

*Cognigen* | *DILIsym Services* | *Lixoft*

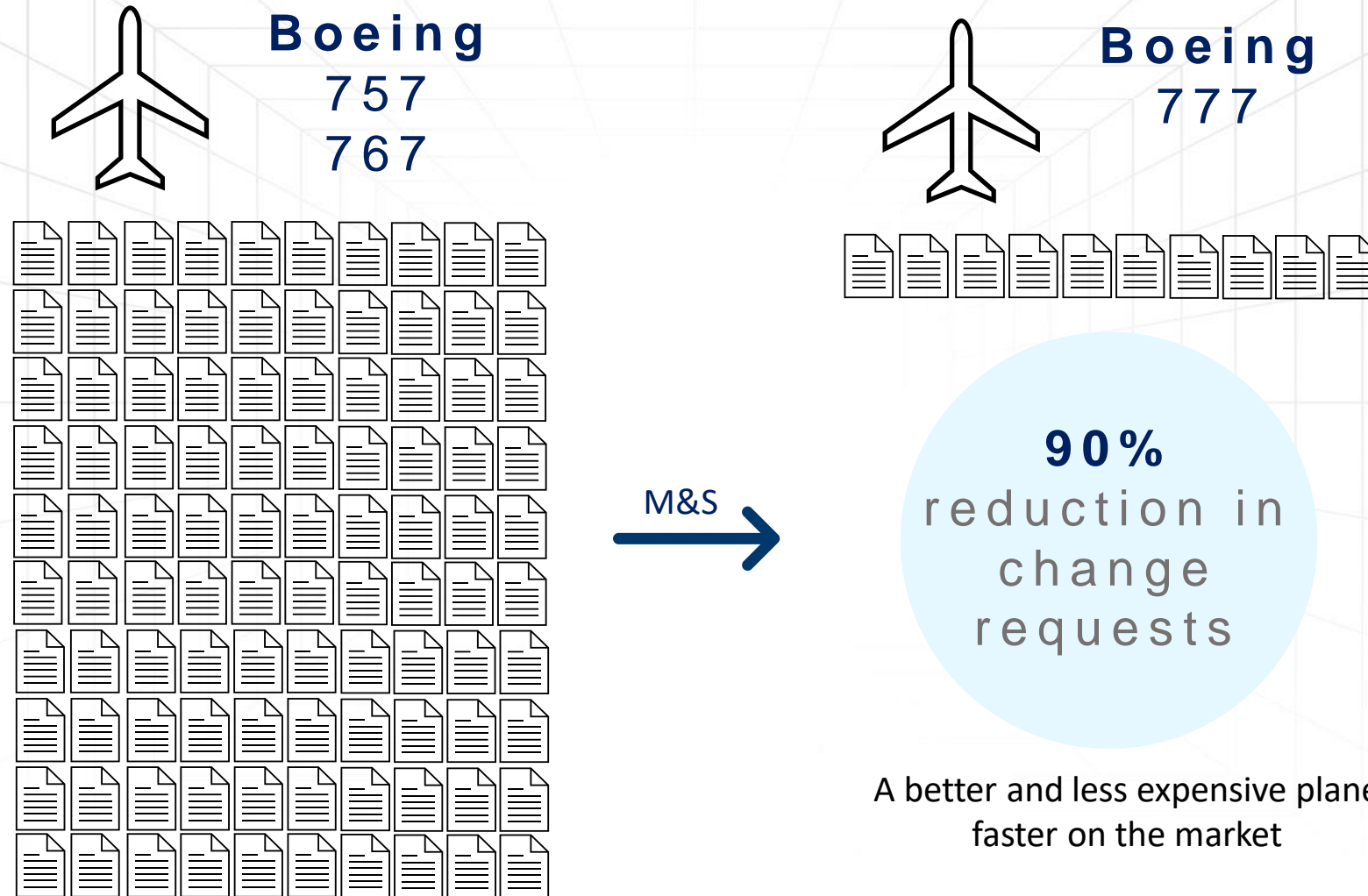
## TriCAMS: Opportunities for Faculty, Postdocs, and Graduate Students

Haiying Zhou, Director of Simulation Technologies, SLP  
([haiying.zhou@simulations-plus.com](mailto:haiying.zhou@simulations-plus.com))

James Beaudoin, Sr. Scientist, DSS Division  
([james.beaudoin@simulations-plus.com](mailto:james.beaudoin@simulations-plus.com))

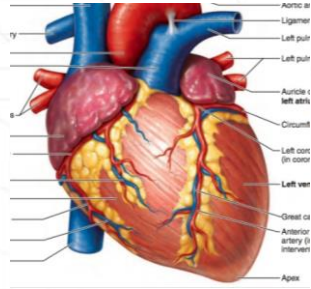
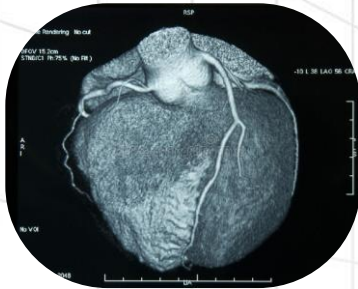
September 17, 2022

# Why Modeling & Simulation?

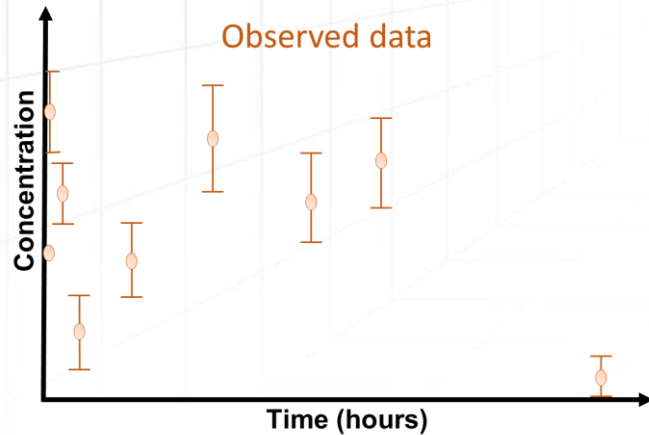


# Principles of Modeling

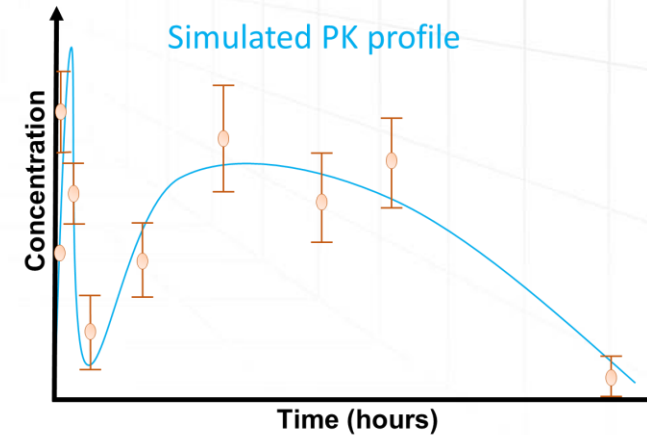
Simplified representation of a system



<3

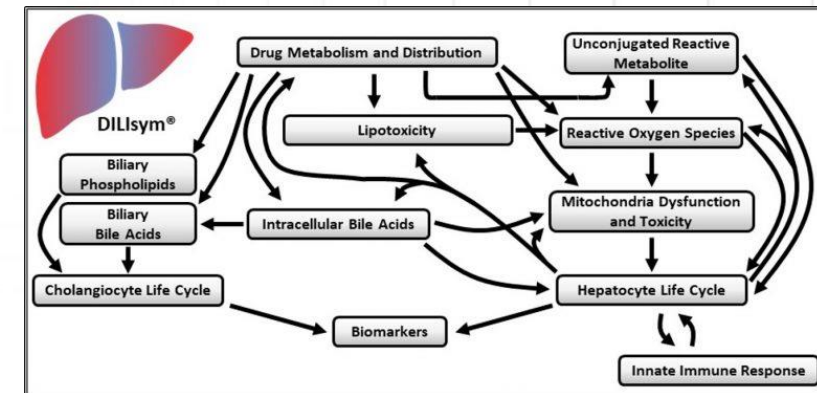
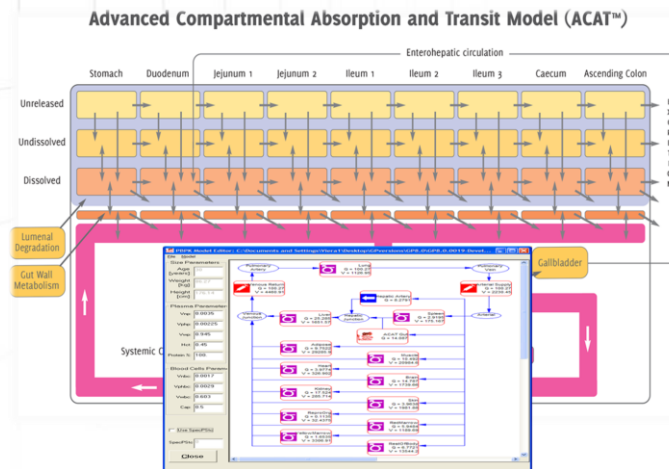
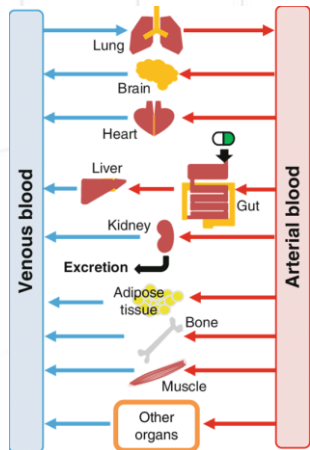
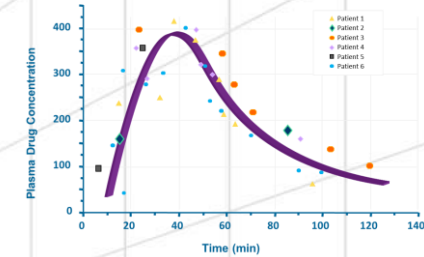
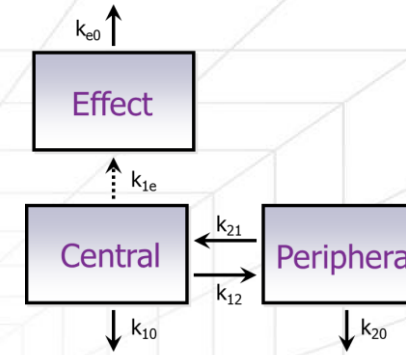


$$C_t = f(t, \text{dose}, \text{route})$$



# SimulationsPlus Allows for Various Types of Modeling

- Empirical modeling → Cognigen and Lixoft Divisions
  - Population pharmacokinetics (PopPK)
  - Pharmacokinetics-pharmacodynamics (PK-PD)
- Mechanistic modeling → Simulations Plus and DILIsym Services Division
  - Physiologically-based pharmacokinetics (PBPK)
  - Quantitative systems toxicology (QST) and pharmacology (QSP)



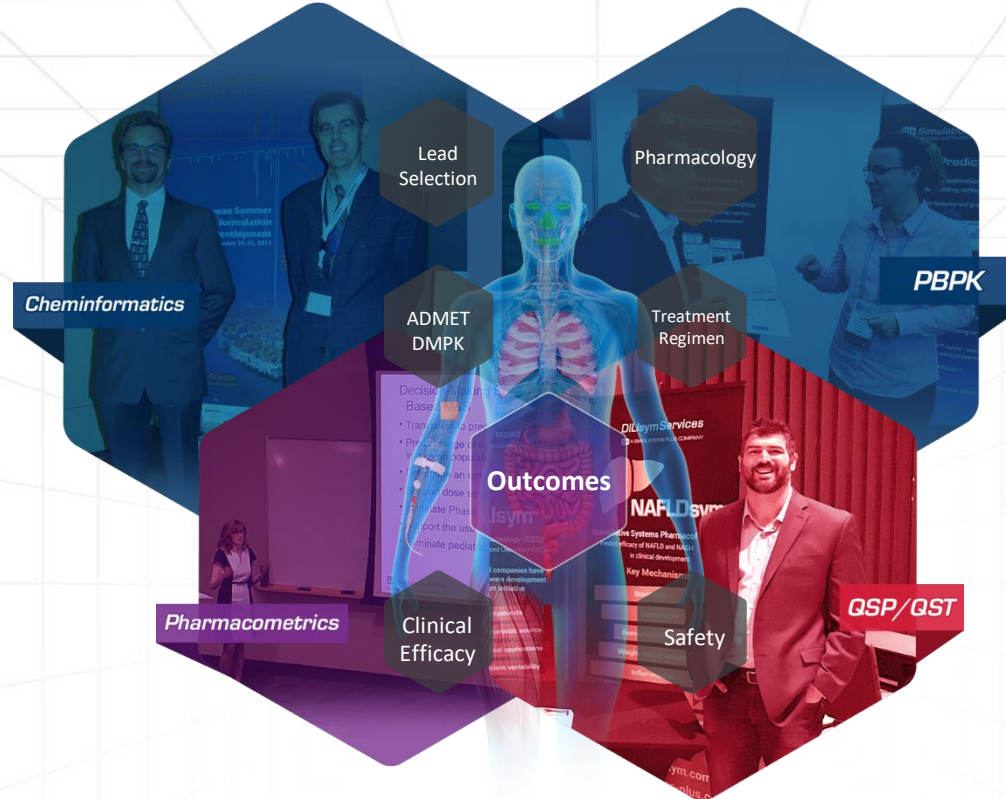
Learn more: <https://www.simulations-plus.com/about/> (Simulations Plus); <https://www.simulations-plus.com/cognigen/> (Cognigen Division), <https://www.simulations-plus.com/dilisymservices/> (DILIsym Services Division); <https://www.simulations-plus.com/lixoft/> (Lixoft Division)



# At *SimulationsPlus* We Put It All Together

## Science

- Seamless collaboration
- Integrated, innovative solutions to meet client needs



## Business

- Resources available to get the job done on time
- One-stop shopping – single vendor for all *in silico* drug development needs a client may have

**We have the solutions and the people  
to address the drug development questions any client may have**

Simulations Plus and its Cognigen, DILIsym Services and Lixoft Divisions consist of multidisciplinary teams of pharmaceutical scientists, applied and computational mathematicians, (bio)chemists, engineers, statisticians, nutritionists and more!

Learn more: <https://www.simulations-plus.com/about/> (Simulations Plus); <https://www.simulations-plus.com/cognigen/> (Cognigen Division), <https://www.simulations-plus.com/dilysym-services/> (DILIsym Services Division); <https://www.simulations-plus.com/lixoft/> (Lixoft Division)

NASDAQ: SLP | CONFIDENTIAL

# Our Solutions Inform the Entire Drug Development Process



**MD** **AP**  ADMET Cheminformatics

**GP** **D+** **M+** 

PBPK/PBBM

**DS** **NS** **RS** **IS** 

QSP/QST

   **PK** 

Pharmacometrics








Regulatory Interactions

Learn more: <https://www.simulations-plus.com/about/> (Simulations Plus); <https://www.simulations-plus.com/cognigen/> (Cognigen Division), <https://www.simulations-plus.com/dilysm-services/> (DILIsym Services Division); <https://www.simulations-plus.com/lixoft/> (Lixoft Division)

NASDAQ: SLP | CONFIDENTIAL

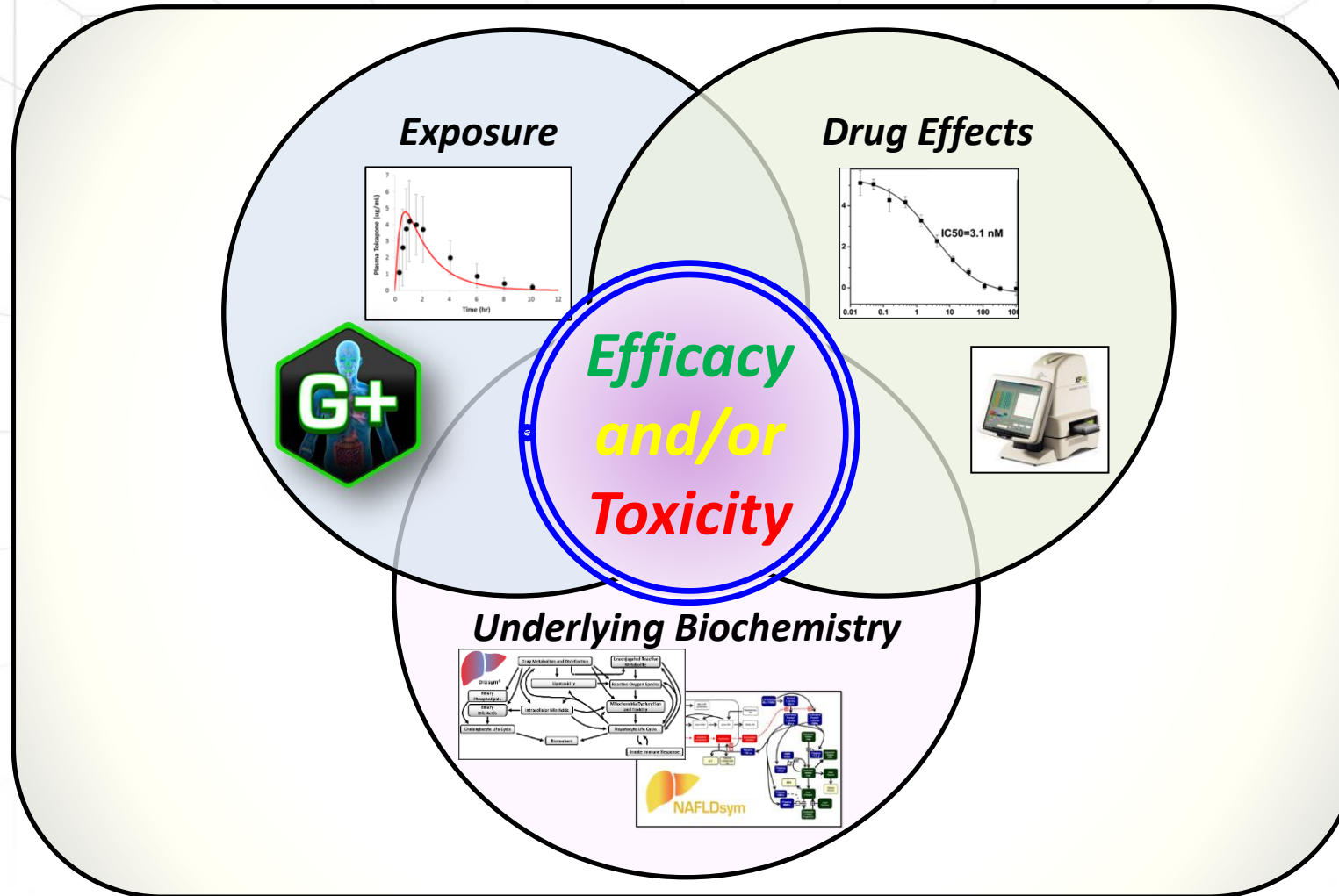
# DILIsym Services QSP/QST Platforms

	Model	Disease area	Key References	Primary biomarkers included:	Number of compounds/ targets evaluated
QSP	NAFLDsym 	Non-Alcoholic Fatty Liver Disease and Non-Alcoholic Steatohepatitis	Kenz 2020, Kenz 2019, Longo 2018, Siler 2018, Siler 2022	Histologic NAS, histologic fibrosis score Liver fat (MRI), plasma ALT	25-30
	IPFsym 	Idiopathic pulmonary fibrosis	Siler 2021	Forced vital capacity; high resolution computed tomography	6
	ILDsym 	Interstitial lung disease	Kenz 2022	Forced vital capacity; high resolution computed tomography	5
	CARDIOsym	Cardiac recovery following myocardial infarction	Kenz 2021	Cardiomyocytes, myofibroblasts, collagen	2
	KIDNEYsym	Kidney diuresis	--	Urine volume; urinary sodium loss	3
	GOUTsym	Gout Emphasis on hyperuricemia	--	Uric acid	5
	MITOsym	Hepatocyte bioenergetics	Yang 2015	Oxygen consumption rate; ATP concentrations	>70
QST	DILIsym 	Drug induced liver injury	Shoda 2017, Battista 2020, Eichenbaum 2020	Plasma ALT, plasma AST, plasma bilirubin	>70
	RENAsym 	Drug induced kidney injury	Gebremichael 2020	Urine KIM-1, urine $\alpha$ GST, serum creatinine	10

Learn more: <https://www.simulations-plus.com/dilisyms-services/> (DILIsym Services Division)

NASDAQ: SLP | CONFIDENTIAL

# DILIsym Services Uses QSP and QST Modeling to Predict Efficacy and Safety of Drugs in Development



Learn more: <https://www.simulations-plus.com/dilisyms-services/> (DILIsym Services Division)

NASDAQ: SLP | CONFIDENTIAL



# SLP University+ and Internship+ Programs Are Great Opportunities for Current Academics

## SLP University+ Program

Offering free access to Simulations Plus software to universities worldwide



### SLP UNIVERSITY+ PROGRAM

The University+ program offers one-year access to Simulations Plus software to students and educators at accredited universities worldwide, renewable if eligibility conditions are met. Our goal is to increase modeling and simulation (M&S) learning and education that will promote the next generation of scientists and set them up today for success tomorrow.

Learn more: <https://www.simulations-plus.com/software/slp-university-program/>

## Internship+

Through our [University+](#) and [Internship+](#) programs, Simulations Plus scientists mentor students each year from across the globe to provide hands-on learning in mechanistic modeling and simulation research. Our internships allow students to apply their academic knowledge and prepare for a career in modeling & simulation science using our industry-leading software tools under the guidance of experts! Check out the bios below to learn more about our interns and the projects they are working on.

Visit our [Careers](#) page to learn more about our [internships](#) and other exciting job opportunities.

### INTERNSHIP+ PROGRAM

Prepare for your future in model-informed drug development (MIDD). Simulations Plus can provide you with a unique opportunity to expand your professional horizons and develop your skills. Prepare yourself for a career in mechanistic modeling & simulation science by gaining hands-on experience with our industry-leading software tools under the guidance of experts!

Learn more: [https://www.simulations-plus.com/wp-content/uploads/Internship-Flyer\\_FINAL-11.08.2021.pdf](https://www.simulations-plus.com/wp-content/uploads/Internship-Flyer_FINAL-11.08.2021.pdf)

# Simulations Plus Is Involved in Multiple Academic (and Government) Collaborations, and Is Always Interested in New Potential Collaborations

## Partners and Collaborators

At Simulations Plus, we strive to improve the productivity of science-based research and development through the use of our technology. We realize, however, that this is something we cannot do alone, and we actively collaborate with a variety of universities, contract research organizations (CROs), distributors, and government agencies to help meet our (and their) client's goals. Below is a partial list of the partnerships we have formed to continue advancing the use of modeling & simulation approaches.

Interested in working with us and/or utilizing our technology to support clients? Our team is ready to discuss your needs today.

### Academic Collaborators

We are always interested in speaking with professors & students on ways in which we can support academic research and coursework:

The University of Buffalo, UB Center of Excellence in Pharmacokinetics and Pharmacodynamics

University of Maryland

University of Florida, College of Pharmacy

### Government Collaborations

Much of the momentum behind the increased use of PBPK modeling has been driven by regulatory agencies around the world, who all have access to our software, and we are happy to partner with several of them on different projects:

National Toxicology Program: We have been collaborating with scientists from the U.S. EPA/NIEHS/NTP for several years on the use of GastroPlus® and ADMET Predictor® to efficiently screen the Tox21 library – more details can be found here:

- ✓ Simulations Plus Extends Research Agreement with National Institute of Environmental Health Sciences
- ✓ U.S. Environmental Protection Agency Purchases Multiple Licenses of Simulations Plus Software

U.S. FDA: We have been very fortunate to receive 2 funded grant awards from the FDA to continue to enhance the GastroPlus platform, and most divisions have access to the software – more details can be found here:

- ✓ FDA's Office of New Drug Products Places Order for 50 Additional Licenses to GastroPlus™
- ✓ Simulations Plus Awarded New Cooperative Agreement with FDA
- ✓ Simulations Plus Wins Cooperative Agreement with FDA
- ✓ Regulatory Agencies in Asia and the U.S. Purchase Multiple Licenses of Simulations Plus Software
- ✓ Simulations Plus Signs Research Collaboration Agreement with FDA

National Institutes of Health: We are thankful the NIH supports our mission to help modernize drug development and reduce the time and costs associated with developing new therapies. Building on our expertise in drug-induced liver injury and nonalcoholic fatty liver disease, RENAsym® will expand our Quantitative Systems Pharmacology (QSP) offerings to include potential damage to the kidney. More details can be found here:

- ✓ Simulations Plus Subsidiary DILIsym Awarded Grant for up to \$1.7 Million For Model Development
- ✓ DILIsym Services was awarded a Phase II \$1.5M NIH SBIR grant to continue development of RENAsym, software for predicting drug-induced kidney injury
- ✓ Policy on Disclosure and Management of Financial Conflicts of Interest related to Public Health Service Research
- ✓ CDC
- ✓ EMA
- ✓ Health Canada
- ✓ NMPA
- ✓ PMDA
- ✓ US EPA
- ✓ US Army
- ✓ Walter Reed Army Institute of Research

Learn more: <https://www.simulations-plus.com/about/partners-and-collaborators/>

# Various Entry-Level and More Advanced Job Opportunities Are Available on a Regular Basis

## Internship+

Buffalo, NY, Lancaster, CA, Paris, France, Research Triangle Park, NC

Simulation  
creative  
horizon

## Cheminformatics Scientist

Remote Work

We are  
to work  
mole

## Sr. PBPK Modeler

Buffalo, NY, Lancaster, CA, Paris, France, Remote Work, Research Triangle Park, NC

We are  
model  
popul

## Jr. PBPK Modeler

Buffalo, NY, Lancaster, CA, Paris, France, Remote Work, Research Triangle Park, NC

We are  
PBPK/P  
design/c

## QT/C++ Programmer

Remote Work

We are lo  
in all pha  
simulatio

## Pharmacometrician

Buffalo, NY, Lancaster, CA, Paris, France, Remote Work, Research Triangle Park, NC

Cognigen  
will enga  
simulatio

## QSP/QST Modeling Scientist

Buffalo, NY, Lancaster, CA, Paris, France, Remote Work, Research Triangle Park, NC

Modeling and Simulation Scientist at the DILIsym Services division focused on developing and using simulation platforms for drug toxicity and efficacy. This position can work from any of our corporate office locations or remotely.

Learn more: <https://www.simulations-plus.com/about/careers/>