

Phoenix WinNonlin[®] User's Guide

Applies to: Phoenix WinNonlin 8.1



Phoenix WinNonlin Version 8.1

Phoenix® WinNonlin®, Phoenix NLMETM, IVIVC ToolkitTM, CDISC® Navigator, AutoPilot ToolkitTM, Job Management SystemTM (JMSTM), Pharsight Knowledgebase ServerTM (PKSTM), Trial SimulatorTM, Validation SuiteTM copyright ©2005-2018, Certara, L.P. All rights reserved. This software and the accompanying documentation are owned by Certara, L.P. The software and the accompanying documentation may be used only as authorized in the license agreement controlling such use. No part of this software or the accompanying documentation may be reproduced, transmitted, or translated, in any form or by any means, electronic, mechanical, manual, optical, or otherwise, except as expressly provided by the license agreement or with the prior written permission of Certara, L.P.

This product may contain the following software that is provided to Certara, L.P. under license: Formula One® copyright 1993-2018 Open-Text Corporation. All rights reserved. Microsoft® .NET Framework copyright 2018 Microsoft Corporation. All rights reserved. Tab Pro ActiveX 2.0.0.45 copyright 1996-2018, GrapeCity, Inc. All rights reserved. Sentinel™ RMS 8.4.0.900 copyright 2006-2018 Gemalto NV. All rights reserved. Microsoft XML Parser version 3.0 copyright 1998-2018 Microsoft Corporation. All rights reserved. Websites Screenshot DLL 1.6 copyright 2008-2018 WebsitesScreenshot.com. All rights reserved. Certara, L.P. has agreement to use and redistribute licenses for the following software: Syncfusion Essential Studio Enterprise 15.4.0.17 copyright 2001-2018 Syncfusion Inc. All rights reserved. Minimal Gnu for Windows (MinGW, http://mingw.org/), copyright 2004-2018 Free Software Foundation, Inc. This product may also contain the following royalty free software: DotNetbar 1.0.0.24030 (with custom code changes) copyright 1996-2018 DevComponents LLC. All rights reserved. Xceed zip Library 2.0.116.0 copyright 1994-2018 Xceed Software Inc. All rights reserved. IMSL® copyright 2018 Rogue Wave Software, Inc. All rights reserved.

Information in the documentation is subject to change without notice and does not represent a commitment on the part of Certara, L.P. The documentation contains information proprietary to Certara, L.P. and is for use by its affiliates' and designates' customers only. Use of the information contained in the documentation for any purpose other than that for which it is intended is not authorized. None of Certara, L.P., nor any of the contributors to this document makes any representation or warranty, nor shall any warranty be implied, as to the completeness, accuracy, or usefulness of the information contained in this document, nor do they assume any responsibility for liability or damage of any kind which may result from the use of such information.

Destination Control Statement

All technical data contained in the documentation are subject to the export control laws of the United States of America. Disclosure to nationals of other countries may violate such laws. It is the reader's responsibility to determine the applicable regulations and to comply with them.

United States Government Rights

This software and accompanying documentation constitute "commercial computer software" and "commercial computer software documentation" as such terms are used in 48 CFR 12.212 (Sept. 1995). United States Government end users acquire the Software under the following terms: (i) for acquisition by or on behalf of civilian agencies, consistent with the policy set forth in 48 CFR 12.212 (Sept. 1995); or (ii) for acquisition by or on behalf of units of the Department of Defense, consistent with the policies set forth in 48 CFR 227.7202-1 (June 1995) and 227.7202-3 (June 1995). The manufacturer is Certara, L.P., 100 Overlook Center, Suite 101, Princeton, New Jersey, 08540.

Trademarks

AutoPilot Toolkit, IVIVC Toolkit, Job Management System, JMS, NLME, Pharsight Knowledgebase Server, PKS, Phoenix, Trial Simulator, Validation Suite, WinNonlin are trademarks or registered trademarks of Certara, L.P. NONMEM is a registered trademark of ICON Development Solutions. S-PLUS is a registered trademark of Insightful Corporation. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc. in the USA and other countries. Sentinel RMS is a trademark of Gemalto NV. Microsoft, MS, .NET, SQL Server Compact Edition, the Internet Explorer logo, the Office logo, Microsoft Word, Microsoft Excel, Microsoft PowerPoint®, Windows, the Windows logo, the Windows Start logo, and the XL design (the Microsoft Excel logo) are trademarks or registered trademarks of Microsoft Corporation. Pentium 4 and Core 2 are trademarks or registered trademarks of Intel Corporation. Adobe, Acrobat, Acrobat Reader, and the Adobe PDF logo are registered trademarks of Adobe Systems Incorporated. All other brand or product names mentioned in this documentation are trademarks or registered trademarks of their respective companies or organizations.

Additional third party software acknowledgements

Software for Locally-Weighted Regression

The authors of this software are Cleveland, Grosse, and Shyu. Copyright © 1989, 1992 by AT&T. Permission to use, copy, modify, and distribute this software for any purpose without fee is hereby granted, provided that this entire notice is included in all copies of any software which is or includes a copy or modification of this software and in all copies of the supporting documentation for such software.

This software is being provided "as is", without any express or implied warranty. In particular, neither the authors nor AT&T make any representation or warranty or any kind concerning the merchantability of this software or its fitness for any particular purpose.

LAPACK

Copyright $\ensuremath{\mathbb{C}}$ 1992-2007 The University of Tennessee. All rights reserved.

Redistribution and use in source and binary forms, with or without modification, are permitted provided that the following conditions are met:

Redistributions of source code must retain the above copyright notice, this list of conditions and the following disclaimer.

Redistributions in binary form must reproduce the above copyright notice, this list of conditions and the following disclaimer listed in this license in the documentation and/or other materials provided with the distribution.

Neither the name of the copyright holders nor the names of its contributors may be used to endorse or promote products derived from this software without specific prior written permission.



This software is provided by the copyright holders and contributors "as is" and any express or implied warranties, including, but not limited to, the implied warranties of merchantability and fitness for a particular purpose are disclaimed. In no event shall the copyright owner or contributors be liable for any direct, indirect, incidental, special, exemplary, or consequential damages (including, but not limited to, procurement of substitute goods or services; loss of use, data, or profits; or business interruption) however caused and on any theory of liability, whether in contract, strict liability, or tort (including negligence or otherwise) arising in any way out of the use of this software, even if advised of the possibility of such damage.

NLog

Copyright © 2004-2006 Jaroslaw Kowalski < jaak@jkowalski.net>. All rights reserved.

Redistribution and use in source and binary forms, with or without modification, are permitted provided that the following conditions are met:

Redistributions of source code must retain the above copyright notice, this list of conditions and the following disclaimer.

Redistributions in binary form must reproduce the above copyright notice, this list of conditions and the following disclaimer in the documentation and/or other materials provided with the distribution.

Neither the name of Jaroslaw Kowalski nor the names of its contributors may be used to endorse or promote products derived from this software without specific prior written permission.

This software is provided by the copyright holders and contributors "as is" and any express or implied warranties, including, but not limited to, the implied warranties of merchantability and fitness for a particular purpose are disclaimed. In no event shall the copyright owner or contributors be liable for any direct, indirect, incidental, special, exemplary, or consequential damages (including, but not limited to, procurement of substitute goods or services; loss of use, data, or profits; or business interruption) however caused and on any theory of liability, whether in contract, strict liability, or tort (including negligence or otherwise) arising in any way out of the use of this software, even if advised of the possibility of such damage.



Certara, L.P. 100 Overlook Center, Suite 101, Princeton, NJ, 08540 USA Telephone: +1.609.716.7900 www.certara.com



Contents

	List of Figures	XV
	List of Tables	xx
Chapter 1	Introduction	25
	The Phoenix platform	25
	Certara contact information	26
Chapter 2	Noncompartmental Analysis	27
	Object user interface	
	Main Mappings panel	
	Dosing panel	
	Slopes Selector panel	
	Slopes panel	
	Partial Areas panel	
	Therapeutic Response panel	34
	Units panel	35
	Parameter Names panel	36
	Options tab	
	User Defined Parameters tab	
	Rules tab	41
	Plots tab	42
	Results	42
	Worksheet output	42
	Plot output	43
	NCA computations	44
	Time deviations in steady-state data	
	Data checking and pre-treatment	44
	Lambda Z or slope estimation settings	
	Lambda Z or slope range selection	46
	Calculation of Lambda Z	47
	Calculation of slopes for effect data	47
	Limitations of Lambda Z and slope estimation	
	Partial areas	
	Therapeutic response	
	Therapeutic response windows	
	* *	



DOCKET

Explore Litigation Insights



Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time** alerts and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.

