NMQual:
A Tool to Automate Installation and Facilitate Qualification of NONMEM

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Bill Knebel¹, Tim Bergsma², Leonid Gibiansky¹, Jeffrey T. Hane¹,
Marc R. Gastonguay¹

Metrum Research Group LLC¹, Avon, CT 06001, USA ; Empidonax Consulting², Quaker Hill, CT 06375, USA

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Background

• Bugfixes and other source code changes in NONMEM often occur following the initial installation.

• This can often result in the user or company making a decision to not implement a bugfix or set of bugfixes based on the nature of the bug fix.
  – Likelihood of encountering the bug
  – Difficulty in updating all NONMEM installations

• If a decision is made to update the installation, keeping the source code current can be difficult for a number of reasons.
  – Manual modification of source code
  – Lack of automated method to implement bugfixes
  – Lack of control over installation/user once source code changes are implemented
Background

• Why is it important to keep NONMEM source code up to date (in a controlled manner)?
  – Difficult to know apriori if a given bugfix is important
  – Scientists using NONMEM should not have to question whether a given bugfix is implemented.
  – Reproducibility of results across scientists and between company and regulatory authorities

(see ECPAG 2004 presentation – http://www.ecpag.org/presentations/2004/workshops/6_Gobburu_Session_II.pdf)

– Recent presentations at industry meetings have indicated that a “qualified” install of NONMEM is likely to be required by regulatory authorities in the future (ECPAG 2004 and AAPS 2004).
Development Goal and Process

• Develop a tool (NMQual) to facilitate the automated installation and qualification of NONMEM on PC’s running Windows and/or Linux

• Developed according to modern software life-cycle practices
  – User requirements
  – Design specifications
  – Implementation and development
  – Validation/verification via a formal plan
  – Installation and operation qualification
  – Training
  – Operation, maintenance/change control, and retirement
User Requirements

• Ability to update the NONMEM source code with all bugfixes
• Implement any user or site specific changes
• Install NONMEM with minimal user intervention
• Maintain an electronic trail of all changes made during the installation
• Test installation as part of overall qualification
• Allow a NONMEM run to be linked to a specific installation and any related code changes
• Automated implementation of several NONMEM test cases for operational qualification
Introduction

• What is NMQual?
  – A set of perl scripts to automate and test/qualify the installation of NONMEM (PC Windows or Linux)

• What are the system requirements to run NMQual?
  – Windows XP or Linux (developed/tested on SUSE 9.2 but other versions -Mandrake, RedHat, Debian- likely to work)
  – A working installation of Perl (Active State for Windows or Perl v5.8 or above for Linux)
  – A copy of the current (April 15th, 2004) GloboMax NONMEM CDROM
  – G77 or Compaq fortran compiler
Introduction

• What does NMQual do?
  – Install current version of NONMEM with all bugfixes to date (automatically)
  – User/site specific changes to NONMEM can also be implemented (if requested)
  – Test the installation and operation of NONMEM via a set of control streams
NMQual

- Run from a command prompt with a minimal set of arguments
  - Source and install directory, fortran command (g77 or df), optimization (y/n), nopause
- Default installation (supervised install) allows user to follow install and requires user input to acknowledge installation steps
- Setting “nopause” option allows unattended install except for insertion of NONMEM CDROM
NMQual
NONMENMEM Installation

NMQual started from command line:
perl nmqual.p source installation fortran optimize
“perl nmqual.p d:/nonmem_v1.1 c:/nmvg77 g77 y”

Bugfixes via XML file
(changes.xml)

Platform/compiler specific changes via XML file
(changes.[g77-linux].xml)

Site/user specific changes via XML file
(changes.options.xml)

NONMENM CDROM (April 15th, 2004) inserted
changes to source code are made
original source files renamed to *.for.old
comments inserted into *.for files at location of bugfix/change
NONMENM compiled

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Perl script to run NONMEM is generated and the path variable in windows/linux is updated

NONMEM directories (nm, pr, tl, tr) marked read-only and checksum ran on directories

Install log created that lists all bugfixes, compiler, and site specific changes, user, optimization, checksum results, and date/time

NONMEM Installation Complete!!
Reboot of windows or logout/login in linux

NONMEM installation can be tested by running test.p script
“perl test.p 3 4 5 6 7 8”

test.p runs control3 – control7 plus additional parent/metabolite model

Results of test.p written to test log
Running NONMEM

NONMEM run started from command line:
perl -S nmvg77.p 100.ctl 100.lst

checksum for nm, pr, tl, and tr directories

checksum passed

compile and run NONMEM

NONMEM run complete: control stream and date/time stamp - output - install log, test log, and date/time stamp

checksum failed
run stops
Benefits of NMQual

• Ensures a consistent and current NONMEM install across all NONMEM users
• Allows for the execution of NONMEM from any directory without the need for copying key files from the install directory
• Allows for different versions of NONMEM to be installed and used on same computer/project
• Maintains a link between a given NONMEM run and installation via the install and test log appended to each output file
Benefits of NMQual

• Provides a basis for the formal “qualification” of a NONMEM installation
• Ensures consistency of results across users, sites, and regulatory authorities
• Implements most of the suggested good practices for the qualification of NONMEM (see ECPAG 2004 presentation referenced in Slide 5)
• Simple mechanism to improve the quality control of NONMEM installations
  – checksum process eliminates possibility of user changes to source code
Limitations of NMQual

• Use of NMQual to install NONMEM does not automatically result in a “qualified” NONMEM installation
  – Additional document trail around the installation and qualification process is required for both NMQual and NONMEM
  – Metrum RG can assist in the development of the document trail, the customization of NMQual for installation/qualification, and in IT training

• Set of test scripts/control streams currently available is limited, but additional test scripts are planned for the future
Access to NMQual

• NMQual freely available (soon) as an iso image download from Metrum RG web site
  http://www.metrumrg.com

• Once burned to a CDROM the downloaded version of NMQual is fully functional.

• A set of installation instructions and FAQ’s will be available on the Metrum RG web site.