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GastroPlus® v9.8.3

September 2022

Dear GastroPlus User,

Thank you for your interest in the <u>GastroPlus</u> PBBM / PBPK modeling and simulation platform. Our development team continues to work hard to make GastroPlus the most advanced and reliable simulation program for drug absorption, pharmacokinetics, and pharmacodynamics in the world today.

1. Updates in version 9.8.3

- ACATTM Model:
 - Increased flexibility in defining suspension dosing
- <u>Additional Dosage Route Module</u>:
 - Ocular:
 - Added melanosome trapping
 - Oral Cavity:
 - Option to include oral cavity dosage forms in Mixed Multiple Doses
- PBPKPlus[™] Module:
 - NEW: NAFL and NASH disease population groups
 - NEW: swine/pig PBPK model
- <u>ADMET Predictor® Module</u>:
 - Added mouse-specific property prediction models
- Metabolism and Transporter Module:
 - New enzyme and transporter expression levels for human, mouse, swine, minipig, and rabbit models
- Compartmental PK:
 - Option to synchronize liver first pass extraction during the optimization of liver clearance
- Population Simulator:
 - Improved interoperability with Monolix to save outputs from the population simulations in Monolix-compatible formats
- General Features:
 - Set Excel as the default output format for PSA and population simulations
 - Bug fixes

2. Updates in version 9.8.2

- ACATTM Model:
 - Incorporated nonlinear bile salt effects
 - Added FeSSIF-V2 as a default recipe for the biorelevant solubility input
 - Improved suspension dosing (combination of solution and solid particles)
 - Added predefined FDA low-fat meal options
- <u>Additional Dosage Route Module:</u>
 - Intramuscular:
 - Added option to modify intramuscular Kp with compartmental PK model;

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- New built-in mouse intramuscular physiology
- Ocular:
 - Added option to include melanin binding in Sclera and Retina;
 - New built-in physiologies for Dutch belted and New Zealand white rabbits
- <u>PDPlusTM Module</u>:
 - New PD model for intraocular pressure
- <u>Metabolism and Transporter Module</u>:
 - o New built-in enzyme expression levels and ontogeny functions
 - o Improved automated Km and Vmax fitting
- Population Simulator:
 - o Improved workflow for Fed/Fasted virtual bioequivalence simulations
 - Bug fixes related to parameter sampling and saving in the output file
 - Bug fixes related to plotting of crossover trials
- General Features:
 - Added option to specify fu,ent (unbound in enterocytes) directly in the main GastroPlus window
 - Expanded information saved in the simulation output files
 - o Maintain user-defined parameter ranges between subsequent PSA runs
 - o Bug fixes

3. Installation of GastroPlus on your computer/network

GastroPlus is designed to run on Windows 10 and 11 systems, or Mac computers through Parallels (or similar Windows virtualization). The software can be installed from the *.zip package retrieved from our ShareFile <u>online portal</u>, either as a "standalone" installation on your computer or as a "network installation" on your local area network. Refer to the installation manual or our <u>website</u> for instructions.

Before GastroPlus can be run from your installation, it must be activated. The activation process is handled via email with our licensing department at <u>licensing@simulations-plus.com</u> or +1-661-723-7723.

4. GastroPlus tutorial

GastroPlus includes an extensive help file with an updated tutorial. Prospective customers can use this tutorial during the evaluation of GastroPlus, for new and existing customers it can assist with validating a computer system (i.e., running tutorials to confirm the same results are generated on your computer versus what is reported in the tutorial).

The tutorial document contains step-by-step instructions for running GastroPlus simulations. A few standard simulations and their use in drug development are described. Data for running these simulations are also provided wherever necessary, along with the nature and source. The tutorial data files are present in the Tutorials folder *after* installing GastroPlus on your computer.

5. Customer support

As part of our Personal Consultation Program, Simulations Plus has assigned scientists to serve you in your use of GastroPlus. Feel free to contact them for guidance on techniques for using the program better, suggestions, and bug reports.

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We stand ready to help. If you would like advice on techniques for using the program most effectively in your research, please contact us.

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We look forward to assisting in any way we can.

Best regards,

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