



## New Features of NONMEM 7.5

ICON is committed to providing the most advanced analysis methods and tools for the pharmaceutical industry through continued enhancements to the NONMEM<sup>®</sup> software, the industry standard for population pharmacokinetic/ pharmacodynamics analysis; ensuring pharmaceutical companies may continue to use this trusted analysis tool, incorporating classical as well as new analysis algorithms for present day pharmaceutical development. In addition, PDx-Pop<sup>®</sup>, a graphical interface working in concert with NONMEM<sup>®</sup>, integrates with existing tools and its own automated methods to expedite the population modeling and analysis, providing optimal flexibility and increased efficiency and functionality.

### **NONMEM 7.5 is scheduled for release in October 2020, and will have the following new features:**

Simulated etas and sigmas may retain separate seed chains during simulation. This is useful if you generate data from two separate data file templates which differ only in the number of data points among subjects, but you have the same number of subjects, and you wish to retain the same etas between the two data sets generated across replications (subproblems).

Simulated eta samples may be rejected and call NONMEM to create a new sample with the EXIT statement. You can filter simulated values to create “normal truncated” distributions, for example.

A table, root.vpt, is created, which incorporates variance-covariances associated with etas as well as those associated with thetas (or omegas and sigmas). To present the comparable total standard errors in a user defined table, set VARCALC=3.

Variance-covariance matrix information can be imported from previous runs, and used to evaluate total standard errors of user defined items in tables, or to bring in variance-covariance matrices from alternative sources (IMP,SAEM,BAYES,SIR), as priors for TNPRI problems.

Increased flexibility has been added to \$PRIOR TNPRI to allow additional sources to provide the prior information.

Thetas may be simulated as a t-distribution.

The option TBLN has been added to \$EST METHOD=CHAIN and \$CHAIN records to allow selecting a table within a raw output file.

Additional records allow block specific setting of degrees of freedom information for LKJ decorrelation priors. Also, user-defined probability densities to the diagonal standard deviations to these blocks may be defined.

A Delay Differential Equation solver (ADVAN16) is now available (ADVAN17 if there are also equilibrium compartments) is now available.

The IDFORMAT option in the \$TABLE record allows a specialized format for ID (such as integer format) that is different from the other items in the table.



Thetas may be symbolically named at the \$THETA record, in conjunction with the initial values specified.

For MCMC Bayesian analysis the .phi table now contains the average of phi() values collected throughout the stationary distribution (positive iterations) phase, with conditional variances. In addition, variances for phi/etc of levels above subject level (when using \$LEVEL) are also now available.

Prepare a Single Burn-In for Multiple Stationary Chains. Because the burn-in of NUTS is computationally expensive, you can use the MSF file to perform a one-time burn-in in one control stream file, and then have subsequent control stream files use the burn-in information (including the mass density information) and evaluate their stationary phases in parallel (at different starting seeds).

Optimal Design is now available.

New options to replicate subjects in a data file are available, to facilitate simulations, avoiding the need to create replicate subjects data outside of NONMEM.

Techniques to incorporate partial differential equations (PDE) into ODE problems

A new way of modeling steady state dosing is available.

Individual parameter samples during BAYES analysis can be conveniently collected without additional user code required.

Collect samples of individual BAYES parameters, while keeping the population parameters fixed.

New format specifiers (FORMAT=q, c, QCSV, and CSV) offer compressed (no spaces) comma delimited file outputs.

You may increase the number of significant digits displayed for population parameter results in the NONMEM report file.

Additional options for SIR covariance of estimates sampling have been added to improve stability in sampling.

Some improvements in assessing nested random effects above subject level.