

Simulations Plus presents  
The GastroPlus™ PBPK Modeling & Simulation Workshop:  
From Lead Optimization to Clinical Development



October 15 - 17 at the University of Florida

Simulations Plus, the industry's leading provider of simulation and modeling software for drug discovery and development, will be hosting its "GastroPlus™ PBPK Modeling & Simulation Workshop: From Lead Optimization to Clinical Development" at the University of Florida in Orlando, Florida on October 15 - 17, 2018.

This three-day, hands-on course provides a working knowledge of the theories and application of our state-of-the-art PBPK modeling and simulation software to support internal research and regulatory interactions. A combination of presentations and interactive examples, taken from actual industry experience and using GastroPlus, illustrate how to recognize and deal with the multiple interacting phenomena that affect the absorption, pharmacokinetics, pharmacodynamics, and DDIs of drugs as they progress to the clinic.



Department of Pharmaceutics Lake Nona  
University of Florida  
6550 Sanger Road, Office 467  
Orlando, FL 32827

Attendance for this event is limited, so register today!

## Who should attend?

This workshop is appropriate for graduate students, research scientists, and engineers in the areas of medicinal chemistry, DMPK, ADME, biopharmaceutics, and clinical pharmacology. Prior experience with GastroPlus is not required. The course will use GastroPlus for all case studies, but the guiding principles will be taught in a software-independent manner. Class size is limited to encourage interaction with the course instructors and among attendees. Interaction and networking among scientists is an important and valuable part of the experience!

## What will you learn?

Upon completion of this course, you should have a solid understanding of the interactions that exist among the various mechanistic phenomena affecting drug dissolution, mechanistic absorption, pharmacokinetics (employing both compartmental PK and physiologically based pharmacokinetics - PBPK), pharmacodynamics, and DDIs.

### You will understand and learn to recognize potential interactions among such factors as:

- pKa – ionization effects on dissolution, precipitation, absorption, and distribution
- solubility and permeability changes in the various environments in the gastrointestinal tract
- differences in physiology between human and preclinical species
- transit times through various gut regions and how and why they may vary
- formulation effects, including particle size distributions and controlled release dosage forms
- influx and efflux transporters in the gut wall and in other tissues
- metabolizing enzymes in the gut wall and in other tissues
- renal clearance and its variables

### You will gain experience with:

- screening compound libraries for absorption and bioavailability using chemical structures
- recognizing when to use PBPK vs. standard compartmental PK models
- predicting first-in-human doses with available preclinical and *in vitro* data
- assessing formulation strategies such as micronization and nanoparticles
- simulating populations including selected mixes of ages, gender ratios, ethnicities, and disease states
- estimating local concentration of drug following dermal and pulmonary administration
- determining the impact of food on the absorption/exposure of different drugs
- modeling nonlinear absorption and/or metabolism kinetics
- evaluating drug-drug interaction (DDI) risks using data at different stages
- understanding optimization methods, objective function weighting, and constraints

## How will the workshop operate?

All presentation files and data sets needed to run case studies will be available in electronic format. All attendees will be responsible for bringing their own laptop computers, with GastroPlus™ and ADMET Predictor™ installed prior to the course.

GastroPlus and ADMET Predictor software training is best done in an environment where each person operates the program and takes an active part in running simulations along with the instructor. As much as possible, the training uses PowerPoint slides to introduce software features. Once a feature is discussed, trainees then use it on their individual computers to see how it works. We find this instruction method to be much more effective than starting with a lecture that explains the entire program and later having students operate the program.

Continental breakfast, refreshment breaks, and lunch will be provided.



## Agenda

The training schedule presented here is a general guideline. We encourage questions as we go along, and we will take the time needed to ensure that everyone understands each point before we move to the next. We will use examples that we have developed for a wide variety of drugs. These examples have been selected to illustrate the various aspects of the ACAT™, TCAT™, PCAT™, & PBPK models, the types of analyses available, how to interpret the results of simulations, and typical caveats.

### Monday, October 15

**8:30 AM:** Welcome and an overview of the ADMET Predictor™ and GastroPlus™ modeling platforms

**8:45 AM:** Applications: QSAR/PBPK modeling integration – defining inputs through chemical structures and in silico F% simulations in animals and humans to drive lead optimization

**10:00 AM:** Break

**10:15 AM:** Applications: QSAR/PBPK modeling integration – defining inputs through chemical structures and in silico F% simulations in animals and humans to drive lead optimization (continued)

**11:00 AM:** Basics behind dissolution & passive absorption modeling (particle size distributions, Z-factor options, the ACAT™ model)

**12:00 PM:** Lunch

**1:00 PM:** Applications: Basics behind dissolution & passive absorption modeling (particle size distributions, Z-factor options, the ACAT™ model) (continued)

**3:00 PM:** Break

**3:15 PM:** Systemic PBPK modeling (clearance-based IVIVE, FIH oral predictions, parameter sensitivity analysis)

**5:00 PM:** Adjourn

### Tuesday, October 16

**8:30 AM:** Systemic PBPK modeling (clearance-based IVIVE, FIH oral predictions, parameter sensitivity analysis) (continued)

**10:00 AM:** Break

**10:15 AM:** Systemic PBPK modeling (transporter-based IVIVE, FIH oral predictions, parameter sensitivity analysis)

**12:00 PM:** Lunch

**1:00 PM:** Applications: Nonlinear PK modeling (incorporation of in vitro  $V_{max}/K_m$  data)

**2:30 PM:** Applications: DDI risk assessment

**3:00 PM:** Break

**3:15 PM:** Applications: DDI risk assessment (continued)

**5:00 PM:** Adjourn

### Wednesday, October 17

**8:30 AM:** PBPK/PD modeling to inform dose selection

**10:00 AM:** Break

**10:15 AM:** Special population predictions (pediatrics, disease states)

**12:00 PM:** Lunch

**1:00 PM:** Applications: Food effect modeling

**3:00 PM:** Break

**3:15 PM:** Applications: Additional dosage routes (mechanistic pulmonary and dermal absorption models)

**5:00 PM:** Adjourn

Note – topics not covered in this agenda include:

- Mechanistic IVIVCs and virtual bioequivalence trial simulations
- PBPK modeling of biologics (large molecules)
- Enterohepatic circulation
- Additional dosage routes (mechanistic ocular, oral cavity, and intramuscular injection absorption models)

# REGISTRATION FORM

Attendance is limited • Please register by October 1, 2018

Please fill in this form and return to: Ms. Renee Bouche  
Email: renee@simulations-plus.com | Phone: +1-661-723-7723 ext. 227 | Fax: +1-661-723-5524

## The GastroPlus™ PBPK Modeling & Simulation Workshop: From Lead Optimization to Clinical Development on October 15 - 17, 2018 at the University of Florida

Title: Professor / Dr. / Mr. / Mrs. / Miss / Ms.

FIRST NAME: \_\_\_\_\_

LAST NAME: \_\_\_\_\_

COMPANY: \_\_\_\_\_

POSITION: \_\_\_\_\_

DEPARTMENT: \_\_\_\_\_

ADDRESS: \_\_\_\_\_

TELEPHONE: \_\_\_\_\_

EMAIL: \_\_\_\_\_

PURCHASE ORDER NO. (if applicable): \_\_\_\_\_

Cost for the workshop is \$750 per person for anyone who is not affiliated with the University of Florida. Price includes all workshop materials, continental breakfast, refreshment breaks, and lunch each day. Also, a one (1) month single-user license to GastroPlus™ and ADMET Predictor™, with all optional modules, will be available after the workshop.

Hotel accommodation is not included with registration.

### Method of payment (Please check one)

Credit card (a confirmation message will be sent to the email address provided)

Name on card: \_\_\_\_\_ Email: \_\_\_\_\_ Tel: \_\_\_\_\_

Card billing address: \_\_\_\_\_

\_\_\_\_\_ Zip/Post Code: \_\_\_\_\_

Type of card:  Visa  MasterCard  AMEX Card Number: \_\_\_\_\_

Expires: \_\_\_\_\_ Security code: \_\_\_\_\_

Payment by check (you will be invoiced upon receipt of your completed registration form)

Payment by wire transfer (you will receive wire transfer information upon receipt of your completed registration form)

Payment online (you will be redirected to the payment portal when registering online at [simulations-plus.com/workshops](http://simulations-plus.com/workshops))

### Terms and Conditions

Cancellation Policy: Cancellations made prior to October 1, 2018 will be eligible for an 80% refund. Refunds for cancellations will be honored up to 45 days after the date of payment for credit card transactions. Substitutions are allowed up to 10 days before the event.

Payment Terms: Following completion and return of the registration form, the total fee must be paid within 30 days of receipt of invoice. All fees must be paid in full prior to the start of the workshop.