



**Advanced Features of NONMEM 7 Workshop**

**Date of Meeting:** 6 June 2016  
**Location:** PAGE 2016 – Lisbon, Portugal  
**Instructors:** Robert J. Bauer, Ph.D., Brian Sadler, Ph.D.

**Agenda Items:**

	<b>"Advanced Features of NONMEM 7" – Presentation:</b>		
1.	<b>Introduction</b>		8:30 – 8:45 AM
2.	<b>Modifications and Enhancements to NONMEM 7</b> <ul style="list-style-type: none"> <li>- Conversion of Fortran 77 to Fortran 90/95</li> <li>- Centralized Error Processing</li> <li>- Improvements in Gradient Methods</li> <li>- Decreased Incidence of Estimation Failure Due to Numerical Problems</li> <li>- Added Option to Specify Step-Size for Gradient Calculation</li> <li>- Increased Number of Data Items and Label Lengths</li> <li>- Flexible Numerical Formats for Input and Output <ul style="list-style-type: none"> <li>- Added Information in Standard Results File</li> <li>- Identifier Tags for Certain Sections</li> </ul> </li> <li>- Shrinkage of Variance</li> <li>- Additional Output Files Easily Readable by Post-Processing Software</li> <li>- Additional Weighted Residuals outputs (conditional, exact versions)</li> </ul>		8:45 – 9:30 AM
3.	<b>New Methods Available in NONMEM 7, Theory, Overview</b> <ul style="list-style-type: none"> <li>- Monte Carlo Importance Sampling Expectation Maximization (EM) (IMP)</li> <li>- Markov Chain Monte Carlo (MCMC) Stochastic Approximation EM (SAEM)</li> <li>- Iterative Two Stage (ITS)</li> </ul>		9:30 – 10:00 AM
4.	<b>Break</b>		10:00 – 10:15 AM
5.	<b>Mu Modeling</b> <ul style="list-style-type: none"> <li>- Model Modifications That Improve Efficiency of EM Methods (Mu Modeling)</li> </ul>		10:15 – 11:00 AM
6.	<b>Examples for EM Methods (hands-on)</b> <ul style="list-style-type: none"> <li>- Basic two compartment model problem, incorporate Mu Model</li> </ul>		11:00 AM – 12:00 PM
7.	<b>Lunch</b>		12:00 – 1:00 PM
8.	<b>Examples for EM Methods (hands-on)</b> <ul style="list-style-type: none"> <li>- Two compartment model with age and gender covariates</li> </ul>		1:00 – 2:00 PM
9.	<b>Bayesian Analysis (hands-on)</b> <ul style="list-style-type: none"> <li>- MCMC Bayesian Analysis (BAYES)</li> <li>- Prior information for MCMC Bayesian Analysis, including new</li> </ul>		2:00 – 3:00 PM

	NONMEM 7.3 feature of adding priors to SIGMA parameters - Revisit two compartment model, adding Bayesian analysis		
10.	<b>Break</b>		3:00 – 3:15 PM
11.	<b>More Examples with EM and Bayesian Analysis</b> -Population mixture model problem - Interoccasion variability problem using enhanced abbreviated code feature of NONMEM 7.3 - Inter-site variability example of NONMEM 7.3 - Modeling transit compartment problem with multiple doses, using DO loop feature of abbreviated code in NONMEM 7.3 -Receptor Mediated Clearance		3:15 – 4:15 PM
12.	<b>Additional Considerations for EM and Bayesian Analysis</b> - Termination Testing - Making Numerically Stable Models - Categorical data problem		4:15 – 4:30 PM
13.	<b>Additional Features to NONMEM 7.2.0 and NONMEM 7.3</b> • Parallel Computing, the Parafire • Dynamic Memory Allocation, use of \$SIZES • Extended formatting for \$TABLE files (RFORMAT, LFORMAT) • Alternative convergence criterion for FOCE (CTYPE=4) • Additional Output Files: o XML version of NONMEM report file o Shrinkage information: shk file o Conditional means and variances for mixture sub-populations: .phm file o FO/FOCE/LAPLACE gradients: .grd file o Monte Carlo, EM, Bayesian convergence diagnostics: .cnv file • NONMEM 7.3 features: o Increased number of mixed effects levels o Symbolic references to thetas, etas and epsilons for easier coding o DO loop usage and indexing of thetas, etas and epsilons in abbreviated code o AUTO option and optimization of EM options by NONMEM o Monte Carlo search algorithms to improve estimations in FOCE o Built-in conditional individual weighted residuals (CIWRES) o Greater control in assessing average eta shrinkage o Bootstrap tools for simulation o quasi-random Monte Carlo extended to simulations and all Monte Carlo methods ➤		4:30 – 5:00 PM
15.	<b>PDx-Pop Interface For NONMEM 7</b> - Real-Time Graphical Monitoring of Objective Function - Interaction with NONMEM Run o Toggle Switch for Console Printing of Iterations o Switch to End a Problem Gracefully o Switch to End a NONMEM Gracefully - Extended Summary Output - Graphical Display of Parameter Sampling History (BAYES) - Setting Up and Running Multiple Analysis Chains Simultaneously - Graphical and Tabular Summary of Multiple Analysis Chains (BAYES) - initial Parameters Variation Test - PDx-Pop on Linux and MAC OS X		5:00 – 5:15 PM
16.	<b>Question and Answer Session</b>		5:15 PM