the Phoenix WinNonlin Validation Suite against the reference files?**

A: Yes, all of the output generated by Phoenix WinNonlin on the machine to be qualified is placed in output files in a folder architecture that mirrors the reference files. Therefore one could easily manually compare the output results against the reference results. Also, there is a log file that contains the results of the testing, so one could also use that to see the output results and to ensure that what is exported into the Validation Run Report has not been "edited" in any way.

**Q: How much detail is provided to explain the testing of the calculations and statistics, particularly for the standard PK parameters/measurements (AUC, C/Tmax, Mean/SD, etc.)**

A: Testing of the calculations is not a part of the test cases that are executed in the Validation Suite, as this is done at Pharsight as part of the internal validation of the computational engines within Phoenix WinNonlin. The Validation Suite product includes a Computational Model Validation Report document which provides information regarding the testing of the calculations and statistics. For the testing that is summarized in this document, Phoenix WinNonlin results were compared against results obtained by an independent method (e.g., a SAS PROC).

**Q: Can I use the Validation Suite to validate Phoenix WinNonlin within Citrix?**

A: Yes, but only on the computer where Phoenix WinNonlin resides. Validation cannot be performed from a Citrix client; only on the application server where Phoenix WinNonlin is installed.

**Q: What do I do if some of the scripts fail validation?**

A: Once the Validation Suite has completed the list of test scripts the user has chosen to run, it will display a report of all of the test scripts and whether each passed or failed. A user would drill-down into any scripts that failed to discover the reason for the failure. Inside a specific failed test script, the user would be able to see all of the steps leading up to the failure and a screen shot(s) of the computer at the point of failure (e.g., an appointment reminder from Outlook popped up and prevented the Val Suite from interacting with the GUI). There are several program settings or variables that can be altered in the Validation Suite (e.g., how long should the Validation Suite wait on the computer to return an answer or refresh a screen) that could increase the likelihood of the computer passing a specific script when a script failure is due to something in the environment which is unrelated to the functionality of Phoenix WinNonlin. Once the cause of a failure is identified and resolved, the specific script or scripts that failed can be re-run with a second report generated to demonstrate the passage of the previously failed test script(s).

**Q: Is there a requirements document, or identification of the functional or user requirements in one of these template documents? Is there a link between these requirements and what is tested in the Validation Suite?**

A: A Requirements Specification template is included in the Validation Suite which can be used as a starting point for users to document their intended use of Phoenix WinNonlin in their environment. With the descriptions of the test cases included in the Validation Suite User's Guide, the user can develop traceability between required functionality and testing of that functionality by the Validation Suite. The user can then determine if any additional testing is required to satisfy the documented requirements.

**Q: To what extent do the Run Report and the Validation Summary Report templates document the testing that was done by the customer? Do they only reference the running of the Validation Suite, or is additional user testing described/included?**

A: The automated Validation Run Report summarizes the results of the automated test scripts that are executed by the Validation Suite based on the selections of the user. The Validation Summary Report document template included with the Validation Suite is a document that "closes the loop" on the validation activities defined in the Validation Plan. If the user added additional testing (i.e., testing other than that executed by the Validation Suite) in the Test Plan, then the results of those additional tests would need to be included in the Validation Summary Report.

**Q: How can I use software to validate software from the same vendor?**

A: Some in industry believe that they "can't use validation information from a vendor." However, the FDA states in their *General Principles of Software Validation* guidance document: "A [user] may conduct a validation using their own personnel or may depend upon a third party such as the equipment/software vendor or a consultant. In any case, the [user] retains the ultimate responsibility for ensuring that the software is validated."

**Q: How can I get support for the Phoenix WinNonlin Validation Suite?**

A: First, please consult the documentation provided with your software or visit [www.Pharsight.com/support](http://www.Pharsight.com/support). If further assistance is needed, contact Pharsight technical support by e-mail, customer support portal (preferred), phone, fax, or post.

- Customer Support Portal [www.Pharsight.com/support](http://www.Pharsight.com/support)
- E-mail: support@pharsight.com
- Phone/voice mail: +1-919-852-4620 (US)  
+1-919-852-4620 (EU/India)  
+81 471-74-9918 (Japan)
- Fax: +1-919-859-6871
- Post: Pharsight Corporation  
5625 Dillard Drive, Suite 205  
Cary, North Carolina 27518