Phoenix® Getting StartedGuide

Applies to:

Phoenix WinNonlin® 8.3
Phoenix NLME™ 8.3

IVIVC Toolkit™ 8.3 for Phoenix WinNonlin®
Validation Suite™ 8.3

CDISC® Navigator 8.3
AutoPilot Toolkit™ 8.3 for Phoenix

Legal Notice

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Phoenix Installation and Licensing

This section contains installation instructions and licensing information for the Phoenix platform and its modules, such as Phoenix NLME, the IVIVC Toolkit. The generic term Phoenix is used to simplify terminology.

Topics in this section include:

System and hardware requirements

Phoenix is a software platform built on the Microsoft .NET 4.7 framework. It uses the MinGW (Minimalist GNU for Windows) compiler to create PML (Phoenix Modeling Language) models. Phoenix also uses MPICH2 to allow usage of multiple CPUs and CPU cores. All software prerequisites needed to use basic Phoenix functions are included in the Phoenix installation file. Extended Phoenix functions have additional software requirements.

Phoenix NLME-specific information

GNU compilers are 64-bit version 4.9.x and the MPI version is 1.4.1p.

Phoenix NLME only works on 64-bit systems.

NLME jobs can be executed on remote Linux hosts and Torque/SGE grids from a Phoenix Windows installation.

If user accounts have limitations in executing command prompt commands, users will not able to execute NLME objects. The **Prevent access to the Command Prompt** policy for users must be changed from **Enabled** to **Disabled**.

Required software

Windows® Installer 3.1 can be downloaded through the Microsoft Update service or by downloading the Windows Installer 3.1 redistributable from the Microsoft download page.

A PDF reader, such as Adobe Reader, must be installed to access PDF files of various software documents, such as the Validation Suite report.

Compatibility with operating system versions

Phoenix is compatible with the following desktop operating system versions with the English (United States), Kanji (Japan), French (France), Spanish (Spain), German (Germany), or Simplified Chinese (China) language packs and with a Regional Options setting of English (United States):

- Windows 8.1 (32 and 64-bit*) Update KB2919355, using a keyboard and mouse, both Professional and Enterprise editions; not RT (Mobile), not on a tablet

- Windows 10 (64-bit) version 1607 or greater, using a keyboard and mouse, Professional edition

*Phoenix NLME only works on 64-bit systems.

Phoenix is compatible with the following server operating system versions (for direct access or for access via a desktop with a terminal server application), with English (United States) operating system/language pack and Regional Options setting of English (United States):

Windows Server 2016

Windows Server 2019

Note: Phoenix is a desktop application that requires isolated resources in order to perform optimally. If you wish to deploy this desktop application in an enterprise type fashion, such as through Citrix, it is important that it be done in a manner that will isolate the recommended amount of resources to each user, such as through a VDI (virtual desktop infrastructure). Publishing Phoenix from a shared resource sever with multiple users is not recommended.

Compatible third-party software

Third-party tools that are to be used as plug-ins need to be installed on the server. The following third-party software programs are compatible with Phoenix.

Microsoft Office 2013, 2016, 2019 local installation and usage of Office 365 (32 and 64-bit). Web version of Office 365 is not compatible with Phoenix for the tools that use Office.

SAS: versions up to and including 9.4 (32 and 64-bit)

NONMEM: 7.1.2, 7.2, and 7.3 (32 and 64-bit)

SigmaPlot as a third party tool: 11.1 through 12.5

SigmaPlot as used by AutoPilot Toolkit 2.x for Phoenix: 11.1, 11.2, 12.2, 12.3, and 12.5

R for the R object and for Linux Grid computing: versions up to and including 3.6.0

R for Windows MPI-cluster processing for NLME: R 3.6.0.

PsN: versions up to and including 4.7.0 (only with the operating system version(s) and NONMEM version(s) with which each PsN version is compatible).
Note: PsN 3.4.2 and 3.6.7 are not compatible with server operating system versions or with German, Spanish, or Chinese language operating system versions/language packs.

See also "Phoenix 64-bit versus 32-bit version".

Note: When Phoenix is installed and configured to run on a Windows operating system version where its Regional Language settings are not US English, SAS and SigmaPlot objects cannot be executed.

Compatible Certara software

Phoenix can be installed on the same computer with other current Certara software products.

It is not guaranteed that a project created with a newer version of Phoenix can successfully load on older versions of Phoenix. The system will warn the user if the project cannot be loaded. The opposite (backwards compatibility) is guaranteed, although, in some cases, settings or models are automatically updated to new options. Warnings are given when these automatic updates occur and the user should review the loaded settings and model.

Hardware requirements

Processor

Minimum Requirement: Intel i5 processor 3 GHz
Recommended*: Intel i7 processor 4 GHz

RAM

Minimum Requirement: 8 GB of RAM
Recommended*: 16 GB of RAM

Internal Storage Device

Minimum Requirement: 1 GB 7200 RPM Magnetic HD
Recommended*: 1 GB SSD

*Especially for large datasets and large projects.

Installing Phoenix

The instructions for installing Phoenix WinNonlin and Phoenix NLME are the same.

Note: To allow Phoenix to correctly process projects created in English locales, standards and formats must be set to US English. Using the Control Panel, navigate to the Region and Language settings. Select **English (United States)** as the format, then click **Additional Settings** and set the decimal symbol for numbers and currency to be a period (**.**) and, finally, set the list separator to be a comma (**,**).

To install Phoenix

Any previous version of Phoenix must be uninstalled before the latest version can be installed. The installer only checks for an installation of the previous version, it does not check for versions older than the previous one. If you have an older Phoenix version, you will need to manually uninstall it, using **Start > Certara > Uninstall Phoenix** or the Control Panel, before installing the latest Phoenix version.

1. Extract the ZIP file that contains the installation files.

2. Double-click `Setup.exe` to run the Phoenix Installation wizard.

   For Windows 7 and Windows Server: right-click `Setup.exe` and select **Run As**. Enter Administrative credentials in the *User Account Control* dialog.

   `Setup.exe` detects the operating system and starts the appropriate executable.

When the installer is started, it checks for the following:
   - an installation of the previous version of Phoenix
   - the appropriate version of the .NET framework
   - the LegacyWNL components and Microsoft Visual C++ components

The user is notified if any of these requirements are not met and the installer will proceed to uninstall/install the necessary items. A forced reboot must be done to complete the installation.

To continue with the Phoenix installation, double-click `Setup.exe`.

To continue the installation

1. On the Phoenix Setup wizard Welcome screen, click **Next** to display the Setup Type screen.
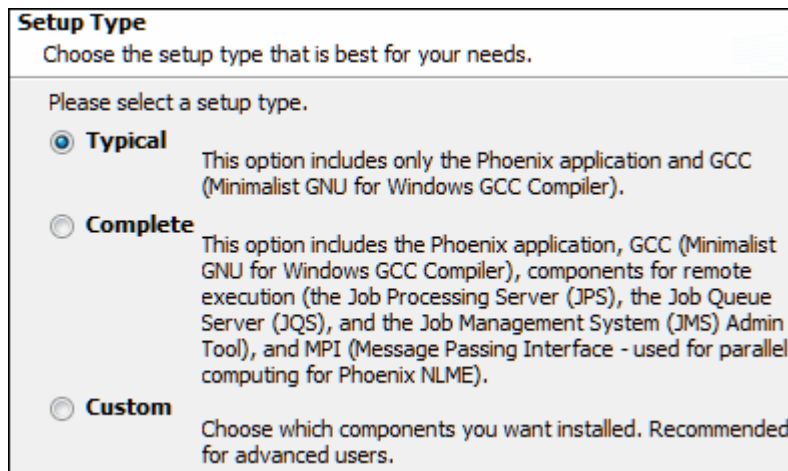
Figure 202-1. Setup Type screen

2. Select a setup type.

   Typical is the default setup type. Only the Phoenix application and GCC (Minimalist GNU for Windows GCC Compiler) are installed.

   Complete installs the Phoenix application, GCC, components for remote execution (JPS, JQS, and JMS), and MPI (for parallel computing for Phoenix NLME).

   Custom allows the user to select the items to install. Recommended for advanced users.
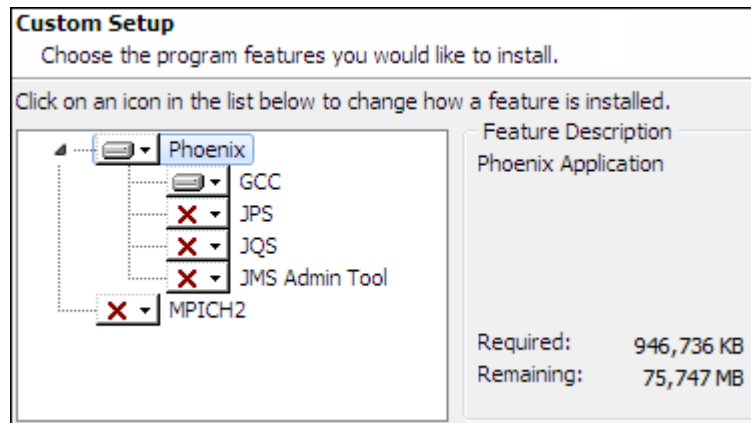
*Figure 202-2. Custom Setup screen — displayed only when **Custom** is selected as the setup type.*

   The GCC component will be installed to `C:\PHSTMinGW64` whether the user retains the default installation location or selects an alternate location.

3. Click **Next** to display the Destination Folder screen.
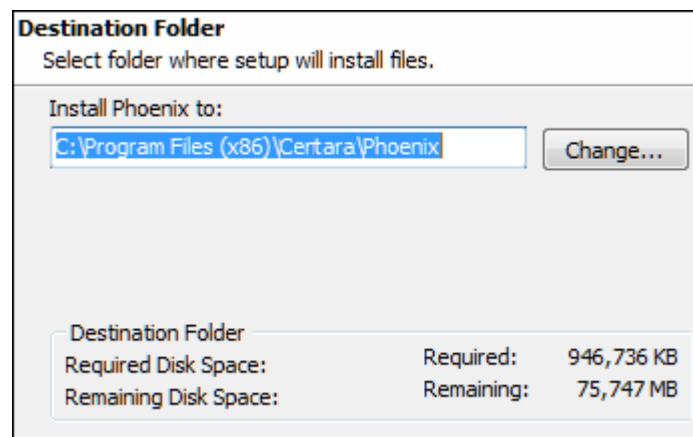
Figure 202-3. Destination Folder screen

4. Specify a destination folder and click **Next** to display the Ready to Install screen.

5. In the Ready to Install screen, use the **Back** button to return to the previous screens to make any changes to the installation or click **Next** to continue the installation process.

    Once installation is finished, the "Completed the Installation of Phoenix" screen is displayed.

6. To complete the installation, the computer should be restarted. However, if restarting needs to be delayed, uncheck the **Restart now** checkbox.

7. Click **Finish** to complete the installation.

Note: If MPICH2 was installed, it is recommended that users open TCP ports on their computers to avoid firewall messages when using the MPICH2 software. See "Opening TCP ports for MPICH2" for instructions on opening TCP ports.

Post-installation considerations

Configuring Phoenix for international use
Opening TCP ports for MPICH2
Executables to be white-listed
Installed folders requiring read/write permission
Modifying, updating, or removing an installation

Configuring Phoenix for international use

When Phoenix is installed on systems that do not use the United States region, then some regional display information must be changed before Phoenix can be used. (The following instructions assume Windows 8.1 KB2919355 is being used.)

Caution: If the settings are not changed then Phoenix cannot correctly run projects that are created in the English (United States) region.

•   In the Control Panel, open the *Regional and Language* dialog (in Windows 8.1, click **Clock, Language, and Region** and then click **Region and Language**).

- In the *Regional and Language* dialog, select **English (United States)** as the region.

  If the region information cannot be changed, then users must set the decimal symbol to a period (**.**) for numbers and currency, and the list separator symbol to a comma (**,**).

- Click the **Additional settings** button. The *Customize Format* dialog is displayed.

- In the **Decimal symbol** menu, change the decimal symbol to a period (**.**).

- In the **List separator** menu, select a comma (**,**).

- Select the **Currency** tab.

- In the **Decimal symbol** menu, change the decimal symbol to a period (**.**).

- Click **OK** and then **OK** in the *Regional and Language* to save the changes.

Note: When Phoenix is installed and configured to run on a Windows operating system version where its Regional Language settings are not US English, SAS and SigmaPlot objects cannot be executed.

Note: For operating systems with Regional Language settings set to Japanese, the default Calendar type should be set to **Western Calendar (Japanese)** in order for `.xpt` files to be exported correctly.

Opening TCP ports for MPICH2

MPICH2 is an implementation of the *M*essage *P*assing *I*nterface (MPI) standard, which allows users to process Phoenix models using multiple CPUs or CPUs with multiple cores.

MPICH2 must use certain TCP ports. If TCP ports are not opened for MPICH2, and the computer uses a software firewall, then the firewall might display alerts each time MPICH2 is run. The multiple alerts are displayed because the executable that uses MPICH2 is compiled dynamically with each execution, so adding an exemption in a firewall for MPICH2 might work only temporarily.

Users can restrict MPICH2 to use a range of ports, and open those ports in a firewall to avoid the multiple warnings. To do this, run the batch tool `<Phoenix_install_dir>\MPICH2-1.4.1\tools\mpiPortTool.bat` as an administrator and open the recommended ports 10000 to 11000. (Please contact your IT support personnel for help with opening ports in a networked computing environment.)

Executables to be white-listed

There are executables that may be flagged/quarantined by different antivirus software. This can cause Phoenix applications to function improperly or even fail. To avoid these types of problems, the following items should be included in an exception list for virus protection by your IT professional.

wnlnca.exe in C:\Program Files (x86)\Certara\Phoenix\application\Plugins\WnlModeling\

Phoenix.exe in C:\Program Files (x86)\Certara\Phoenix\application\

Phoenix32.exe in C:\Program Files (x86)\Certara\Phoenix\application\

ChiDistribution.exe in C:\Program Files (x86)\Certara\Phoenix\application\lib\

TDL5.exe in C:\Program Files (x86)\Certara\Phoenix\application\lib\NLME\Executables\

In addition, the following folders (and their sub-folders) may need to be added to the exception list:

C:\Users\%UserName%\AppData\Roaming\Certara

C:\Users\%UserName%\AppData\Local\Temp

C:\Users\%UserName%\Documents\Certara Projects

C:\Program Files (x86)\Certara

C:\ProgramData\Certara

C:\PHSTMinGW

C:\PHSTMinGW64

Installed folders requiring read/write permission

For environments where a Phoenix installation is being shared, users should have read/write permission for `C:\ProgramData\Certara`.

When creating custom tables, users should have read/write permission for `C:\Program Files (x86)\Certara\Phoenix\application\Plugins\Table\Custom`.

Modifying, updating, or removing an installation

If Phoenix is already installed, then users can double-click the `Setup.exe` or the `Setup.msi` file to update or modify a Phoenix installation.

1. Double-click the `Setup.exe` or the `Setup.msi` file to display the Welcome screen.

2. Select a maintenance operation.

    Modify Available Options is the default selection type and provides options to install updates to the existing application.

    Repair Application re-installs over the existing application to replace possibly corrupt files.

    Uninstall removes all files from the Phoenix installation folder that were originally part of the installation, including files associated with GCC and MPICH2. The uninstall process ***does not*** uninstall any .NET framework versions or C++ runtime versions that were installed as prerequisites, nor does it uninstall the LegacyWNL file.

3. Click **Next**.
    • If **Modify Available Options** is selected, the *Custom Setup* dialog is displayed.
    • If **Repair Application** is selected, the *Ready to Install Phoenix* dialog is displayed. Phoenix will be re-installed based on the user selections made when Phoenix was originally installed.
    • If **Uninstall** is selected, the *Ready to Install Phoenix* dialog is displayed.

Note: During the uninstall process, if a dialog is displayed stating that the application called MPICH2 Process Manager needs to be closed before continuing, accept the default to automatically close the application and click **OK**. If an *Application Requirements* dialog is displayed stating that requirements must be processed before continuing, click **Next**.

Silent installation of Phoenix

Administrators can remotely install Phoenix on users' computers in "silent" mode using scripting. This allows large organizations to "push out" installation updates to computers overnight without any user interaction.

The command to issue is the following. This can be run from a command prompt, from the directory where the Phoenix `setup.exe` file is located.

```
setup.exe /s MINIMUM=FALSE COMPLETE=TRUE DESKTOPDIR=C:\Users\Pub-
lic\Desktop
```

where:

> `/s`: Tells the install to be silent (no UI is displayed)
> `MINIMUM=FALSE`: Specifies that it will not just be Phoenix installed
> `COMPLETE=TRUE`: Specifies that MPICH and JMS are also to be installed
> `DESKTOPDIR=C:\Users\Public\Desktop`: Specifies the location to put the Phoenix shortcut. Specifying the Public profile will ensure ALL users receive the shortcut.

As part of scripting the installation (PowerShell is being used in the following example):

Start-Process <*PATH_TO_PHOENIX_EXECUTABLE*> *-ArgumentList* "`/s MINI-MUM=FALSE COMPLETE=TRUE DESKTOPDIR=C:\Users\Public\Desktop`" *-Wait*

Italicized text above indicates PowerShell syntax needed to properly execute the command, as well as wait for a successful completion before continuing.

Phoenix 64-bit versus 32-bit version

Both the 64-bit and 32-bit versions of Phoenix, namely Phoenix and Phoenix32, are available to users with 64-bit operating systems. Users of 32-bit operating systems are unable to launch Phoenix as a 64-bit application. Any features not available in Phoenix 64-bit are available in the 32-bit version, on the same system.

Functional differences between 32-bit and 64-bit

Phoenix 64-bit has all the same features as Phoenix running in 32-bit, except for the specific differences outlined here. The following functionality descriptions refer only to the 64-bit version.

- **Executables**: Executables that do not support 64-bit fail validation if the user tries to execute them. Users can still open, save, create and interact (limited in some cases) with all executables but are not able to execute them if not supported in 64-bit. These executables are: SigmaPlot and AP.

- **File I/O**: Not all file formats supported in 32-bit are supported in 64-bit. Primarily due to COM interaction with legacy WNL components used to read the file formats. This is the case for importing files from the desktop as well as Certara Integral. (The exception is WNL 5 scenarios from PKS. Scenarios are well-formed workspaces that can be loaded without additional user intervention in a separate process space which is why they are supported.)

  PWO, PMO, PTO, PCO, BQL, TDF, XML, LML, CMD, IVC, MAP
  WNL workspaces (WSP, PWS)
  ODBC Import

  In the case of the legacy files the user is given a warning that the file format is not supported in 64-bit. For ODBC, the menu options are not displayed to the user. To import these legacy files,

run Phoenix32.exe to import the data and save the project. The saved project can then be loaded into 64-bit Phoenix.

Compatibility exceptions

Projects created in the 32-bit or 64-bit versions of the application work in both versions. JMS/RMS work with Phoenix regardless of the bit level of the server or client components. 32-bit Phoenix can communicate with 64-bit JMS/RMS, 64-bit Phoenix can communicate with 32-bit JMS/RMS. Certara Integral works with both versions of Phoenix.

Job Management Service (JMS)

The JMS queue and job processor components (queue: JQS, job processor: JPS) support 32 and 64-bit versions. The AnyCPU versions are the default. If a user or admin needs to use the 32-bit versions of JQS or JPS they are also installed as `jqs32.exe` and `jps32.exe`. To use the 32-bit versions the services must be stopped and the 32-bit versions must be renamed to `jqs.exe` and `jps.exe` respectively.

Licensing of Phoenix software

This section contains the following topics:

Phoenix Licensing Service

The Phoenix Licensing Service is the system Phoenix uses to manage user licenses. When a user starts Phoenix for the first time the Licensing Service is the first Phoenix service that is initialized, and a message is displayed that you are running an unlicensed version of the software, if no license is detected. The Licensing Service is integrated into the Phoenix *Preferences* dialog, which can be accessed by selecting **Preferences** in the **Edit** menu.

Users have several options to install or acquire a license. Users can activate their copy of Phoenix by using online and offline activation, or users can connect to a license server to acquire a license for online or offline use.

License key code types

Phoenix requires the installation of a license key code. There are two types of license key codes:

- **Named User**: a license key code that activates the software on (i) a single machine that may be accessed by the individual named end user for that license or (ii) a single host machine or server ("Host Server") that may be accessed by any of the named end users as part of the license agreement. A Named User License means that only one named person can use each license and that named person has the right to unlimited access to the software. A Named User License is not based on concurrent users, but instead on an actual named user basis.

- **Commuter**: a license key code that is retrieved from a network. Commuter licenses give users temporary offline authorization to use Phoenix while away from the network where their license server resides.

  Commuter licenses can be used for a specified period of time and are subject to a hold time during which they cannot be checked out by another user. This protects users who need to make changes to a Phoenix project after they close Phoenix from immediately losing their license key to another user on the network.

  Customers must work with Certara Sales and the Licensing Administrator to determine how many of their licenses should contain the commuter feature and the length of time that commuter enabled licenses are valid after they have been checked out from the license server. The time-out period cannot be altered after the license has been installed.

Note: The commuter license option is only available if the Sentinel™ RMS 8.x license server is used with Phoenix.

Product and authorization codes

A product code and an authorization code are included with each license or set of licenses purchased. The primary delivery system for acquiring the Phoenix application is downloading the installation files from a Certara server. Certara's download and support page is located at https://support.certara.com.

When Phoenix is purchased, customers are sent an email with the four things necessary to use Phoenix:

- The application and license server download link.
- The authorization code.
- The product code.
- The license code generation Web site link.

Please include the product code in all correspondence with Certara about the product and its license, including license renewals, software updates, and product upgrades.

License activation

1. Run Phoenix as an administrator.
    - Right-click the Phoenix icon on the desktop and select **Run as administrator**.
    - In the *User Account Control* dialog, enter the administrator login information and click **Yes**.

2. Select **Edit > Preferences** from the Phoenix menubar.

3. In the navigation panel, expand the **Licensing** node and select **License Acquisition**.
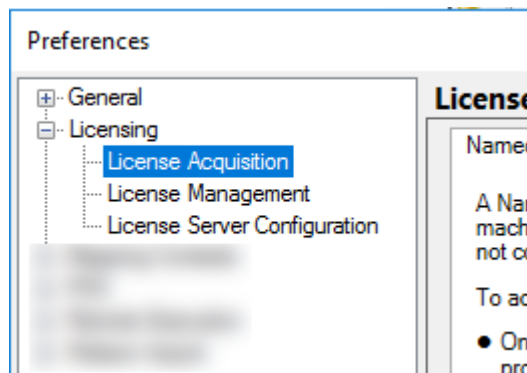
4. On the right side of the *Preferences* dialog, select the **Online** tab.
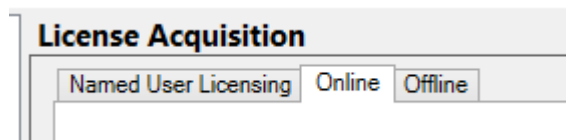
5. In the Online tab, click **Test** to check that you have access to the Authentication Server for online license activation. If the test is unsuccessful, go to the "Offline activation" section.

6. Copy the *entire* authentication code given in the email.
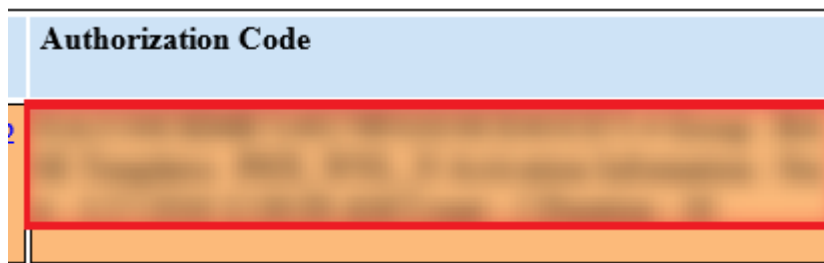
7. In the *Preferences* dialog, paste the copied code into the step 2 text field and click the **Activate** button.
    A verification pop-up confirming that the activation was successful.

Note: If your machine does not have internet access, or if the Online Activation failed, refer to the "Offline activation" section.

8. Click **OK** to close the pop-up verification.

9. In the navigation pane of the *Preferences* dialog, select the **License Management** node.

10. Verify that the correct license now appears. An example of a correctly installed local license is shown below:
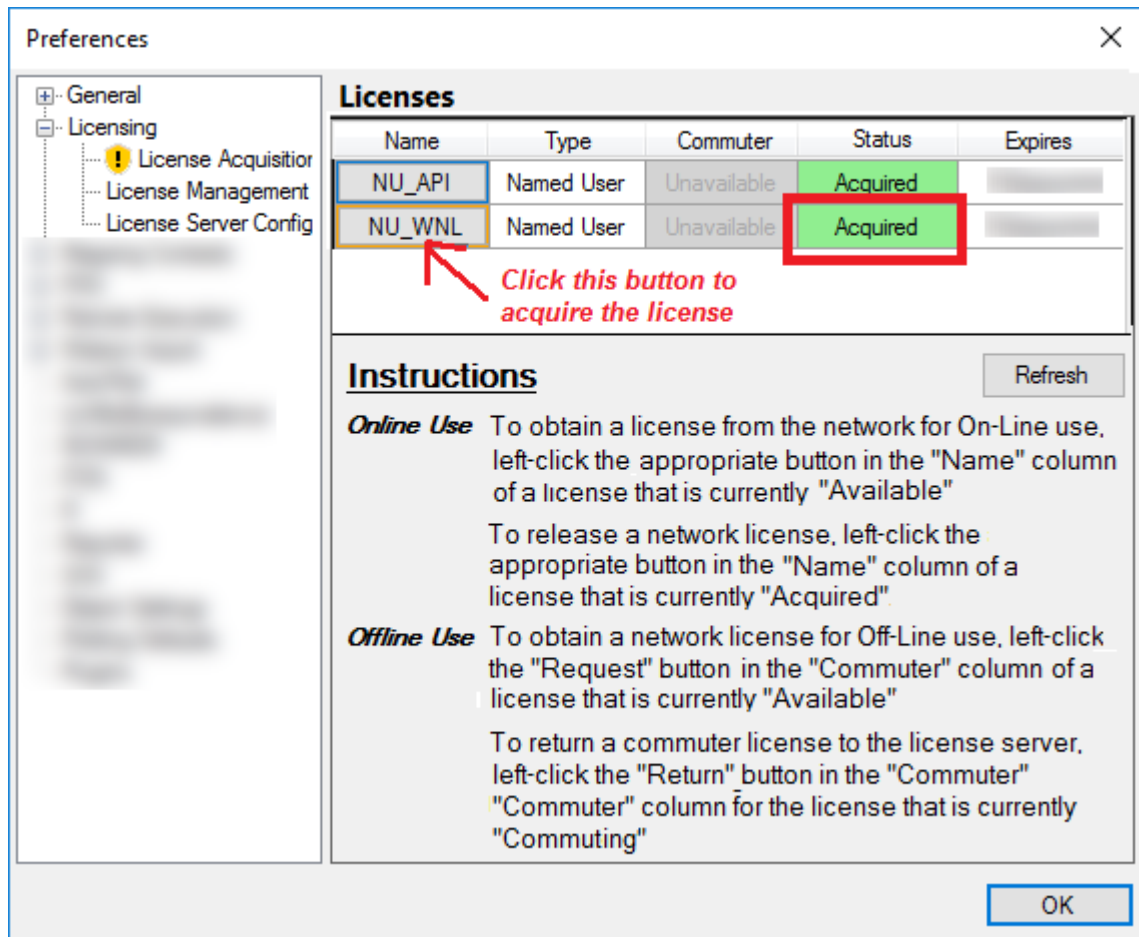
If the License Management window shows a successfully "Acquired" license, you are done with the license activation and are ready to use your Phoenix application.

Offline activation

Use either of the Options below to perform an Off-line License Activation:

Option 1:

• Login at: https://support.certara.com/login and then click the **License Generation** link.

• Copy your Authentication Code (from the license email) and paste it into the web page.

• Click the **Copy Lock Code** button in the *Preferences* dialog and paste the information into the **Locking Code** field in the web page.

• Click **Request License**.

An example is shown below:

- Copy the *entire* license code that is displayed in the bottom box.

- Paste the license code information into the field in the Offline tab of the *Preferences* dialog.

- Click **Install** to install the license you received through the website.

Option 2:

In the Offline tab of the *Preferences* dialog, click the **Email Certara license administrator** link to request instructions for an Offline activation. Include the following information in the email:

- Your System Lock Code (click the **Copy Lock Code** button in the *Preferences* dialog and paste the information into the email).
- Your order number from the Subject line of your license email (C-0xxxxx)

Certara Licensing will use the System Lock Code to make a license code for your machine, and email it back with instructions to do an Offline activation.

License management

The License Management panel in the *Preferences* dialog allows users to see which license types are available and acquired.
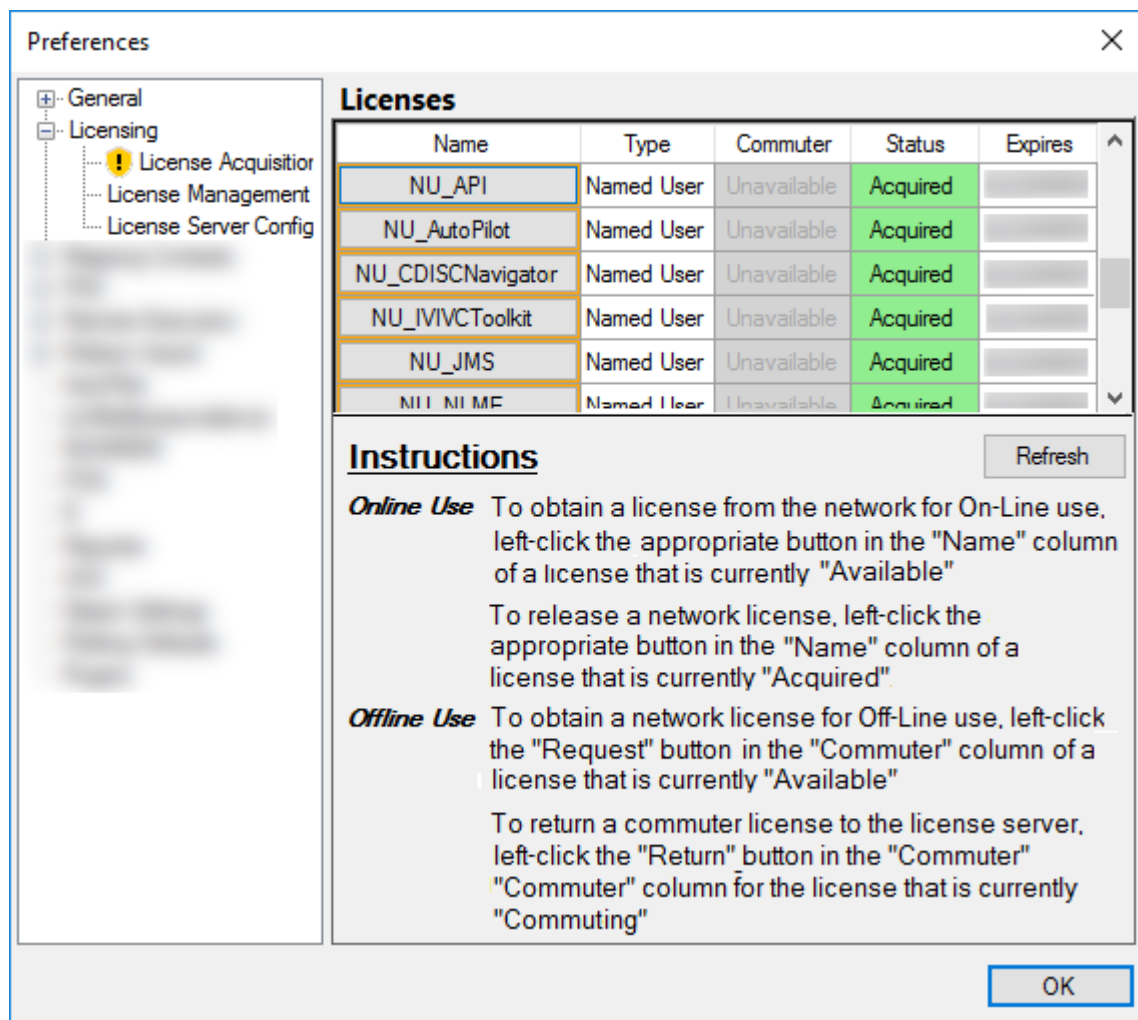
Figure 203-1. License Management preferences

Name: Lists the names of available licenses.
Type: Lists whether the license is a named user or named user server license.
Commuter: Lists licenses that are available to be commuted.
Status: Lists the status (Available, Acquired, etc.) of licenses
Expires: Lists the license expiration date.

To use the License Management dialog

1. Select **Edit > Preferences**.

2. In the *Preferences* dialog, expand the **Licensing** node in the menu tree by clicking the (**+**) signs.

3. Select **License Management**.

Local named user licenses

There are no options for local named user licenses in the License Management screen.

Named user server licenses

- To use a named user server license, click a license name in the **Name** column. The license status is changed to Acquired.

- Click the license name again to return the license. The license status is now Available.

Commuter licenses

- If a commuter license is available, click **Request** in the Commuter column. If the commuter license is acquired, its status is changed to Commuting.

   The date the commuter license expires is listed in the Expires column.

- To return a commuter license, click **Release** to release the license.

- Click **Refresh** to update the list of available licenses.

License Server configuration

The License Server Configuration panel allows users to add license server IP addresses to Phoenix. The number of available license servers is determined by the customer. Some versions of Sentinel license servers support redundant license servers.

The License Server Configuration panel has three fields: Name, IP Address, and Status. The Name field contains the name of the license server, the IP Address field contains the IP address of the license server, and the Status field contains the connection status.
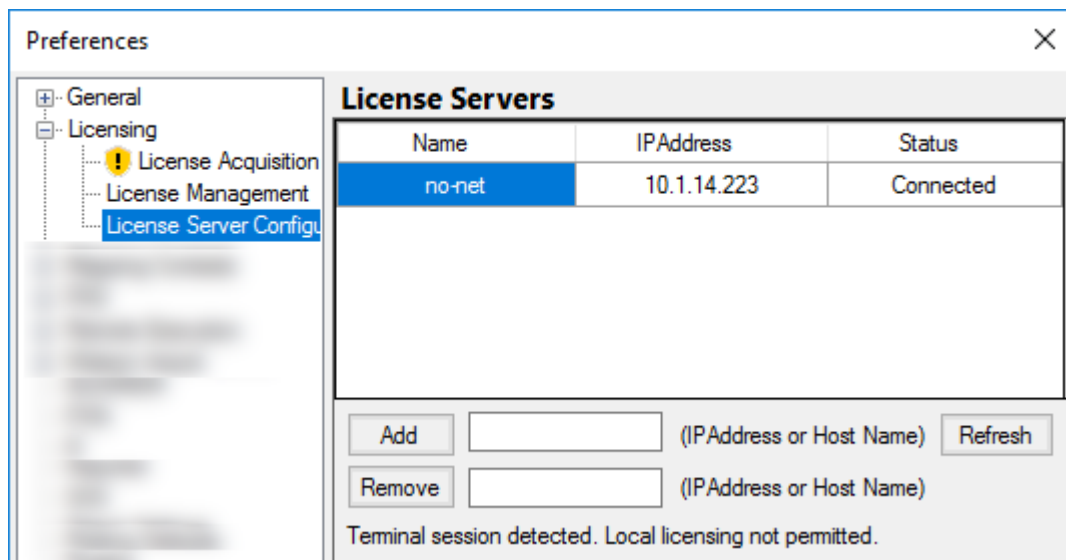
Figure 203-2. License Server Configuration panel

To use the License Server Management screen

- To *add* a license server, enter the IP address of the server in the **IP Address or Host Name** field and click **Add**.

- To *remove* a license server, enter the IP address of the server in the **IP Address** field and click **Remove**.

- To *update* the list of available license servers, click **Refresh**.

Testing the Phoenix installation

The following instructions test the installation of Phoenix WinNonlin by using a number of the sample files provided with the software. This chapter 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 set of Validation Suite Products is available from Certara. Contact the Certara sales department for more information.

Start Phoenix and create a new project

1. Double-click the Phoenix icon ( ) on your desktop to start Phoenix.

Note: AutoPilot users running on 64-bit operating systems should run the 32-bit version of Phoenix (**Phoenix32**) as opposed to the 64-bit version. The Phoenix desktop icon should be updated to reference the Phoenix32 executable as well.

2. Select **File > New Project** to create a new project. A new project is created in the Object Browser.

3. Name the new project `Install Test.`

The left panel's default view is the Object Browser, which contains the project, and the other folders and objects that are contained in the project. The right viewing panel's default view is blank, unless one of the project folders or the workflow is selected.
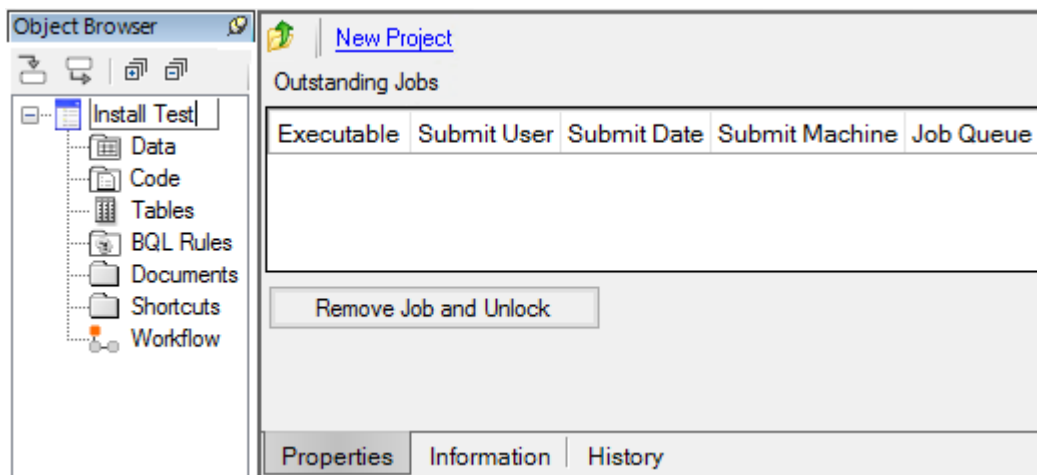
Figure 204-1. Creation of Install Test project denotes successful installation test

Confirm license installation

The ability to execute different Phoenix plug-ins depends on the license type installed. Use the *Preferences* dialog to check the installed Phoenix license(s).

1. Select **Edit > Preferences** to access the *Preferences* dialog.

2. Select **Licensing > License Management** to access the list of available licenses.

3. Confirm that the purchased license or licenses are listed in the Licenses panel.

Confirm plug-in startup

The Phoenix architecture is based on a series of plug-ins that allow different features to be enabled or disabled. Phoenix initializes these plug-ins when the application starts. The default setting is for all plug-ins to initialize when Phoenix starts. The plug-in initialization is independent of the installed license(s).

1. In the *Preferences* dialog, click **Plugins** to view the list of available plug-ins.
   - The Plugins panel on the right contains three tabs: **General**, **System**, and **Non-loaded**.
   - Each plug-in has two possible states, **Started** and **Stopped**.
   - All plug-ins are started the first time Phoenix is started.
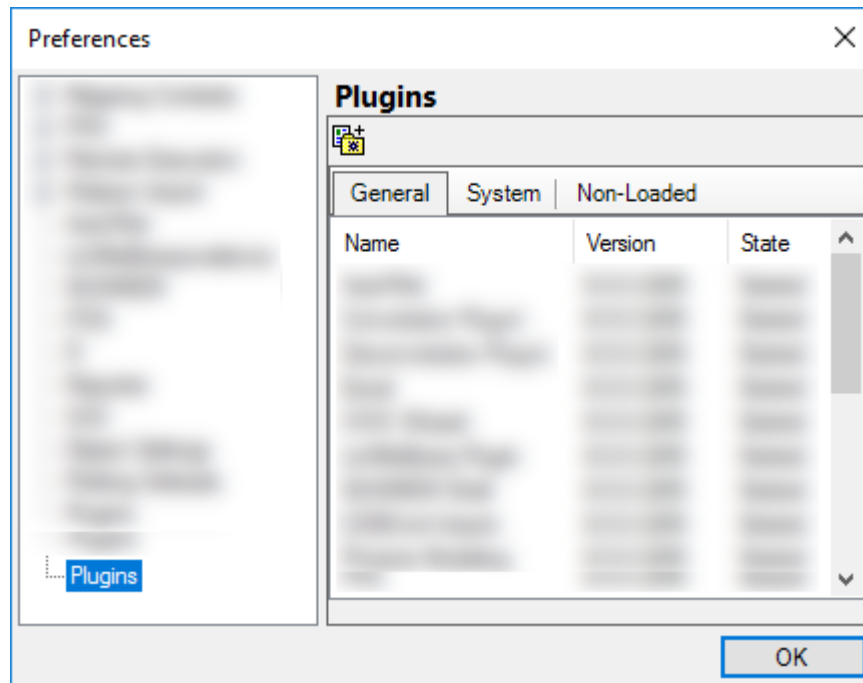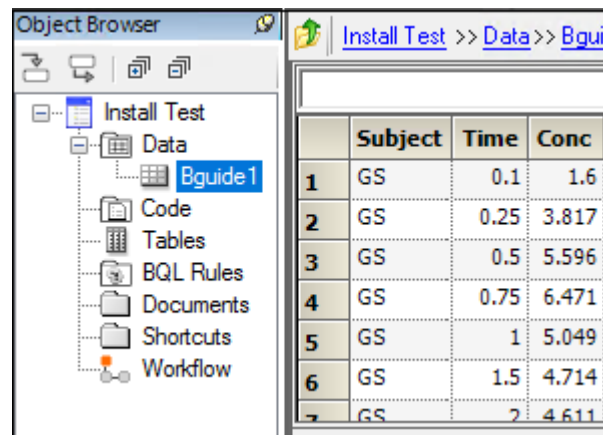
Figure 204-2. Plugins Preferences panel

2. Select the **General**, **System**, and **Non-loaded** tabs to see the review the state of each plug-in type and to confirm they are started.

3. Click **OK** to exit the *Preferences* dialog.

Import a dataset

The dataset `Bguide1.dat` is used to test key Phoenix functions.

1. Select **File > Import**, click (**Import File** icon), or right-click the Data Folder in the Object Browser and select **Import** to display the *Import File(s)* dialog.

2. Navigate to `<Phoenix_install_dir>\application\Examples\WinNonlin\Supporting files)`.

3. Select the file **Bguide1.dat** and click **Open**.
   The *File Import Wizard* dialog is displayed. The dialog is used to assign options for how the data are imported and presented.

4. Click **Finish**. The dataset is added to the project Data folder and the worksheet is displayed in the right viewing panel.
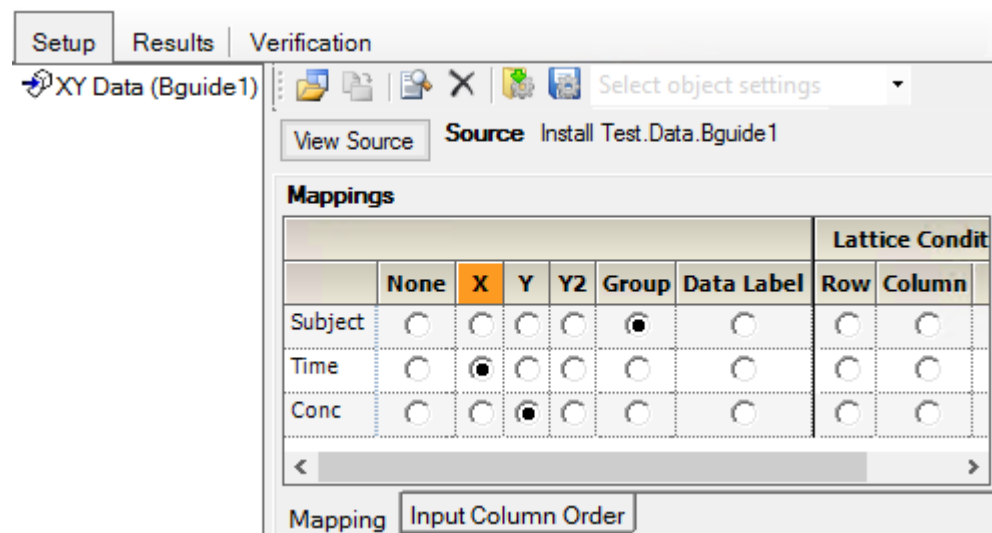
Figure 204-3. View of a dataset

Create a plot

1. Select the Workflow object in the Object Browser and then select **Insert > Plotting > XY Plot**.
   Or
   Right-click the Workflow object and select **New > Plotting > XY Plot**.

   The **XY Plot** object is added to the workflow in the Object Browser and is automatically opened in the right viewing panel. The default view of an object is the Setup tab, which contains all the steps necessary to set up an object.

2. Use the pointer to drag the **Bguide1** worksheet from the Data folder to the XY Data Mappings panel.

3. Use the option buttons in the XY Data Mappings panel to map the data types to the following contexts:
   Map **Subject** to the **Group** context.
   Map **Time** to the **X** context.
   Map **Conc** to the **Y** context.

Figure 204-4. Context mapping for XY Plot

4. Click ▶ (**Execute** icon) to execute the workflow.
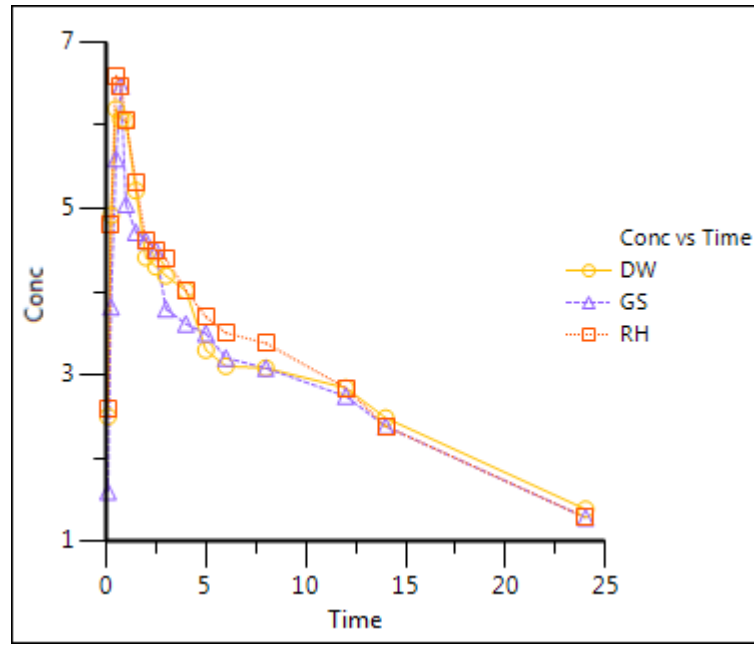
Figure 204-5. XY Plot results

5. Now use the Bguide1 dataset to test the Table object and its summary statistics function.

Create a table

1. Add the Table object to the workflow by selecting the **Workflow** object in the Object Browser and then selecting **Insert > Reporting > Table**.

2. Map the dataset Bguide1 as the input source for the Table object by dragging the **Bguide1** worksheet from the Data folder to the Table object Main Mappings panel.

3. Use the option buttons in the Main Mappings panel to map the data types to the following contexts:
Map **Subject** to the **Stratification Row** context.
Leave **Time** mapped to **None**.
Map **Conc** to the **Data** context.

4. In the Options tab (located below the Setup tab, specify which table type the Table object is to use by selecting **Table 1 - Column Summary by Row Stratification** from the **Table Type** menu.

5. Select the **Page Break on Row Stratification** checkbox.
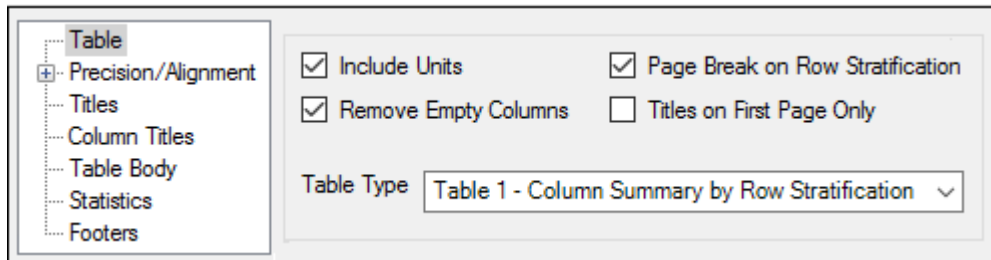
Figure 204-6. Setting Table object options

6. Select the **Statistics** tab, which is located underneath the Setup tab.

7. Click **Select All** to select all output statistics.

8. Execute the object.

The results are presented as three HTML tables in the Results tab. Compare the tables in the Results tab to the tables pictured below.

Subject		Conc
DW	N	16
	NMiss	0
	NObs	16
	Mean	4.004
	SD	1.432
	SE	0.358
	Variance	2.051
	CV%	35.8
	Min	1.39
	Median	4.10
	Max	6.20
	Range	4.81
	Mean Log	1.3179
	SD Log	0.4039
	Geometric Mean	3.736
	Geometric SD	1.498
	Geometric CV%	42.10
	CI 95% Lower	0.95
	CI 95% Upper	7.06
	CI 95% Lower Mean	3.24
	CI 95% Upper Mean	4.77
	CI 95% Lower Var	1.12
	CI 95% Upper Var	4.91
	CI GEO 95% Lower	1.58
	CI GEO 95% Upper	8.84

CI 95% Lower GEO Mean	3.01
CI 95% Upper GEO Mean	4.63
Lower 1SD	2.572
Upper 1SD	5.436
GEO Lower 1SD	2.494
GEO Upper 1SD	5.595
1%	1.39
2.5%	1.39
5%	1.39
10%	2.15
25%	2.90
50%	4.10
75%	5.14
90%	6.11
95%	6.20
97.5%	6.20
99%	6.20
IQR	2.24
Sum	64.06
Harmonic Mean	3.434
Skewness	0.0595
Skewness Pop	0.0537
Kurtosis	-0.8084
Kurtosis Pop	-0.9299
Pseudo SD	1.7578
KS PValue	0.96

Figure 204-7. Resulting HTML table for subject DW

Subject		Conc
GS	N	16
	NMiss	0
	NObs	16
	Mean	3.748
	SD	1.394
	SE	0.348
	Variance	1.942
	CV%	37.2
	Min	1.29
	Median	3.70
	Max	6.47
	Range	5.18
	Mean Log	1.2432
	SD Log	0.4334
	Geometric Mean	3.467
	Geometric SD	1.543
	Geometric CV%	45.46
	CI 95% Lower	0.78
	CI 95% Upper	6.72
	CI 95% Lower Mean	3.01
	CI 95% Upper Mean	4.49
	CI 95% Lower Var	1.06
	CI 95% Upper Var	4.65
	CI GEO 95% Lower	1.38
	CI GEO 95% Upper	8.73

CI 95% Lower GEO Mean	2.75
CI 95% Upper GEO Mean	4.37
Lower 1SD	2.354
Upper 1SD	5.141
GEO Lower 1SD	2.247
GEO Upper 1SD	5.348
1%	1.29
2.5%	1.29
5%	1.29
10%	1.51
25%	2.83
50%	3.70
75%	4.69
90%	5.86
95%	6.47
97.5%	6.47
99%	6.47
IQR	1.86
Sum	59.96
Harmonic Mean	3.141
Skewness	0.0524
Skewness Pop	0.0473
Kurtosis	-0.1695
Kurtosis Pop	-0.4740
Pseudo SD	1.7519
KS PValue	0.99

Figure 204-8. Resulting HTML table for subject GS

Subject		Conc
RH	N	16
	NMiss	0
	NObs	16
	Mean	4.154
	SD	1.502
	SE	0.375
	Variance	2.255
	CV%	36.2
	Min	1.29
	Median	4.20
	Max	6.60
	Range	5.31
	Mean Log	1.3500
	SD Log	0.4241
	Geometric Mean	3.857
	Geometric SD	1.528
	Geometric CV%	44.39
	CI 95% Lower	0.95
	CI 95% Upper	7.35
	CI 95% Lower Mean	3.35
	CI 95% Upper Mean	4.95
	CI 95% Lower Var	1.23
	CI 95% Upper Var	5.40
	CI GEO 95% Lower	1.56
	CI GEO 95% Upper	9.52

CI 95% Lower GEO Mean	3.08
CI 95% Upper GEO Mean	4.84
Lower 1SD	2.652
Upper 1SD	5.656
GEO Lower 1SD	2.524
GEO Upper 1SD	5.895
1%	1.29
2.5%	1.29
5%	1.29
10%	2.05
25%	2.98
50%	4.20
75%	5.19
90%	6.51
95%	6.60
97.5%	6.60
99%	6.60
IQR	2.21
Sum	66.46
Harmonic Mean	3.503
Skewness	-0.0029
Skewness Pop	-0.0027
Kurtosis	-0.4545
Kurtosis Pop	-0.6773
Pseudo SD	2.0453
KS PValue	1.00

Figure 204-9. Resulting HTML table for subject RH

Confirm noncompartmental analysis functions

1. Select **File > Load Project**. The *Load Project* dialog is displayed.

2. Navigate to `<Phoenix_install_dir>\application\Examples\WinNonlin`.

3. Select **Multiple_Profiles.phxproj** and click **Open**.

   This project contains:
   - A dataset worksheet (profiles)
   - A worksheet of dosing information (Dosing published from NCA)
   - An XY Plot object
   - An NCA model object
   - A Descriptive Statistics object
   - A Data Wizard object
   - An X-Categorical XY Plot object

4. Expand the workflow node.

5. Select the **NCA** model object in the Object Browser.

6. Select items in the Setup tab list to explore the data mappings and option settings.

7. Execute the object.

Text output

The **Core output** contains the model settings and the same data as the worksheets, but presented in plain ASCII text. If there were errors in the model they would be listed here. Part of this file is shown below:

```
…
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations:   12
Dose time:       0.00
Dose amount:       100.00
Calculation method: Linear Trapezoidal with Linear Interpolation
Weighting for lambda_z calculations: Uniform weighting
Lambda_z method: Find best fit for lambda_z, Log regression
Compute Concentrations at: 75

Summary Table
-------------
 Time   Conc.   Pred. Residual    AUC          AUMC       Weight
  min    ng/ml  ng/ml  ng/ml    min*ng/ml   min*min*ng/ml
 ---------------------------------------------------------------
0.0000 0.0000                    0.0000        0.0000
5.000  1816.                      4540.       2.270e+04
10.00  1687.                     1.330e+04    8.756e+04
15.00* 286.8   327.4 -40.61     1.823e+04    1.405e+05    1.000
20.00* 323.7   311.1  12.65     1.976e+04    1.674e+05    1.000
30.00* 321.5   280.8  40.75     2.290e+04    2.480e+05    1.000
45.00* 237.3   240.7 -3.445     2.717e+04    4.004e+05    1.000
60.00* 218.0   206.4  11.56     3.059e+04    5.786e+06    1.000
90.00* 192.6   151.8  40.80     3.675e+04    1.035e+06    1.000
120.0* 123.8   111.6  12.18     4.149e+04    1.518e+06    1.000
180.0* 40.00   60.35 -20.35     4.641e+04    2.179e+06    1.000
240.0* 36.20   32.63  3.572     4.869e+04    2.656e+06    1.000
360.0* 5.500   9.538 -4.038     5.119e+04    3.296e+06    1.000
480.0* 4.300   2.788  1.512     5.178e+04    3.539e+06    1.000
```

The **Settings** file lists all the settings used to specify the noncompartmental analysis.

```
…
   Sort: Subject, Form
   Time: Time [min]
   Concentration: Conc [ng/mL]
   Carry:
Dosing: (Internal)
Slopes: (Internal)
Partial Areas: (Internal)
Therapeutic Response: <None>
Units: (Internal)
Parameter Names: <None>
…
Plasma Model
Title=Processing Multiple Profiles with Model 200
Linear Trapezoidal Linear Interpolation
Sparse=False
Weighting=Uniform Weighting; 0
Dose Type=Extravascular
Dose Unit=ng
Dose Normalization=None
Compute Concentrations at: 75
```

Output data

The NCA object creates seven results worksheets: Dosing Used, Exclusions, Final Parameters, Final Parameters Pivoted, Partial Areas, Plot Titles, Slopes Settings, and Summary Table. Selections from the Final Parameters and Summary Table worksheets are shown below.

	Subject	Form	Parameter	Units	Estimate
1	1	Capsule	N_Samples		12
2	1	Capsule	Dose	ng	100
3	1	Capsule	Rsq		0.99267305
4	1	Capsule	Rsq_adjusted		0.99084131
5	1	Capsule	Corr_XY		-0.99632979
6	1	Capsule	No_points_lambda_z		6
7	1	Capsule	Lambda_z	1/min	0.016987622
8	1	Capsule	Lambda_z_intercept		6.8975665
9	1	Capsule	Lambda_z_lower	min	45
10	1	Capsule	Lambda_z_upper	min	240
11	1	Capsule	HL_Lambda_z	min	40.803072
12	1	Capsule	Span		4.7790519
13	1	Capsule	Tlag	min	0
14	1	Capsule	Tmax	min	15
15	1	Capsule	Cmax	ng/mL	2069.167
16	1	Capsule	Cmax_D	ng/mL/ng	20.69167
17	1	Capsule	Tlast	min	240
18	1	Capsule	Clast	ng/mL	19.31667
19	1	Capsule	Clast_pred	ng/mL	16.785864
20	1	Capsule	AUClast	min*ng/mL	72987.921
21	1	Capsule	AUClast_D	min*ng/mL/ng	729.87921
22	1	Capsule	AUCall	min*ng/mL	72987.921
23	1	Capsule	AUCINF_obs	min*ng/mL	74125.023
24	1	Capsule	AUCINF_D_obs	min*ng/mL/ng	741.25023
25	1	Capsule	AUC_%Extrap_obs	%	1.5340334
26	1	Capsule	Vz_F_obs	mL	0.079415003
27	1	Capsule	Cl_F_obs	mL/min	0.0013490721
28	1	Capsule	AUCINF_pred	min*ng/mL	73976.044
29	1	Capsule	AUCINF_D_pred	min*ng/mL/ng	739.76044
30	1	Capsule	AUC_%Extrap_pred	%	1.3357341
31	1	Capsule	Vz_F_pred	mL	0.079574936
32	1	Capsule	Cl_F_pred	mL/min	0.001351789
33	1	Capsule	AUMClast	min*min*ng/mL	3398545.5
34	1	Capsule	AUMCINF_obs	min*min*ng/mL	3738387.3
35	1	Capsule	AUMC_%Extrap_obs	%	9.090598
36	1	Capsule	AUMCINF_pred	min*min*ng/mL	3693862.3
37	1	Capsule	AUMC_%Extrap_pred	%	7.9947977
38	1	Capsule	MRTlast	min	46.563122
39	1	Capsule	MRTINF_obs	min	50.433539
40	1	Capsule	MRTINF_pred	min	49.933223
41	1	Capsule	AUC0_120	min*ng/mL	66331.921
42	1	Capsule	C75	ng/mL	288.54165

Figure 204-10. Final Parameters worksheet

	Subj	Form	Time (min)	lambda_	Conc (ng/mL)	Predicted (ng/mL)	Residual (ng/mL)	AUC (min*ng/mL)	AUMC (min*min*ng)	Weight
1	1	Capsule	0		0			0	0	0
2	1	Capsule	5		340.3167			850.79175	4253.9588	0
3	1	Capsule	10		1914			6486.5835	56357.918	0
4	1	Capsule	15		2069.167			16444.501	181801.68	0
5	1	Capsule	20		1470.917			25294.711	332941.29	0
6	1	Capsule	30		788.75			36593.046	598345.49	0
7	1	Capsule	45	*	496.4167	460.87344	35.543259	46231.796	943354.88	1
8	1	Capsule	60	*	372.8333	357.20475	15.628553	52751.171	1278670.5	1
9	1	Capsule	90	*	204.25	214.57954	-10.329536	61407.421	1889958	1
10	1	Capsule	120	*	124.05	128.90192	-4.8519188	66331.921	2388985.5	1
11	1	Capsule	180	*	39.25	46.515912	-7.2659123	71230.921	3047515.5	1
12	1	Capsule	240	*	19.31667	16.785864	2.5308059	72987.921	3398545.5	1
13	1	Tablet	0		0			0	0	0
14	1	Tablet	5		1474.2			3685.5	18427.5	0
15	1	Tablet	10		2475			13558.5	98730	0
16	1	Tablet	15		949.3			22119.25	196203.75	0
17	1	Tablet	20		665.7			26156.75	265087.5	0
18	1	Tablet	30		426.6			31618.25	395647.5	0
19	1	Tablet	45		293.3			37017.5	590621.25	0
20	1	Tablet	60		232			40957.25	794010	0
21	1	Tablet	90		168.6			46966.25	1230420	0
22	1	Tablet	120		108.4			51121.25	1653150	0
23	1	Tablet	180	*	45.7	52.948237	-7.2482367	55744.25	2290170	1
24	1	Tablet	240	*	15.2	12.18823	3.0117702	57571.25	2646390	1
25	1	Tablet	360	*	0.6	0.64583102	-0.0458310	58519.25	2878230	1

Figure 204-11. Summary Table worksheet

Plots

A total of 12 plots are generated; one for each of two formulations, for each of the six subjects. The first two charts for subject one are shown below.
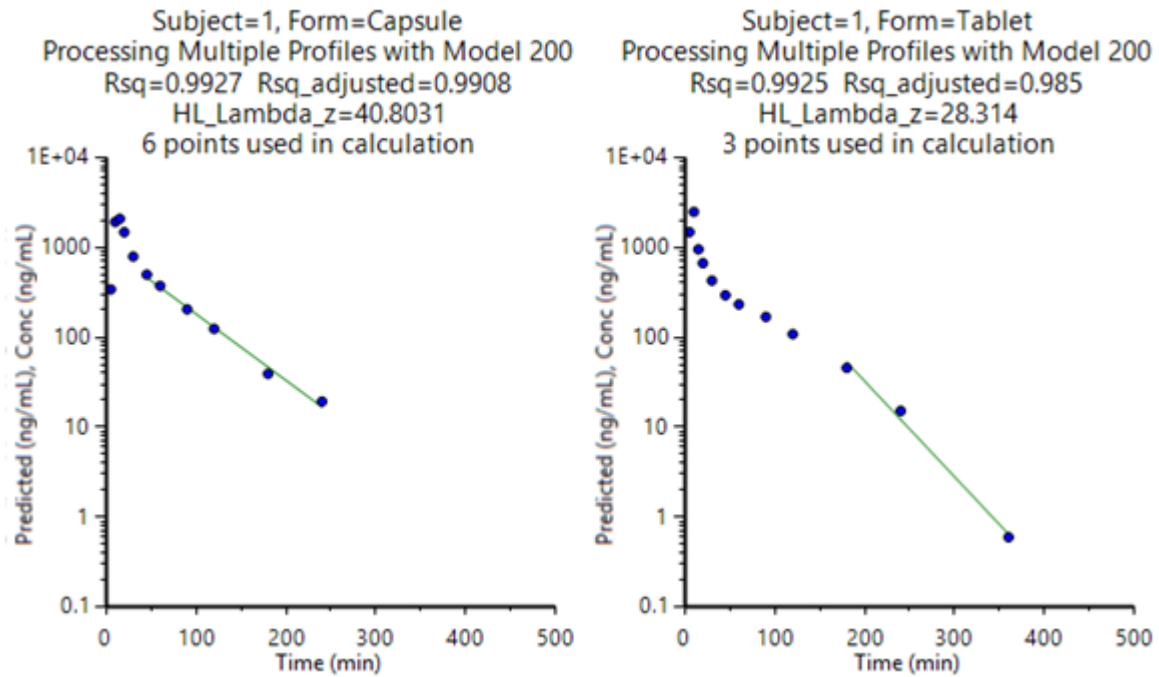
Figure 204-12. Plots for subject one, capsule and tablet formulation

Confirm pharmacokinetic modeling functions

1. Select **File > Load Project**. The *Load Project* dialog is displayed.

2. Navigate to `<Phoenix_install_dir>\application\Examples\WinNonlin`.

3. Select **PK_Model.phxproj** and click **Open**.

   This project contains:
   - A dataset worksheet (study1).
   - An XY Plot object.
   - A PK model object.

4. Expand the workflow node.

5. Select the **PK** Model object in the Object Browser.

6. Select items in the Setup tab list to explore the model's data mappings and option settings.

   The imported PK Model object uses PK Model 3, which is a one-compartment model with 1st order absorption.

7. Execute the object.

Worksheet results

The PK Model object's output worksheets partially include Condition Numbers, Diagnostics, Dosing Used, Final Parameters, Initial Estimates, Secondary Parameters, and Summary Table. The Final Parameters, Secondary Parameters, and Summary Table worksheets are shown below.

	Sub	Par	Units	Estimate	StdError	CV%	UnivarCI_L	UnivarCI_U	PlanarCI_L	PlanarCI_U
1	1	V_F	mL	301.28617	5.4850738	1.8205528	289.3352	313.23713	283.22832	319.34401
2	1	K01	1/hr	2.1586326	0.090628388	4.1984166	1.96117	2.3560951	1.8602676	2.4569975
3	1	K10	1/hr	0.21483403	0.007340839	3.4169816	0.1988397	0.23082837	0.19066667	0.2390014

Figure 204-13. Final Parameters worksheet

	Subject	Parameter	Units	Estimate	StdError	CV%
1	1	AUC	hr*ng/mL	30.899234	0.63214664	2.0458327
2	1	K01_HL	hr	0.32110476	0.013467848	4.1942224
3	1	K10_HL	hr	3.226431	0.11013642	3.413568
4	1	CL_F	mL/hr	64.726523	1.3255206	2.0478785
5	1	Tmax	hr	1.1870389	0.026332083	2.2182999
6	1	Cmax	ng/mL	5.1439722	0.046900364	0.91175384

Figure 204-14. Secondary Parameters worksheet

	Sub	Time_obs (hr)	Conc_obs (ng/mL)	Time (hr)	Conc (ng/mL)	Predicted (ng/mL)	Residual (ng/mL)	W	SE_Yhat	Standard_Re
1	1	0.1	1.29	0.1	1.29	1.2745998	0.015400175	1	0.033025914	0.15795305
2	1	0.25	2.81	0.25	2.81	2.6889731	0.12102695	1	0.055940643	1.4005554
3	1	0.5	4.16	0.5	4.16	4.1158923	0.044107747	1	0.058589906	0.52112365
4	1	0.75	4.6	0.75	4.6	4.8144531	-0.21445309	1	0.049693255	-2.3788162
5	1	1	5.13	1	5.13	5.0953875	0.034612464	1	0.045856544	0.37556116
6	1	1.5	5.03	1.5	5.03	5.051743	-0.021742964	1	0.050117469	-0.24181407
7	1	2	4.78	2	4.78	4.6987536	0.081246401	1	0.050279037	0.90448852
8	1	2.5	4.39	2.5	4.39	4.2750813	0.11491872	1	0.045791316	1.2464824
9	1	3	3.68	3	3.68	3.8583222	-0.17832217	1	0.041419535	-1.8922238
10	1	4	3.2	4	3.2	3.1202607	0.079739284	1	0.040325291	0.84190556
11	1	5	2.55	5	2.55	2.5179435	0.03205647	1	0.044871579	0.34601201
12	1	6	2.03	6	2.03	2.0312675	-0.001267533	1	0.048709632	-0.013977098
13	1	8	1.28	8	1.28	1.3218078	-0.041807823	1	0.049677892	-0.46370881
14	1	12	0.552	12	0.552	0.5597105	-0.007710497	1	0.037020818	-0.080273645
15	1	14	0.321	14	0.321	0.36421764	-0.043217644	1	0.029360941	-0.43802838

Figure 204-15. Summary Table worksheet

Text output

The **Core output** text results include all model settings and iterations, including the output from the worksheets. Any model errors would be listed here. Part of this file is shown below.

```
…
Listing of input commands
 MODEL 3
 NVAR 3
 NPOI 1000
 XNUM 2
 YNUM 3
 NCON 3
 CONS 1,2,0
 METH 2'Gauss-Newton (Levenberg and Hartley)
 ITER 50
 INIT 0.25,1.81,0.23
 MISS '.'
 DATA 'WINNLIN.DAT'
 BEGIN
```

The **Settings** file lists all the settings used to specify the noncompartmental analysis. Part of this file is shown below.

```
…
Main: PK Model.Data.study1
   Sort: Subject
   Time: Time [hr]
   Concentration: Conc [ng/mL]
   Carry:
Dosing: (Internal)
Initial Estimates: (Internal)
Units: (Internal)
***** Other Parameters *****
…
PK 3-[PK]
Gauss-Newton (Levenberg and Hartley)
Convergence criteria of 0.0001 used during minimization process
50 maximum iterations allowed during minimization process
```

Plots

The plot results include Observed Y and Predicted Y vs X, Partial Derivatives Plot, Predicted Y vs Observed Y, Predicted Y vs X, Residual Y vs Predicted Y, and Residual Y vs X. Some plot results are shown below.
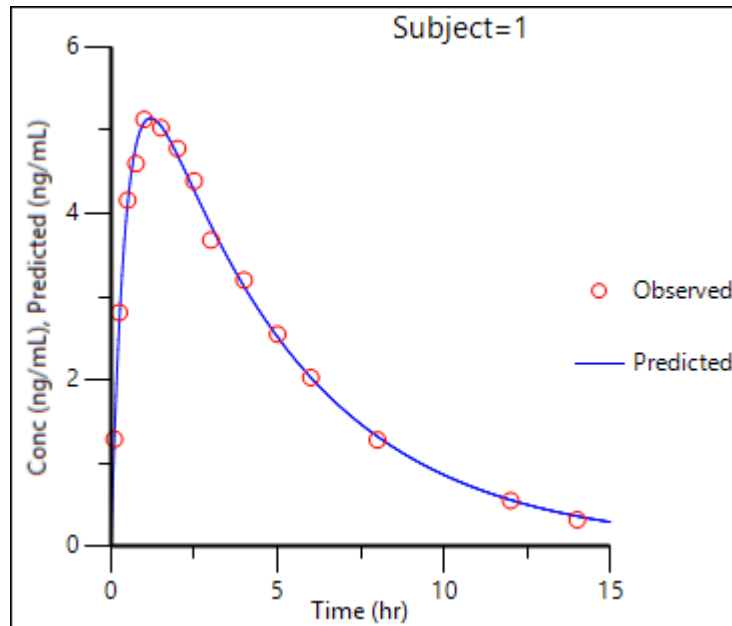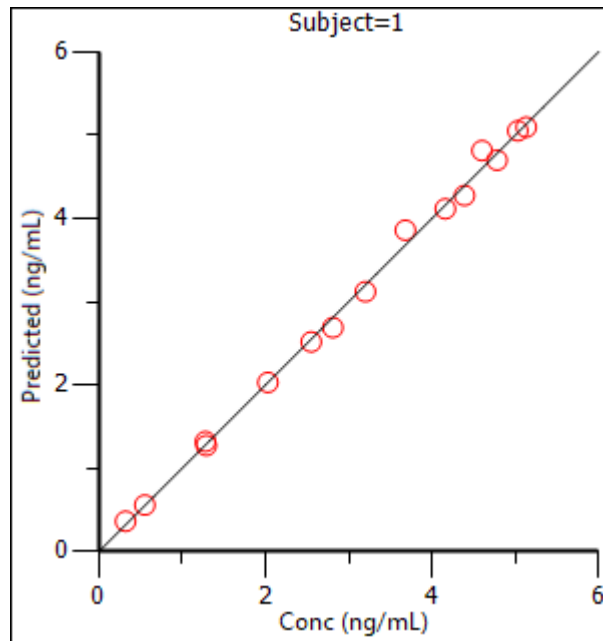

Figure 204-16. Observed Y and Predicted Y vs X

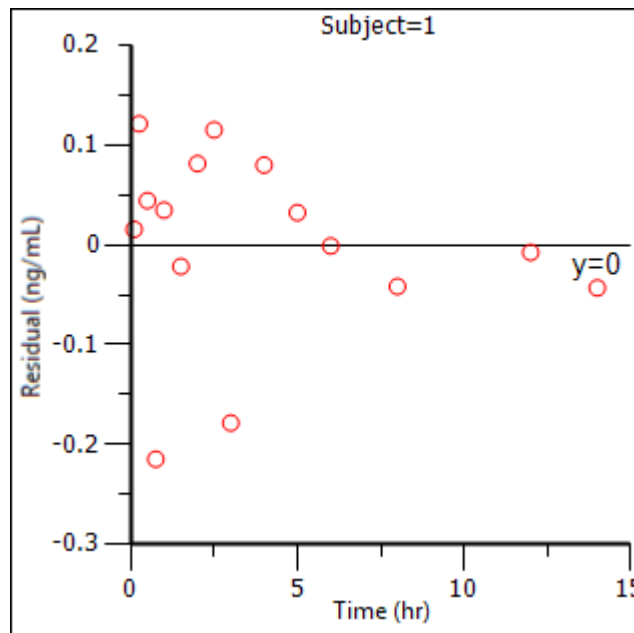*Figure 204-17. Predicted Y vs Observed Y*

Figure 204-18. Residual Y vs X

Confirm bioequivalence functions

1. Select the **Install Test** project in the Object Browser.

2. Select **File > Import**.

3. In the *Import File(s)* dialog, navigate to `<Phoenix_install_dir>\application\Exam-ples\WinNonlin\Supporting files`.

4. Select the file `Seq2Per4.csv` and click **Open**.

5. In the *File Import Wizard* dialog, click **Finish**. The dataset is added to the project Data folder.

6. Select the project workflow in the Object Browser and then select **Insert > Computation Tools > Bioequivalence**.
The **Bioequivalence** object is added to the workflow in the Object Browser.

Note: The default settings for a new Bioequivalence model are **Crossover** as the type of study and **Average** as the type of bioequivalence.

7. Use the pointer to drag the **Seq2Per4** worksheet from the Data folder to the Main Mappings panel.
The Seq2Per4 dataset is mapped to the Bioequivalence object.

8. Use the option button in the Main Mappings panel to map **AUC** to the **Dependent** context.

   The following data types are automatically mapped to contexts when the dataset is mapped to the Bioequivalence model.
   Sequence is mapped to the **Sequence** context.
   Subject is mapped to the **Subject** context.
   Period is mapped to the **Period** context.
   Formulation is mapped to the **Formulation** context.
   AUC is mapped to the **Dependent** context.

9. In the Model tab (located below the Setup tab), ensure that **Crossover** is selected as the **Type** of study, **Average** is selected as the **Type of Bioequivalence**, and **R** is selected as the **Reference Formulation**.

Figure 204-19. Settings for a Bioequivalence model

10. Select the **Fixed Effects** tab, which is located below the Setup tab.
    Ln(x) is automatically selected in the **Dependent Variables Transformation** menu. Do not change this setting.

11. Execute the object.

Output data

The bioequivalence model worksheet output partially includes Average Bioequivalence, Diagnostics, Final Fixed Parameters, Final and Initial Variance Parameters, Least Squares Means, and Sequential Tests. The Diagnostics, Final Variance Parameters, and Sequential Tests worksheets are shown below.

	Depend	Units	FormVar	FormR	RefLSM	RefLSM_S	RefGeoL	Test	TestLSM	TestLSM_
1	Ln(AUC)		Formulation	R	5.5537097	0.10472836	258.1936	T	5.7481984	0.1196125

TestGeoLSM	Difference	Diff_SE	Diff_DF	Ratio_%Ref_	CI_80_Lower	CI_80_Upper
313.62513	0.19448871	0.09348619	24.829354	121.46898	107.40168	137.37878

CI_90_Lower	CI_90_Upper	CI_95_Lower	CI_95_Upper	t1_TOST	t2_TOST	Prob_80_00
103.53701	142.50665	100.1885	147.26953	4.4673151	-0.30651416	7.514E-05

Prob_125_00	MaxProb	TotalProb	Power_TOST	AHpval	Power_80_20	Prob_Eq_Var
0.38088443	0.38088443	0.38095957	0.08554966	0.38080929	0.7482755	

Figure 204-20. Average Bioequivalence worksheet

	Dependent	Units	Diagnostic	Value
1	Ln(AUC)		Total Observatio	48
2	Ln(AUC)		Observations Us	48
3	Ln(AUC)		Obs. Missing Mo	0
4	Ln(AUC)		Residual SS	0
5	Ln(AUC)		Residual df	0
6	Ln(AUC)		Convergence	Achieved
7	Ln(AUC)		REML log(likelih	-19.238555
8	Ln(AUC)		-2 * REML log(li	38.477111
9	Ln(AUC)		Akaike's Inform	60.477111
10	Ln(AUC)		Schwarz's Bayes	79.591476
11	Ln(AUC)		Hessian eigenva	855.2051
12	Ln(AUC)		Hessian eigenva	715.32814
13	Ln(AUC)		Hessian eigenva	158.63358
14	Ln(AUC)		Hessian eigenva	63.03212
15	Ln(AUC)		Hessian eigenva	21.604278

Figure 204-21. Diagnostics worksheet

	Dependent	Units	Parameter	Estimate
1	Ln(AUC)		lambda(1,1)_11	0.27893988
2	Ln(AUC)		lambda(1,2)_11	0.35567907
3	Ln(AUC)		lambda(2,2)_11	-1.97E-13
4	Ln(AUC)		Var(Period*For	0.10761781
5	Ln(AUC)		Var(Period*For	0.09035641

Figure 204-22. Final Variance Parameters worksheet

	Dependent	Units	Hypothesis	Numer_DF	Denom_DF	F_stat	P_value
1	Ln(AUC)		int	1	10.008139	3055.0348	8.9E-14
2	Ln(AUC)		Sequence	1	10.008139	0.095274924	0.7639047
3	Ln(AUC)		Formulation	1	24.829354	4.328066	0.047965077
4	Ln(AUC)		Period	3	28.392036	2.1673487	0.11384356

Figure 204-23. Sequential Tests worksheet

This concludes the Phoenix installation tests.

Test installation of Phoenix NLME

This section tests Phoenix WinNonlin's population modeling functions. This test is not intended as a full validation of population modeling.

Users who have purchased a license for Phoenix NLME can use the Maximum Likelihood Models object to create and test population models. After Phoenix is installed, follow the steps below to confirm that population modeling is working correctly.

If any problems are encountered during this installation test, report the issue to Customer Support.

Start Phoenix and create a project

1. Double-click the Phoenix icon ( ) on your desktop to start Phoenix.

2. Select **File > New Project** to create a new project. A new project is created in the Object Browser.

3. Name the new project `Installation Project`.

4. To verify active licenses select **Help > About Phoenix**. For this installation test to work users must have an active license for Phoenix NLME 8.1.

Confirm population modeling functionality

This example verifies that the Phoenix NLME license and the Minimal GNU C++ compiler are correctly installed and configured. If Phoenix is being used without population modeling functionality, then skip this part of the installation test.

1. Select **File > Import**.

2. In the *Import File(s)* dialog, navigate to `<Phoenix_install_dir>\application\Examples\NLME\Supporting files`.

3. Select **theopp.csv** and click **Open**.

4. In the *File Import Wizard* dialog, click **Finish**. The dataset is added to the project Data folder and the worksheet is opened.

5. Select the workflow object in the Object Browser.

6. Select **File > Load Workflow Template**.

7. In the dialog, navigate to `<Phoenix_install_dir>\application\Examples\NLME\Supporting files`.

8. Select **Diagonal Model.phxtmplt** and click **Open**.

WinNonlin template files store information about settings and internal worksheets, but do not store external data sources.

The template file adds a one-compartment, 1st order absorption model that uses weight as a covariate. The model uses the FOCE L-B (First Order Conditional Estimation with the Lindstrom-Bates iterative algorithm) run method.

• Select the Structural, Parameters, and Run Options tabs to examine the model configuration.

The Parameters tab contains several sub-tabs that list fixed effects, random effects, and covariates.

9. Use the pointer to drag the **theopp** worksheet from the Data folder to the Main Mappings panel.

The theopp dataset is mapped to the Diagonal model and the study variables **xid**, **dose**, **time**, **yobs**, and **wt** are automatically mapped to the contexts **ID**, **Aa**, **Time**, **CObs**, and **wt**, respectively.

10. Execute the object.

11. Close the *NLME Job Status* dialog by clicking the X in the upper right corner.

Verify the results

1. Select the **Verification** tab.

The Verification Results state that the model successfully executed, and that no errors occurred.
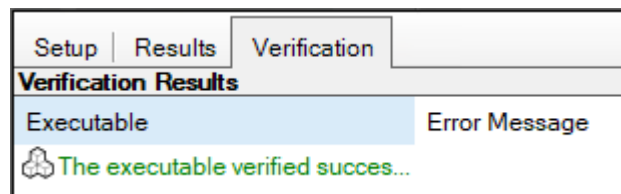

Figure 204-24. Verification tab

2. Select the **Results** tab.

The model object produces text files, plots, and worksheets. The output types are listed below.

Output data

The model creates 23 worksheet results. Some of the output worksheets are Eta, EtaCovariate, Omega, and Theta. Not all worksheets listed under Output Data contain results.

Confirm the accuracy of some of the output in order to complete the installation test.

1. In the Output Data, select the Theta worksheet and confirm that the following estimates are the same (after rounding):
tvKa   1.55696
tvV   0.455554
tvCl   0.0402882
stdev0 0.692202

	Scenario	Param	Estimate	Units	Stderr	CV%	2.5% CI	97.5% CI	Var. Inf
1		tvKa	1.5569604		0.1577445	10.131568	1.2447663	1.8691545	
2		tvV	0.45555382		0.021240349	4.6625334	0.41351677	0.49759086	
3		tvCl	0.040288243		0.0035422835	8.7923505	0.033277665	0.047298821	
4		stdev0	0.69220223		0.049209233	7.1090833	0.59481161	0.78959284	

Figure 204-25. Theta worksheet

	Scenario	xid	nV	nKa	nCl	nV_shrink	nKa_shrink	nCl_shrink
1		1	-0.209411	0.127672	-0.62549	0.148239	0.056501	0.154346
2		2	-0.0257136	0.22751	0.0881794	0.234426	0.072118	0.135127
3		3	0.0435623	0.393174	-0.00059655	0.204953	0.078919	0.149193
4		4	-0.0468817	-0.25137	-0.0792458	0.262562	0.065061	0.153702
5		5	0.068973	-0.0692733	0.0800722	0.193197	0.049368	0.108945
6		6	0.0970105	-0.307421	0.212374	0.402893	0.1041	0.204487
7		7	0.0994328	-0.80097	0.21714	0.456722	0.08528	0.171494
8		8	0.0831916	-0.148401	0.137447	0.306627	0.080195	0.165974
9		9	-0.189691	1.42661	-0.175047	0.155803	0.234206	0.168354
10		10	-0.0246066	-0.767507	-0.209189	0.261928	0.049456	0.134938
11		11	0.193702	0.749686	0.34077	0.21555	0.096903	0.147827
12		12	-0.0863166	-0.538814	0.00485868	0.27301	0.054083	0.109486

Figure 204-26. Eta worksheet

Plots

Thirty-nine plots are listed in the Plots section. Not all listed plots have results.

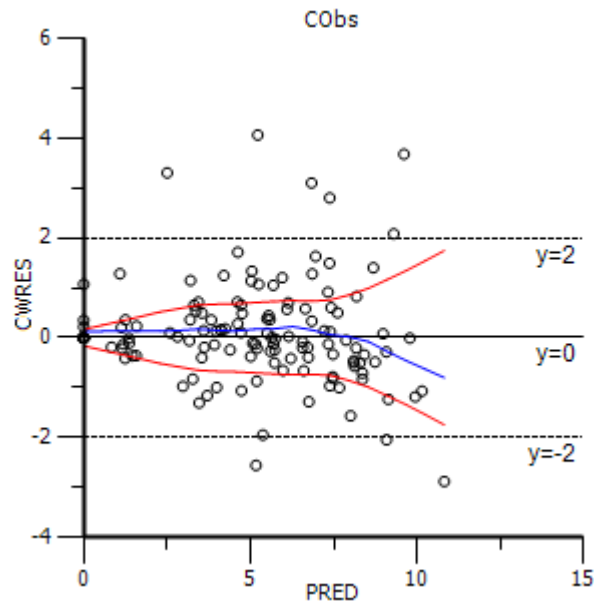1. In the Plot output, select Pop CWRES vs PRED and compare it to the screen shot below:

Figure 204-27. Pop CWRES vs PRED

Text output

The Maximum Likelihood Models object creates six text files. The Settings text file lists model settings, part of which is shown below.

```
…
  Sort:
  ID: xid
  Aa: dose
  Time: time
  CObs: yobs
  wt: wt
…
test(){
  deriv(Aa = -Ka * Aa)
  deriv(A1 = Ka * Aa - Cl * C)
  dosepoint(Aa)
  C=A1/V
  error(CEps = 1)
  observe(CObs = C + CEps)
  stparm(Ka = tvKa * exp(nKa))
  stparm(V = tvV * exp(nV))
  stparm(Cl = tvCl * exp(nCl))
  covariate(wt)
  fixef(tvKa = c(, 1.54697,))
  fixef(tvV = c(, 0.455465,))
  fixef(tvCl = c(, 0.0402979,))
  ranef(diag(nV, nKa, nCl)=c(0.01809, 0.41265, 0.06997))
}
------------------------------------
id("xid")
time("time")
dose(Aa<-"dose")
covr(wt<-"wt")
obs(CObs<-"yobs")
table(file="posthoc.csv", time(0), Ka,V,Cl)
------------------------------------
Run Options
Method: FOCE L-B
N Iter:1000
Input sorted by subject+time
Enabling automatic log transform (if applicable)
ODE solver method: matrix exponent
Method of computing standard errors: Central Diff
Hessian standard errors
Confidence Level %95
Simple run was performed
```

This concludes the installation test for Phoenix NLME. Close project without saving it.

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