PAGE Satellite workshop:
New features and advanced methods
for model building and evaluation in NONMEM VI
Marseille, France, 15th, 16th and 17th June 2008

Overview

The pharmacometrics group at Uppsala University has been involved in developing NONMEM models and methodology for over fifteen years. They have been involved in the testing and evaluation of NONMEM VI as it has been developed during the last decade. Several research projects have focused on new functionality in NONMEM VI. In parallel, diagnostics for model building have been developed, evaluated and integrated into NONMEM VI-adapted versions of the programs Perl-speaks-NONMEM (PsN) and Xpose 4 (described below). In this course, some of the most exciting new features of NONMEM VI will be presented and how these tools can be used in the development and evaluation of non-linear mixed effects models.

Agenda (3 full days)

The course will last for 3 days and consists of both lectures and hands-on computer exercises. Participants will use NONMEM VI, PsN and Xpose 4. PsN and Xpose 4 are freeware and may be installed on participants' computers for use after the course. In addition to the agenda below consultation sessions will be offered during each day of the course.

Day 1 - Model building and diagnostics using NONMEM VI
- Introduction to new features in NONMEM VI
- Introduction to diagnostics for NONMEM runs
- Automation of NONMEM runs using PsN
- Improved model building and diagnostics using PsN and XPOSE 4
  - Shrinkage-corrected Empirical Bayes based diagnostics
  - Conditional weighted residuals
- Hands-on computer exercises with NONMEM VI, PsN and XPOSE

Day 2 - Advanced methods in NONMEM VI and simulation based diagnostics
- Simulation based diagnostics: Using PsN and XPOSE 4
  - Simulation based diagnostic references
  - Visual and numerical predictive checks
- The use of prior information on parameter values in NONMEM evaluations
- Simultaneous Modeling of Continuous and Categorical Data
- Handling data below the limit of quantification (BLQ)
- Additional new features in NONMEM VI
- Hands-on computer exercises with NONMEM VI, PsN and XPOSE

Day 3 - Advanced methods in NONMEM VI and computer intense diagnostics
- Using nonparametric parameter estimation in model building using NONMEM
- Computer intense model building and diagnostics using PsN and NONMEM
  - Bootstrapping
  - Case deletion diagnostics
  - Individual objective function value
- Hands-on computer exercises with NONMEM VI, PsN and XPOSE

Prerequisite
Having used NONMEM and understanding population PK-PD modelling
and/or having attended a NONMEM basic workshop

Instructors

Prof. Mats Karlsson

Mats Karlsson is professor of Pharmacometrics at Uppsala University, Sweden where he leads a research group of about twenty five modellers. He received his PhD in pharmacokinetics from this university in 1989 and has been a research fellow at University of Glasgow and University of California, San Francisco, and a visiting professor at Georgetown University, Washington DC. He has received the Giorgio Segre Prize from EUFEPS and is editor for the Journal of Pharmacokinetics and Pharmacodynamics. His research interests focus on methodological aspects of non-linear mixed effects model building and applied PKPD modelling. He has published over one hundred fifty original research articles in the area of PK and PKPD.

Dr Andrew Hooker

Andrew Hooker is an assistant professor of pharmacometrics at Uppsala University, Sweden. Andrew received his PhD in Bioengineering from the University of Washington, Seattle, USA in 2003, and then moved to Sweden as a Pfizer post-doctoral fellow at Uppsala University. His research focuses on methodological problems associated with building and evaluating pharmacometric models as well as population optimal experimental design for non-linear mixed effects models. Andrew is a primary developer of both Xpose 4 and the population optimal experimental design program PopED.

Ms Radojka Savic

Radojka Savic joined the Pharmacometric research group at Uppsala University, Sweden in 2003 after receiving her pharmacist degree from University of Belgrade, Serbia. Since then, she has been actively working on evaluating new features of NONMEM VI. Her research interests focus on nonparametric methods for population analysis, improved diagnostics for NONMEM VI and development of new absorption models.

Technical Assistance: **Pontus Pihlgren**

Details

The course will emphasize hands on training, with the participants working on their own computers. Participants should bring their own computer. They will run all programs from an USB memory-stick and will not be required to install any programs on their computer. In case a participant needs a computer, he should indicate it to the organizers.

Xpose 4 is a model building aid for population analysis using NONMEM. It facilitates data set checkout, exploration and visualization, model diagnostics, candidate covariate identification and model comparison. Xpose 4 has been rewritten in the programming language R with a modular and object oriented design allowing for integration into nearly any model building platform. New functionality in Xpose 4 allows the user to create simulation based reference diagnostics, compute the conditional weighted residuals and modify standard Xpose graphics to create publication quality figures. Xpose 4 also makes use of the new features in NONMEM VI allowing for the visualization of non-parametric parameter distributions and individual objective function contributions. Freely available at xpose.sf.net.

Perl-speaks-NONMEM (PsN) is a collection of Perl modules and programs aiding in the development of non-linear mixed effect models using NONMEM. The functionality ranges from simpler tasks such as parameter estimate extraction from output files, data file sub setting and resampling, to advanced computer-intensive statistical methods. PsN includes both stand-alone tools as well as development libraries for method developers. Freely available at psn.sf.net.

PRACTICAL INFORMATION

NONMEM VI 3 days Satellite Workshop (15-17 June 2008)
Registration Fees, VAT included:

With own laptop   **Industry:** 1700 €   **Reduced fees for Academic**: 1200 €

With rental laptop   **Industry:** 1850 €   **Reduced fees for Academic**: 1350 €

Registration fees include: syllabus; 1 USB Key loaded with all software; morning and afternoon refreshment breaks and lunches on the 3 days; In addition a complementary welcome dining cocktail on Saturday 15th and a dinner at restaurant on Sunday June 16th 2008 will be offered.

➔ Attendance is strictly limited to 50
➔ Number of "reduced fees" for Academics and students is limited.
➔ Registration and academic fees will be offered on the basis of *first come, first served*

Workshop location:
Novotel Marseille Vieux Port
36, Boulevard Charles Livon, 13007 MARSEILLE, FRANCE
☎ : (+33) 496 11 42 11 ;   Fax : (+33) 496 11 42 20;
Located in the heart of the city, the hotel overlooks the world famous *Old Harbour*. It is situated in a green environment with panoramic terrace and stunning views.

The **City of Marseille** is surrounded by Mediterranean Sea. As the capital of the third economic region of France and the first industrial and services pole of the south of France, it can easily be reached by plane, train (high speed connection from Lyon or Paris), freeway or even … boat.

Workshop Organised by AP²POP; contact persons:

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NONMEM VI Satellite Workshop Registration process:
Through the PAGE web page, starting on February 15th 2008

You will receive after February 15 a special code to log into the *Atout Organisation Science* web-site (see http://www.page-meeting.org/) to finalize and pay your PAGE registration fee and reserve a hotel room.

If you are willing to register to the NONMEM VI workshop, payment to PAGE and workshop will have to be performed simultaneously as a single operation.

NB
1. No registration to the workshop will be possible later on through the web site: the only possibility is to register to the workshop at the same time you pay your PAGE registration.
2. All organisational information concerning the workshop will be obtained through the Workshop Organising Committee listed above, not from *Atout Organisation Science*.
3. Accommodation is not provided. Participants will have to book their hotel through *Atout Organisation Science* web-site or through a list of close by hotels that will be send out to the registrants.