

NONMEM Users Guide - Part III
NONMEM 7.4.3 Installation Guide

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by

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PREFACE

The NONMEM Installation Guide contains more details on NONMEM installation than are needed by most users. If NONMEM is to be installed under Microsoft Windows/MS-DOS or Unix/Linux/OS X, look first at the README_743 document on the CD. It describes an easy installation using SETUP74.BAT (for Windows/MS-DOS) and SETUP74 (for Unix/Linux/OS X).

All files are distributed on a single CD. There is no single-precision version of NONMEM 7. You must replace all of NONMEM, PREDPP, and NM-TRAN. Do not mix new and old versions of the various components of the NONMEM system!

The MS-DOS installation utility is now called SETUP74.BAT. The UNIX installation utility is called SETUP74. UNIX shell scripts NMFE74 and MS-DOS batch file NMFE74.BAT are used to run NONMEM 7.4. They both have an option "recompile" that allows the source code to be recompiled easily after a change to SIZES.

There is a single INCLUDE file named SIZES.f90. This file contains all the constants pertaining to NM-TRAN, NONMEM, and PREDPP. Many of the constants can be changed with the \$SIZES record in a control stream file, although still some require modification in SIZES.f90, and recompilation of the NM-TRAN and NONMEM system.

When re-running old NONMEM problems, please be aware of the following facts:

NONMEM output changes slightly with each version.

It is possible that the results of the Estimation and Covariance Steps may be different than with earlier versions of NONMEM.

Old Model Specification files (MSF's) *cannot* be re-used with a new release.

Old Fortran subroutines (e.g., PRED, MODEL, PK, DES, AES routines) (whether user-coded or generated by NM-TRAN) *cannot* be re-used without certain modifications.

Old NM-TRAN control streams and NM-TRAN data files can be re-used. Old NONMEM data files can be re-used.

In general, we have tried to make NONMEM 7.4 upwards compatible from earlier versions of NONMEM 7.

In the hardcopy and pdf versions of this guide, significant changes to the content versus the NONMEM 7.3 have been made. The appropriate citation to use for the NONMEM software and these guides is:

Beal SL, Sheiner LB, Boeckmann AJ, and Bauer RJ (eds) NONMEM 7.4 Users Guides. (1989–2017). ICON plc, Gaithersburg, MD. <https://nonmem.iconplc.com/nonmem743/guides>

Chapter I - Introduction

1. How to Use This Guide

This guide describes how to install and test the NONMEM system, which consists of NM-TRAN, NONMEM, and PREDPP Version 7.4. The NONMEM system is distributed as FORTRAN 95 source code. There is only one version of NONMEM 7.4; this guide tells how to modify the installation in order to customize it for your computer and your operating system.

The first chapter describes system and compiler requirements and discusses certain decisions that must be made before installation begins. Later chapters give step by step instructions for installing the major components of the system, testing them, and running them.

Please follow these steps when installing the NONMEM system:

1. Read this Users Guide III. It describes the various components of the NONMEM system and how they are used. Please familiarize yourself with the components of the NONMEM system and how they relate to each other.
2. Review decisions. The people who will use NONMEM should be consulted on these decisions.
3. Follow the instructions on installation.
4. If any questions or persistent problems arise regarding installation, please phone the NONMEM consultant at (301) 944-6807 between the hours of 8:00AM and 5:00PM EDT, or preferably send electronic mail to: nmconsult@iconplc.com.
5. You may also ask questions of other NONMEM users by way of the NONMEM Users Network, described in Section 6.

Please do not make ANY changes to the source code other than the ones described in this guide without first talking to the NONMEM consultant. Unless such changes are approved, the NONMEM consultant cannot help you with problems which may arise. The NONMEM consultant is familiar with the problems you will encounter during the installation, and will be able to suggest the best fix for your situation.

2. System Requirements

2.1. Memory Requirements (RAM)

The size of a NONMEM executable ("load module") varies considerably, depending on which optional routines are included. However, all modern computers can run NONMEM 7 easily.

2.2. Compiler Requirements

The compiler must implement the ANSI FORTRAN 95 standard. The Essential Lahey Fortran 90 Compiler does **not** support the complete Fortran 95 standard and is **not** suitable for use with NONMEM, although other Lahey Fortran compilers can be used. In addition the compiler must implement certain other features:

1. It must allow the default length of integer variables to be 4 bytes. *All subroutines must be compiled with the default length of integer variables as 4 bytes.*
2. It must allow variables of different types to share the same storage area using the EQUIVALENCE statement.
3. It is desirable that floating point underflow be permitted to occur silently, but *only* if the resulting value is set to zero; this is the default action specified by the IEEE 754 standard for floating point arithmetic.
4. It must allow the FORTRAN INCLUDE statement. It is part of the FORTRAN 95 language. If your system does not permit INCLUDE statements, please contact the NONMEM consultant.

NONMEM 7.4 has been successfully compiled using the following compilers:

- 1) Intel Fortran 8.0 and higher, for Windows, MAC OSX, or Linux
- 2) GNU gfortran version 4.6.0 for Windows, or version 4.4.0 20090219 Trunc version 144289 for Linux.
- 3) SUN/Solaris using f95
- 4) MAC OSX 10.6 (Snow Leopard)

2.3. Speed Requirements

NONMEM run times vary greatly, depending on the amount of data and the complexity of the model. Extensive use is made of floating point arithmetic, so it is necessary to have a floating point (math) processor. With most modern machines, simple problems with moderate size population data sets, such as are used in the various examples in the Users Guide, will run in a reasonable amount of time (no more than an hour, often much less). With more complicated problems, run times can be as much as 10 hours or more. Machines with speeds of 1 GHz or more are preferred.

Prior to installing NONMEM a test of your compiler is appropriate to assure that your compiler

is properly configured. An example of such a test is given in the Installation Chapter IV.

2.4. Disk Space Requirements

The NONMEM system is read from the NONMEM distribution medium in the form of encrypted FORTRAN 95 source code. Chapter II describes the number of bytes of storage required for each file on the medium. On most systems, the compiled object code (binary code) occupies more disk space than does the original source code. In general, at least 400 MB of disk storage are desirable during the installation of NONMEM. Additional storage will be needed for the user files: input data files, output reports, etc.

3. Additional Documentation

All other volumes of the NONMEM Users Guide should be available for reference as needed during the installation process. In particular, examples of input and output to be used as test cases during the installation are found in NONMEM Users Guide, Parts I and VI. The inputs are recorded on the distribution medium. The results files can be found at

<https://nonmem.iconplc.com/nonmem743/STDResults/>

The additional documentation is:

Part I - Users Basic Guide

A step by step discussion of various NONMEM features and statistical concepts involved in using NONMEM. Of historical interest for early versions of NONMEM. Part V should be read first.

Part II - Users Supplemental Guide

A continuation of Part I which includes some special features of NONMEM.

Part IV - NM-TRAN Guide

A complete reference guide to NM-TRAN (which includes the Data Preprocessor).

Part V - NONMEM Introductory Guide

A guide for beginning users of NM-TRAN/NONMEM-PREDPP. A NONMEM user should read the Introductory Guide first.

Part VI - PREDPP Guide

A complete reference guide to PREDPP.

Part VII - Conditional Estimation Methods

A description of these methods and some guidelines for their use.

Part VIII - Help Guide

A fast way to locate information on a given word or topic. The content of the Help Guide is also supplied on the NONMEM distribution medium for on-line use.

NONMEM V Supplemental Guide

Describes changes found with NONMEM V of which the user should be aware, especially if he used earlier versions of NONMEM.

Introduction to Version VI

Describes changes and new features found with NONMEM VI of which the user should be aware, especially if he used earlier versions of NONMEM.

Introduction to NONMEM 7.4 (nm743.pdf, intro7.pdf)

Describes changes from NONMEM VI Release 2.0, to 7.1.0, 7.1.2, 7.2.0, 7.3.0, 7.4.1, 7.4.2, and 7.4.3.

readme_743.pdf

The NONMEM Distribution medium contains files readme_743.pdf (The names may change with future releases.) The ".pdf" file may be viewed with Adobe Acrobat Reader. You may print it. Their content is identical with chapter IV of this installation guide. The "readme" contains important information that was developed too late for inclusion in this guide. Be sure to read it.

Nonmem7_technical_guide.pdf

Technical and mathematical guide on the expectation-maximization population and Monte Carlo analysis methods in the NONMEM 7 Program.

cv_guide, cvs_guide, ida_guide, idas_guide

These guides are for the ADVAN14 (CVODES) and ADVAN15 (IDAS) PREDPP systems.

Emails and Technical Newsletters

From time to time, emails and technical newsletters are sent to all current NONMEM licensees. These describe how to fix bugs discovered in the code and may give hints and suggestions on the installation and use of the system. Please be sure to review all emails and technical newsletters, if any, that accompany the NONMEM distribution medium. If you think you may be missing relevant newsletters, please call the NONMEM consultant.

See also Section 7 of this chapter for a list of internet sites from which bug memos and fixes may be obtained.

5. A Few Remarks about the Examples

In the following chapters, complete examples of operating system commands and features are given for two commonly used operating systems: UNIX (specifically, Ubuntu Linux), and MS-DOS (specifically, an MS-DOS window running under Microsoft Windows XP, using Intel Fortran 9.0 and higher). MS-DOS examples can also be used with Microsoft Windows 7 and Vista.

The UNIX examples all use commands for the Bourne shell.

Only UNIX and MS-DOS examples are included because these are the only operating systems with which we have first hand experience. NONMEM has been installed under a variety of other operating systems.

The examples, suitably modified for local differences, may suffice for many users. For other operating systems, they may be helpful as samples of what can be done. For example, NONMEM 7.4 has been installed on a MacBook Pro running OS X using the UNIX/Linux installation instructions.

People who are proficient in the use of their local operating system may well choose to do things differently.

6. The NONMEM Users Network

You and the NONMEM users at your site are invited to participate in the NONMEM Users Network. It is an electronic mailing list, not a news group. A user with a question, remark, or discussion which he believes might interest or help other NONMEM users sends the item to a single e-mail address. The item is automatically broadcast to every e-mail address on the network. The mail is not reviewed by anyone before it is broadcast. The NONMEM Users Network helps users worldwide communicate with each other, share information, and solve problems. In addition, technical newsletters describing bug fixes may be sent via e-mail to the network, as well as by ordinary (paper) mail to all licensees.

To be added to the mailing list (or to be removed from it), please send a request containing your e-mail address to:

nmusers-request@iconplc.com.

Thereafter, to send an item to the network, send it to:

nmusers@globomaxnm.com.

You may send questions to the network even if you are not actually on the mailing list, but be sure to include your e-mail address for replies.

7. Internet Sites

Bug lists may be found at the following sites:

https://nonmem.iconplc.com/nonmem743/nm743_bug_list.pdf

https://nonmem.iconplc.com/nonmem730/nm730_bug_list.pdf

https://nonmem.iconplc.com/nonmem720/nm720_bug_list.pdf

https://nonmem.iconplc.com/nonmem712/nm712_bug_list.pdf

https://nonmem.iconplc.com/nonmem710/nonmem_7.1.0_bug_List_5_NOV_2009.pdf

https://nonmem.iconplc.com/nonmem/NONMEM_VI_buglist

https://nonmem.iconplc.com/nonmem/NONMEM_V_buglist

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Chapter II - How to Read the NONMEM Distribution Medium

This chapter describes the contents of NONMEM distribution medium, and describes how to read the files.

1. Media Characteristics

NONMEM source code, On-line Help files, and Users Guides are distributed on a single CD. Only one version of NONMEM is distributed. Changes to the source code should not be required to specialize it to a particular computer system.

2. Contents of the Distribution Medium

2.1. Top Directory

These files provide scripts and executables that are needed for installing NONMEM in several environments.

```
BuildEnvironmentWindowforNONMEM.pdf
install_Darwin
install_Darwin_32
install_darwin_32.txt
install_Darwin_powerpc
install_Linux
install_SunOS
install_SunOS_i386
install_Win.exe
nm743.pdf
NONMEM-PDx-Pop-Support.pdf
nonmem.lic
readme_743.pdf
SETUP74
SETUP74.bat
unzip.exe
unzip.SunOS
```

2.2. compilers

This directory contains gfortran compilers for several operating systems that have been shown to work with NONMEM 7.4

```
gcc-trunk-i686.tar.gz
gfortran-4.5.0-x86_64-SnowLeopard.dmg
gfortran-macosx-x86.dmg
gfortran-windows-460.exe
```

Each subdirectory is described separately below.

2.3. mpich2

Directory mpich2 contains files for installing the message passing interface system for parallel computing.

```
mpich2-1.2.1-installguide.pdf
```

```

mpich2-1.2.1-userguide.pdf
mpich2-1.2.1-windevguide.pdf
mpich2-1.2.1p1-win-ia32.msi
mpich2-1.4.1-installguide.pdf
mpich2-1.4.1-userguide.pdf
mpich2-1.4.1-windevguide.pdf
mpich2-1.4.1p1-win-x86-64.msi
mpich2_1.2.1.1.orig.tar.gz
README_vin.mht
RELEASE_NOTES.txt

```

2.4. NONMEM_7.4.x

```

guides.zip
help.zip
html.zip
nonmem74e.zip
nonmem74r.zip

```

2.5. guides.zip

The zip file guides.zip contains all parts of the NONMEM Users Guide as PDF files. These files may be searched and displayed on-line. They may also be printed.

Name of Documentation	Description/Title
I.pdf	Users Basic Guide
II.pdf	Users Supplemental Guide
III.pdf	NONMEM 7.4 Installation Guide
IV.pdf	NM-TRAN Guide
V.pdf	Introductory Guide
VI.pdf	PREDPP Guide
VII.pdf	Conditional Estimation Methods
VIII.pdf	Help Guide
nm743.pdf	Introduction To Nonmem 7.4.3
Supp.pdf	NONMEM V Supplemental Guide
Intro.pdf	Introduction to Version VI
Nonmem7_technical_guide.pdf	Technical Guide on the Expectation-Maximization Population and Monte Carlo Analysis Methods in the NONMEM 7 Program
cvs_guide.pdf	Guide on CVODES (ADVAN14)
cv_guide.pdf	Guide on CVODE (ADVAN14)
idas_guide.pdf	Guide on IDAS (ADVAN15)
ida_guide.pdf	Guide on IDA (ADVAN15)

2.6. help.zip

This zip file contains help files for the console help system. The file helptools.zip contains files that is useful with on-line help files in the MS-DOS platform.

2.7. html.zip

This zip file contains files for the help system that can be navigated using an internet browser such as Windows Internet Explorer.

3. Storage of the Distribution Medium

Once the source code has been read, the CD (if you acquired one) should be stored in a safe place for subsequent use. If you erase the source code from disk after installation, you will have to read it back from the original medium to make corrections or changes. If at some future time you wish to transfer NONMEM to a different computer, you should re-install it from the original medium. If you terminate your NONMEM license, you must destroy all computer files containing NONMEM system source, binary code, and derivative products, and return the medium to the distributor, ICON Plc Development Solutions.

Chapter III - The New Features and Bug Fixes of NONMEM 7.4 compared to NONMEM 7.3.0

New features and bugs fixes from previous version to NONMEM 7.4 are listed in section I.1 of guides\nm743.pdf

Chapter IV - How to Install and Test NONMEM

1.0 General

These notes describe some fairly quick ways to install NONMEM. In particular, these notes cover:

Installation on a Windows system from a CD-ROM or directory

Installation on a UNIX or Linux or Mac OS X system from a CD-ROM or directory

Compiler test for Windows systems

Additional Mac OS X issues

Installation of NONMEM_7.4.3 is very similar to that of NONMEM_7.3.0. To install NONMEM, a FORTRAN compiler must already have been installed on your system. Parts of NONMEM 7.4.3 are provided as unencrypted source code, which can be modified by the user, and other parts are encrypted and cannot be directly accessed or modified by the user. Two "SETUP" scripts, SETUP74.bat and SETUP74, are currently available, the first for Windows and the second for Linux, Unix, and Mac OS X. These scripts are used to install NONMEM with ifort (Intel Fortran 90/95), gfortran or g95. If you use g95, it is recommended that the latest version from ftp.g95.org be used, especially with Mac OS X or Linux. However, g95 has not been tested extensively with NONMEM 7.4.3, and may not be able to compile the routines needed for parallel processing with the MPI method. Furthermore, g95 compiled NONMEM programs are known to execute very slowly, and among the free compilers, GNU gfortran is preferred. Recent versions of gfortran are available at <http://gcc.gnu.org/wiki/GFortranBinaries> and are in the compilers directory of the CD. See also Section 6.0 Additional software for compilers.

2.0 SETUP74 Scripts

SETUP74.bat and SETUP74 include a default designation ifort for the FORTRAN compiler. However, the "default compiler" may not be the one that has been installed on your system. Please acquaint yourself with which FORTRAN compiler has been installed, and perhaps more importantly, with the command name that designates this compiler. Then if this compiler is not the default compiler and/or its designation is not the default designation, you can override the default designation. System environmental variables associated with the compiler should be set before proceeding. Please see the documentation for your compiler and the document on the NONMEM distribution CD-ROM, NONMEM-PDx-Pop-Support.pdf, that contains information

on how to set the system environment variables via the Windows Control Panel. The BuildEnvironmentWindowforNONMEM.pdf provides additional information on setting up environment variables for installation with the Intel Fortran compiler on Windows. See also section 11.7 on how to set the environment variables just during the period of NONMEM execution using nmloc.

3.0 HELP Files

The command-line nmhelp utility for Windows has been improved. It is still possible that nmhelp.exe does not work on all versions of Windows at this time. Niclas Jonsson has given us permission to include the html files produced by nmhelp2html. SETUP74.bat and SETUP74 will copy this directory to the NONMEM 7.4.3 installation directory. To access this help facility double click on the index.htm (not \$index.htm) file. If you detect a problem in using the html files, please report this to us.

4.0 License File

License File: A license file named nonmem.lic is included on the NONMEM7.4.3.zip file or CD. However, it will expire soon. The contact person for the license should contact ICON Development Solutions via e-mail IDSSOFTWARE@iconplc.com requesting a new license and providing the name of the licensee (company and department or individual). A new nonmem.lic file with an expiration date corresponding to the next license renewal date will be sent by return e-mail.

5.0 Free MPI Software

Directory mpich2 of nm743CD contains a number of files that implement MPI-2.2, the Message Passing Interface (MPI) method of parallel processing.

The contents of this directory is discussed in the **Parallel Computing** Section of Introduction to NONMEM 7.4.3 (nm743.pdf, available in the guides directory after installation of NONMEM). Note that MPICH2 need not be installed if parallel processing is not used, as will be the case with the typical single-CPU single-core installation of NONMEM. SETUP74 does not copy the directory to the nm743 directory. The installer material (zip file, unzipped contents, or CD) should be retained in case this directory is to be used in the future.

6.0 Free Compilers

Directory compilers of the nm743CD contain the following files:

gcc-trunk-i686.tar.gz (gfortran for Linux)
 gfortran-windows-460.exe (gfortran 4.6.0 for Windows)
 gfortran-4.5.0-x86_64-SnowLeopard.dmg (gfortran 4.5.0 for Mac OS X 10.6)
 gfortran-macosx-x86.dmg (gfortran 4.5.0 for Mac OS X 10.5)

Same as the files with the same names on the web site. See below.

The ftp folder, <https://nonmem.iconplc.com/nonmem7/compilers>, contains free compilers available under public license that have been found to work correctly with NONMEM 7. The

compilers currently available in the directory are listed below. Please read the associated license agreements after installation of the compiler and comply appropriately with the stated requirements.

"gfortran-windows.exe" is a GNU gfortran compiler (version 4.5.0) that may be used on 64-bit versions of Microsoft Windows (e.g. Vista 64-bit) as well as 32-bit versions. It requires the user to manually create an appropriate LIBRARY_PATH environment variable after installing the compiler. The file was originally obtained from <http://gcc.gnu.org/wiki/GFortranBinaries>.

"gfortran-windows-460.exe" is not the latest GNU gfortran compiler (version 4.6.0) but has been tested for NONMEM 7.4.3.

"gcc-trunk-i686.tar.gz" is a GNU gfortran compiler (version 4.4.0) that may be used on 32-bit versions of Linux operating systems. The file "GFortranBinaries32Linux - GCC Wiki.mht" found in this directory contains information regarding the installation of this compiler. The file was originally obtained from <http://gcc.gnu.org/wiki/GFortranBinaries>.

"gfortran-4.5.0-x86_64-SnowLeopard.dmg" is a GNU gfortran compiler (version 4.5.0) that may be used on 64-bit Mac OS X such as 10.6 (Snow Leopard). Click on the file or type the command "open 4.5.0-x86_64-SnowLeopard.dmg" to install.

The file was originally obtained from <http://gcc.gnu.org/wiki/GFortranBinaries>.

"gfortran-macosx-x86.dmg" is a GNU gfortran compiler (version 4.5.0) that may be used on 32-bit versions of the Mac OS X such as 10.5 (Leopard). Click on the file or type the command "open gfortran-macosx-x86.dmg" to install. The version we provide (from 2009) is difficult to find on the web as of current writing (2010) because web sites such as gcc.gnu.org have packaged the Snow Leopard version under the older name. If you installed gfortran 4.5.0 and cannot run it because it is the wrong architecture, uninstall it with command

"sudo rm -r /usr/local/bin/gfortran /usr/local/gfortran /Library/Receipts/gfortran.pkg"

As more compilers are tested they will be added to the ftp folder as a convenience for NONMEM users. It is the responsibility of the user to read and comply with all GNU license requirements.

Keep in mind that the free compilers undergo frequent modifications. It is the user's responsibility to choose a version that works properly with NONMEM 7.

Note that installing from a dmg on a Mac may be done by clicking on the dmg file in finder, or by opening a terminal window and typing the commands "cd Downloads; opendmg".

The user may have to change the Apple menu "System Preferences, Security and Privacy, Allow apps downloaded from:" to allow "App Store and identified developers." Click "OK" on an alert box during the install itself to allow gfortran.pkg to be opened from an unidentified developer. It may also be necessary to go back to Security and Privacy and click on "Open Anyway".

Instructions for gfortran on macOS Sierra Version 10.12

Install the command line developer tools (see IV.9.1 Missing Unix commands) if this has not been done already.

Apple-style installers for macOS may be found at <http://gcc.gnu.org/wiki/GFortranBinaries>.

Click on MacOS.

You will find a list such as the following:

macOS Sierra (10.12): [download gfortran 6.3](#)

OS X El Capitan (10.11): [download gfortran 6.1](#)

OS X Yosemite (10.10): [download gfortran 5.2](#) or [gfortran 4.9.2](#)

OS X Mavericks (10.9): [download gfortran 4.9.0](#) or [gfortran 4.8.2](#)

OS X Mountain Lion (10.8): [download gfortran 4.8.2](#)

OS X Lion (10.7): [download gfortran 4.8.2](#)

Detailed instructions can be found [here](#).

Click on “download gfortran 6.3” to download **gfortran-6.3-Sierra.dmg**

Install this like any dmg (see above). Be sure to click open and read README.html, and to install the corresponding command-line tools by typing the command

xcode-select --install

Users who installed NONMEM before upgrading to Sierra from a previous release of MacOS may find that gfortran versions such as 5.2 and 6.1 continue to work after the upgrade and there is no need to re-install gfortran or NONMEM. To learn what version of gfortran you are using, type the command

gfortran --version.

You should receive several lines of text, including something like:

GNU Fortran (GCC) 6.3.0

If gfortran fails after the upgrade and needs to be reinstalled, the following command will remove the previous version:

```
sudo rm -r /usr/local/gfortran /usr/local/bin/gfortran
```

Now try re-installing gfortran as above.

Regardless of the approach that you use to install gfortran, it is necessary that the \$PATH environment variable knows the location of gfortran. It is usually installed in /usr/local/gfortran. However, it is symbolically linked to /usr/local/bin/gfortran (and /usr/local/bin is almost always in \$PATH). Sometimes the command “rehash” may be needed to make sure \$PATH is up to date.

Now NONMEM must be reinstalled with the new gfortran, using the SETUP74 command.

An error message such as the following may occur during the NONMEM install if the command-line tools are not the correct versions:

util/test.c:1:19: fatal error: stdio.h: No such file or directory

Be sure to type `xcode-select` as above.

Additional Comments: The name suggested for the NONMEM 7.4.3 installation directory, `nm743`, may be changed. E.g., if this directory already exists and contains a pre-release version of NONMEM, then one should use a name such as `nm743_1.0` instead. Directories (`c:\nm743` and `/Users/Shared/nm743`) are only suggestions. In previous versions of this guide, `/opt` was suggested rather than `/Users/Shared`. With Mac OS, `/Users/Shared` is preferable because it avoids the need for root permission when NONMEM is installed. Or install in the user's home directory `$HOME/nm743`, which is suggested below. Other directories may be used in a server-type installation.

With NONMEM 7.1, the `SETUP` command offered a choice for sizes ("reg", "big", "same"). Beginning with NONMEM 7.2, this choice is ignored. It is in effect always "same" and is shown as "same" in all examples. However, some constants in `SIZES` are not dynamically allocated (for example, `LSTEXT`; see help entry for sizes). To change such a constant, stop the installation (or reinstallation) at the point where `SETUP74` pauses with the message "Changes to License file, resource/SIZES.f90 and other resource files may be made here." In the target directory (e.g., `C:\nm743\resource`), edit `SIZES.f90` (be sure to copy the original as a backup), and retype the `SETUP74` command as before. Use option "rec" (recompile) rather than "norec".

7.0 Note on Parallelization

When using Intel Fortran compiler 11.1 or 12.0, the results of an FOCE analysis may differ slightly when running in single CPU mode versus parallel processing mode, but the results should still be very similar in well posed problems. Adding the compiler switch `/O1` may make the results between single CPI and parallel processing more consistent, although NONMEM runs may execute more slowly. To add this switch, insert `/O1` after `Ob1ti` in `SETUP74.bat` (line 245), or `-O1` in `SETUP74` (lines 381,384). Then use the appropriate `SETUP74` script for installation. Should this still result in slightly different results between single CPI and parallel processing mode, try the following compiler options in place of the ones that are in the `SETUP74` scripts:

For `SETUP74`:

```
-fp-model strict -Gs -nologo -nbs -w
```

For `SETUP74.bat`:

```
/fp:strict /Gs /nologo /nbs /w
```

Note that all examples of commands are to be typed on one line, even though they may appear to be split between two lines. The `SETUP` command should be run in the foreground, not the background.

8.0 Installation on a Windows system from a CD-ROM or Directory.

Easy Install:

If you are content to use a pre-supplied gfortran compiler, then the following easy install method is suitable for most Windows users.

Easy installers for NONMEM 7.4.3

Please visit the site at
<https://nonmem.iconplc.com/nonmem743>

And download one of the following, and follow the instructions:

Windows 7 64 bit Easy Install:

Installer:
NONMEM743_64gfortran463.exe

installation instructions:
Download NONMEM743_64gfortran463.exe

Once downloaded, run the program (start->run, or run from a dos window).
Obtain password from IDSSOFTWARE@iconplc.com
Answer questions.

After installation, there should be a nm74g64 icon on your desktop. Click on it, and a command window will open.

The program has an expired license file. Therefore, copy your up-to-date license file nonmem.lic to the directory
\\nm74g64\\license
This needs to be done only once.

Then execute the test problem
nmfe74 control5 control5.txt -prdefault

The objective function should be about 104.56

This version has its own gfortran with a built-in path to it, and is designed to be run from any command window.

There is no need to run the SETUP74 script.

If you are using PDxPop5, then run PDxPop5 and in the configuration section, "Tools > Edit Configuration insert c:\\nm74g64 as the NONMEM directory, and GFORTTRAN as the compiler.

Windows XP 32 bit Easy Install

Installer:
NONMEM743_gfortran460.exe

installation instructions:

Download nonmem743_gfortran460.exe

Once downloaded, run the program (start->run, or run from a dos window).

Obtain password from IDSSOFTWARE@iconplc.com

Answer questions.

After installation, there should be a nm74g ICON on your desktop. Click on it, and a command window will open.

The program has expired license file. Therefore, copy your up-to-date license file nonmem.lic to the directory

\nm74g\license

This needs to be done only once.

Then execute the test problem

```
nmfe74 control5 control5.txt -prdefault
```

The objective function should be about 104.56

This version has its own gfortran with a built-in path to it, and is designed to be run from any command window.

There is no need to run the SETUP74 script.

If you are using PDxPop5, then run PDxPop5 and in the configuration section, "Tools > Edit Configuration insert c:\nm74g as the NONMEM directory, and GFORTTRAN as the compiler.

General Install:

For more general installation, using your favorite compiler version, the instructions below apply to the following compilers: Compaq/Digital Visual Fortran versions 6.6c to 6.6d, Intel Fortran for Windows 7, 8, 9, 10, 11, and recent versions of GNU gfortran and g95. Installation on Windows Vista or Windows 7 requires that the User Account Control be turned off. (On Vista the path is: Control Panel -> User Accounts -> Turn User Account Control on or off. Remove the check mark. UAC can be turned back on after installation. With Windows 7, the computer must be restarted after turning off UAC.)

Permanently setting the system environment variable for the compiler is highly recommended for use with PDx-Pop and so that you do not need to run a separate script or batch file every time you want to run NONMEM. See the document on the NONMEM distribution CD-ROM, NONMEM-PDx-Pop-Support.pdf, for information on how to set the system environment variables via the Windows Control Panel. The BuildEnvironmentWindowforNONMEM.pdf provides additional information on setting up environment variables for installation with the Intel Fortran compiler on Windows.

To install NONMEM 7.4.3 follow these steps:

Read all these instruction before beginning installation.

Download the nm743CD image from a zip file:

<https://nonmem.iconplc.com/nonmem743/NONMEM7.4.3.zip>

Once downloaded, unzip the file (password is obtained from IDSSOFTWARE@iconplc.com), making sure options to extract sub-directories and use of folder names are turned on.

A directory called c:\nm743CD should be produced (or wherever you decided to place the directory). Then execute the SETUP74 script to install nm743. Specific instructions for Linux, Mac or Solaris system are found in section IV.7, below.

Open a DOS terminal window. Change to the directory of nm743CD or whatever the location is you chose for the installer files:

```
cd nm743CD
```

At the command prompt, type the SETUP74 command and appropriate positional options.

```
SETUP74 cd h f o ar s r i u zf zu
```

The options are:

```
cd = source path (e.g. d:\)
h   = name of NONMEM 7.4.3 directory
f   = command for FORTRAN compiles
o   = optimization (y / n)
ar  = full path name of lib/ar command
s   = same (SIZES.f90)
r   = norec (no recompile) / rec (recompile)
i   = i (interactive) / q (non-interactive)
u   = unzip program
zf  = encrypted source files
zu  = unencrypted files
```

The defaults are:

```
SETUP74 D: C:\nm743 ifort y link same rec i unzip.exe nonmem74e.zip
nonmem74r.zip
```

The default source path d: refers to a CDROM drive, but the usual usage now is to use the unzipped contents of NONMEM 7.4.3.zip. If the gfortran compiler is used, and the installation is to proceed with user interaction, then the command is

```
SETUP74 c:\nm743CD C:\nm743 gfortran y ar same rec i
```

Note that c:\nm743CD should be replaced with the location you actually unzipped the NONMEM7.4.3.zip file.

Typical commands for other compilers, installing into [c:\nm743](#), are:

Compaq Visual Fortran: `SETUP74 c:\nm743CD C:\nm743 df y link same rec i`

gfortran: `SETUP74 c:\nm743CD C:\nm743 gfortran y ar same rec i`

Intel Fortran 7 compiler: `SETUP74 c:\nm743CD C:\nm743 ifl y link same rec i`

Intel Fortran 8 and higher: `SETUP74 c:\nm743CD C:\nm743 ifort y link same rec i`

Note that with gfortran and g95, the ar command must be specified instead of link.

For installation from a CD, the source location should be the CD drive letter (such as d:) , followed by the directory name nm743CD, E.g.,

```
SETUP74 d:\nm743CD C:\nm743 ifort y link same rec i
```

For a non-interactive installation, change the final argument from i to q.

E.g.,

```
SETUP74 D:\nm743CD C:\nm743 ifort y link same rec q
```

You may ignore messages such as the following:

(a) Messages that appear at the terminal during SETUP (not new to nm74):

```
/Applications/Xcode.app/Contents/Developer/Toolchains/XcodeDefault.xctoolchain/usr/bin/ranli
b: file: resource.a(NM_INTERFACE.o) has no symbols
etc.
```

(b) Messages in finish.txt (new to nm74)

Error messages regarding klu and superlmt:

```
sundials/sundials_klu_impl.h:28:17: fatal error: klu.h: No such file or directory
#include "klu.h"
etc.
```

A note on building the CVODES (ADVAN14) and IDAS (ADVAN15) C routines.

ADVAN14 and ADVAN15 use differential equation solvers that are descendants of ADVAN13 and ADVAN9, respectively. Most users will not need the additional versatility of these two new solvers. If you have large models, they may be of advantage. If you are using GNU gfortran, then the C routines should compile with the gcc command, which is part of the gfortran system. However, if you are using intel Fortran, and you wish to use Intel C compiler, then you will need to purchase the Intel C compiler separately. The Intel C compiler command is icl. Alternatively, you can install the free GNU software and use its gcc compiler, which can be linked to the intel fortran compiled code.

It is not necessary to resolve the issue of C compilation at the time of installation. After installation, you can execute one of the following scripts in a terminal (command) window from the `..\pr` directory:

`cvcde_build.bat`

Execute this batch file if you used intel Fortran, and you have Intel C compiler available.

Remember to set the compiler options similar to how you compiled the Fortran code of NONMEM (see your `SETUP74.bat` file for the compiler options you used).

`cvcde_buildg(64).bat`

Execute this batch file (32 bit or 64 bit version) if you use gfortran for compiling the Fortran code of NONMEM.

`Cvcde_buildg(64)_to_ifort.bat`

Execute this batch file (32 bit or 64 bit version) if you used intel Fortran, and you do not have Intel C compiler available, but you have GNU gcc/gfortran installed.

Test the NONMEM installation:

The `SETUP74` script will run an installation test using

`nmfe74 CONTROL5 REPORT5.txt`

where `CONTROL5` is the control stream file, and `REPORT5.txt` is the NONMEM report file. The objective function value from the test run will be displayed. The file `"run\REPORT5.txt"` will contain the complete results of the run and should be similar to `"run\REPORT5IDS.txt"`.

The examples directory contains control streams and data files for the examples described in the "Introduction to NONMEM 7.4.3" document (see `guides\nm743.pdf`). Result files for these examples are also provided for reference. Note, however, that results from different compilers, and sometimes between single versus parallel computing, may vary somewhat, although they should not differ statistically significantly.

For implementation of parallelization, See Section I.55 of `nm743.pdf`.

New to NONMEM 7.2, and continued to later versions, are sample `".pnm"` files in the `run` directory.

9.0 Installation on a Linux, Mac or Solaris system from a CD-ROM or Directory

The instructions below apply to the following system configurations: Linux or Mac or Solaris, with Intel 9,10,11, or recent versions of g95 or GNU gfortran.

Permanently setting the system environment variable for the compiler is highly recommended for use with PDx-Pop and so that you do not need to run a separate script or batch file every time you want to run NONMEM.

Downloading the NONMEM7.4.3 CD Image from ICON's NONMEM ftp site:

Open a Safari or Google Chrome or other browser window. Type into the search bar:

<https://nonmem.iconplc.com/nonmem743>

or other suitable sub-directory

Click on the file NONMEM7.4.3.zip

This should start the download.

When it is finished, open a terminal window for the remainder of the install.

(Note: Do not try to unzip the file NONMEM7.4.3.zip in Finder. This will attempt to use the Apple Archive utility, which will fail with an error message.)

To open a terminal window, open a Finder window, click on Applications, click on Utilities, click on Terminal.app. Any shell (e.g, bash or csh) may be used.

In the terminal window, type

```
cd Downloads
```

```
unzip NONMEM7.4.3.zip
```

```
(password is obtained from IDSSOFTWARE@iconplc.com)
```

```
cd nm743CD
```

Now proceed to instruction 5 below for the SETUP74 command with the following options:

- Option cd (source path) should be \$HOME/Downloads/nm743CD
- Option h (NONMEM 7.4 directory) is up to you. \$HOME/nm743 is suggested.

If gfortran is installed, the command would be as follows:

```
/bin/bash SETUP74 $HOME/Downloads/nm743CD $HOME/nm743 gfortran
```

NONMEM 7.4 will be installed in directory nm743, in the user's home directory.

Any new terminal window that is opened will be in the user's home directory.

To install NONMEM 7.4.3 from a CD, follow these steps:

1. Read all these instruction before beginning installation.
2. Open a Terminal window. Any shell (e.g, bash or csh) may be used.
3. Place the NONMEM_7.4.3 CD in the CD drive.

The path for the CD will differ from one OS to another. Possible locations for auto mounting include:

Solaris 10: /cdrom/cdrom0

Redhat: /mnt/cdrom

ubuntu: /media/cdrom

Other Linux: /cdrom

Mac OS X: /Volumes/NONMEM_7.4.3

4. Change to the CD, e.g., "cd /mnt/cdrom "

5. Type /bin/bash SETUP74 command and appropriate positional options.

```
/bin/bash SETUP74 cd h f o ar s r i u zf zu
```

The options are:

```
cd = source path (e.g. /mnt/cdrom) .
h = name of NONMEM 7.4 directory
f = command for FORTRAN compiles
o = optimization (y | n)
ar = full path name of ar command
s = same (SIZES.f90)
r = norec (no recompile) | rec (recompile)
i = i (interactive) | q (non-interactive)
u = unzip program
zf = encrypted source files
zu = unencrypted files
```

Default:

```
SETUP74 /mnt/cdrom /Users/Shared/nm743 ifort y /usr/bin/ar same rec i
unzip nonmem74e.zip nonmem74r.zip
```

If the gfortran compiler is used and NONMEM 7.4.3 is to be installed from the CD located at /mnt/cdrom0 into the /Users/Shared/nm743 directory with optimization, the default ar command is to be used, and the installation is to proceed with user interaction, then the command is:

```
/bin/bash SETUP74 /mnt/cdrom0 /Users/Shared/nm743 gfortran y ar same
rec i
```

Typical commands for other compilers, installing into [/Users/Shared/nm743](#) are:

gfortran:

```
/bin/bash SETUP74 /mnt/cdrom0 /Users/Shared/nm743 gfortran y ar same
rec i
```

Intel Fortran 8-11:

```
/bin/bash SETUP74 /mnt/cdrom0 /Users/Shared/nm743 ifort y ar same rec
i
```

For installation from a directory, copy the files from the CD to the directory from which the installation will be performed, or unzip the NONMEM7.4.3.zip file into the directory from which installation will be performed. The path to this directory is the first argument for the `/bin/bash SETUP74` command.

E.g.,

```
/bin/bash SETUP74 /Users/Shared/Downloads/nm743CD
/Users/Shared/nm743 ifort y ar same rec i
```

For Solaris with f95, include the path to ar and unzip, e.g.,

```
/bin/bash SETUP74 /Users/Shared/Downloads/nm743CD
/Users/Shared/nm743 f95 y /usr/ccs/bin/ar same rec i
unzip
```

The installation may fail on Solaris 10 with the message

```
./util/dotest: line 74: gcc: command not found
Could not assemble util/test.c with gcc
Compiler f95 and/or install program cannot be run
```

If so, copy the CD to your own directory. Edit `SETUP74` and change

```
./util/dotest $f
```

to

```
# ./util/dotest $f
```

Now do the installation from your own directory.

For a non-interactive installation, change the final argument from `i` to `q`.

E.g.,

```
/bin/bash SETUP74 /Users/Shared/Downloads/nm743CD
/Users/Shared/nm743 f95 y /usr/ccs/bin/ar same rec q
```

You may ignore messages such as the following:

(a) Messages that appear at the terminal during `SETUP` (not new to nm74):

```
/Applications/Xcode.app/Contents/Developer/Toolchains/XcodeDefault.xctoolchain/usr/bin/ranli
b: file: resource.a(NM_INTERFACE.o) has no symbols
etc.
```

(b) Messages in `finish.txt` (new to nm74)

```
In file included from cvodes_klu.c:28:0:
sundials/sundials_klu_impl.h:28:17: fatal error: klu.h: No such file or directory
#include "klu.h"
etc.
```

A note on building the CVODES (ADVAN14) and IDAS (ADVAN15) C routines.

ADVAN14 and ADVAN15 use differential equation solvers that are descendants of ADVAN13 and ADVAN9, respectively. Most users will not need the additional versatility of these two new solvers. If you have large models, they may be of advantage. If you are using GNU gfortran, then the C routines should compile with the gcc command, which is part of the gfortran system. However, if you are using intel Fortran, and you wish to use Intel C compiler, then you will need to purchase the Intel C compiler separately. The Intel C compiler command is icl. Alternatively, you can install the free GNU software and use its gcc compiler, which can be linked to the intel fortran compiled code.

It is not necessary to resolve the issue of C compilation at the time of installation. After installation, you can execute one of the following scripts in a terminal (command) window from the ..\pr directory:

`cvode_build.bsh`

Execute this script file if you used intel Fortran, and you have Intel C compiler available.

Remember to set the compiler options similar to how you compiled the Fortran code of NONMEM (see your SETUP74.bat file for the compiler options you used).

`cvode_buildg.bsh`

Execute this batch file if you use gfortran for compiling the Fortran code of NONMEM. You may also execute this script file if you used intel Fortran, and you do not have Intel C compiler available, but you have GNU gcc/gfortran installed.

6. Test the NONMEM installation:

The SETUP74 script will run an installation test using

`nmfe74 CONTROL5 REPORT5.txt`

and will display the objective function value from the test run and the objective function from the reference file, `REPORT5IDS.txt`. The file "run/REPORT5.txt" will contain the complete results of the run and should be similar to "run/REPORT5IDS.txt".

The examples directory contains control streams and data files for the examples described in the "Introduction to NONMEM 7.4.3" document (see `guides/nm743.pdf`). Result files for these examples are also provided for reference. The user may want to run these examples as well for a more extensive qualification of the installation.

For implementation of parallelization, See Section I.55 of `nm743.pdf`.

New to NONMEM 7.2 are sample ".pnm" files in the run directory.

10.0 Compiler test for Windows systems

Due to the fact that most installation problems are caused by incomplete compiler or linker installation, prior to installing NONMEM a test of your compiler is appropriate to assure that your compiler is properly configured. An example of Fortran source code follows. Create a file named `hello.for` using Notepad.exe containing the following text:

```
C234567
      program test
      WRITE (6,*) "Hello, NONMEM World!"
      end
```

(The first line begins with column 1 ([this is a comment line that acts as a column number guide], lines 2,3, & 4 begin in column 7.)

Save the file and compile it from a DOS command line using the compiler command for your compiler.

For Intel 8, 9, 10, 11, "ifort hello.for"

For g95, "g95 hello.for -o hello.exe"

For gfortran, "gfortran hello.for -o hello.exe"

For Digital/Compaq, "df hello.for"

Run the compiled program at the command line, by typing hello followed by the Enter key. If successful, the output will be as expected:

```
C:\>ifort hello.for -o hello.exe
```

```
C:\>hello
Hello, NONMEM World!
```

```
C:\>
```

If not successful, you will get an error either indicating that the compiler was not found:

'ifort' is not recognized as an internal or external command, operable program or batch file.

or a compiler error of some other type.

The most probable cause of these errors is that the environment variables for the compiler and/or the linker (Microsoft Visual Studio provides the linker for Digital/Compaq and Intel Fortran) are not set so that these programs may be run from a DOS window. This requires that the environment variables are set for the system which is usually done using the Control Panel if the installation for the compiler or MS Visual Studio has not set them. The compiler test must be successful before you can install NONMEM. Please note that this simple compiler test may not detect problems with the linking process.

11.0 Mac OS X issues

11.1 Missing Unix commands

Mac OS X may not include certain Unix commands that are needed for NONMEM installation: ar as ranlib ld gcc make

It is possible that they have been previously installed. In a terminal window type the command

gcc

If the response is

i686-apple-darwin10-gcc-4.2.1: no input files

(or fatal error: no input files, or something similar) then the commands have been installed.

Proceed as directed above for Mac OS X installation.

If the response is “gcc: Command not found”), then these commands must be installed before NONMEM can be installed. There are several ways this can be done.

With macOS Sierra Version 11.12 (and some earlier versions starting with Mavericks 10.9), the response to gcc may be an alert box containing this text:

The “gcc” command requires the command line developer tools.

Would you like to install the tools now?

Choose [Install](#) to continue. Choose Get Xcode to install Xcode and the command line developer tools from the App Store.

Click on the blue [Install](#) button. This will install the necessary commands from the App Store without the full Xcode package. You must be connected to the internet.

With other earlier versions of Mac OSX, it may be necessary to install the version of Xcode that corresponds to the OS X version.

These can be found by browsing <https://developer.apple.com/download/more/>

You may have to create a developer login, but this should be free with your Apple ID.

It may be easier to upgrade to Sierra than to download Xcode.

Upgrades to Sierra from OS X Yosemite 10.10 and OS X El Capitan 10.11 have been performed easily. We have no experience with upgrades to Sierra from older versions of OS X.

Be sure to backup your system before attempting any upgrade.

Installation of gcc may require some time (more than 20 minutes for some setups), so be patient.

The following information was written for earlier versions of NONMEM and MacOS.

You may install them from the Mac OS X Install Disks.

For example, with Mac OS X version 10.5 (Leopard), Xcode Tools is on Install Disc 2.

Click on “Xcode Tools” and then “Xcode Tools.mpkg”

Only the UNIX Development Tools need be installed.

If you do not have the Install Disks, you may register with Apple as a developer at

<http://developer.apple.com/technologies/tools/xcode.html>

and get the Xcode Free Download package for your version of Mac OS X.

For Mac OS X 10.6 (Snow Leopard), click on “Xcode 3 Free Download “ and “Mac Dev Center”. Only the UNIX Development Tools need be installed.

There is a discussion of these two options at http://www.webmo.net/support/fortran_osx.html
See SOFTWARE DEVELOPMENT UTILITIES AND C COMPILER

When gcc and the other commands have been installed, proceed as directed above for Mac OS X installation.

11.2 Choosing 32-bit vs. 64-bit binaries

The compiler and gcc must produce the same kind of binaries by default.

The util directory contains two files: test.c test.f90

Check that they produce the same kind of binaries, e.g.,

On Mac OS X 10.6 (Snow Leopard)

```
% gfortran test.f90; file a.out
a.out: Mach-O 64-bit executable x86_64
% gcc test.c ; file a.out
a.out: Mach-O 64-bit executable x86_64
```

On Mac OS X 10.5 (Leopard)

```
% gfortran test.f90; file a.out
a.out: Mach-O executable i386
% gcc test.c ; file a.out
a.out: Mach-O executable i386
```

SETUP74 will work correctly with gfortran when the a.out's are consistent.

If you have a compiler other than gfortran and the a.out's are inconsistent, contact us and we will work with you on this.

11.3 Mounting file systems for MPI

It is easier to use afp (Apple Filing Protocol) than nfs .

To export a file system or folder to another Mac:

Select the Apple menu / System Preferences / Sharing / File Sharing

Under “shared folders:” click + and select the folder e.g., mydir

Under “users:” click + and select the users.

To mount a file system or folder from another Mac:

Open a finder window.

You should see the hostname of the other computer listed under “Shared”

Click on it. Click on “connect as”

Enter the username and password.

Click on the folder, e.g., mydir

The file system or folder will be mounted as /Volumes/mydir

E.g., in a terminal window: % ls /Volumes/mydir

11.4 Enabling ssh with no password for OS X

Select the Apple menu / System Preferences / Sharing / Remote Login
 The instructions for Linux (using ssh-keygen) should work on Mac OS X.
 There may be an interaction with keychain, and this may be problematic.

If “ssh -n “cannot be made to work, you can use the workaround for mpdboot described in the MPICH2 Installer’s Guide.

See ‘start the daemons “by hand”’ on page 7 of mpich2-1.2.1-installguide.pdf

11.5 Installing MPICH2

MPICH2 must be compiled and installed for Mac OS X.
 Please look at mpich2/README_vin.mht and the other documents.

First, see what kind of binaries have been installed, e.g.,
`% cd /opt/nm743/mpi/mpi_ling (or mpi_lini, with ifort):`
`% file mpi.o`

You will see either of the following:
 mpi.o: Mach-O 64-bit object x86_64
 mpi.o: Mach-O object i386
 “i386” indicates 32 bit binaries.

Suggested options for the configure step:

If SETUP74 installed 64 bit binaries:

```
./configure --prefix=/usr/local/mpi64 CFLAGS="-m64" FFLAGS="-m64" --enable-f90 --
disable-cxx | & tee c.txt
```

If SETUP74 installed 32 bit binaries:

```
./configure --prefix=/usr/local/mpi32 --enable-f90 | & tee c.txt
```

Either way, continues with
`make |& tee m.txt`
`make install |& tee mi.txt`

Then replace libmpich.a, in the NONMEM 74 directory, e.g, if 64 bit was installed:

```
cd /opt/nm743/mpi/mpi_ling
cp libmpich.a libmpich.a.orig
cp /usr/local/mpi64/lib/libmpich.a libmpich.a
```

11.6 Using the Correct MPI commands

The user's path should be set so that commands such as mpirun and mpf90 from MPICH2 are used instead of the corresponding Open MPI commands native to Mac OS X.

For example, if 64 bit was installed, the following is suggested prior to doing one or more NONMEM runs with MPI in a csh window:

```
% set path = (/usr/local/mpi64/bin $path)
```

If this is not done, the message may appear:

Unfortunately, this installation of Open MPI was not compiled with Fortran 90 support. As such, the mpif90 compiler is non-functional.

11.7 Setting up NONMEM's environment Variable System

A feature of the execution script file nmfe74 is that the path to the fortran compiler system and MPI system that is appropriate for NONMEM may be specified in a script file that could have the following environment variables defined:

```
compilerpath
mpibinpath
mpilibpath
mpilibname
```

Comments in these files are provided for instructions about each of these environment variables. These paths will be temporarily added to the front of the PATH environment variable, so that the appropriate compiler or MPI system is called to service NONMEM. In the past, conflicts with other installed fortran compilers from other applications would prevent the appropriate compiler from being used for the NONMEM system. This location file method allows NONMEM to be forced to look in a particular location.

The location file should be called nmloc.bat or nmloc by convention. It may be specified at the nmfe74 command line by the -locfile option, for example:

```
nmfe74 myfile.ctl myfile.res -locfile=nmloc.bat
```

If -locfile is not specified, the nmfe74 script looks in the present working directory for nmloc.bat (windows) or nmloc (linux). If this file is not found, it looks in the top directory of the NONMEM installed directory. Thus, the file nmloc.bat (Windows) or nmloc (Linux) in the top nonmem installed directory serves as the default location file, and may be modified, or used as a template and placed in the working directory or specified in the -locfile option on the command line. If a particular environment variable in the above list is not found or is not defined, then nmfe74 will behave as in earlier versions, and rely on the presently existing PATH for finding the compiler and MPI system. The nmfe74 script will display a statement as to what path it will use.

To find environment variables for your fortran compiler, you can use the "which" command in Linux based operating systems. Open a terminal window and type the command

```
which gfortran
or
```

which ifort
depending on your compiler.

As an example, this may return
/usr/local/bin/gfortran

Next, locate the file nmloc in the top directory of your NONMEM installation. The environment variable “compilerpath” needs to be modified to point to this directory, for example:
compilerpath=/usr/local/bin:/usr/bin

You can do the same for finding the path to your MPI system:

which mpiexec

or whatever the executable name of your MPI system is, and populate the environment variable “mpibinpath” in the nmloc file.

Chapter V – Modification of Execution

1.0. Version Identification

NONMEM is an evolving program, and changes are made from time to time. Version and level numbers together identify a particular instance of NONMEM. The first line of a NONMEM output report gives version and level numbers. These numbers identify the instance of NONMEM used to generate the output. As a result of implementing bug fixes that are announced in an email or newsletter, the level number is automatically changed.

In SIZES.f90 there is a level number given in a DATA statement similar to the follow-ing:

```
MODULE VERSION
CHARACTER(LEN=80)    :: LEV
DATA LEV/'7.4.3'/ ! Version No.
END MODULE VERSION
```

Do not change this version number.

2.0. Bug Fixes in NONMEM 7.4

Bug fixes to NONMEM 7.4 will be issued to nmusers, and uploaded to https://nonmem.iconplc.com/nonmem743/nm743_bug_list.pdf

3.0. SIZES

Certain constants are used by NONMEM to control array and buffer sizes, and may be changed by the user, many of them by using the \$SIZES record in their control stream file.

For permanent changes, values may be changed in SIZES.f90. Values that are changed in SIZES.f90 take affect after all the appropriate NONMEM source modules have been recompiled and, if a binary library is used, after the binary library has been rebuilt. Note that PREDPP and NM-TRAN Routines also use constants from SIZES. If you change a constant in SIZES, comments will tell you if other components of the NONMEM system should be recompiled.

Several of the constants in SIZES are of special interest.

3.1. Changing the Number of Theta's, Eta's, and Epsilon's

LTH gives the maximum number of theta's allowable.

LVR2 controls the maximum number of eta's permitted when the Laplacian Method is used.

The values in SIZES on the distribution medium are as follows.

```
PARAMETER (LTH=100)
PARAMETER (LVR=30)
PARAMETER (LVR2=20)
```

NM-TRAN dynamically sizes LTH and LVR for you, which can be over-ridden by the user, by

inserting the following line in the beginning of the control stream file, for example:

```
$SIZES LTH=150 LVR=60 LVR2=60
```

Constants LTH, LVR, and LVR2 may also be permanently increased in SIZES.f90, but you should not decrease them.

3.2. Increasing the Number of Observations per Individual Record

As of NONMEM 7.3, the maximum number of observations for a given individual is assessed by NMTRAN. It is possible that the calculation may be inadequate. If this constant is not adequate, NONMEM will produce an error message such as the following.

```
TOT. NO. OF OBSERVATIONS IN INDIVIDUAL REC NO.      1 (IN INDIVIDUAL REC
ORDERING)
EXCEEDS  250
```

To increase this limit, add the following record as the first executable line in the control stream file:

```
$SIZES NO=500
```

And re-run the problem again.

3.3. Changing the Size of Common NMPRD4 (LNP4)

Common NMPRD4 is used for communication between NONMEM and the PRED subroutine (and also for communication between user-supplied routines for PREDPP). To change its size, specify in the control stream file,

```
$SIZES LNP4=5000
```

Or some other appropriate. Typically, users who write abbreviated code will consider making this change only when the following error message is produced by NM-TRAN:

```
288  SIZE OF NMPRD4 EXCEEDED; LNP4 IS TOO SMALL IN NMTRAN AND NONMEM
```

When abbreviated code is not used, positions in NMPRD4 are assigned explicitly in user-supplied code. Users can determine for themselves if the common area is too small for their needs.

3.4. Changing the Size of NONMEM Buffers (LIMxx)

See Changing the Size of NONMEM Buffers in Introduction to NONMEM 7.4, nm743.pdf.

3.5. Increasing the Number of Mixture Models

Should NMTRAN fail to provide a sufficient size for number of mixture models, the size can be changed, by inserting the following line at the beginning of the control stream file:

```
$SIZES MMX=15
```

Change the value MMX to the desired value.

3.6. Increasing the Number of Individual Records in the Data Set

See Changing the Size of NONMEM Buffers in Introduction to NONMEM 7.4, nm743.pdf.

3.7. Increasing the Max. No. of Points of Support with Nonparametric Estimate

With the Nonparametric method (\$NONPARAMETRIC), the points of support are the posthoc estimates of each eta, which is essentially equal to the number of individuals in the data set. (An individual record has a value of the ID data item that is different from that of the previous individual record.)

This limit is set by constant LSUPP. If this constant is not adequate, NONMEM will produce an error message such as the following.

```
NONPARAMETRIC ESTIMATE NOT OBTAINABLE WHEN NO. OF INDIVIDUALS
EXCEEDS 4050
```

Change the value LSUPP to the desired value.

```
$SIZES LSUPP=6000
```

4.0. Modifying System Action in the Event of Floating Point Exceptions

Floating point arithmetic (e.g., division by zero, overflow, or underflow) sometimes occur during a NONMEM run. See Users Guide V, Chapter 13, Section 4.5. The ANSI FORTRAN 95 standard does not specify what should happen when a floating point exception occurs. Consequently, each operating system and compiler takes a different action, ranging from an immediate abort of the program to continuation with no warning that such an event occurred. Some systems, however, permit the user to control the situation. We recommend that installers check the FORTRAN Users Guide or equivalent documentation for their system and learn how to give their users some means of controlling the actions taken by their system.

It is always safe to ignore floating point underflow, *provided* that the resulting value is set to zero; this is the default action specified by the IEEE 754 standard for floating point arithmetic. For other error conditions, the run should stop and produce as much diagnostic information as possible when an error occurs. so that the cause of the errors can be investigated. Second, if the user concludes that the errors are benign and are unavoidable, it should be possible for him to cause the errors to be ignored.

See Section 2.1.3 for code that can be used with Sun FORTRAN compilers.

With some compilers, a compiler option can be used to specify how floating point exceptions are handled. For example, with Intel Visual Fortran, we suggest the option

```
/fpe:0
```

With Sun FORTRAN, we suggest

```
-fnonstd
```

These options request that the program stop if floating-point overflow, division by zero, or an invalid operation exception occurs. With Sun, the message "illegal instruction" appears. Both also request that underflow to zero occur for excessively tiny quantities.

If the compiler produces fatal error messages, or if you are concerned about warning messages, contact the NONMEM consultant. Do not attempt to fix the source code yourself! Phone at (301) 944-6807 or send e-mail to nmconsult@iconplc.com.

5.0. NONMEM Routines CRIT, MIX, PRIOR, CONTR, CCONTR, CONSTRAINT, USMETA, SPTWO

These are NONMEM dummy routines ("stubs") that may be replaced by user-written subroutines. Specify the name of the routine on the \$SUBROUTINES record, as in this example.

```
$SUBROUTINES .... MIX=subname ...
```

NM-TRAN opens the file named "subname" and copies it to FSUBS.

Similarly, if the \$MIX block of abbreviated code is present, then a generated code for MIX is present in FSUBS, or, if NM-TRAN Library routines are used, the NM-TRAN Library MIX routine must be included in the NONMEM executable.

Because NONMEM routines are obtained from a binary library (nonmem.a or nonmem.lib), the linker uses the MIX subroutine in FSUBS (or the NM-TRAN library) rather than the MIX routine from NONMEM.

6.0. PREDPP Routines, INFN, TRANS

These are PREDPP routines that may be replaced by user-written subroutines. Again, this is done by specifying the name of the routine on the \$SUBROUTINES record, as in this example.

```
$SUBROUTINES .... INFN=subname
```

NM-TRAN opens the file named "subname" and copies it to FSUBS. The information in FREPORT causes NMLINK6 to omit PREDPP's INFN routine from the list of files in LINK.LNK.

7.0. User Utility Routines

User-supplied routines and NM-TRAN verbatim code may contain calls to other user-supplied subroutines, which are referred to as *user utility routines*. Such routines may be included in the NONMEM executable module. First, they may be listed as OTHER routines on the \$SUBROUTINES record, as in this example.

```
$SUBROUTINES .... OTHER=BSPLINE
```

NM-TRAN opens the file named "BSPLINE" and copies it to FSUBS. It is compiled and included in the NONMEM executable.

A second way permits pre-compiled routines or libraries to be included automatically. The OTHER option is not used. Instead, the nmfe74 shell script or nmfe74.bat batch file should be modified. Locate the line u= or set u=, respectively.

Two examples of how this line might be changed are given for UNIX, and two examples are given for MS-DOS:

UNIX:

```
set u="/.../.../mylib.a"
```

MSDOS:

```
Set u=BSPLINES.obj
```

```
set u="\...\\...\\mylib.lib"
```

In the first examples, an object module BSPLINE is included in the NONMEM executable whether or not it is used in a given run. In the second example, "/.../.../mylib.a" stands for the full path of a binary library. Modules from this library are included only if actually called. In both nmfe74 and nmfe74.bat, the order presented to the linker is: nonmem library followed by user library or modules (\$n \$u in UNIX and %n% %u% in MS-DOS). As a result, the user utility routines cannot themselves call NONMEM utility routines such as CHOL or SUPP. If they do call NONMEM routines, the order must be reversed (\$u \$n in UNIX and %u% %n% in MS-DOS). This must be done with care because a routine in a user library having the same name as a NONMEM routine will be used instead of the NONMEM routine.

8.0. User Supplied Routines

Users may choose to substitute their own subroutines for certain default NONMEM-PREDPP routines, as follows:

NONMEM routines: CRIT, MIX, PRIOR, CONTR, CCONTR, CONSTRAINT, USMETA, SPTWO.

PREDPP routines: INFN and TRANS.

Users may also supply their own complete PK, ERROR, MODEL, DES, and AES sub-routines, rather than use NM-TRAN abbreviated code (\$PK, etc.). They may also supply a TOL subroutine rather than supply a value on the \$SUBROUTINES record.

NONMEM and PREDPP should be installed in such a manner that substitutions are possible.

Substitutions are specified to NM-TRAN on the \$SUBROUTINES record. For example, if a user-supplied MIX routine is used with file name MIXUSER, the option MIX=MIXUSER appears on the \$SUBROUTINES record. NM-TRAN uses such information in two ways:

Substitutions are documented in the FREPORT file, which contains a complete description of the composition of the NONMEM-PREDPP executable.

All user-supplied subroutines are copied to file FSUBS, to help in the construction of the actual executable.

9.0. User Files

A user might supply a subroutine that requires I/O. FORTRAN logical units in the range 51-2000 may be used. If user files are output, it can be important to close them properly before the NONMEM run terminates. Use of the NONMEM utility FILES can help perform this function.

10.0. The Files Utility

Whenever a FORTRAN OPEN statement or a CLOSE statement is executed in a user-supplied routine, NONMEM should be informed. This should be done as follows. Immediately after the OPEN or CLOSE statement is executed, a call should be issued to a NONMEM utility subroutine called FILES. The form of the call is simply:

```
CALL FILES (IUNIT)
```

where IUNIT is the number of the logical unit involved in the OPEN or CLOSE statement. When this is done, if a file is open when NONMEM terminates, the file is properly closed.

If reads or writes are issued to a given unit, but no OPEN statement for this unit is executed, then when ICALL is 0, a call to FILES should be issued (before any I/O statement).

11.0. NM-TRAN Include Lines

The NM-TRAN control file may contain one or more lines of the form

```
INCLUDE filename
```

The file with name "filename" is an *NM-TRAN include file*. NMTRAN opens the include file, reads it to end-of-file and includes its contents in place of the INCLUDE record. The contents of the include file may be any portion of an NM-TRAN control stream: control records and/or abbreviated code.

12.0. Uninstalling NONMEM 7

NONMEM may be uninstalled with the following DOS command
rmdir /q /s nonmemdir

or unix command:
`rm -r nonmemdir`

Chapter VI - Other Files on the Distribution Medium

This chapter discusses the remaining files on the distribution medium.

1. Files for Installation Tests

In Chapters III, IV and V, we recommend that you try simple test cases after installing each component of the NONMEM system. The files necessary for these tests are printed in other Users Guides, and are also provided on the distribution medium. These files are located in the util directory of the installed nonmem directory:

PRED1 - PRED subroutine for Chapter III (NONMEM)

Printed as Figure 1 in NONMEM Users Guide I.

CONTROL1 - Control file for Chapter III (NONMEM)

Printed as Figure 2 in NONMEM Users Guide I.

PK1 - PK subroutine for Chapter IV (PREDPP)

Printed as Figure 7 in NONMEM Users Guide VI.

ERROR1 - ERROR subroutine for Chapter IV (PREDPP)

Printed as Figure 11 in NONMEM Users Guide VI.

CONTROL2 - Control file for Chapter IV (PREDPP)

Printed as Figure 25 in NONMEM Users Guide VI.

CONTROL3 - Control file for Chapter V (NM-TRAN)

Printed in Appendix IX in NONMEM Users Guide IV.

DATA3 - Data file for Chapter V (NM-TRAN)

Printed in Appendix IX in NONMEM Users Guide IV.

2. Phenobarbital and Theophylline Data Files

PHENO - Phenobarbital Data

This is the complete data for the Phenobarbital example used in NONMEM Users Guide V (Introductory), Chapters II and XI. The record length is 80 bytes. There are 745 lines in the file.

THEO - Theophylline Data for PRED

This is the theophylline data for the first illustrative run of Chapter I, Section 2.5 of this guide, which uses PRED abbreviated code, not PREDPP. The data are printed in Users Guide IV, Appendix II. The record length is 80 bytes. There are 132 lines in the file.

THEOPP - Theophylline Data for PREDPP

This is the theophylline data for the second, third, and fourth illustrative runs of Chapter I, Section 2.5, of this guide, which use PREDPP. The data are printed in NONMEM Users Guide IV, Appendix VI. The record length is 80 bytes. There are 144 lines in the file. Note that the data of THEO are identical to that of THEOPP, except that each subject's dose amount is recorded separately from his first plasma concentration, as required with PREDPP.

3. NM-TRAN Control Streams for Illustrative Runs

CONTROL4 - Theophylline control file: PRED abbreviated code

This is a double precision version of the the NM-TRAN control stream for the first illustrative run of Chapter I, Section 2.5, of this guide. The contents of the file is printed in Users Guide IV, Chapter I. The data of file "THEO" should be used with this control stream.

CONTROL5 - Theophylline control file: PREDPP with ADVAN2

This is a double precision version of the NM-TRAN control stream for the second illustrative run of Chapter I, Section 2.5. The contents of the file is printed in Users Guide IV, Chapter V.

The data of file "THEOPP" should be used with this control stream. It produces essentially the same result as the first illustrative run, but uses PREDPP and the One Compartment Model with First Order Absorption (ADVAN2).

CONTROL6 - Theophylline control file: PREDPP with ADVAN7

This is a double precision version of the NM-TRAN control stream for the third illustrative run of Chapter I, Section 2.5. The contents of the file is printed in Users Guide IV, Appendix VIII. The data of file "THEOPP" should be used with this control stream. It produces essentially the same result as the second illustrative run, but uses PREDPP and the General Linear Method with Real Eigenvalues (ADVAN7). Normally, one would not use ADVAN7 when it is possible to use ADVAN2 because of the increased run time, but this is done here to provide an illustration of comparative executable sizes and run times.

CONTROL7 - Theophylline control file: PREDPP with ADVAN6

This is a double precision version of the NM-TRAN control stream for the fourth illustrative run of Chapter I, Section 2.5. The contents of the file is printed in Users Guide IV, Appendix VIII. The data of file "THEOPP" should be used with this control stream. It produces essentially the same result as the second illustrative run, but uses the General Non-Linear Kinetics Method (ADVAN6). Normally, one would not use ADVAN6 when it is possible to use ADVAN2 because of the increased run time, but this is done here to provide an illustration of comparative executable sizes and run times.

4. Example Control Stream Files

Additional control stream files are located in the examples directory. Accompanying them are standard NONMEM result files, with which you may compare with your run. These examples are described in Introduction to NONMEM 7.4 guide.

Chapter VII - NONMEM Users Guide and On-line Help

This chapter discusses documentation that can be found on the NONMEM distribution medium.

1.0. PDF Guides

The guides directory contains all parts of the NONMEM Users Guide as PDF files. These files may be searched and displayed on-line. They may also be printed.

Name of Documentation	Description/Title
I.pdf	Users Basic Guide
II.pdf	Users Supplemental Guide
III.pdf	NONMEM 7.4 Installation Guide
IV.pdf	NM-TRAN Guide
V.pdf	Introductory Guide
VI.pdf	PREDPP Guide
VII.pdf	Conditional Estimation Methods
VIII.pdf	Help Guide
nm743.pdf	Introduction To Nonmem 7.4.3
Supp.pdf	NONMEM V Supplemental Guide
Intro.pdf	Introduction to Version VI
Nonmem7_technical_guide.pdf	Technical Guide on the Expectation-Maximization Population and Monte Carlo Analysis Methods in the NONMEM 7 Program
cvs_guide.pdf	Guide on CVODES (ADVAN14)
cv_guide.pdf	Guide on CVODE (ADVAN14)
idas_guide.pdf	Guide on IDAS (ADVAN15)
ida_guide.pdf	Guide on IDA (ADVAN15)

2. On-line Help

Directories help and html contain the same material that is distributed as pdf files NONMEM Users Guide Part I- Part VIII, Help Guide. In addition, they contain files that enable the material to be searched and displayed conveniently when installed on a computer. When installed as suggested, they implement the *On-line Help* feature of NONMEM. Their installation and use is optional.

2.1. HTML help

The HTML versions work with all web browsers such as Internet Explorer, Netscape, Firefox, etc., and can be used with all operating systems. As of NONMEM VI 2.0, the html directories contain sub-directories I, II, III, etc, containing NONMEM Users Guides I, II, III, etc. in html format. These are provided so that references between and within Users Guides can be followed by the browser as hyperlinks. This feature is not fully implemented.

Start a web browser such as Internet Explorer, Netscape, or Firefox. On the File menu, you should find a button called Open or Open File. Type (or browse for) the directory, e.g., `c:\nm743\html` or `/export/home/nm743/html`. Type the file name `index.htm` (not `$index.htm`). This should open a page with the title

This is the main index of Hyper-NMhelp.

You may find it convenient to bookmark the page.

The use of Hyper-NMhelp is straightforward. Note that the keywords may be grouped somewhat differently than they are with the command-line on-line help described in the following sections.

2.2 COMMAND-LINE HELP (nmhelp)

Help files are intended for command-line usage, and may be useful when working from a UNIX or MS-DOS command prompt, or if there is no web browser available. Dos_tools allow convenient command-line help under MS-DOS. Users with other operating systems can use the command-line Help material, but they may have to create their own user-interface for search and display; the UNIX and MS-DOS examples may serve as convenient starting points.

The Help Guides consists of two sections: an index, which is printed in two parts (RESERVED WORDS and MISCELLANEOUS TOPICS); and over 200 individual discussions, which are also printed in two parts (DETAILED DESCRIPTIONS and EXAMPLES). In the Help directory, a file named `index` contains both parts of the printed index, in a format designed for use by the UNIX and DOS tools included on the distribution medium. Also on the Help Guide directory are over 200 files with names of the form `xxxx.xxx`, each of which contains the text of a single individual discussion. These files are referred to collectively as "detailed description files" in the examples below. (The suffix identifies the content. For example, examples have names ending with the suffix `exa`.)

If you opted to have the help manual installed when you ran `SETUP74`, then the `nonmem` directory (such as `c:\nm743\help` or `/export/home/nm743/help`) will contain the console/command line help system, `nmhelp`. The `nmhelp` file is either a DOS executable (`nmhelp.exe`), or a Unix bash script (`nmhelp`).

To use the `nmhelp` system in DOS, you must be in the help directory,

```
cd c:\nm743\help
```

Then select a topic, such as:

```
nmhelp ADVAN9
```

To use the `nmhelp` system in unix,

```
cd ~/nm743/help
```

Then select a topic, such as:

```
./nmhelp ADVAN9
```

In unix, you may execute `nmhelp` from any directory if you do the following. Insert the following line into your login file, such as the file `.bashrc` in your user directory:

```
alias nmhelp=~ /nm743/help/nmhelp
```

or whatever directory your nonmem directory is located. Then, you may enter
 nmhelp
 from any directory.

To get information on the command nmhelp itself, enter "nmhelp help"

To get a list of the topics available, enter "nmhelp".

To get information on a given reserved word or topic, enter "nmhelp" followed by the reserved word or topic. For example,

```
nmhelp nonlinear
```

Help for nonlinear is available in the following documents:

1 ADVAN10	4 NONMEM model
2 ADVAN6 ADVAN8	5 NONMEM program
3 ADVAN9	6 Michaelis Menten example

Your choices:

```
enter "p number" to print a document (e.g., p1 or p 1)
enter the number of the document you wish to see
enter <CR> to see document number 1
enter q <CR> to quit this list
```

A number 1 through 6 may be entered, and the appropriate document will be displayed at the terminal. You may then enter a different number to display a different document.

2.3. Information about the DOS Tools Components (nmhelp.exe)

nmhelp.exe

A compiled C-program that searches for and displays detailed description documents. It must be used on a 386-based DOS system or higher. It uses utility programs from the Free Software Foundation.

nmhelp.c

The source code for nmhelp, in case it is necessary to re-compile it on your system. A C or C++ compiler will be required if you choose to modify the code and create a new nmhelp.exe by running nmhelp_win.bat; we do not provide it.
 gawk.exe, grep.exe

Compiled utility programs from the Free Software Foundation. Must be used on a 386-based DOS system or higher.

Other files in the Dos_tools directory are gnulic.txt (a license agreement from the Free Software Foundation which should be read by anyone who wishes to make the utilities available to others).

2.4. Using nmhelp with Ordinary MS-DOS commands

Here is a very rudimentary way to search and display the contents of the Help Guide, using ordinary DOS commands. A better way involves the use of nmhelp, described in the previous section.

Change to the directory into which you read the Help files.

To get information on a given reserved word or topic, enter "find" followed by the reserved word or topic in quotes (""). For example,

```
find "nonlinear" index
```

```
----- INDEX
advan10.ppp~ ADVAN10~ nonlinear kinetics model
advan68.ppp~ ADVAN6 ADVAN8~ general nonlinear kinetics model advan68.ppp~
ADVAN6 ADVAN8~ nonlinear kinetics model advan9.ppp~ ADVAN9~ general
nonlinear kinetics model advan9.ppp~ ADVAN9~ nonlinear kinetics model
nonmod.gen~ NONMEM model~ nonmem nonlinear mixed effects model nonpro.gen~
NONMEM program~ nonmem nonlinear mixed effects model michaeli.exa~ Michaelis
Menten example~ nonlinear kinetics model
```

The first column lists detailed description files. The second column gives their titles. The third column gives the context in which the search word "nonlinear" appears as a keyword in these files. (The column delimiter is the character ~).

To display a document in the list, enter "more" followed by the filename. For example,

```
more < advan10.ppp
```