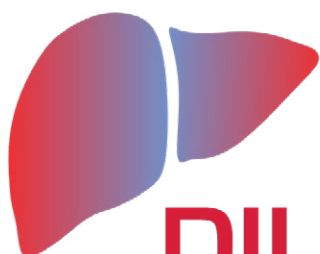


DILIsym Services, a Simulations Plus company, presents:  
The DILIsym® 2-Day Training Workshop



September 12 - 13 in Research Triangle Park, North Carolina



**DILIsym**®

DILIsym Services, a Simulations Plus company, will be hosting its “DILIsym® 2-Day Training Workshop” in Research Triangle Park, North Carolina on September 12 - 13, 2018.

This two-day, hands-on course provides a working knowledge of the basic theories and application of state-of-the-art quantitative system toxicology (QST) modeling and simulation software (DILIsym®) for the analysis of the potential for drugs and drug candidates to cause drug-induced liver injury (DILI), or for the investigation of mechanisms involved in a documented DILI

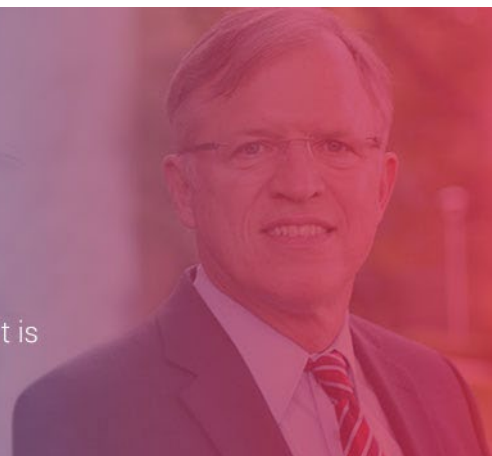
event. A combination of presentations and interactive examples using DILIsym will illustrate how to gather the appropriate *in vitro* toxicity data, derive DILIsym related toxicity parameters, conduct simulations of expected outcomes and analyze results for impacting decisions.

Lecture on assessing liver safety in clinical trials by:

Paul B. Watkins, M.D.

Director of UNC Institute for Drug Safety Sciences  
Professor of Pharmacy, Medicine & Public Health

“DILI remains a major problem for drug developers and regulators and DILIsym is helping address this challenge. It is being used successfully in a growing number of pharma companies and has been recently licensed to the FDA.”



Attendance for this event is limited, so register today!



**SimulationsPlus**

SCIENCE + SOFTWARE = SUCCESS

42505 10th Street West • Lancaster, CA 93534 • USA • phone: +1-661-723-7723

fax: +1-661-723-5524 • email: [info@simulations-plus.com](mailto:info@simulations-plus.com) • [www.simulations-plus.com](http://www.simulations-plus.com) • NASDAQ: SLP

## Who should attend?

This workshop is appropriate for pharmaceutical/biotechnology scientists and engineers in the areas of toxicology, clinical pharmacology, pharmacovigilance, DMPK and ADME. This is a beginner's course - prior experience with DILIsym is not required. The course will use DILIsym 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 industry, government, and academic 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 actions on the liver that could result in a safety risk to patients.

### You will understand the following important aspects of liver safety investigation:

- primary mechanisms often involved in DILI events, including mitochondrial dysfunction, oxidative stress production, lipotoxicity and bile acid transporter inhibition
- *in vitro* assay design, execution and stage-wise approach considerations for:
  - o high content imaging techniques to assess oxidative stress, GSH content, ATP, etc.
  - o the Seahorse XF analyzer assay for a detailed analysis of mitochondrial effects
  - o bile acid transporter inhibition IC50 and Ki studies
- pharmacokinetics including prediction of liver concentrations and how this impacts DILI predictions
- differences between early (discovery) stage approaches and late stage (clinical) approaches
- accepted and novel liver safety biomarkers
- general concepts accepted by regulators related to DILI monitoring and detection

### You will gain basic experience with:

- translating *in vitro* data into DILIsym parameter values
- simulating expected DILI outcomes for humans, rats, mice and dogs
- utilizing simulated populations (SimPops™) to:
  - o assess expected outcomes on a population level, including rare responses expected as the treated population grows
  - o understand how disease populations may respond differently from healthy volunteers
- understanding and using the:
  - o DILIsym optimization feature
  - o DILIsym clinical monitoring feature capable of allowing dynamic dose titration or cessation depending on liver safety outcomes in real time
  - o DILIsym Data Comparisons feature for validating key concepts represented in DILIsym
  - o DILIsym Specified Data feature that allows for direct input of PK information to drive DILI predictions directly from GastroPlus™ and other simulators
  - o DILIsym sensitivity analysis capabilities for determining uncertainty around predictions prior to making decisions
- examples of DILIsym use within the regulatory arena where development programs were impacted through QST
- using simulated outcomes to help better design mechanistic *in vitro* toxicology studies



**SimulationsPlus**

SCIENCE + SOFTWARE = SUCCESS

42505 10th Street West • Lancaster, CA 93534 • USA • phone: +1-661-723-7723

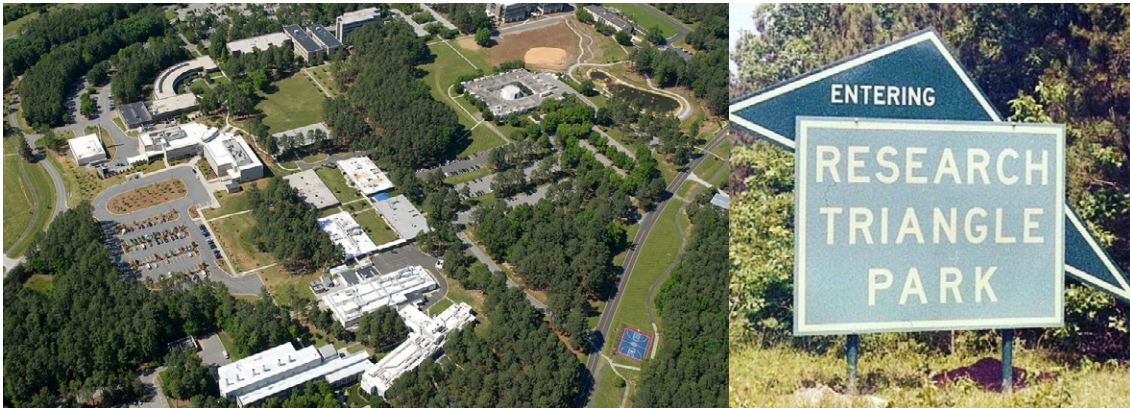
fax: +1-661-723-5524 • email: [info@simulations-plus.com](mailto:info@simulations-plus.com) • [www.simulations-plus.com](http://www.simulations-plus.com) • NASDAQ: SLP

## 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.

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

## Where will this be held?

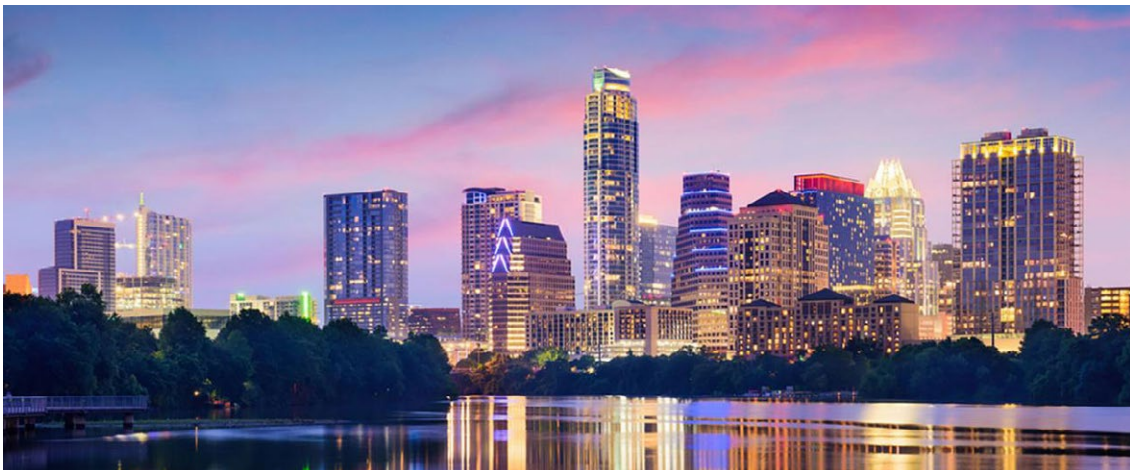


### **Marriott at Research Triangle Park**

4700 Guardian Drive

Durham, North Carolina 27703

+1-919-941-6200





# REGISTRATION FORM

Attendance is limited • Please register by September 3, 2018

Please fill in this form and return to Patti Steele (psteale@dilisym.com)  
To register by phone, please call Patti at +1-919-558-1297

## The DILIsym® 2-Day Training Workshop September 12 - 13, 2018 in Research Triangle Park, North Carolina

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

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

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

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

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

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

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

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

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

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

Free for industry members and license holders, free for academic/government license holders, USD \$600 per person (industry non DILI-sim members), and \$300 (government/academic non-license holders). Includes all workshop materials, continental breakfast, refreshment breaks, and lunch each day.

Hotel accommodations are 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 August 24, 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.



SCIENCE + SOFTWARE = SUCCESS

42505 10th Street West • Lancaster, CA 93534 • USA • phone: +1-661-723-7723  
fax: +1-661-723-5524 • email: [info@simulations-plus.com](mailto:info@simulations-plus.com) • [www.simulations-plus.com](http://www.simulations-plus.com) • NASDAQ: SLP