Creating a Roadmap to Quantitative Systems Pharmacology-Informed Rare Disease Drug Development

University of Maryland Center of Excellence in Regulatory Science and Innovation
Food and Drug Administration
Public Workshop
May 11, 2023 | 10:00 AM – 5:05 PM Eastern Time

Biographies

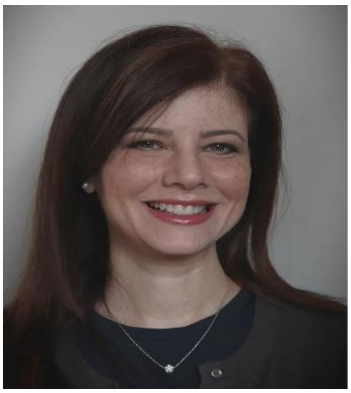
Sydney Stern, PhD
Clinical Pharmacology Reviewer
DTPM | OCP | OTS | CDER | FDA

Dr. Sydney Stern is a clinical pharmacology reviewer in the Division of Translational and Precision Medicine (DTPM) in the Office of Clinical Pharmacology at the FDA. She received a Master of Science in Clinical Research and a Ph.D. at University of Maryland Baltimore in Pharmaceutical Sciences. During her PhD, she developed a small molecule dual activator to improve the bioactivation of cyclophosphamide, a prodrug, and protect cardiomyocytes against doxorubicin-induced toxicity in the treatment of breast cancer. She has extensive experience with in vitro/in vivo extrapolation, particularly with liver-based toxicity models, and has led several big data projects in the rare disease space. She has also led a pilot program, called From Cells to Communities, at University of Maryland Baltimore in collaboration with the Marlene and Stewart Greenbaum Comprehensive Cancer Center to enhance bidirectional learning of early-stage scientists and cancer patients. Additionally, she has served on Sarcoma Patient Advocacy Global Network (SPAEN) and the Life Raft Group Consensus Committees for creating standardized guidelines for rare diseases such as tenosynovial giant cell tumor. Sydney's rare disease expertise has led to the creation of many patient and physician programs for diseases such as giant cell tumor of the bone and tenosynovial giant cell tumor.

Issam Zineh, PharmD, MPH, FCP, FCCP
Director of the Office of Clinical Pharmacology
OCP | OTS | CDER | FDA

Dr. Issam Zineh is Director of the Office of Clinical Pharmacology (OCP) at the U.S Food and Drug Administration (FDA). He has held various leadership positions at the FDA including Associate Director for Genomics (2008-2012), Co-Director of the CDER Biomarker Qualification Program (2009-2015), and serves on the CDER Medical Policy Council and other CDER-wide governance committees. Dr. Zineh received his PharmD from Northeastern University and completed his residency at Duke University Medical Center. He completed a fellowship in cardiovascular pharmacogenomics at the University of Florida (UF) where he also obtained his MPH in Health Policy and Management. Prior to joining FDA in 2008, Dr. Zineh was on faculty at the UF Colleges of Pharmacy and Medicine and Associate Director of the UF Center for Pharmacogenomics. He is a recognized expert in the fields of drug development and evaluation, clinical pharmacology, pharmacotherapy, and precision medicine. As Director of OCP, Dr. Zineh leads a staff of over 250 regulatory, research, program/project management, and administrative staff in FDA's efforts to enhance drug development and promote regulatory innovation through clinical pharmacology and experimental medicine.

Hilary Vernon, MD, PhD
Associate Professor of Genetic Medicine, Department of Genetic Medicine
Johns Hopkins University School of Medicine



Dr. Hilary Vernon's research interests include understanding intermediary metabolism in mitochondrial disorders and inborn errors of metabolism. Dr. Vernon is the director of the Mitochondrial Medicine Center at Johns Hopkins Hospital and the Barth Syndrome Interdisciplinary Clinic at the Kennedy Krieger Institute. She is also the co-director of the Department of Genetic Medicine Clinical Trials Unit at Johns Hopkins University School of Medicine.

Dr. Vernon received her MD and PhD from Rutgers University, New Brunswick, NJ, USA. She completed residencies in Genetics and Pediatrics at Johns Hopkins University, and a fellowship in Clinical Laboratory Biochemical Genetics at Johns Hopkins University. She is board certified in Pediatrics, Clinical Genetics, and Clinical Laboratory Biochemical Genetics.

Kapil Gadkar, PhD
Staff Scientist, Senior Director
Denali Therapeutics

Dr. Kapil Gadkar is a Staff Scientist, Senior Director, and the Head of the Quantitative Pharmacology Group at Denali Therapeutics. Kapil Gadkar earned his PhD in Chemical Engineering from UC-Santa Barbara. He has spent 15+ years developing and applying mathematical models to support drug development. He and his team at Denali Therapeutics currently support the discovery and development of drug therapeutics towards defeating neurodegeneration. Prior to joining Denali Therapeutics, Dr. Gadkar was in the Quantitative Systems Pharmacology Group at Genentech, where he worked in a wide range of therapeutic areas including Immunology, Oncology, Ophthalmology, Cardiovascular disease, and Neuroscience. Dr. Gadkar also has a keen interest in teaching and takes every opportunity to lecture in topics related to Modeling and Simulation in Drug Development to undergraduate and graduate students in short courses and workshops.

Gary An, MD, FACS
Professor of Surgery and Vice Chair of Surgical Research, Department of Surgery
University of Vermont Larner College of Medicine

Dr. Gary An is a Professor of Surgery and Vice-Chairman for Surgical Research in the Department of Surgery at the University of Vermont Larner College of Medicine. He is a clinically active trauma/critical care surgeon who has worked on the application of complex systems analysis, agent-based modeling and in silico trials to study sepsis, inflammation, wound healing, host-pathogen interactions and cancer since 1999. He is one of the co-founders of Translational Systems Biology, a discipline that promotes the use of multi-scale mechanistic simulation models to cross the Valley of Death of Drug Development. He asserts that the biggest bottleneck in drug development/repurposing is the inability to effectively predict the effect of a molecular manipulation of cellular behavior (e.g. a drug) demonstrated to be effective in pre-clinical studies or with existing clinical usage when it is then applied in a novel clinical context. His work consists of the development of multiscale, cell-based computer simulations and the integration of machine learning and artificial intelligence with such models to represent the individual diversity within clinical populations (e.g. populations of medical digital twins for in silico trials) and for discovery and development of therapeutic control modalities.

Valeriu Damian, PhD
Senior Director, System Modeling & Translational Biology, Computational Sciences, Medicine Design, R&D
GSK-Upper Providence

Dr. Valeriu Damian is leading the Systems Modeling and Translational Biology group in GlaxoSmithKline. The group is responsible for providing translational modeling support for all therapeutic areas in GSK. This includes Physiological Based PK (PBPK), PK/PD, Quantitative Systems Pharmacology and Toxicology (QSP/T) modeling for all modalities and delivery routes.

Valeriu holds a PhD in Computer Science from University of Iowa and a Computer Engineering diploma from Politehnica University of Bucharest in Romania.

Throughout his 23 years carrier in GSK Valeriu focus has been on integrating diverse scientific ideas from multiple disciplines – mathematics, informatics, chemistry, physics, biology, and engineering – into mechanistically based models and demonstrated their capability to interpret available data, to enhance understanding, to suggest testable hypotheses, to push the scientific boundaries and ultimately to bring better, faster and more affordable medication to the patients. Valeriu made significant contributions to PBPK modeling of inhaled, transdermal, ocular, and long acting injectable delivery as well as QSP model development. In 2018, Valeriu was the chair for the QSP Special Interest Group in ISoP and ASCPT Systems Pharmacology community leader in 2022/2023.

Steven Chang, BS EE, MS EE
President & CEO
Immunetrics, Inc.

Steven Chang is a successful technology entrepreneur with more than 30 years of experience in identifying emerging market needs and combining state of the art technologies and resources to meet those needs. He helped start Immunetrics over 20 years ago and has led the company's efforts to make QSP disease modeling an integral part of analyzing and designing modern clinical trials.

Robert Schuck, PharmD, PhD
Deputy Director
DTPM | OCP | CDER | FDA

Dr. Robert Schuck is the Deputy Director of the Division of Translational and Precision Medicine (DTPM) in the Office of Clinical Pharmacology (OCP) at the FDA. DTPM is a multidisciplinary team consisting of translational scientists with clinical pharmacology, human genomics, epidemiology, and molecular biology expertise. The division focuses on regulatory review, research, and policy development in the areas of pharmacogenomics, biomarker qualification, drugs for rare diseases and inborn errors of metabolism, and genetically targeted therapies.

Before joining the FDA in 2013, he received his PharmD from the University of Michigan College of Pharmacy in 2008 then completed his PhD in Pharmaceutical Sciences at the University of North Carolina Eshelman School of Pharmacy in 2013.

Kerry Jo Lee, MD
Associate Director for Rare Diseases
DRDMG | OND | CDER | FDA

Dr. Kerry Jo Lee is the Associate Director for Rare Diseases in the Division of Rare Diseases and Medical Genetics, Office of New Drugs (OND), Center for Drug Evaluation and Research (CDER). In this role, she leads the Rare Diseases Team, a multidisciplinary rare disease programming and policy team that works to promote their mission to facilitate, support, and accelerate the development of drugs and therapeutic biologics for rare diseases, and serves as the program management office for CDER's Accelerating Rare diseases Cures (ARC) Program. Dr. Lee joined the FDA as a medical officer in 2014 with the former Division of Gastroenterology and Inborn Errors Products, OND, CDER. Dr. Lee then moved to a position as a clinical advisor for the Office of New Drug Policy, CDER, where she served as a lead in the areas of benefit-risk assessment, modernization efforts (including the integrated review for marketing applications), and real-world data/evidence programming before serving in her current position.

Dr. Lee is a pediatric gastroenterologist/hepatologist and a graduate of Princeton University and the New York University School of Medicine with an honors degree conferred in microbiology. She completed her residency in pediatrics at the Children's Hospital of Los Angeles followed by a post-doctoral clinical fellowship in Pediatric Gastroenterology, Hepatology, and Nutrition at Columbia University College of Physicians and Surgeons in New York. Dr. Lee maintains a steadfast interest in international policy and bioethics and worked for several years at the former National Bioethics Advisory Commission on reports advising the executive branch on ethical and policy issues in both international and domestic clinical trials.

Jane P.F. Bai, PhD
Expert Regulatory Scientist
DARS | OCP | CDER | FDA

Dr. Jane Bai is Expert Regulatory Scientist with the expertise in systems pharmacology at the US Food and Drug Administration. Dr. Bai has served on the NIH National Institute of Biomedical Imaging and Bioengineering Interagency Modeling and Analysis Group as one of three FDA representatives since 2021. Dr. Bai received a Master's degree in Applied Mathematics in 1990, and PhD in Pharmaceutics in 1990 from the University of Michigan, Ann Arbor, Michigan. Dr. Bai was on the faculty of Pharmaceutics Department of the University of Minnesota Twin Cities between 1990-1996; and was named PhRMA Starter (1992) and AAPS Young Investigator (1994). From 1996 to 2004, she was an entrepreneur developing and licensing to several pharmaceutical companies an in-silico software, OraSpotter®, for predicting the fraction dose absorbed in humans. Dr. Bai has published 80 peer-reviewed papers and book chapters and co-edited the book entitled "Systems Medicine," which was published by Spring Nature in 2022.

Cynthia J. (C.J.) Musante, PhD
Vice President of Scientific Research & Global Head of Quantitative Systems Pharmacology
Pfizer, Inc.

Dr. Cynthia J. (C.J.) Musante is Vice President of Scientific Research and Global Head of Quantitative Systems Pharmacology (QSP) at Pfizer Inc. She received her PhD in Applied Mathematics from North Carolina State University and has over twenty years of experience in QSP modeling. At Pfizer, her group is responsible for developing and applying systems models and disease platforms across the portfolio to enhance the robustness and quality of decision-making at the program- and therapeutic strategy-level. CJ is an advocate for model informed drug development, both internally and externally. She is a frequent organizer and invited speaker at national and international conferences, and currently serves as President of the International Society of Pharmacometrics (ISoP).

Jie (Jack) Wang, PhD
Team Leader, Rare Diseases and Inborn Errors of Metabolism
DTPM | OCP | CDER | FDA

Dr. Jie (Jack) Wang is the team leader for the Rare Diseases and Inborn Errors of Metabolism review team in the Division of Translational and Precision Medicine in the FDA's Office of Clinical Pharmacology (OCP). He also currently serves as Vice Chair of the Biologics Oversight Board and a steering committee member of Rare Disease Scientific Interest Group in OCP. Dr. Wang joined the FDA in 2011 and has served as a reviewer and team leader for clinical pharmacology review teams responsible for evaluating IND, NDA, and BLA for drugs and biologics in multiple therapeutic areas. He has authored or co-authored over 30 peer-reviewed journal articles and 40 abstracts in the areas of pharmacokinetics, pharmacodynamics, biopharmaceutics, immunogenicity, gene therapy, and nanomedicine. He received his BS in Pharmacy from Beijing Medical University, his MS in Pharmaceutical Sciences from Peking University, and his PhD in Pharmaceutics from The Ohio State University.

Stephen Schmidt, BPharm, PhD, FCP
Endowed Professor, Department of Pharmaceutics
Director, Center for Pharmaceutics and Systems Pharmacology
University of Florida

Dr. Stephan Schmidt is an endowed Professor in the Department of Pharmaceutics at the University of Florida, where he also serves as the Director for the Center for Pharmacometrics and Systems Pharmacology. He received his BS in Pharmacy from the Friedrich-Alexander University in Erlangen, Germany, and his PhD in Pharmacy from the University of Florida in Gainesville, USA. Following a post-doctoral fellowship at the Leiden-Amsterdam Center for Drug Research, he rejoined the University of Florida as faculty in 2012. Dr. Schmidt's research focuses on the development and application of mechanism/physiologically-based drug-disease trial models to address clinically relevant questions in the area of antimicrobial chemotherapy, chronic progressive diseases, special patient populations, and drug-drug interactions. He published more than 140 peer-reviewed scientific manuscripts, eight book chapters, and two textbooks, including the fifth edition of Rowland and Tozer's Clinical Pharmacokinetics and Pharmacodynamics textbook, one of the world-wide leading textbooks in the quantitative clinical pharmacology arena. He received numerous awards including the University of Florida Excellence Award for Assistant Professors in 2013, the Tanabe Young Investigator Award from the American College of Clinical Pharmacology (ACCP) in 2016, the Outstanding Doctoral Thesis Mentoring Award from UF's College of Pharmacy in 2018, and the Excellence in Academia, MIDD+ Scientific Conference Award in 2021. Dr. Schmidt serves as clinical pharmacology section editor of the *European Journal of Pharmaceutical Sciences* as well as editorial board member of the *Journal of Clinical Pharmacology* and the *European Journal of Pharmaceutical Sciences*, and Scientific Advisor to the Editors of the *Journal of Pharmaceutical Sciences*.

Susana Zaph, PhD
Senior Director, Head of Translational Disease Modeling-Rare and Neuro
Sanofi

Dr. Susana Zaph is a Senior Director at Sanofi, where she leads the Translational Disease Modeling team covering the Rare and Neurology therapeutic areas developing QSP-based models that support drug development programs in lysosomal storage diseases, rare hematology, and gene therapy. Dr Zaph holds a PhD in Pharmacology from Mount Sinai School of Medicine, followed by a tenured track academic position leading a systems biology research group. Dr. Zaph is the leading author of several publications, and presentations in systems biology and QSP. Dr. Zaph is a member of the Innovation & Quality (IQ) Consortium Working Group on QSP and is part of the American Conference of Pharmacometrics (ACoP) scientific programming committee.

Brian J. Schmidt, PhD
Executive Director, Head of Quantitative Systems Pharmacology & Physiologically Based Pharmacokinetics Department
Bristol Myers Squibb

Dr. Brian J. Schmidt is an Executive Director and the head of the Quantitative Systems Pharmacology & Physiologically Based Pharmacokinetics department at Bristol Myers Squibb. Brian earned his PhD in Biomedical Engineering at the University of Virginia. He received postdoctoral training in systems biology and computational biology at the University of Virginia; University of California, San Diego; and Sanford-Burnham Medical Research Institute. He also previously performed research as a dynamics engineer in QSP at Entelos. Brian joined BMS in 2014. He has made a number of contributions to the field of mechanistic modeling, including development of models, development of new algorithms for calibrating mechanistic models to data, software tools, application of modeling to improve decision making at various stages throughout discovery and clinical development, and the application of models for regulatory interactions. E-mail: brian.schmidt@bms.com

Raj Madabushi, PhD
Associate Director, Guidance and Scientific Policy
OCP | OTS | CDER | FDA

Dr. Rajanikanth (Raj) Madabushi has over 15 years of regulatory experience. As a Pharmacometrics Reviewer and Clinical Pharmacology Team Lead, Dr. Madabushi has played a key role in the advancement and application of quantitative clinical pharmacology approaches for regulatory decision making and addressing various drug development issues. He currently serves as the Associate Director, Guidance and Scientific Policy in the Immediate Office of Office of Clinical Pharmacology. Dr. Madabushi is also the CDER Point-of-Contact for the MIDD Paired Meeting Program and the Rapporteur for ICH M12 Expert Working Group – Drug Interaction Studies. Dr. Madabushi received his PhD in Pharmaceutical Sciences from Birla Institute of Technology and Sciences (BITS), Pilani, India.

Tina Hernandez-Boussard, PhD, MPH, MS, FACMI
Associate Dean for Research
Professor of Medicine, of Biomedical Data Science, of Surgery and, by courtesy, Epidemiology and Population Health
Director, Health Informatics, Stanford Center for Clinical and Translational Research, and Education
Stanford School of Medicine

Dr. Tina Hernandez-Boussard is an Associate Dean of Research and Professor at Stanford University in Medicine (Biomedical Informatics), Biomedical Data Sciences, Surgery and Epidemiology & Population Health (by courtesy). Her background and expertise are in the field of biomedical informatics, health services research, and epidemiology. In her current work, Dr. Hernandez-Boussard develops and evaluates AI technology using multimodal data to accurately and efficiently monitor, measure, and predict healthcare outcomes. Her work is used to improve patient outcomes, healthcare delivery, and guide policy.

Hao Zhu, PhD, Mstat
Division Director, Division of Pharmacometrics
OCP | OTS | CDER | FDA

Dr. Hao Zhu is the director of the Division of Pharmacometrics, Office of Clinical Pharmacology, Office of Translational Science, Center of Drug Evaluation and Research, U.S. Food and Drug Administration. Dr. Zhu received his Ph.D. in Pharmaceutical Sciences and Master in Statistics from the University of Florida. He started his career in modeling and simulation teams in Johnson & Johnson and Bristol-Myers-Squibb. He joined FDA as a pharmacometrics reviewer more than 15 years ago. Dr. Zhu has been a clinical pharmacology team leader for more than 6 years and a QT-IRT scientific lead for two years. Then he became the deputy director at the Division of Pharmacometrics. His division reviews the pharmacometrics related submissions and supports pharmacometrics-related policy development.

Christina Friedrich, PhD
Chief Engineer
Rosa & Co.

Dr. Christina Friedrich is the Chief Engineer at Rosa & Co, a drug development advisory firm. Dr. Friedrich has a PhD in Management Science and Engineering from Stanford University and over 20 years of experience in developing and applying quantitative systems pharmacology models to support development of pharmaceuticals and consumer products. Her therapeutic area expertise includes a wide range of metabolic, immunological, and nervous system disorders. She has a long-standing interest in advancing methodologies and applications for the effective use of mechanistic QSP models.

Justin C. Earp, PhD
Lead Pharmacokineticist
DPM | OCP | OTS | CDER | FDA

Dr. Justin Earp is team lead in the Division of Pharmacometrics for anti-viral and anti-infective products. Dr. Earp joined the Division of Pharmacometrics as a reviewer in 2008 and has served as a reviewer on over 150 IND and NDA & BLA reviews. Between 2016 and 2019, he was the scientific lead for biosimilar and biologic products in the division. Over the past 15 years he has also served on a number of working groups including: the ISOP working group for the assessment of PK drug-drug interactions via population PK and the AAPS working group for the assessment of therapeutic protein drug-drug interactions via population PK, as well as the OND/OTS safety analytics control board, and co-chair for the OCP QSP SIG.

Before joining the FDA, Dr. Justin Earp received his Bachelor's of Science in Biochemistry with a minor in applied mathematics from the University of Arizona, Tucson in May 2002. In 2008, Dr. Earp received his doctorate in Pharmaceutical Sciences from the State University of New York at Buffalo.

Markus Ries, MD, PhD, MHSc, FCP
Professor, Pediatric Neurology and Metabolic Medicine, Center for Rare Diseases, Center for Pediatric and Adolescent Medicine
Heidelberg University Hospital

Dr. Markus Ries is a Professor, board certified Physician-Scientist, and research group leader at the Center for Pediatric and Adolescent Medicine, Pediatric Neurology and Metabolic Medicine, Heidelberg University Hospital, Heidelberg, Germany (www.linkedin.com/in/markusries/). He had an active role in five successful drug registration programs and has drug development experience with biologics and small molecules, both early and late stage development. Dr. Ries has clinical, academic and biopharmaceutical industry expertise in neurosciences/neurometabolics and complex multisystemic health conditions. He is multilingual (German, English, French, and Spanish) with broad professional international experience (US, EU, UK, Latin America, Japan). Dr. Ries has an MD from the University of Mainz, Germany, a PhD (biochemistry) from the University of Bonn, Germany, and a Master of Health Sciences in Clinical Research from Duke University, Durham, NC. He received postgraduate clinical and research training at the University Hospitals of Mainz and Heidelberg, both in Germany, and the National Institutes of Health, Bethesda, MD. Dr. Ries has authored 100 papers and his current h-index is 36 (https://katalog.ub.uni-heidelberg.de/cgi-bin/heibibprofil.cgi?gnd=136385338&sprache=ENG). He is an editor in the Journal of Inherited Metabolic Disease and PLOS ONE as well as a Fellow of the American College of Clinical Pharmacology. Dr. Ries and his family have lived in the US and EU. His clinical interest is developmental neurology. Being an expert in community resilience in catastrophes and crises, Dr. Ries served as a Lieutenant Colonel in the Medical Corps of the Federal Armed Forces of Germany during the COVID-19 pandemic disaster response.

Audra Stinchcomb, PhD
Professor, Pharmaceutical Sciences
University of Maryland School of Pharmacy

Dr. Audra Stinchcomb is Professor of Pharmaceutical Sciences at the University of Maryland School of Pharmacy. She is also currently the chief scientific officer and co-founder of F6 Pharma Inc., a palliative care product company. She received her Bachelor's in Pharmacy from the University of Colorado, and a PhD in Pharmaceutics from the University of Michigan. She completed a postdoctoral fellowship at UCSF. She was a professor at the University of Kentucky from 2001-11, and joined the faculty at the School of Pharmacy in November 2011. She is a Fellow of the American Association of Pharmaceutical Scientists. Dr. Stinchcomb's research interests span across many disciplines, including pharmaceutics, drug delivery, medicinal chemistry, neuroscience, dermatology, bioengineering, regulatory science, and translational research models.

James Polli, PhD
Professor and Ralph F. Shangraw/Noxell Endowed Chair in Industrial Pharmacy and Pharmaceutics
University of Maryland School of Pharmacy

Dr. James Polli is Professor of Pharmaceutical Sciences and Ralph F. Shangraw/Noxell Endowed Professor in Industrial Pharmacy and Pharmaceutics at University of Maryland. His research interest is oral drug absorption. His two main research interests are 1) maximizing oral bioavailability through formulation and chemical approaches and 2) developing public quality standards for oral dosage forms. He has served as advisor to 24 PhD graduates. He is co-Director of the University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI; www.cersi.umd.edu) and the Center for Research on Complex Generics (CRCG; www.complexgenerics.org), each an FDA-funded collaborative agreement with the Agency. He is Director of the online M.S. in Regulatory Science program (www.pharmacy.umaryland.edu/regulatoryscience).

He is a fellow of the American Association for Pharmaceutical Scientists and until recently served as an editor of its flagship journal Pharmaceutical Research for 12 years. He is a member of the University of Maryland General Clinical Research Center Advisory Committee and the University of Maryland institutional review board (IRB). He is a member of the Scientific Advisory Board of Simulations Plus.