

WinNonlin[®]

Getting Started Guide

WinNonlin® Version 4.1

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Installation

System requirements

WinNonlin Professional

The following system configuration is needed for WinNonlin[®] Professional.

Table 1-1. System requirements for WinNonlin Professional

Item	Minimum	Recommended
System software	Windows 98, 2000, XP or NT with service pack 3 or later, or Citrix MetaFrame XP	Windows 2000
Browser (to view online help)	Microsoft Internet Explorer 5.0 or higher	
Processor	Pentium 133 MHz	Pentium 350 MHz or faster
RAM	32 MB	64 MB
Hard disk space: system drive ^a	70 MB	
Hard disk space: installation drive ^b	60 MB	
Graphics		SVGA

a. Hard drive on which the operating system is loaded, typically the C drive.

b. Hard drive onto which WinNonlin will be installed.

Note: Installation on Windows NT or Windows 2000 requires administrator rights.

WinNonlin Enterprise with PKS

WinNonlin Enterprise can serve as a client interface for the Pharsight Knowledgebase Server™ (PKS). This functionality requires a faster processor and more memory than are needed to run WinNonlin without PKS.

The following system configuration is recommended to use WinNonlin Enterprise with PKS.

Table 1-2. System requirements for WinNonlin Enterprise with PKS

Item	Minimum	Recommended
System software	Windows 98, 2000, XP or NT with service pack 3 or later, or Citrix MetaFrame XP	Windows 2000
Browser (to view online help)	Microsoft Internet Explorer 5.0 or higher	Internet Explorer 6.0 or higher
Processor	Pentium III 500MHz	Pentium III 700MHz
RAM	128 MB	192 MB
Hard disk space: system drive ^a	70 MB	
Hard disk space: installation drive ^b	60 MB	
Graphics		SVGA

a. Hard drive on which the operating system is loaded, typically the C drive.

b. Hard drive onto which WinNonlin will be installed.

Installing WinNonlin

WinNonlin installation requires read/write access to: 1. the Windows system directory; 2. the installation directory, and 3. the directory in which WinNonlin stores common files (C:\PROGRAM FILES\COMMON FILES\PHARSIGHT). The files in items 1 and 3 above are used internally by the application.

Note: Installation instructions for the Pharsight Knowledgebase Server appear separately, in the *PKS System Administrator's Guide*.

Pharsight common files

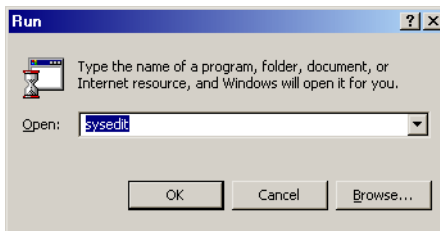
Installing WinNonlin on a machine that has WinNonMix[®] or Trial Simulator installed may update some common files, shared between products. The other Pharsight products will continue to operate correctly.

Temporary files directory

It is possible to specify the location to which WinNonlin will store temporary files. This is done by setting the TMP and TEMP environment variables in the Windows operating system. The WinNonlin user must have read/write access to the temporary file location(s). Changing this setting requires administrative rights on the machine.

To set the temporary files directory on Windows 98:

1. In the Windows **Start** menu, choose **Run...**
2. Run the System Configuration Editor as follows:



- a. Type `sysedit` in the Open field.
 - b. Click **OK**.
3. Add the temporary directory definition to the file AUTOEXEC.BAT. For example, to set the temporary directory to C:\TEMP:
 - a. In the autoexec.bat window, enter the text:

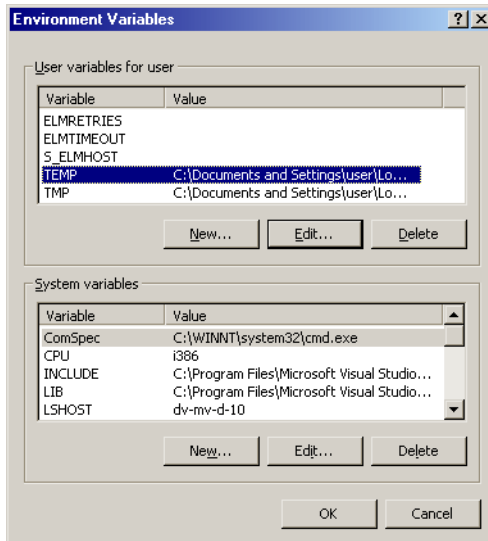
```
SET TMP=C:\TEMP
```

```
SET TEMP=C:\TEMP
```

- b. Save the file and exit the System Configuration Editor, by choosing **File>Save**, then **File>Exit** in the menus.

To set the temporary files directory on Windows NT or Windows 2000:

1. In the Windows **Start** menu, choose **Settings>Control Panel**.
2. Open the **System** control panel, **Advanced** tab.
3. Click on the **Environment Variables** button to open the following dialog.



4. Use the upper **Edit** button to set the variables *TMP* and *TEMP* in the User Variables list box. Set both to point to the desired temporary files directory. Make sure that the directory path exists on the machine.

Note: This action changes the temporary files directory for all applications on the system.

Updating WinNonlin

If a prior version of WinNonlin has been installed on the machine, the installation wizard will identify and uninstall it. If WinNonlin 3.1 or earlier exists on the machine, it may be necessary to manually uninstall it.

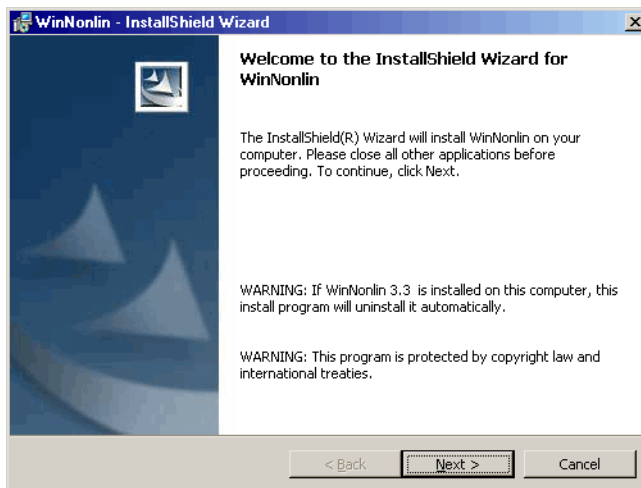
The installation procedure

To install WinNonlin:

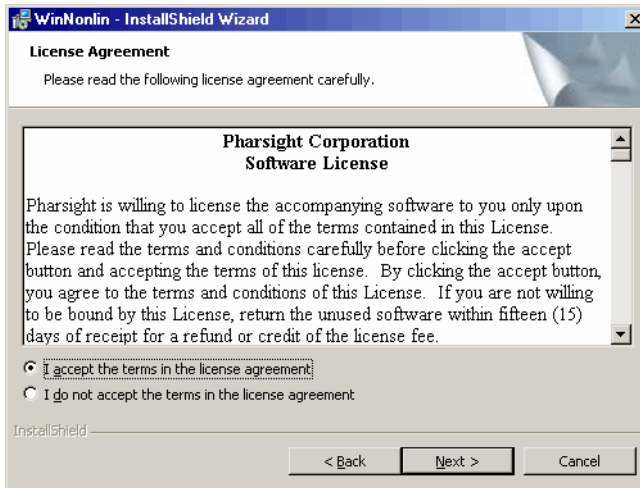
1. Close all Windows applications.
2. If an anti-virus program is running on the machine, turn it off before installing WinNonlin. Anti-virus programs can severely degrade installation performance. If the WinNonlin CD must be checked for viruses, run the virus scanning software on the CD (being sure to scan all compressed files) before installing the application.
3. Insert the WinNonlin CD into the machine's CD-ROM drive.
4. If the Installation Wizard does not start automatically:
 - a. From the Windows **Start** menu select **Run**.
 - b. In the Run dialog box, type `d:\setup`, where d is the letter assigned to the CD-ROM drive, and click **OK**.
5. The software will scan the machine for a previous installation of WinNonlin. If one is located, step through the un-installation process, and click the **Finish** button when it completes. Any previously-installed license will be saved to be applied to the new version. Re-launch the installer (step 4 above) to proceed.

Note: It may be necessary to manually uninstall WinNonlin versions prior to 3.1.

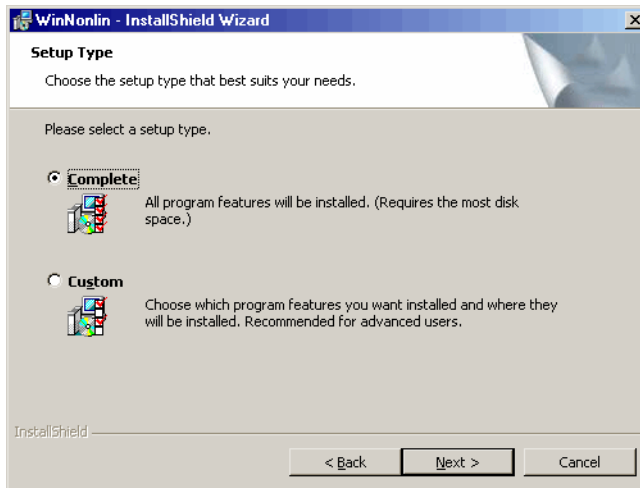
6. The InstallShield Wizard for WinNonlin will appear.



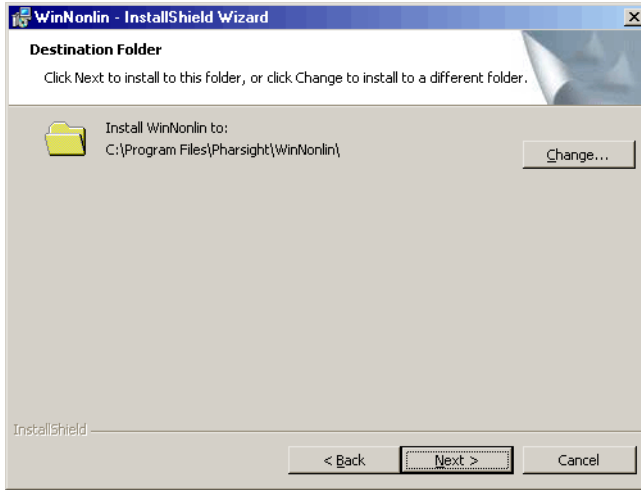
7. Click **Next** to proceed to the license agreement.



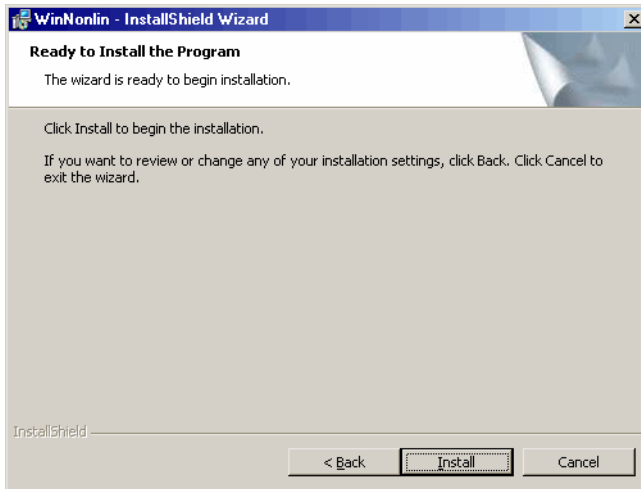
8. Read the agreement. To accept its terms and proceed with the installation, select **I accept the terms of the license agreement** and click **Next**. Else, please contact Pharsight's sales department at sales@pharsight.com.



9. Both Complete and Custom installations will install the WinNonlin software, Pharsight Licensing Manager, and WinNonlin user documentation and example files. The Custom install will indicate the disk space required: approximately 40 MB.



10. Click **Next** to proceed with the installation. Use the **Change...** button in this dialog to set the directory to contain the WinNonlin program files.
11. Click **Next**.



12. Click **Install** to load the following content:

Table 1-3. WinNonlin installation content

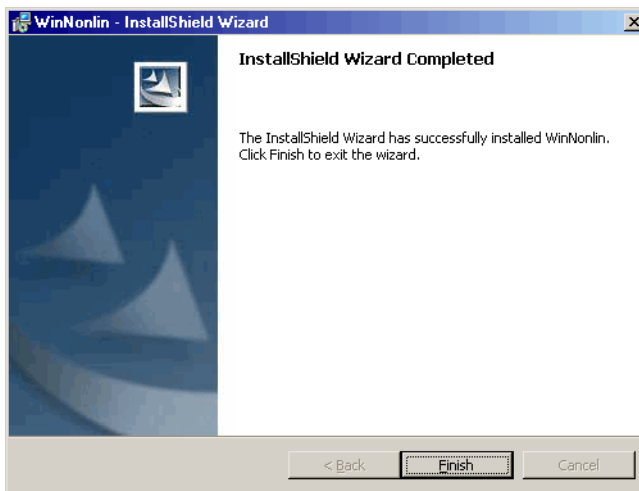
Description	Default location
WinNonlin software and online help	C:\Program Files\Pharsight\WinNonlin

Table 1-3. WinNonlin installation content

Description	Default location
Pharsight License Wizard	C:\Program Files\Pharsight\WinNonlin
Example data files	C:\Program Files\Pharsight\WinNonlin\Examples
User manuals	C:\Program Files\Pharsight\WinNonlin\WNL4.1 User Docs

Note: Network Administrators and Information Technology personnel may contact Pharsight Customer Support (support@pharsight.com) for a complete list of files that are installed with WinNonlin 4.1, and their default locations.

The InstallShield Wizard will reappear when the installation is complete.



13. Click **Finish** to exit the wizard.
14. WinNonlin includes a 30-day license. Installation of an annual license is required for WinNonlin to continue running after the trial license expires:
 - a. If a current license from a prior WinNonlin installation exists on the machine, no action is required. The Install Wizard will automatically load the previous license for use with the new version of WinNonlin.
 - b. If the installation is new, or the prior license has expired, follow the instructions in [Chapter 2](#) to install or update the product license.

CAUTION: The WinNonlin CD jewel case contains the product ID number and license key code. These numbers are required for installing a license, purchasing renewals or upgrades, and obtaining customer support. Store the CD and jewel case in a safe place.

Licensing

Installation and renewal of WinNonlin software licenses

The license key code and product tracking ID

WinNonlin requires installation of a current annual license key code. There are two types of license key codes:

1. A *node license key code* activates the software on the machine on which it is installed. The license agreement restricts installation of the software and license to a single personal computer (PC) per node license.
2. A *floating license key code* enables multiple PC's in a networked environment to run the product using a shared pool of software licenses. The number of simultaneous users is limited to the total number of licenses on the license server.

One license key code and one product tracking ID are included with each license or set of licenses purchased. For mail shipments, the key code and product tracking ID are located on the packing slip shipped with the software, and on the product's CD jewel case. The packing slip indicates the type of license purchased. For electronic license renewals, the key code, product tracking ID and license type are sent by e-mail.

Please include the product tracking ID in all correspondence with Pharsight Corporation about the product and its license, including license renewals, software updates and product upgrades.

Existing license key codes

The WinNonlin installation program will search for any previously-installed WinNonlin license key code. If a current key code is located, the installation will automatically set it up for use with the updated WinNonlin software.

Installing a node license key code

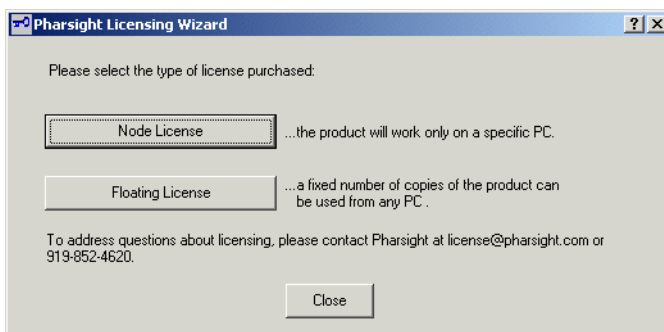
WinNonlin must be installed before the license key code can be installed. See “Installing WinNonlin” on page 2.

The same procedure is used to install a new license or renew an existing one.

To install a node license:

1. From the Windows **Start** menu, select **Programs>Pharsight>WinNonlin 4.1>Pharsight License Wizard**.

This opens the Pharsight Licensing Wizard.



2. Choose the **Node License** button. This opens the following dialog. Any previously-installed WinNonlin license key code will be detected and pre-filled in the License Key Code field.

Pharsight Licensing Wizard

Install Node License

Follow the steps below to install or update a Pharsight product node license key code.

1. Type or paste in the Product Tracking ID, included with your product shipment or license renewal e-mail. This number will be needed for all correspondence with Pharsight regarding this product license.
Product Tracking ID:
2. Please enter the following user contact information (optional).
User Name: Department:
Company: E-mail:
Title: Phone:
3. Type or paste in the license key. The license key was included with your product shipment or sent by Pharsight via e-mail.
License Key Code:
4. Click this button to install the license key.
5. The information entered above will be saved to a file called lservrc, located in the directory containing your Pharsight software. To expedite requests for license renewals, upgrades, or additions, include the lservrc file in e-mail to Pharsight at license@pharsight.com.

<< Back Exit

3. Enter the Product Tracking ID, which was included with the WinNonlin shipment or license renewal e-mail.

Note: The product tracking ID will be needed for future correspondence with Pharsight regarding the software or license. To view it, re-open the Pharsight Licensing Wizard. Alternately, e-mail the license file, LSERVRC in the WinNonlin installation directory, with the service request to support@pharsight.com for technical support or to sales@pharsight.com for license renewals or product upgrades.

4. Enter the user information (optional). This information will be saved in the license key file, LSERVRC, which you may use to provide Pharsight with contact and license information for license renewals and customer support.
5. Enter the license key code. This number was included with your product shipment or license renewal e-mail.
6. Click the **Install License Key** button to save the information to the license key file and install the license.
7. Click **Exit** to close the Pharsight Licensing Wizard. It is now possible to run WinNonlin for the term of the license.

Installing a floating license key code

The Pharsight Floating License Server software must be installed on the server machine before the floating license can be installed and activated on each client machine.

Note: Contact Pharsight Customer Support for suggestions on automated deployment of network (floating) versions of Pharsight software.

To install the floating license server:

1. On the server machine, run the file: \PHARSIGHT FLOATING NETWORK LICENSE SERVER\SETUP.EXE from the WinNonlin CD.
2. Follow the instructions in the installation wizard.

Note: The License Server must be installed in the process space of the intended server machine; that is, it must be installed while operating on the server machine itself, and not via a mapped drive on a client machine.

To install a floating license:

1. Open the Windows **Start** menu on the network server and choose **Programs>Pharsight>Pharsight Floating License Server>Pharsight License Wizard for Server**.

This opens the Pharsight License Wizard for Server dialog, shown below.

Pharsight License Wizard for Server

Install Floating License(s)

Follow the steps below to install or update a Pharsight product floating license key code.

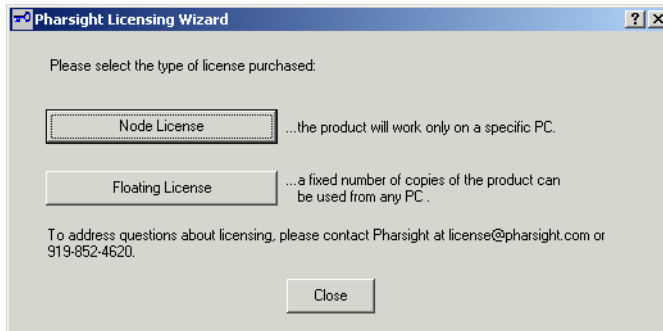
1. Type or paste in the Product Tracking ID, included with your product shipment or license renewal e-mail. This number will be needed for all correspondence with Pharsight regarding this product license.
Product Tracking ID:
2. Please enter the following user contact information (optional).
User Name: Department:
Company: E-mail:
Title: Phone:
3. Type or paste in the license key. The license key was included with your product shipment or sent by Pharsight via e-mail.
License Key Code:
4. Click this button to install the license key.
5. The information entered above will be saved to a file called lserverc, located in the directory containing your Pharsight software. To expedite requests for license renewals, upgrades, or additions, include the lserverc file in e-mail to Pharsight at license@pharsight.com.
6. Install the software on each client machine. For each client, run the License Manager and use the Floating License option to enable the client to access the floating license server.

2. Enter the Product Tracking ID, which was included with your WinNonlin shipment or license renewal e-mail. Refer to this number in all correspondences with Pharsight about this product license.

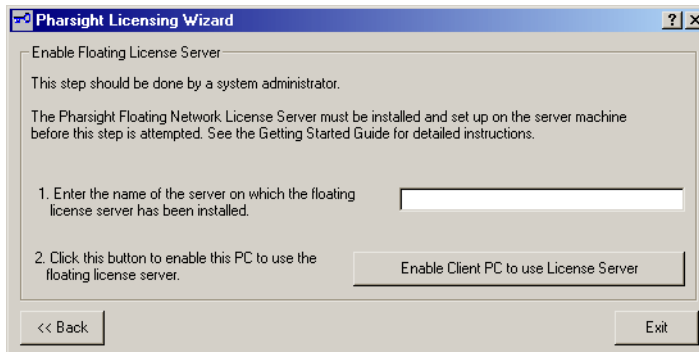
Note: To locate the Product Tracking number after installation, re-open the Pharsight Licensing Wizard; alternately, e-mail the license server file, LSERVERC in the WinNonlin installation directory, to license@pharsight.com.

3. Enter the contact information, if desired. This information will be saved in the license key file, which you may use to provide Pharsight with contact and license information for license renewals and customer support.
4. Enter the license key code, included with your product shipment or license renewal e-mail.
5. Click the **Install License Key** button to save the information to the license key file and install the license. Click **OK** in the confirmatory dialog.
6. Click the **Exit** button to close the wizard.
7. On each client machine, install WinNonlin following the instructions under “Installing WinNonlin” on page 2, then set up the licensing as follows.

8. From the client machine's Windows **Start** menu, choose **Program Files>Pharsight>WinNonlin>Pharsight License Wizard**.



9. Click the **Floating License** button. The Wizard opens a new dialog requesting the name of the license server.



10. Enter the name of the network server on which the Pharsight Floating Network License Server has been installed.
11. Click **Enable client PC to use License Server**.
12. A message appears confirming installation of the license code. Click **OK**.
13. Click **Exit** to exit the Licensing Wizard. Repeat steps 7-12 above for each client machine on the network.

Renewing a floating license key code

To renew a floating license, enter the new license key code and product tracking ID on the network license server using the Pharsight Floating License Wizard for Server. No changes are necessary on the client machines.

Testing the Installation

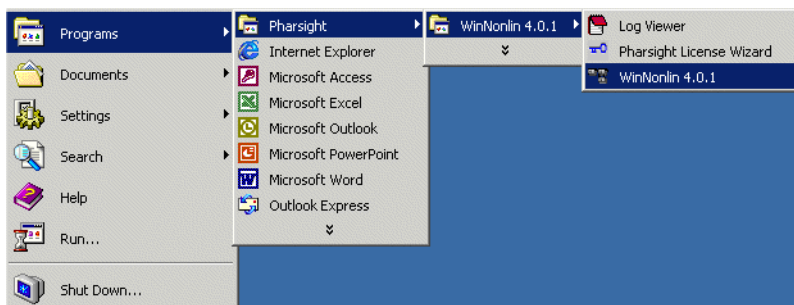
Confirming proper installation of the main WinNonlin functions

Instructions follow to test the installation of WinNonlin using a number of the sample files provided with the software. This is not intended as a full validation of the product. It is intended to test for proper installation of major components of the application. A complete validation kit is available from Pharsight Corporation. Contact the Pharsight sales department for more information.

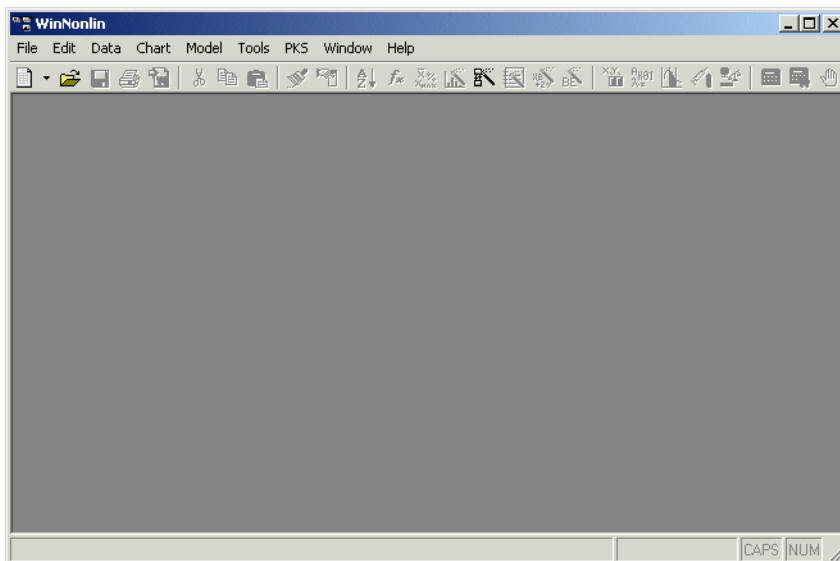
File and window operations

To start WinNonlin:

1. From the Windows **Start** button, choose **Program Files>Pharsight>WinNonlin 4.1>WinNonlin 4.1**. (Path may differ, depending on install location.)



The WinNonlin parent window appears with no file open.

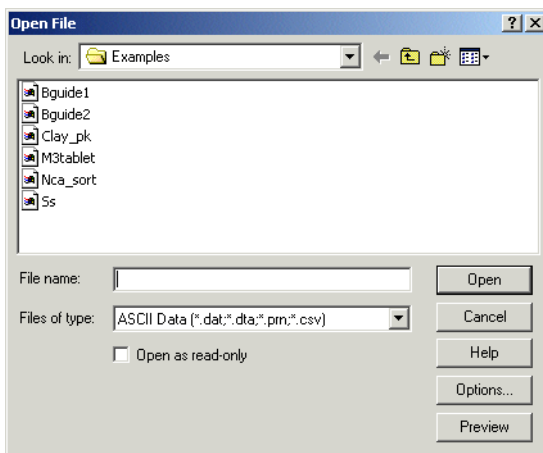


Loading a file

To open a sample file:

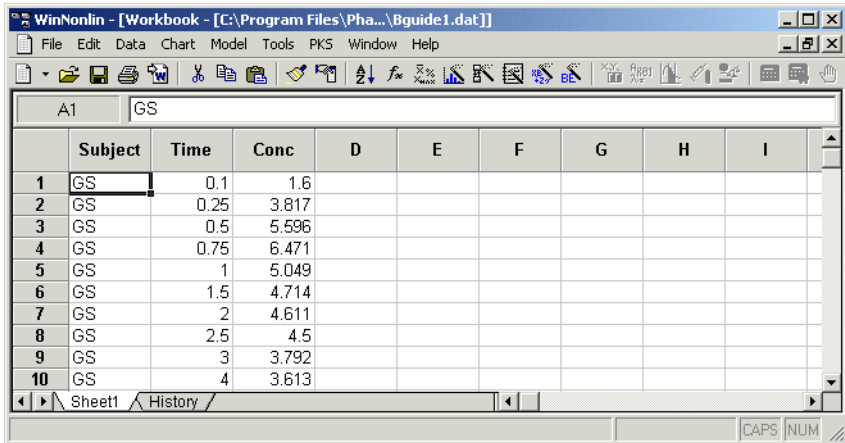


1. Click the **Open** toolbar button, or choose **File>Open** from the WinNonlin menus. The Open File dialog appears.



2. Select **ASCII Data (*.dat, *.dta, *.prn, *.csv)** as the file type.
3. Navigate to the **EXAMPLES** directory inside the **WINNONLIN** install directory.

4. Double-click **BGUIDE1.DAT** in the list of files. The file opens in a workbook window, in the WinNonlin parent window.



The screenshot shows the WinNonlin software interface with a spreadsheet window open. The spreadsheet has the following data:

	Subject	Time	Conc	D	E	F	G	H	I
1	GS	0.1	1.6						
2	GS	0.25	3.817						
3	GS	0.5	5.596						
4	GS	0.75	6.471						
5	GS	1	5.049						
6	GS	1.5	4.714						
7	GS	2	4.611						
8	GS	2.5	4.5						
9	GS	3	3.792						
10	GS	4	3.613						

BGUIDE1.DAT will be used to test key WinNonlin functions.

Creating a chart

To create a chart:

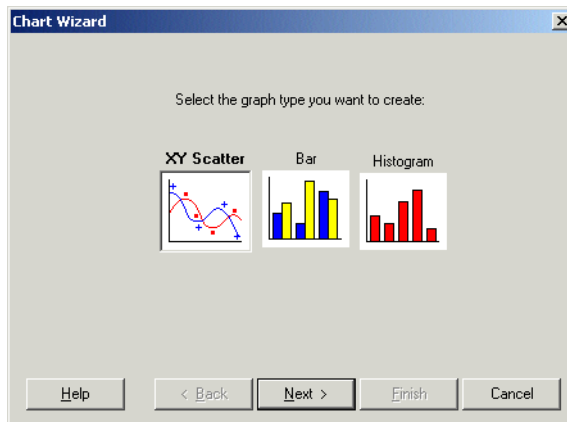


1. Click the **Chart Wizard** toolbar button.

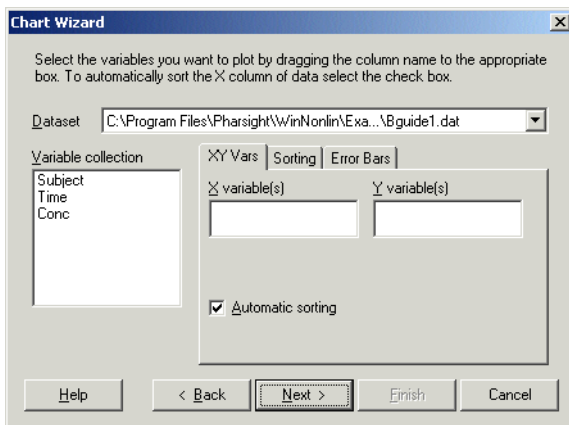
or

Choose **Tools>Chart Wizard** from the **WinNonlin** menus.

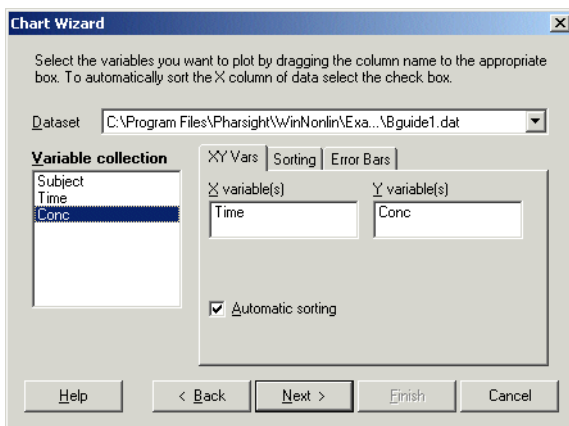
The Chart Wizard appears.



2. Select **XY Scatter** as the graph type and click **Next**. A second dialog appears showing the variables in the BGuide1 dataset.

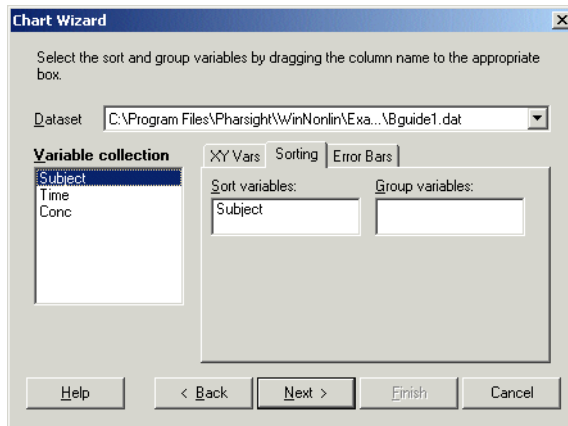



3. Click on **Time** under Variable Collection and drag it to the X-Variable field.
4. Click on **Conc** under Variable Collection and drag it to the Y-Variable field.



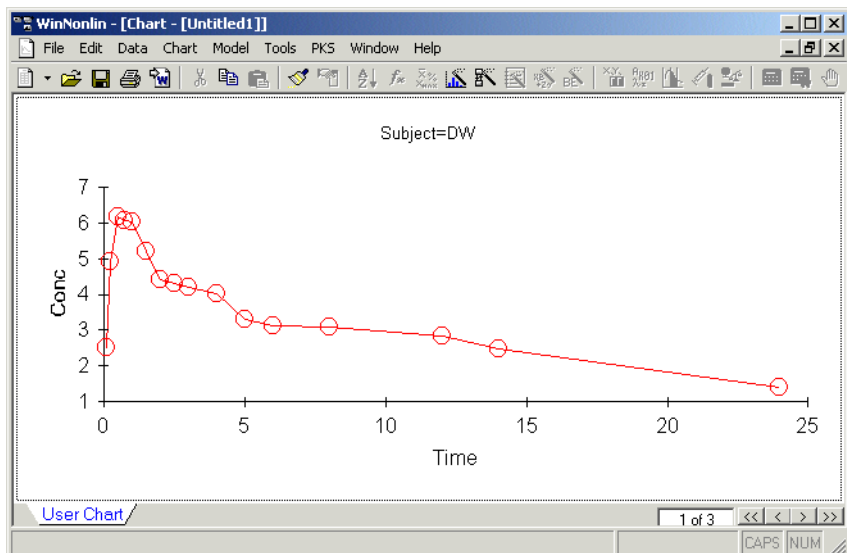
5. Click on the **Sorting** tab.
6. Drag **Subject** to the Sort Variables field. WinNonlin will create separate charts for each unique value of **Subject**.

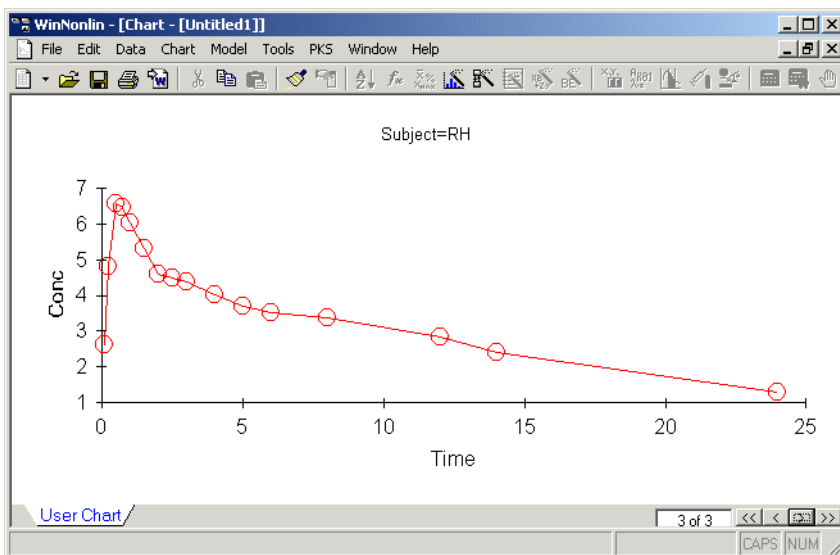
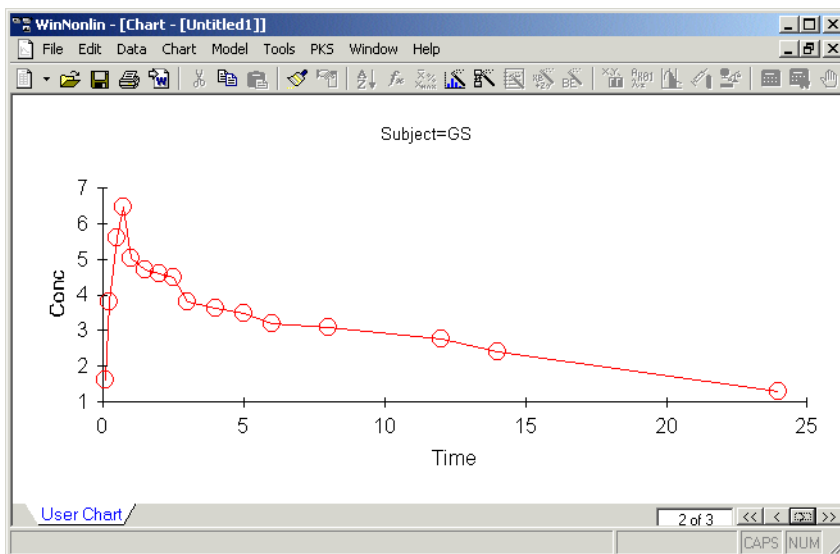
BGuide1 includes three subjects.



7. Click **Next** to proceed to the final Chart Wizard dialog (not shown).
8. Click **Finish** to close the wizard and create the new charts.
9. Use the page buttons  in the lower right corner of the chart window to move between profiles (subjects).

The three charts are shown below, for comparison.



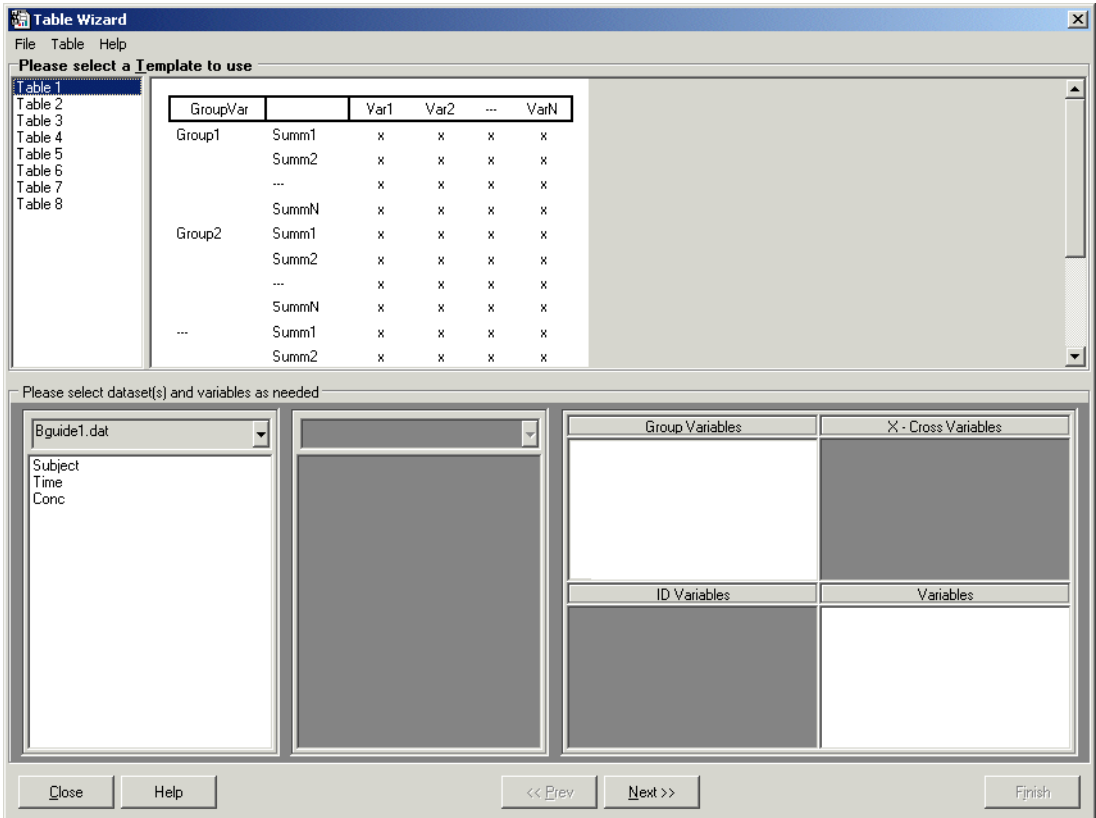


Next, the BGuide1 data set will be used to test the Tables Wizard and its summary statistics function.

Creating a table

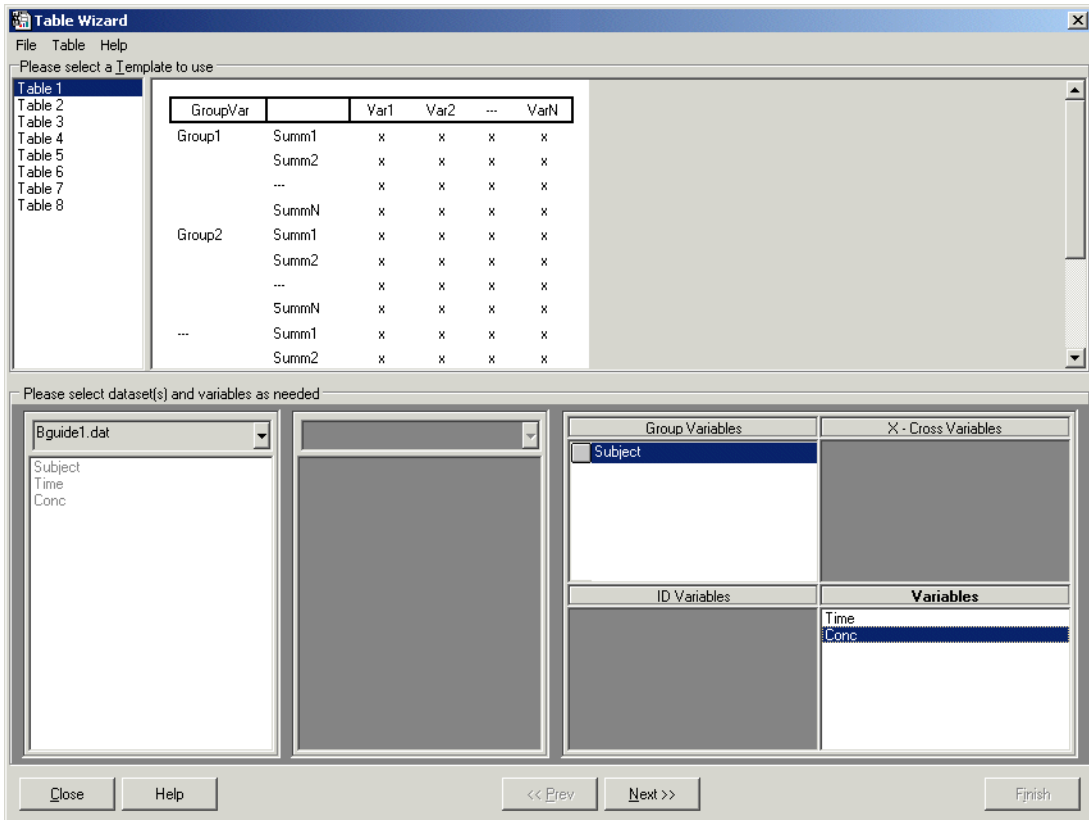
To create a table:

1. Choose **Window>Workbook - BGUIDE1.DAT** in WinNonlin's menus to move the workbook back into the active window.
2. Click the **Table Wizard** toolbar button.



The first dialog in the Table Wizard lists variables (at the bottom left) and the available templates for creating tables (at the top). The fields available in the selected template appear at the bottom right.

3. Select **Table 1** to open a preview of that table format to the right.
4. Drag **Time** and **Conc** to the Variables field.
5. Drag **Subject** to the Group Variables field.

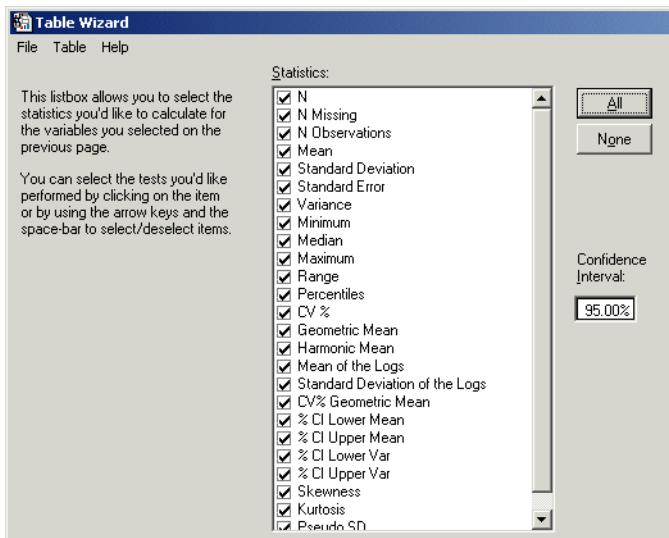


6. Click Next.

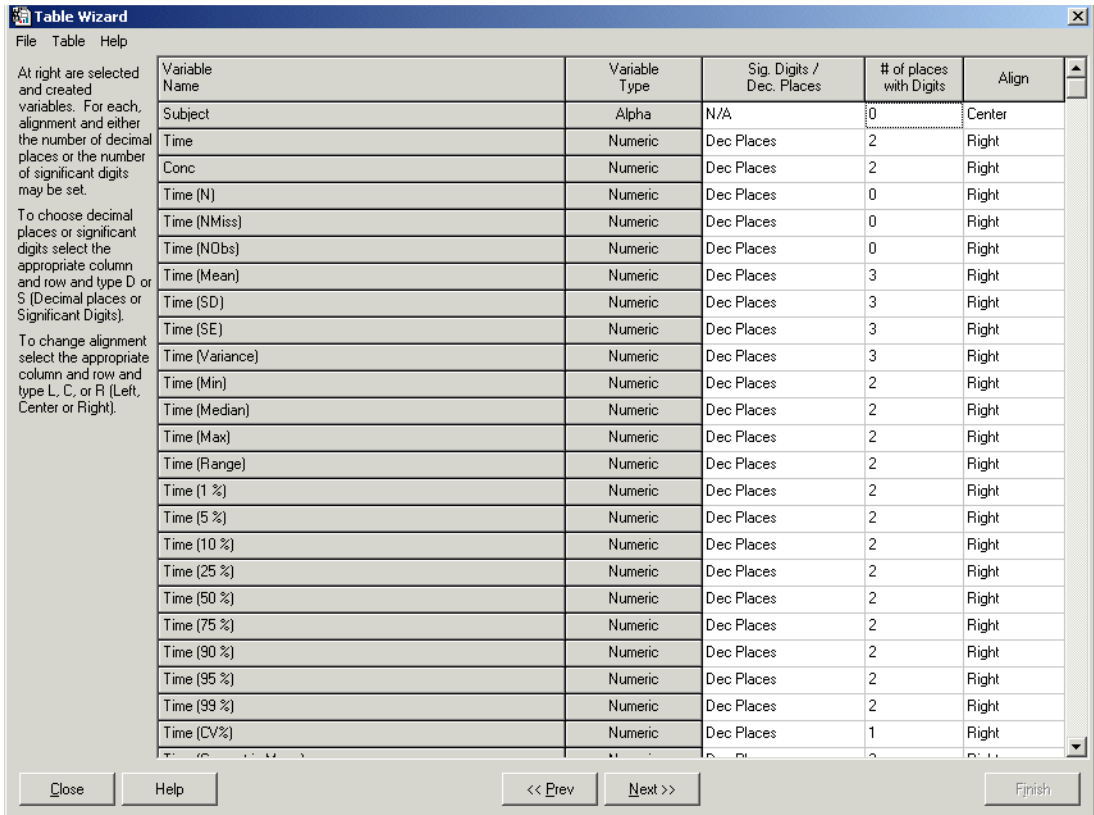
The next dialog in the sequence allows selection of summary statistics to be computed for the selected variables.

7. For this example, click All.

8. Click Next.

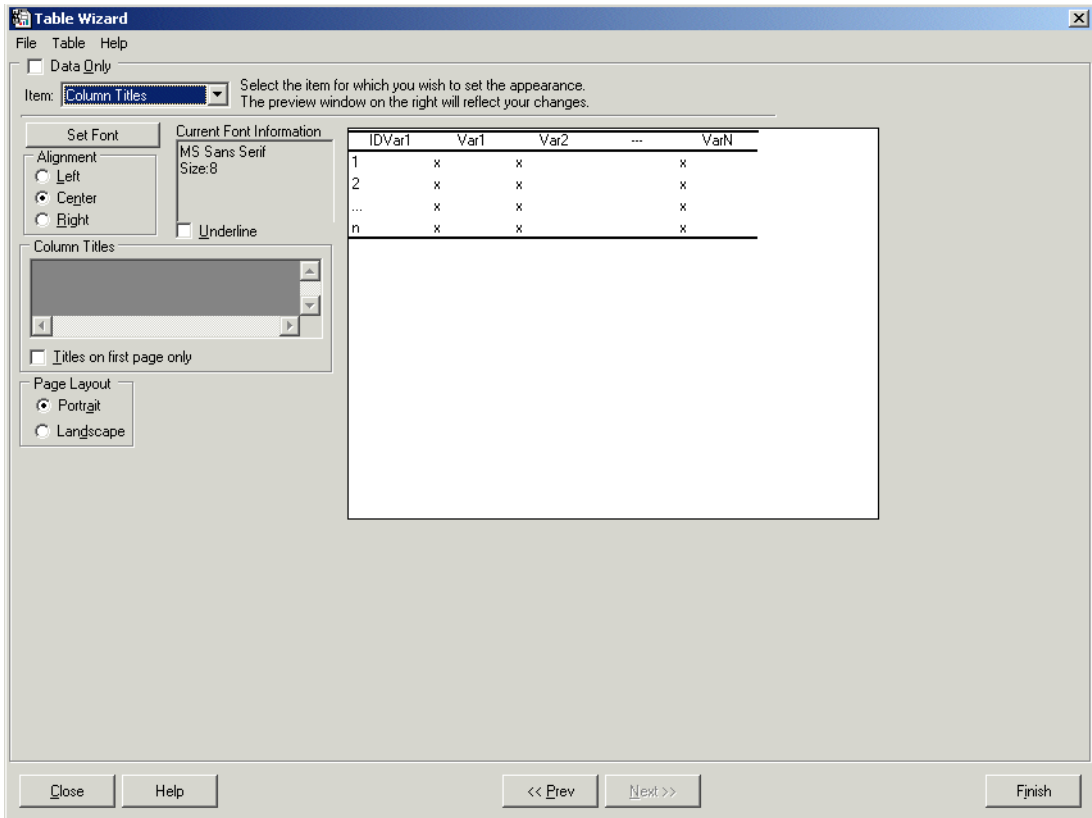


The dialog that appears sets the number of decimal places (or significant figures) and the alignment of numbers in the output table. For this example, accept the default settings.



9. Click **Next**.

The next dialog in the sequence sets formatting of table elements, including the column titles, table body, header, and footer. The default settings will be used here.



10. Click **Finish** to display the table in the Table Wizard window.

11. Click **Create**.

The table should appear in a new workbook window, containing the data shown below.

	A	B	C	D
1	Subject		Time	Conc
2	DW	N	16	16
3		NMiss	0	0
4		NObs	16	16
5		Mean	5.288	4.004
6		SD	6.496	1.432
7		SE	1.624	0.358
8		Variance	42.204	2.051
9		Min	0.10	1.39
10		Median	2.75	4.10
11		Max	24.00	6.20
12		Range	23.90	4.81
13		1 %	0.10	1.39
14		5 %	0.10	1.39
15		10 %	0.21	2.15
16		25 %	0.81	2.90
17		50 %	2.75	4.10
18		75 %	7.50	5.14
19		90 %	17.00	6.11
20		95 %	24.00	6.20
21		99 %	24.00	6.20
22		CV%	122.9	35.8
23		Geometric Mean	2.342	3.736
24		Harmonic Mean	0.756	3.434
25		Mean of the Logs	0.8508	1.3179
26		SD of the Logs	1.5096	0.4039
27		CV% Geometric Mean	296.063	42.099
28		95% CI Lower Mean	1.826	3.241
29		95% CI Upper Mean	8.749	4.767
30		95% CI Lower Var	23.030	1.119
31		95% CI Upper Var	101.094	4.914
32		Skewness	1.7231	0.0537
33		Kurtosis	2.3308	-0.9299
34		Pseudo SD	2.3574	1.7578

	A	B	C	D
35	Subject		Time	Conc
36	GS	N	16	16
37		NMiss	0	0
38		NObs	16	16
39		Mean	5.288	3.748
40		SD	6.496	1.394
41		SE	1.624	0.348
42		Variance	42.204	1.942
43		Min	0.10	1.29
44		Median	2.75	3.70
45		Max	24.00	6.47
46		Range	23.90	5.18
47		1 %	0.10	1.29
48		5 %	0.10	1.29
49		10 %	0.21	1.51
50		25 %	0.81	2.83
51		50 %	2.75	3.70
52		75 %	7.50	4.69
53		90 %	17.00	5.86
54		95 %	24.00	6.47
55		99 %	24.00	6.47
56		CV%	122.9	37.2
57		Geometric Mean	2.342	3.467
58		Harmonic Mean	0.756	3.141
59		Mean of the Logs	0.8508	1.2432
60		SD of the Logs	1.5096	0.4334
61		CV% Geometric Mean	296.063	45.462
62		95% CI Lower Mean	1.826	3.005
63		95% CI Upper Mean	8.749	4.490
64		95% CI Lower Var	23.030	1.060
65		95% CI Upper Var	101.094	4.652
66		Skewness	1.7231	0.0473
67		Kurtosis	2.3308	-0.4740
68		Pseudo SD	2.3574	1.7519

	A	B	C	D
69	Subject		Time	Conc
70	RH	N	16	16
71		NMiss	0	0
72		NObs	16	16
73		Mean	5.288	4.154
74		SD	6.496	1.502
75		SE	1.624	0.375
76		Variance	42.204	2.255
77		Min	0.10	1.29
78		Median	2.75	4.20
79		Max	24.00	6.60
80		Range	23.90	5.31
81		1 %	0.10	1.29
82		5 %	0.10	1.29
83		10 %	0.21	2.05
84		25 %	0.81	2.98
85		50 %	2.75	4.20
86		75 %	7.50	5.19
87		90 %	17.00	6.51
88		95 %	24.00	6.60
89		99 %	24.00	6.60
90		CV%	122.9	36.2
91		Geometric Mean	2.342	3.857
92		Harmonic Mean	0.756	3.503
93		Mean of the Logs	0.8508	1.3500
94		SD of the Logs	1.5096	0.4241
95		CV% Geometric Mean	296.063	44.386
96		95% CI Lower Mean	1.826	3.354
97		95% CI Upper Mean	8.749	4.954
98		95% CI Lower Var	23.030	1.231
99		95% CI Upper Var	101.094	5.402
100		Skewness	1.7231	-0.0027
101		Kurtosis	2.3308	-0.6773
102		Pseudo SD	2.3574	2.0453

12. After comparing the output to these results, choose **File>Close All** from the menus.

Modeling

This section will test an example of pharmacokinetic modeling and an example of noncompartmental analysis.

Compartmental modeling

To run compartmental modeling:

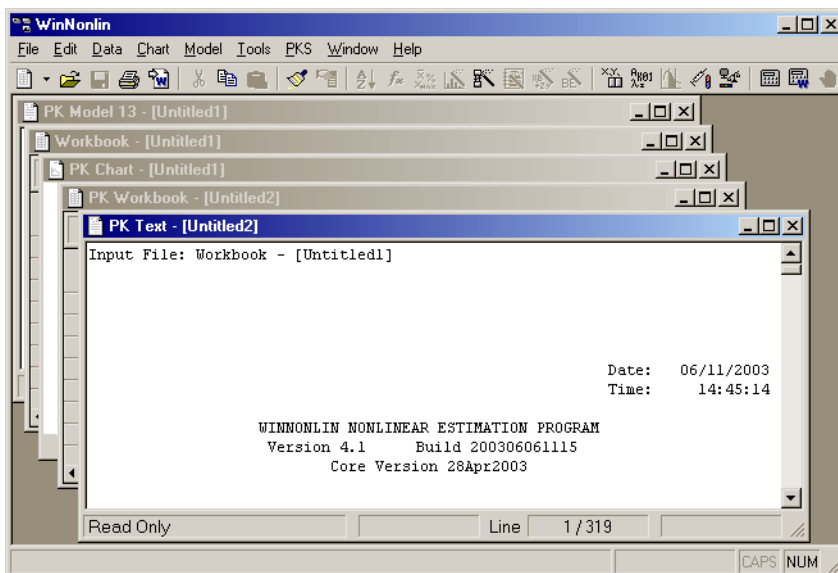


1. Click on the **Open** toolbar button. The File Open dialog appears.
2. Select **Command Files (*.cmd)** in the Files of type list.
3. Select **EXP1.CMD** in the WinNonlin EXAMPLES directory.
4. Click **Open**. This command file loads a data set, PK model, and modeling commands into WinNonlin.
5. Choose **Model>Model Options** from the menus or click on the **Model Options** toolbar button.
6. On the Output Options tab, confirm that workbook, chart and text output are all checked.
7. On the PK Settings tab, un-check the **Transpose Final Parameter Table** option, if necessary.
8. Click **OK**.

	Time (hr)	Conc (ng/ml)	C	D	E	F	G
1	0.1	2.6					
2	0.25	4.817					
3	0.5	6.596					
4	0.75	6.471					
5	1	6.049					
6	1.5	5.314					
7	2	4.611					
8	2.5	4.5					



9. Select **Model>Start Modeling** from the menus or click the **Start Modeling** toolbar button. WinNonlin performs the modeling calculations and generates three new windows: PK Chart, PK Workbook and PK Text.



Workbook output

The output PK Workbook includes tabbed pages (worksheets) containing the following derived data. The same information is found in the PK Text window.

Initial Parameters

	Parameter	Value	Lower	Upper
1	A	6.053	0	60.53
2	B	4.969	0	49.69
3	K01	4.271	0	42.71
4	Alpha	1.362	0	13.62
5	Beta	5.39E-02	0	0.5391

Minimization Process

Iteration	Weighted_SS	A	B	K01	ALPHA	BETA
0	0.703867	6.053	4.969	4.271	1.362	5.39E-02
1	0.271012	8.56	5.003	3.518	1.67	5.40E-02
2	0.262316	10.59	5.002	3.302	1.78	5.40E-02
3	0.258917	12.76	4.999	3.146	1.86	5.38E-02
4	0.252427	14.17	4.997	3.074	1.899	5.38E-02
5	0.247807	15.73	4.995	3.008	1.937	5.37E-02
6	0.244618	17.44	4.994	2.948	1.972	5.37E-02
7	0.213611	21.31	4.972	2.818	1.991	5.33E-02
8	0.201785	24.54	4.97	2.765	2.027	5.32E-02
9	0.199318	24.54	4.97	2.77	2.024	5.32E-02
10	0.199056	25.41	4.97	2.757	2.035	5.32E-02
11	0.198837	26.38	4.971	2.743	2.047	5.32E-02
12	0.19868	27.35	4.971	2.731	2.058	5.32E-02
13	0.198562	28.25	4.972	2.72	2.067	5.32E-02
14	0.19847	29.12	4.972	2.711	2.076	5.32E-02
15	0.198397	29.95	4.973	2.702	2.084	5.33E-02
15	0.19838	30.72	4.973	2.694	2.091	5.33E-02

Final Parameters

	Parameter	Units	Estimate	StdError	CV%
1	A	ng/ml	30.716921	204.064467	664.34
2	B	ng/ml	4.973020	0.136567	2.75
3	K01	1/hr	2.694211	1.940510	72.03
4	Alpha	1/hr	2.091084	1.798209	85.99
5	Beta	1/hr	0.053250	0.002802	5.26

UnivarCI_Lower	UnivarCI_Upper	PlanarCI_Lower	PlanarCI_Upper
-418.427659	479.861501	-792.614929	854.048771
4.672436	5.273604	4.422016	5.524023
-1.576838	6.965261	-5.135096	10.523519
-1.866762	6.048930	-5.164087	9.346255
0.047084	0.059417	0.041946	0.064555

Note: There should be two Final Parameters worksheets: that shown above, and an additional, transposed version. If the format of the Final Parameters worksheet differs from those displayed above, check that the Transpose Final Parameters Table checkbox was not checked in the PK Settings tab of the Model Options dialog (Model>Model Options).

Transposed Final Parameters (partial output shown)

	A (ng/ml)	A_StdError	A_CV%	A_UnivarCI_Lower	A_UnivarCI_Upper	A_PlanarCI_Lower
1	30.716921	204.064467	664.34	-418.427659	479.861501	-792.614929
2						

Dosing

	Constant	Value
1	Stripping Dose	2
2	Number of Doses	1
3	Dose #1	2
4	Time of Dose #1	0

Correlation Matrix

	Parameter	A	B	K01	ALPHA	BETA
1	A	1				
2	B	0.580121	1			
3	K01	-0.998361	-0.55573	1		
4	Alpha	0.998284	0.608346	-0.993373	1	
5	Beta	0.422131	0.835997	-0.403203	0.444629	1

Eigenvalues

	Number	Value
1	1	7909
2	2	110.2
3	3	2.58
4	4	0.6295
5	5	4.33E-07

Condition Numbers

Iteration	Rank	Condition
0	5	51.393440
1	5	125.185646
2	5	188.189029
3	5	277.347719
4	5	348.131752
5	5	445.481653
6	5	580.137434
7	5	926.833867
8	5	1372.700867
9	5	1329.901738
10	5	1492.334332
11	5	1698.682497
12	5	1925.321628
13	5	2160.405315
14	5	2408.231383
15	5	2663.790684

Variance-Covariance Matrix

Parameter	A	B	K01	ALPHA	BETA
A	41642.3				
B	16.1671	1.87E-02			
K01	-395.34	-0.147274	3.76558		
Alpha	366.321	0.149395	-3.46632	3.23356	
Beta	0.241354	3.20E-04	-2.19E-03	2.24E-03	7.85E-06

Summary Table

Time_Obs (hr)	Conc_Obs (ng/ml)	Predicted (ng/ml)	Residual (ng/ml)	Weight	SE_Yhat	Standard_Res
0.1	2.6	2.6067	-0.0067	1.3473	0.0871	-0.0884
0.25	4.817	4.9205	-0.1035	0.7272	0.1027	-0.8667
0.5	6.596	6.3603	0.2357	0.5311	0.1100	1.5941
0.75	6.471	6.4483	0.0227	0.5413	0.1137	0.1592
1	6.049	6.0978	-0.0488	0.5791	0.1029	-0.3406
1.5	5.314	5.2980	0.0160	0.6592	0.1038	0.1240
2	4.611	4.7764	-0.1654	0.7597	0.0914	-1.3336
2.5	4.5	4.4756	0.0244	0.7784	0.0698	0.1805
3	4.392	4.2857	0.1063	0.7976	0.0633	0.7793
4	4.013	4.0254	-0.0124	0.8729	0.0683	-0.0979
5	3.698	3.8114	-0.1134	0.9473	0.0650	-0.9317
6	3.505	3.6131	-0.1081	0.9994	0.0585	-0.8936
8	3.382	3.2480	0.1340	1.0358	0.0490	1.0940
12	2.844	2.6248	0.2192	1.2317	0.0484	1.9764
14	2.383	2.3597	0.0233	1.4700	0.0523	0.2389
24	1.287	1.3854	-0.0984	2.7218	0.0648	-1.9958

Note: The columns Time and Conc are not shown above, as they are the same as Time_Obs and Conc_Obs.

Diagnostics

Function	Item	Value
1	CSS	33.8254
1	WCSS	36.4794
1	SSR	0.209649
1	WSSR	0.19838
1	S	0.134293
1	DF	11
1	CORR_(OBS,PRED)	0.9969
1	AIC	-15.88111
1	SBC	-12.01817

Partial Derivatives

Function	Time (hr)	A	B	K01	ALPHA	BETA
1	0.1	0.05511856	0.26797700	3.16383419	-2.89235866	-0.57417053
1	0.25	0.07076437	0.40667143	3.87839598	-3.88150761	-1.04618521
1	0.5	0.06668793	0.52013676	3.37880878	-3.93213427	-1.76442051
1	0.75	0.05579132	0.60941515	2.60821256	-3.52958898	-2.63671693
1	1	0.04258309	0.67008811	1.83340803	-2.88507230	-3.58807637
1	1.5	0.02099185	0.73531620	0.76233957	-1.62210458	-5.59132849
1	2	0.00932294	0.77957511	0.28350944	-0.81570047	-7.79288041
1	2.5	0.00368610	0.77127511	0.09320432	-0.36260349	-9.60130757
1	3	0.00140859	0.76094563	0.02941437	-0.15473491	-11.35580099
1	4	0.00019822	0.75504018	0.00276968	-0.02663936	-15.01810729
1	5	0.00002665	0.74577064	0.00024346	-0.00428139	-18.54122607
1	6	0.00000346	0.72630517	0.00002026	-0.00065134	-21.66812063
1	8	0.00000005	0.66469703	0.00000013	-0.00001347	-26.43877968
1	12	0.00000000	0.58578794	0.00000000	-0.00000001	-34.94645294
1	14	0.00000000	0.57529492	0.00000000	0.00000000	-40.03841549
1	24	0.00000000	0.45962113	0.00000000	0.00000000	-54.82187973

Predicted Data

	Function	Time (hr)	Predicted (ng/ml)
1	1	0	0
2	1	0	0
3	1	2.50E-02	0.754297
4	1	5.01E-02	1.43673
5	1	7.51E-02	2.05311
6	1	0.1001	2.60883
7	1	0.125125	3.10887
8	1	0.15015	3.55783
9	1	0.175175	3.95996
10	1	0.2002	4.31918
11	1	0.225225	4.63913
12	1	0.25025	4.92315
13	1	0.275275	5.17434
14	1	0.3003	5.39554
15	1	0.325325	5.58937
16	1	0.35035	5.75828
17	1	0.375375	5.90447
18	1	0.4004	6.03002
19	1	0.425425	6.13682
20	1	0.45045	6.2266
21	1	0.475475	6.30096
22	1	0.500501	6.36139
23	1	0.525526	6.40922
24	1	0.550551	6.44571
25	1	0.575576	6.47199

Predicted Data (continued)

	Function	Time (hr)	Predicted (ng/ml)
976	1	24.3744	1.3581
977	1	24.3994	1.35629
978	1	24.4244	1.35448
979	1	24.4494	1.35268
980	1	24.4745	1.35088
981	1	24.4995	1.34908
982	1	24.5245	1.34728
983	1	24.5495	1.34549
984	1	24.5746	1.34369
985	1	24.5996	1.3419
986	1	24.6246	1.34012
987	1	24.6496	1.33833
988	1	24.6747	1.33655
989	1	24.6997	1.33477
990	1	24.7247	1.33299
991	1	24.7497	1.33122
992	1	24.7748	1.32945
993	1	24.7998	1.32768
994	1	24.8248	1.32591
995	1	24.8498	1.32414
996	1	24.8749	1.32238
997	1	24.8999	1.32062
998	1	24.9249	1.31886
999	1	24.9499	1.3171
1000	1	24.975	1.31535
1001	1	25	1.3136

Secondary Parameters

	Parameter	Units	Estimate	StdError	CV%
1	K10	1/hr	0.123914	0.086593	69.88
2	K12	1/hr	1.121807	1.542586	137.51
3	K21	1/hr	0.898614	0.182791	20.34
4	AUC	hr*ng/ml	94.832014	3.267991	3.45
5	K01-HL	hr	0.257273	0.185116	71.95
6	K10-HL	hr	5.593768	3.895151	69.63
7	Alpha-HL	hr	0.331477	0.284766	85.91
8	Beta-HL	hr	13.016765	0.684205	5.26
9	V1_F	ml	0.170198	0.116810	68.63
10	CL_F	ml/hr	0.021090	0.000728	3.45
11	V2_F	ml	0.212471	0.107523	50.61
12	CLD2_F	ml/hr	0.190929	0.131827	69.05
13	Tmax	hr	0.643786	0.021305	3.31
14	Cmax	ng/ml	6.499829	0.113816	1.75

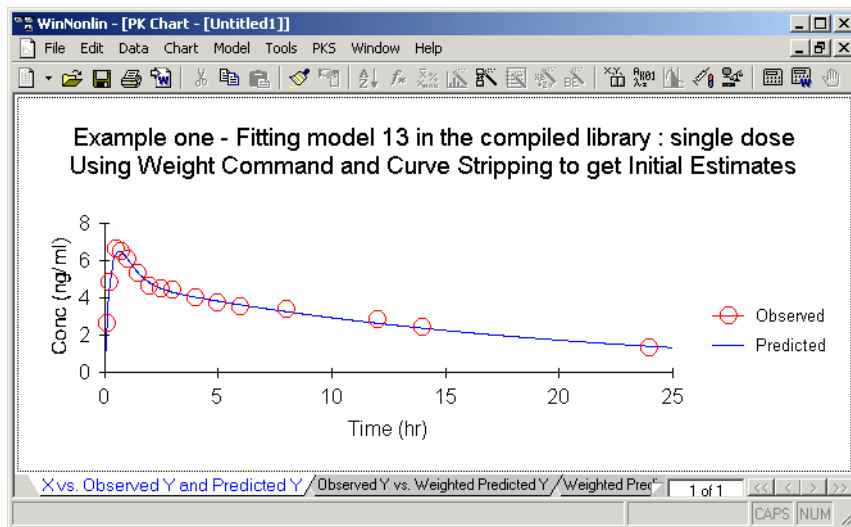
Transposed Secondary Parameters (partial output shown)

	K10 (1/hr)	K10_StdError	K10_CV%	K12 (1/hr)	K12_StdError	K12_CV%	K21 (1/hr)	K21_StdError	K21_CV%
1	0.123914	0.086593	69.88	1.121807	1.542586	137.51	0.898614	0.182791	20.34

User Settings

Example one - Fitting model 13 in the compiled library : single dose
Using Weight Command and Curve Stripping to get Initial Estimates
PK Model 13 - [Untitled1]
Weighted analysis using WEIGHT = -1
Gauss-Newton (Levenberg and Hartley) method used
Convergence criteria of 0.0001 used during minimization process
50 maximum iterations allowed during minimization process

Chart output



Additional chart types, not shown here, are produced in the model fitting.

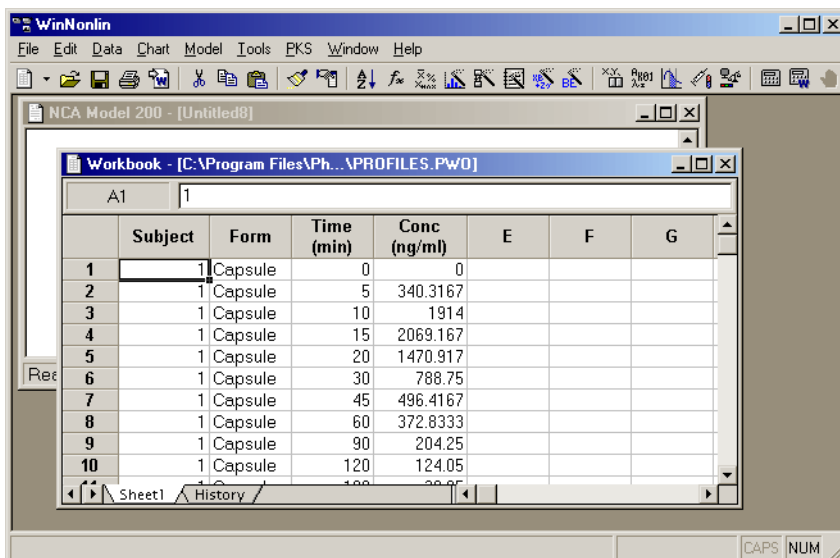
Note: The output displayed in this chapter is intended only to test for proper installation of WinNonlin, and is not a full validation of the software. Those interested in a validation kit should send e-mail to sales@pharsight.com.

10. Close all open windows (**File>Close All**) in WinNonlin before proceeding to the next test, noncompartmental analysis.

Noncompartmental analysis

To run noncompartmental analysis:

1. Open the command file PROFILES.CMD from the WinNonlin EXAMPLES directory. This will load a data set, model, and modeling settings.



	Subject	Form	Time (min)	Conc (ng/ml)	E	F	G
1	1	Capsule	0	0			
2	1	Capsule	5	340.3167			
3	1	Capsule	10	1914			
4	1	Capsule	15	2069.167			
5	1	Capsule	20	1470.917			
6	1	Capsule	30	788.75			
7	1	Capsule	45	496.4167			
8	1	Capsule	60	372.8333			
9	1	Capsule	90	204.25			
10	1	Capsule	120	124.05			

2. Choose **Model>Model Options** from the menus.
3. On the Output Options tab of the Model Options dialog, confirm that workbook, chart and text output are all checked.
4. Open the NCA Settings tab and un-check **Transpose Final Parameters**, if necessary.
5. Click **OK**.
6. Choose **Model>Start Modeling** from the menus.

Three new output windows appear: NCA Chart, NCA Workbook and NCA Text. The text output contains the same data as the workbook, in ASCII form. Samples from the chart and workbook output are shown below.

Chart output

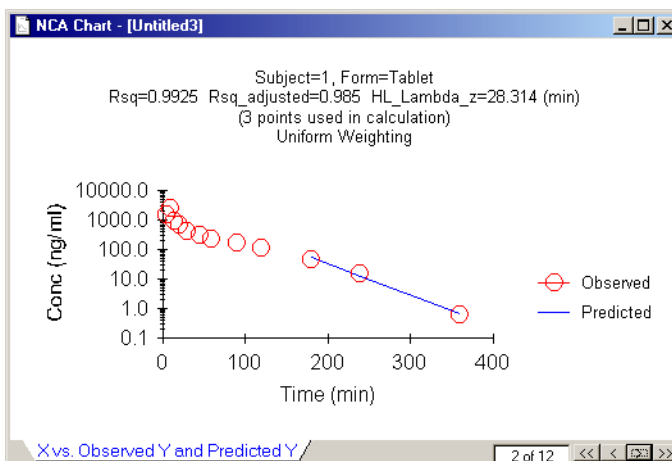
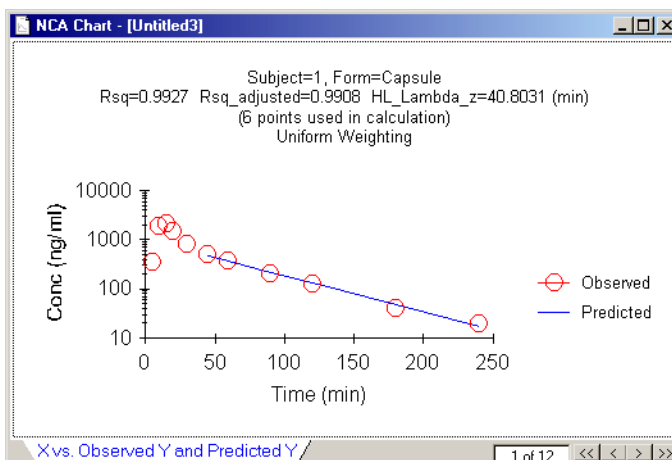


Figure 3-1. Charts for subject 1. Observed and predicted concentrations for the capsule formulation (top) and tablet formulation (bottom).

NCA workbook output

The NCA Workbook contains multiple worksheets. Selections from the data are presented below.

Final Parameters

	Subject	Form	Parameter	Units	Estimate	F
1	1	Capsule	Rsq		0.9927	
2	1	Capsule	Rsq_adjusted		0.9908	
3	1	Capsule	Corr_XY		-0.9963	
4	1	Capsule	No_points_lambda_z		6.0000	
5	1	Capsule	Lambda_z	1/min	0.0170	
6	1	Capsule	Lambda_z_lower	min	45.0000	
7	1	Capsule	Lambda_z_upper	min	240.0000	
8	1	Capsule	HL_Lambda_z	min	40.8031	
9	1	Capsule	Tlag	min	0.0000	
10	1	Capsule	Tmax	min	15.0000	
11	1	Capsule	Cmax	ng/ml	2069.1670	
12	1	Capsule	Tlast	min	240.0000	
13	1	Capsule	Clast	ng/ml	19.3167	
14	1	Capsule	AUClast	min*ng/ml	72987.9209	
15	1	Capsule	AUCall	min*ng/ml	72987.9209	
16	1	Capsule	AUCINF_obs	min*ng/ml	74125.0235	
17	1	Capsule	AUCINF_D_obs	min*ng/ml/ng	741.2502	
18	1	Capsule	AUC_%Extrap_obs	%	1.5340	
19	1	Capsule	Vz_F_obs	ml	0.0794	
20	1	Capsule	Cl_F_obs	ml/min	0.0013	
21	1	Capsule	AUCINF_pred	min*ng/ml	73976.0441	
22	1	Capsule	AUCINF_D_pred	min*ng/ml/ng	739.7604	
23	1	Capsule	AUC_%Extrap_pred	%	1.3357	
24	1	Capsule	Vz_F_pred	ml	0.0796	
25	1	Capsule	Cl_F_pred	ml/min	0.0014	
26	1	Capsule	AUMClast	min*min*ng/ml	3398545.4940	
27	1	Capsule	AUMCINF_obs	min*min*ng/ml	3738387.2505	
28	1	Capsule	AUMC_%Extrap_obs	%	9.0906	
29	1	Capsule	AUMCINF_pred	min*min*ng/ml	3693862.3137	
30	1	Capsule	AUMC_%Extrap_pred	%	7.9948	
31	1	Capsule	MRTlast	min	46.5631	
32	1	Capsule	MRTINF_obs	min	50.4335	
33	1	Capsule	MRTINF_pred	min	49.9332	

Figure 3-2. Final parameter estimates for subject 1, capsule formulation only.

Summary Table

	Subject	Form	Time (min)	Lambda_z_Incl	Conc (ng/ml)	Predicted (ng/ml)	Residual (ng/ml)	AUC (min*ng/ml)	AUMC (min*min*ng/ml)	Weight
1	1	Capsule	0.0000		0.0000			0.0000	0.0000	0.0000
2	1	Capsule	5.0000		340.3167			850.7918	4253.9588	0.0000
3	1	Capsule	10.0000		1914.0000			6486.5835	56357.9175	0.0000
4	1	Capsule	15.0000		2069.1670			16444.5010	181801.6800	0.0000
5	1	Capsule	20.0000		1470.9170			25294.7110	332941.2925	0.0000
6	1	Capsule	30.0000		788.7500			36593.0460	598345.4925	0.0000
7	1	Capsule	45.0000	*	496.4167	460.8734	35.5433	46231.7963	943354.8788	1.0000
8	1	Capsule	60.0000	*	372.8333	357.2047	15.6286	52751.1713	1278670.5000	1.0000
9	1	Capsule	90.0000	*	204.2500	214.5795	-10.3295	61407.4208	1889957.9700	1.0000
10	1	Capsule	120.0000	*	124.0500	128.9019	-4.8519	66331.9208	2388985.4700	1.0000
11	1	Capsule	180.0000	*	39.2500	46.5159	-7.2659	71230.9208	3047515.4700	1.0000
12	1	Capsule	240.0000	*	19.3167	16.7859	2.5308	72987.9209	3398545.4940	1.0000
13	1	Tablet	0.0000		0.0000			0.0000	0.0000	0.0000
14	1	Tablet	5.0000		1474.2000			3685.5000	18427.5000	0.0000
15	1	Tablet	10.0000		2475.0000			13558.5000	98730.0000	0.0000
16	1	Tablet	15.0000		949.3000			22119.2500	196203.7500	0.0000
17	1	Tablet	20.0000		665.7000			26156.7500	265087.5000	0.0000
18	1	Tablet	30.0000		426.6000			31618.2500	396647.5000	0.0000
19	1	Tablet	45.0000		293.3000			37017.5000	590621.2500	0.0000
20	1	Tablet	60.0000		232.0000			40957.2500	794010.0000	0.0000
21	1	Tablet	90.0000		168.6000			46966.2500	1230420.0000	0.0000
22	1	Tablet	120.0000		108.4000			51121.2500	1653150.0000	0.0000
23	1	Tablet	180.0000	*	45.7000	52.9482	-7.2482	55744.2500	2290170.0000	1.0000
24	1	Tablet	240.0000	*	15.2000	12.1882	3.0118	57571.2500	2646390.0000	1.0000
25	1	Tablet	360.0000	*	0.6000	0.6458	-0.0458	58519.2500	2878230.0000	1.0000

Figure 3-3. Summary of noncompartmental analysis for subject 1.

Close all open windows before proceeding to the next example.

Bioequivalence

Average bioequivalence

To test average bioequivalence:

1. Open the file SEQ2PER4.PWO from the WinNonlin EXAMPLES directory.
2. Start the Bioequivalence wizard: choose **Tools>Bioequivalence Wizard** from the menus or click the **Bioequivalence Wizard** toolbar button.
3. In the Bioequivalence Model dialog, make sure **Crossover** is selected as the type of study.
4. Make sure that **Average** is selected as the type of bioequivalence.



The screenshot shows the 'Bioequivalence Model' dialog box. It has a title bar with a close button. The main area contains several groups of controls:

- Type of Study:** Radio buttons for 'Parallel/Other' and 'Crossover' (selected).
- Type of Bioequivalence:** Radio buttons for 'Average' (selected) and 'Population/Individual'.
- Subject:** A dropdown menu with 'Subject' selected.
- Sequence:** A dropdown menu with 'Sequence' selected.
- Period:** A dropdown menu with 'Period' selected.
- Formulation:** A dropdown menu with 'Formulation' selected.
- Reference value:** A dropdown menu with 'R' selected.

On the right side, there are buttons: 'Clear Model', 'Load...', 'Save As...', and 'Previous Model...'. At the bottom, there are buttons: 'Help', '< Back', 'Next >', 'Calculate', and 'Cancel'.

5. Select **R** as the reference value and click **Next**.
6. In the Bioequivalence Fixed Effects dialog, drag **AUC** to the **Dependent Variables** field.

The screenshot shows the 'Bioequivalence Fixed Effects' dialog box. It has a title bar with a close button. The main area is divided into several sections:

- Variable Collection:** An empty list box.
- Sort Variables:** An empty list box.
- Regressors/Covariates:** An empty list box.
- Weight Variable:** An empty text box.
- Classification Variables:** A list box containing 'Sequence', 'Formulation', 'Period', and 'Subject'.
- Dependent Variables:** A list box containing 'AUC'.
- Fixed Effects Confidence Level:** A text box with '95' and a '%' symbol.
- Dependent Variables Transformation:** A dropdown menu with 'Ln(x)' selected.

At the bottom, there is a **Model Specification** section with a text box containing 'Sequence+Formulation+Period' and buttons for '+', '*', '(', and ')'. There is also a checkbox for 'No Intercept' which is unchecked. At the bottom of the dialog are buttons: 'Help', '< Back', 'Next >', 'Calculate', and 'Cancel'.

7. Make sure the Dependent Variables Transformation is set to **Ln(x)**.
8. Click **Calculate**. The new output is generated in a Bioequivalence workbook.

WinNonlin - [Bioequivalence Workbook - [Untitled10]]

File Edit Data Chart Model Tools PKS Window Help

A1 Ln(AUC)

	Dependent	Units	FormVar	FormRef	RefLSM	RefLSM_SE	RefGeoLSM	Test	Test
1	Ln(AUC)		Formulation	R	5.5537	0.1047	258.1936	T	
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									

Average Bioequivalence Ratios Test=T Diagnostics

CAPS NUM

WinNonlin - [Bioequivalence Workbook - [Untitled10]]

File Edit Data Chart Model Tools PKS Window Help

A1 Ln(AUC)

	Dependent	Units	Subject	Sequence	R	T	Test-Ref	Ratio[%Ref]	I
1	Ln(AUC)		10	1	229.5197	223.9187	-5.6010	97.56	
2	Ln(AUC)		11	2	272.6825	421.9909	149.3084	154.76	
3	Ln(AUC)		14	1	327.9440	551.0232	223.0792	168.02	
4	Ln(AUC)		15	2	165.4319	271.3675	105.9357	164.04	
5	Ln(AUC)		18	1	166.7440	170.1700	3.4260	102.05	
6	Ln(AUC)		19	2	205.4969	328.2872	122.7903	159.75	
7	Ln(AUC)		22	1	200.5283	224.5855	24.0572	112.00	
8	Ln(AUC)		23	2	373.6165	443.5175	69.9010	118.71	
9	Ln(AUC)		26	1	471.4524	350.2773	-121.1752	74.30	
10	Ln(AUC)		27	2	224.4060	321.2028	96.7968	143.13	
11	Ln(AUC)		30	1	395.5312	531.1292	135.5980	134.28	
12	Ln(AUC)		31	2	240.6243	192.7472	-47.8771	80.10	
13									
14									
15									

Average Bioequivalence Ratios Test=T Diagnostics

CAPS NUM

WinNonlin - [Bioequivalence Workbook - [Untitled10]]

File Edit Data Chart Model Tools PKS Window Help

A1 Ln(AUC)

	Dependent	Units	Diagnostic	Value	E	F	G
1	Ln(AUC)		Total Observations	48			
2	Ln(AUC)		Observations Used	48			
3	Ln(AUC)		Observations Excluded	0			
4	Ln(AUC)		Residual SS	0.000000			
5	Ln(AUC)		Residual df	0			
6	Ln(AUC)		Convergence	Achieved			
7	Ln(AUC)		REML log(likelihood)	-19.23855533			
8	Ln(AUC)		-2 * REML log(likelihood)	38.477111			
9	Ln(AUC)		Akaike's Information Criterion	60.477111			
10	Ln(AUC)		Schwarz's Bayesian Criterion	79.591476			
11	Ln(AUC)		Hessian eigenvalues #1	855.205104			
12	Ln(AUC)		Hessian eigenvalues #2	715.328145			
13	Ln(AUC)		Hessian eigenvalues #3	158.633578			
14	Ln(AUC)		Hessian eigenvalues #4	63.03212002			
15	Ln(AUC)		Hessian eigenvalues #5	21.60427779			

Navigation: Average Bioequivalence | Ratios Test=T | Diagnostics |

WinNonlin - [Bioequivalence Workbook - [Untitled10]]

File Edit Data Chart Model Tools PKS Window Help

A1 Ln(AUC)

	Dependent	Units	Hypothesis	Numer_DF	Denom_DF	F_stat	P_value	H	I
1	Ln(AUC)		int	1	10.0	3055.03	0.0000		
2	Ln(AUC)		Sequence	1	10.0	0.10	0.7639		
3	Ln(AUC)		Formulation	1	24.8	4.33	0.0480		
4	Ln(AUC)		Period	3	28.4	2.17	0.1138		
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									

Navigation: Ratios Test=T | Diagnostics | Sequential Tests | Partial |

The Partial Tests worksheet is not displayed here.

WinNonlin - [Bioequivalence Workbook - [Untitled10]]

File Edit Data Chart Model Tools PKS Window Help

A1 Ln(AUC)

	Dependent	Units	Effect_Level	Estimate	StdError	Denom_DF	T_stat	P_value	C
1	Ln(AUC)		int	5.5209	0.1714	18.5	32.22	0.0000	
2	Ln(AUC)		Sequence:1	0.0631	0.2045	10.0	0.31	0.7639	
3	Ln(AUC)		Sequence:2	Not estimable					
4	Ln(AUC)		Formulation:R	-0.1945	0.0935	24.8	-2.08	0.0480	
5	Ln(AUC)		Formulation:T	Not estimable					
6	Ln(AUC)		Period:1	0.2301	0.1301	30.8	1.77	0.0868	
7	Ln(AUC)		Period:2	0.3012	0.1280	30.6	2.35	0.0252	
8	Ln(AUC)		Period:3	0.2516	0.1301	30.8	1.93	0.0624	
9	Ln(AUC)		Period:4	Not estimable					
10									
11									
12									
13									
14									
15									

Sequential Tests Partial Tests Final Fixed Parameters

CAPS NUM

WinNonlin - [Bioequivalence Workbook - [Untitled10]]

File Edit Data Chart Model Tools PKS Window Help

A1 Ln(AUC)

	Dependent	Units	Parameter	Estimate	E	F	G
1	Ln(AUC)		lambda(1,1)_11	0.278940			
2	Ln(AUC)		lambda(1,2)_11	0.355679			
3	Ln(AUC)		lambda(2,2)_11	0.000000			
4	Ln(AUC)		Var(Period*Formulation*Subject)_21	0.107618			
5	Ln(AUC)		Var(Period*Formulation*Subject)_22	0.090356			
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							

Partial Tests Final Fixed Parameters Final Variance Parameters

CAPS NUM

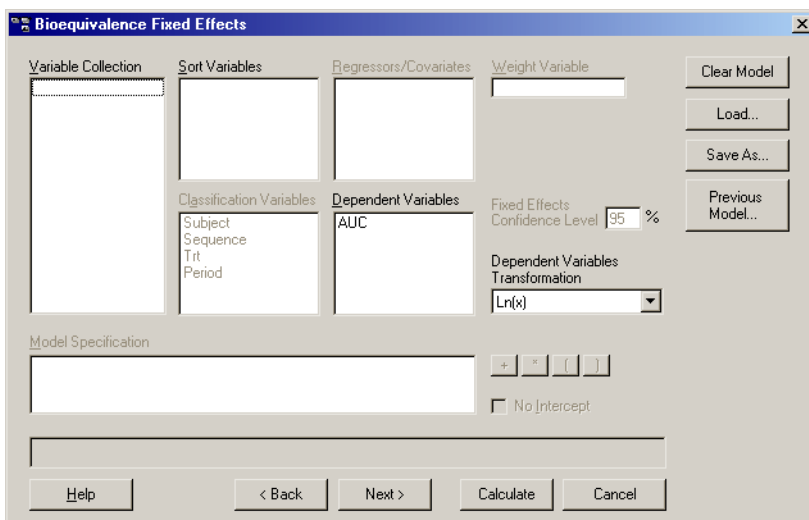
Other worksheets generated from the modeling have been omitted for brevity.

Close all open windows.

Population/individual bioequivalence

To test population/individual bioequivalence:

1. Open the dataset RTR_TRT.PWO from the WinNonlin EXAMPLES directory.
2. Start the Bioequivalence wizard: choose **Tools>Bioequivalence Wizard** from the menus or click the **Bioequivalence Wizard** toolbar button.
3. Select **Population/Individual** as the type of bioequivalence. Crossover is the only study type allowed for population/individual bioequivalence.
4. Select **R** as the reference formulation and click **Next**. The Bioequivalence Fixed Effects dialog appears.
5. For Population/individual bioequivalence the model is preset (by FDA guidelines) and thus the model field cannot be changed. Drag **AUC** from the Variable Collection to the Dependent Variables field.



6. Click **Calculate**. The output appears in a new Bioequivalence workbook.

WinNonlin - [Bioequivalence Workbook - [Untitled12]]

	Dependent	Units	Statistic	Value	Upper_CI	Conclusion
1	Ln(AUC)		Difference(Delta)	-0.4819		
2	Ln(AUC)		Ratio(%Ref)	61.7590		BE not shown for ratio test
3	Ln(AUC)		SigmaR	0.7225		
4	Ln(AUC)		SigmaWR	0.3698		
5	Ln(AUC)		Ref_Pop_eta	-0.5725	0.5755	Pop. BE not shown for refnc-scaling C
6	Ln(AUC)		Const_Pop_eta	0.3355	1.3516	Pop. BE not shown for const-scaling C
7	Ln(AUC)		Mixed_Pop_eta	-0.5725	0.5755	Pop. BE not shown for mixed-scaling C
8	Ln(AUC)		Ref_Indiv_eta	0.4489	1.5076	Indiv. BE not shown for refnc-scaling C
9	Ln(AUC)		Const_Indiv_eta	0.6902	1.7199	Indiv. BE not shown for const-scaling C
10	Ln(AUC)		Mixed_Indiv_eta	0.4489	1.5076	Indiv. BE not shown for mixed-scaling C
11						
12						
13						
14						
15						

Pop./Individual Bioeq Ratios Test=T User Settings

WinNonlin - [Bioequivalence Workbook - [Untitled12]]

	Dependent	Units	Subject	Sequence	R	T	Test-Ref	Ratio[%Ref]	I
1	Ln(AUC)		1	1	109.3996	45.6000	-63.7996	41.68	
2	Ln(AUC)		2	1	39.6482	49.4000	9.7518	124.60	
3	Ln(AUC)		3	1	12.4905	11.1300	-1.3605	89.11	
4	Ln(AUC)		4	1	55.1494	15.3300	-39.8194	27.80	
5	Ln(AUC)		5	1	17.7265	34.4700	16.7435	194.45	
6	Ln(AUC)		6	1	52.4535	16.6100	-35.8435	31.67	
7	Ln(AUC)		7	1	46.0633	25.7900	-20.2733	55.99	
8	Ln(AUC)		8	1	42.7347	46.5300	3.7953	108.88	
9	Ln(AUC)		9	1	34.2911	69.4100	35.1189	202.41	
10	Ln(AUC)		10	1	19.1056	12.8100	-6.2956	67.05	
11	Ln(AUC)		11	2	137.0000	18.4507	-118.5493	13.47	
12	Ln(AUC)		12	2	14.4400	4.8509	-9.5891	33.59	
13	Ln(AUC)		13	2	41.6800	29.8164	-11.8636	71.54	
14	Ln(AUC)		14	2	108.8500	81.8601	-26.9899	75.20	
15	Ln(AUC)		15	2	33.1200	49.1546	16.0346	148.41	

Pop./Individual Bioeq Ratios Test=T User Settings

This bioequivalence example is complete. Close all open windows.

The examples in this chapter test the computational engines to insure that WinNonlin has been installed and operates properly.

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