

## What's New in Trial Simulator 2.2.2

### Objectives

This release of Pharsight® Trial Simulator™ version 2.2.2 (TS 2.2.2) is intended to be used with 32 bit Windows 7 SP1 on English or Kanji (Japanese) environments. It provides the option to use GNU Fortran version 4.5.2 or Intel Fortran 12.1 (with Visual Studio.NET 2008) as the back-end compiler. The GNU Fortran compiler is redistributed with TS2.2.2. At time of installation the user will be given the option to select the compiler of choice. Only the supported versions of the compilers listed above should be used.

Trial Simulator 2.2.2 is now compatible with Microsoft Office 2003, 2007 and 2010.

Trial Simulator 2.2.2 is compatible with S-Plus 6.2 Prime (distributed with TS2.2.2) or with S-Plus 8.2.

Trial Simulator 2.2.2 is a maintenance product version to provide compatibility with Windows 7 SP1 32-bit operating system version on English and Kanji (Japanese) as well as better support for back-end compilers. No design changes, enhancements, or fixes of the functionality have been done. The previous major update was Trial Simulator 2.2, which provided a new scripting capability and enhancements in performance, data access and model building. Major enhancements in the TS2.2 version included the following:

### Enhancements

- *Active-X interface*

An Active-X programmer interface permits Trial Simulator to be run via a scripting engine such as Visual Basic.

- *PBPK modeling*

New features to support modeling of physiologically based pharmacokinetics (PBPK) include:

*Vascular flows*: model drug movement via blood flow between organs.

*Include sets*: alternate subordinate drug models, stored in external files, can be swapped into the main drug model. Include sets might capture species-specific parameters, or compare organ models.

*PBPK libraries*: example models, available in the installation directory under PKPDlib\PBPK\.

- *Cmax block*

At the request of many past users, a Cmax block was added that outputs the time and value of the most recent maximum (optionally minimum) of an arbitrary time function.

- *User-defined link function*

The discrete effect block now supports use of a FORTRAN subroutine for the inverse link function.

- *Performance boost: exclude specific output*

Formulation, response, and event blocks now include an option to suppress database output from that block during simulation, for potential reductions in simulation time.

- *Performance boost: binary simulation output*

For a 2- to 10-fold decrease in simulation time and file size, save output to a sequential binary file. Trial Simulator includes a utility to extract the binary data for analysis in third-party software.

- *Drug model enhancements*

*Replicate-level variability:* import distributions once per replicate or once per center, to evaluate trial designs in the presence of uncertainty in simulation parameters.

*More ports per block:* The maximum number of input and output ports per block has increased from 16 to 32, except on the Multivariate Distribution Block, on which it remains 16.

*Save model as text or XML:* In the drug model library window, drug models can now be saved in two new formats: .xml for XML format or .pmt for an editable textual format.

*New math functions:* Several new functions are available in the Expression Editor, including: base 10 log, 2-argument arctangent, logit(prob), min(a,b) and max(a,b).