



**Using WinNonlin AutoPilot for Fast and Efficient  
Creation of Tables and Graphs for PK Reporting**

**Pharsight Software Products Business Unit**

**Executive Issue Brief**

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# Using WinNonlin AutoPilot for Fast and Efficient Creation of Tables and Graphs for PK Reporting



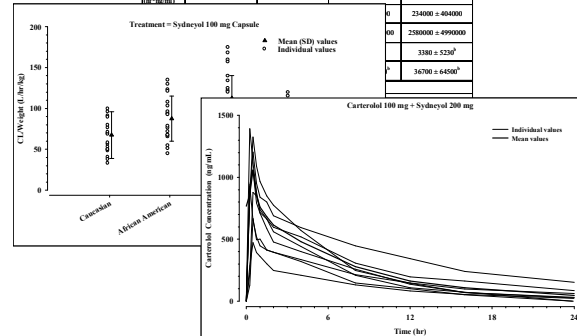
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## Introduction

Pharmacokinetics (PK) Report Automation is a technology that gives companies the means to significantly increase the productivity of their scientific staff while improving the quality and consistency of their PK analyses and reports. When the concept of PK Report Automation is applied to routine and repetitive data analyses and the creation of presentation-quality PK tables and figures, it will noticeably shorten the turn-around time for intermediate and final reports and presentations – making time available that can be used for deeper and more exploratory and in-depth analyses.

Mean ± SD	Analysis = Flynn, Cartertotal			
	Female		Male	
	Cartertotal PK Form A	Cartertotal PK Form B	Cartertotal PK Form A	Cartertotal PK Form B
N	4	4	4	4
$C_{max}$ (ng/ml)	165 ± 205	619 ± 432	668 ± 1180	1030 ± 2130
$T_{max}$ (hr)	0.44 (0.25 - 0.50)	0.63 (0.50 - 0.75)	0.52 (0.25 - 0.75)	0.66 (0.50 - 1.00)
$t_{1/2}$ (hr)	7.02 ± 2.32	4.33 ± 1.11	6.59 ± 1.59	7.39 ± 2.62
AUC <sub>0-∞</sub> (ng·hr/ml)	953 ± 1200	3020 ± 2370	3760 ± 6940	6480 ± 15200
AUC <sub>0-t</sub> (ng·hr/ml)	1040 ± 1280	3120 ± 2450	4080 ± 7450	7270 ± 14500



WinNonlin AutoPilot is a configurable PK Report Automation software product. WinNonlin®, the industry standard for Non-compartmental Analysis (NCA) and PK / PD modeling, is used to perform the NCA analyses and 3<sup>rd</sup> party tools such as SigmaPlot® and Microsoft® Word and Excel® are used to produce report-quality output for regulatory submissions and interim reports and presentations.

## Flexible PK Analysis and PK Output Generation

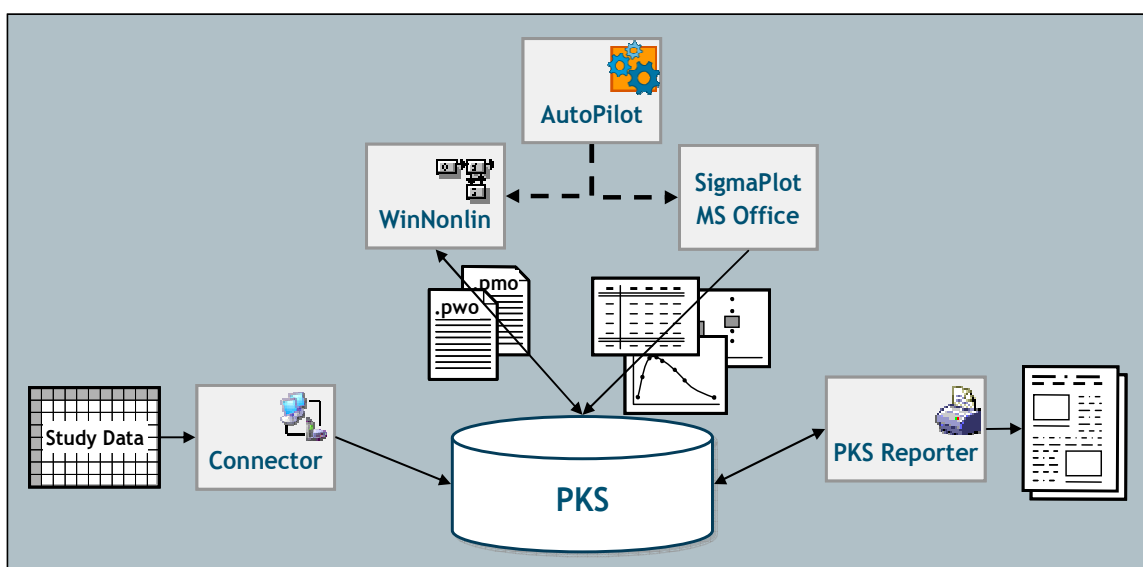
When using AutoPilot, the underlying PK analyses are executed on input study data and the associated WinNonlin model from the file system of the scientist's computer or the Pharsight Knowledgebase Server database. AutoPilot directs WinNonlin to run the analysis and uses the results to produce report-quality PK tables and figures in Microsoft Excel and SigmaPlot<sup>1</sup>. These automation runs are controlled by an easy-to-use, wizard-based user interface which allows the scientist to make the critical selections to meet the requirements of more than 90% of all non-compartmental studies for regulatory submissions. Both parallel and crossover study designs are supported along with common study design types such as

- Bioequivalence and Bioavailability

- Drug-Drug and Food-Drug interactions
- First-In Man and Dose Proportionality
- Special Populations (e.g., renal, hepatic, age)

An additional comparison module provides the ability to compare and to report on the results of previous PK automation runs. The comparison module supports comparative analyses over different dosing routes (bioavailability of IV vs. PO), different dosing regimens (accumulation of single dose versus steady-state), different matrices (calculation of renal clearance), and multiple analytes (parent vs. metabolites).

In reality, report requirements vary from study to study and there is no one-size-fits-all solution for analyses. AutoPilot meets this challenge in a very unique way by providing a flexible user interface that allows extensive configuration of formatting, nomenclature, and business rules that are applied during the execution of analyses and the creation of PK output. The system comes with pre-configured, factory default settings that will allow



users to start working right out-of-the-box. However, every company, even different groups within one company, can easily modify the default settings to efficiently implement an organization's analysis and reporting requirements via the secure administrator module. User's can select from different "System Settings" prior to starting an automation run and make sure their output will meet SOPs and other requirements.

While WinNonlin AutoPilot works off datasets and models from the local file system, there is additional benefit when building an integrated workflow that incorporates integrates Pharsight's industry-leading PK/PD data management repository, Pharsight Knowledgebase Server, and Pharsight PKS Reporter. In this integrated workflow, AutoPilot can read study data and analysis settings directly from PKS, create the desired PK output, and save the results back to PKS in compliance with the U.S. Food and Drug Administration's Electronic Records and Signatures regulation, 21 CFR Part 11. In the next step, PKS Reporter can be used to extract AutoPilot output from PKS to populate the client's own Microsoft Word report templates. This will enable automatic and seamless report updates and secure review and approval of final reports with electronic signatures.

### **Making the Case for PK Automation: "More, faster, better"**

From using AutoPilot, a company can realize benefits in productivity, speed, and quality. AutoPilot enables capturing and implementing best practices and business rules within one department or across organizations to achieve immediate improvements such as:

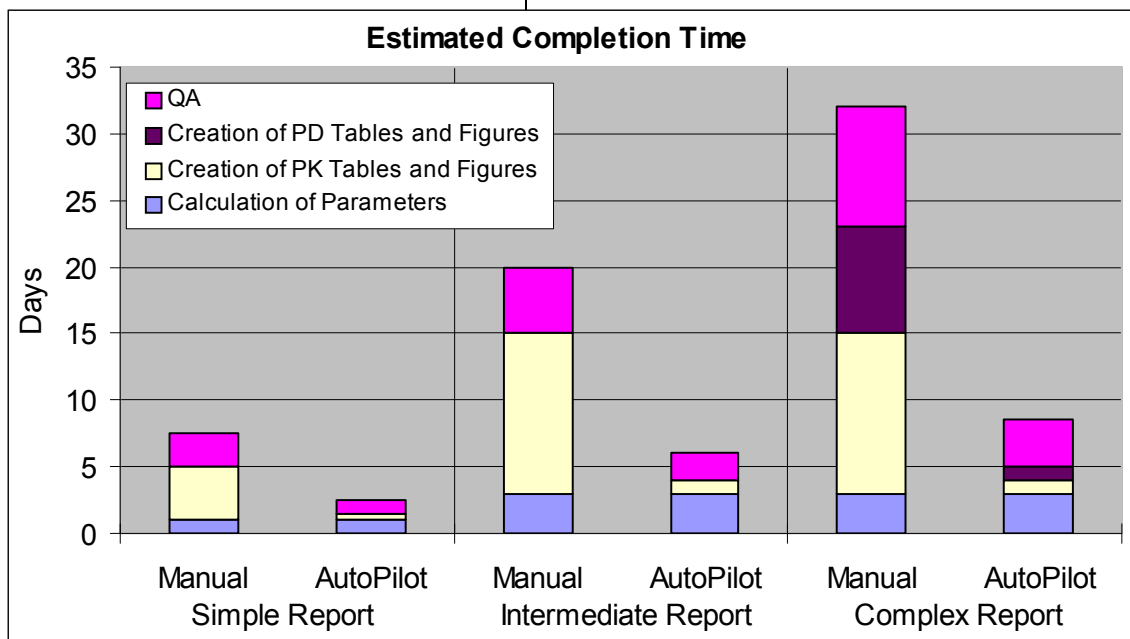
- Increased number of completed PK reports
- Reduced report cycle time (defined as average time to report completion)
- Standardized content and formatting of PK content leading to reduced authoring and review effort and improved consistency and quality of final and intermediate reports and presentations.

On a different level, PK Automation – integrated in a company's workflow – will enable strategic advantages by making the organization more responsive and allow for higher quality results. Benefits include decreasing reporting backlogs and avoiding submission delays and an increased ability to respond to requests for additional interim analyses. Freeing up valuable PK scientists' time to work on trial simulation, population PK modeling, model-based drug profile exploration, or similar complex tasks, instead of focusing them on routine analyses and output creation, can significantly improve the overall drug development process – consistent with proposals in the FDA's Critical Path Initiative. Using AutoPilot can reduce the reliance on outsourcing work to contract research organizations, which directly leads to cost savings.

Pharsight's internal Reporting and Analysis Services Group completed an internal study to estimate the potential savings through the use of PK Automation before implementing AutoPilot. They estimated the time savings from WinNonlin AutoPilot using a parallel study with 5 dose levels and 12 patients per dose level as an example. To estimate the potential savings through using AutoPilot they assumed three different study report types as follows:

- profiles on linear and semi-log arithmetic scale are created.
- An intermediate study report, adding urine analysis to the picture. Obviously, this will add the typical urine PK Parameter tables and urine concentration time profiles to the output that needs to be reported.
- A more complex study report, adding a non-compartmental PD analysis on Absolute Neutrophil Count and a biomarker to the report.

The graph shows the estimated number of days for completion of these reports with and without using AutoPilot to create the PK tables and figures. It



- A simple study report, assuming a WinNonlin non-compartmental analysis of the parent drug and one metabolite in plasma. In tables, nine typical parameters together with standard summary statistics by dose levels are reported. Figures of individual and mean concentration time

clearly shows the time saving using PK Automation compared to creating the PK output manually. With this type of study and the various study reports, time savings are expected to be around 70% with increased savings for more complex study reports.

## Conclusion

WinNonlin AutoPilot provides the infrastructure and tools to manage and effectively automate common or repetitive PK analyses and the creation of the required tables and figures for reports and presentations. Customer defined configurations – including formatting and business rules applied to analyses and to generated output – allow companies to clearly communicate and apply standards for content and layout of PK reports across the organization.

Used in a PKS environment with PKS Reporter, WinNonlin AutoPilot provides standardized, regulatory-compliant, secure, and automated generation of reports, enabling PKS Reporter to pick-up the generated output with automatic report updates and secure review and approval processes.

With or without PKS, WinNonlin AutoPilot can provide significant return on investment through productivity and quality improvements in PK analyses and reporting. Benchmarks show that time savings of around 70% per study report can be expected, with increased benefits for more complex reports.

For additional resources, please visit Pharsight's Website at <http://www.pharsight.com>.

## References:

1. Sample Output generated by WinNonlin® AutoPilot™  
[http://www.pharsight.com/library/AP\\_Sample\\_OUTPUT.pdf](http://www.pharsight.com/library/AP_Sample_OUTPUT.pdf)