

# ISSX Modeling and Simulation Focus Group Newsletter

## FEBRUARY 2022

*The ISSX Modeling and Simulation Focus Group (M&SFG) is chaired by Manthena Varma (Pfizer) and Yuan Chen (Genentech). The goals of this group are to disseminate and promote state-of-the-art research and foster discussion and collaboration among ISSX members on the role of modeling and simulation in drug design, drug development and beyond. In addition to providing a discussion forum, this group will also aim to generate and publish position papers on new vistas in mechanistic PBPK and PK/PD modeling science in relation to drug discovery/development. The focus group will engage members throughout the year via webinars, workshops, and by contributing to ISSX meeting planning.*

**International Society for the Study of Xenobiotics (ISSX)**

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[www.issx.org/page/fg2](http://www.issx.org/page/fg2)  
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## A Note from Ping Zhao

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### ISSX M&SFG 2021 Activities and a Look to 2022

Several months before his sad passing, our founding chair, Professor Hartmut Derendorf advised me to build a strong steering committee (SC) for this ISSX Focus Group with the goal to formalize the M&SFG and step up the group activities. In December, 2020, the SC consisted of members with diverse experience kicked off its first meeting. It has been a great pleasure working with these fellow members to accomplish multiple tasks smoothly and successfully over the past two years.

Organizationally, we decided to have two co-chairs for the SC. Each co-chair has a 2-year term with 1-year overlapping with another co-chair. Dr. Manthena Varma from Pfizer graciously agreed to serve as co-chair for 2021 and 2022. Dr. Nita Patel from Lilly is leading the effort of drafting the M&SFG's charter towards further formalization of the focus group.

Since its inception almost 12 months ago, the M&SFG's SC has successfully executed multiple events. The group's first webinar in 2021 was [dedicated to Professor Derendorf](#) and moderated by Dr. Patel. Professor Derendorf's former PhD student, Dr. Amparo de la Peña (Lilly) highlighted major scientific contributions of Professor Derendorf and reflected on his dedication and commitment to students, post-docs, and alumni. The second webinar [Pharmacokinetics in Renal Impairment: Current State of PBPK Modeling and Regulatory Recommendations](#) offered industry's experience presented by Dr. Yuan Chen (Genentech) and regulatory perspective by Dr. Raj Madabushi (US FDA) on the state of PBPK to predict the effect of renal impairment on a drug's PK. The presentations and a panel discussion were moderated by Dr. Manthena Varma (Pfizer). The panel discussion included additional panelists, Dr. Steven Hall (Lilly), Tycho Heimbech (Merck) and Xinyuan Zhang (US FDA) and garnered input in moving this area from the exploratory to regular implementation. The third event was integrated within the 24th North American ISSX Virtual Meeting. Dr. Manthena Varma (Pfizer) and I moderated a Short Course, Enabling Efficient Drug Discovery and Development via Physiologically-based Pharmacokinetic (PBPK) Modeling, featuring lectures by Professor Amin Rostami (Manchester), Dr. Ernesto Callegari (Pfizer), Professor Yuichi Sugiyama (RIKEN), and Dr. Maria Posada (Lilly). The lectures not only gave attendees an overview of the progress being made in PBPK research but also offered practical drug development case studies. In the 2022 International ISSX and MDO Meeting, the PBPK Short Course has been selected by the organizing committee, and the SC will manage the event by introducing new topics and moderating the discussions.

In 2021, the COVID pandemic made it challenging to hold in-person networking activities. Traditionally, the M&SFG would organize informal events at the meeting among members. However, the pandemic does not prevent us from interacting and networking using online meetings. Moving into 2022, we will consider organizing virtual meet-and-greet with members.

We have lined up a series of exciting events for 2022. The first event in 2022 is an ISSX [Webinar on Quantitative Systems Pharmacology \(QSP\) models](#) moderated by Dr. Venkatesh Pilla Reddy (AstraZeneca). This event features speakers from platform developer, regulatory agency as well as industry on the experience of using QSP models in vaccine development and registration, a topic of great interest under the COVID pandemic. The SC has been busy organizing an online summer workshop on PBPK (June 7-9). This is another great learning opportunity for us to inform the Society and beyond on the state of the science, applications, and knowledge gaps of PBPK. Additionally, under Dr. Venkatesh Pilla Reddy's (AstraZeneca) leadership, the M&SFG and ISSX will join force with American Society of Clinical Pharmacology and Therapeutics (ASCPT) to co-sponsor a workshop on [DDI Risk Assessment - Approaching Global Convergence and Understanding Emerging Innovation](#). Further details can be found in the Upcoming Events section below.

By writing this letter, I announce my stepping-down as a co-chair and meanwhile, with my great pleasure, that Dr. Yuan Chen (Genentech) as the co-chair for 2022-2023. I continue to cherish the early days working with Professor Derendorf to further enhance the visibility of M&S science within the Society. In the past 12 months, I feel extremely fortunate to work with Dr. Varma and all SC members.

It was the SC team that made our accomplishments in 2021 possible. We recently welcomed Dr. Maria Posada from Lilly as our next SC member. In 2022, we will extend SC member invitations to academic and non-profit organizations.

I look forward to working with fellow SC members and Drs. Chen and Varma to make 2022 another successful year for M&SFG and the Society!

Ping

(ISSX M&S FG Co-Chair 2020-2021)

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## Upcoming Webinar

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### A QSP Platform Model for COVID 19 Vaccine Development

**Presenters:** Prof. Piet H. van der Graaf, Dr. Artur Belov, Dr. Osman Yogurtcu, and Dr. Rosalin Arends

**Moderator:** Dr. Venkatesh Pilla Reddy

**February 15, 2022 at 11:00 AM ET USA (16:00 UTC)**

**Registration:** [ISSX Webinar - International Society for the Study of Xenobiotics](#)

**Lectures:**

1. A QSP Platform model for COVID 19 vaccine development: Prof. Piet H. van der Graaf, Certara.
2. CBER's experience with the MIDD Paired Meeting Pilot Program and recent MIDD public workshops: Artur Belov and Osman Yogurtcu, FDA.
3. Industry perspective of using QSP models in Vaccines: Dr. Rosalin Arends, AstraZeneca.

**Abstract:** Quantitative pharmacology approaches can inform clinical development strategies for vaccines similar to how these approaches have been applied for decades for small and large molecules. Therefore, as long as a validated quantitative model is in place, principles of model-informed drug development (MIDD) can be applied to vaccines as well. This would provide enormous value since it would circumvent conducting large and new trials and thus allow predicting efficacy against new variants. It is clear that clinical pharmacology principles are paramount to answer clinical and regulatory questions throughout vaccine development - whether during pandemic outbreaks, exploration of new modalities or adaptive trial designs. By understanding the relationship between biomarkers (e.g., antibody titers) and efficacy in preclinical species, how this translates to the clinic, to inform humoral and cell responses needed for protection will allow for adequate understanding of clinical effects in special populations, posology for new variants, and the potential for drug interactions. Together, these data-driven approaches should be embraced to accelerate the delivery of safe and efficacious vaccines to patients globally.

## ISSX Virtual Summer Workshop

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### Physiologically-based Pharmacokinetic (PBPK) Modeling

June 7-9, 2022 at 10:00 AM ET USA (14:00 UTC)

Registration: [Now Open](#)

#### Sessions:

1. Mechanistic Modeling of PK in Special Population
2. Current State of Biomarker-informed PBPK Modeling to Predict DDIs
3. Successful Drug Development Stories and Learnings

This virtual workshop will be focused on the advancements in the application of PBPK as a mechanistic tool in the discovery and development setting. The workshop has been structured into three sessions with emphasis on emerging trends such as special population, biomarker-informed DDI modeling, and diverse drug development applications. Each session will include lectures and short presentations, the latter will be selected from the pool of abstracts from the students and industry attendees. Additionally, virtual posters are planned, which will provide a platform for students and scholars to interact and discuss ideas and career opportunities.

Additional information will be announced in February 2022.

## PBPK Short Course

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**2022 ISSX/MDO International Meeting**

**September 11-14, 2022**

**The Westin Seattle, Seattle, Washington, USA**

**Registration: Coming Soon!**

**Short Course: Advances in PBPK Approaches in Driving Drug Development Decisions**

**Co-Chairs: Manthena Varma, Pfizer, and Ping Zhao, Bill and Melinda Gates Foundation**

Tentative Lectures:

1. Absorption Predictions: Current Capabilities and Knowing the Gaps  
*Viera Lukacova, Simulations Plus*
2. Understanding Physiology and Systems Parameters in Special Population Models  
*Peter Kilford, Certara*
3. Leveraging Biomarkers in Modeling Transporter-mediated DDIs:  
*Manthena Varma, Pfizer*
4. Biologics  
*Speaker to be announced*

Additional information will be announced soon.

## ISSX M&SFG Steering Committee Members



*Dr. Manthana Varma (Co-Chair)*

**Dr. Manthana Varma** is Research Fellow, at Pfizer Inc. Dr. Varma received his B. Pharm. degree from the Kakatiya University, India in 2000, and an M.S. degree (2001) and PhD in Pharmaceutics (2005), from the National Institute of Pharmaceutical Education and research (NIPER), Punjab, India. Later, Dr. Varma worked as a Post Doctoral Fellow at the Department of Pharmaceutics, University of Minnesota (Minneapolis). In 2008, he joined Worldwide R&D, Pfizer, Groton, CT. Dr. Varma holds an Adjunct faculty position in the Department of Pharmacy of the University of Rhode Island. Manthana is a founding member and Instructor for a three-day Annual workshop on “Transporters in Drug Discovery and Development: Driving Knowledge from Laboratory to Label” at University of Rhode Island. His research is focused in the fields of ADME/PK technologies and strategies in drug design and development, role of drug transporters and transporter-enzyme interplay (extended clearance) in ADME/PK, clinical pharmacokinetics and DDI predictions/evaluation via mechanistic (PBPK) modeling. He published about 130 original articles/reviews/book chapters and presented over 75 presentations at the scientific conferences in these scientific areas.



*Dr. Yuan Chen*

**Dr. Yuan Chen** is a Senior Fellow in the Department of Drug Metabolism and Pharmacokinetics at Genentech. Dr. Chen has 20 years of pharmaceutical industry experience in the drug metabolism and pharmacokinetic discipline working at Genentech and Roche. She has been DMPK project lead for many discovery and development projects in broad therapeutic areas, and contributed to the clinical candidate nomination and filing of IND, NDA and BLA to the regulatory authorities. Dr. Chen’s current research focus is on physiologically-based pharmacokinetic (PBPK) modeling for the prediction of human PK, absorption, and CYP-and transporter-mediated drug-drug interactions. She leads PBPK effort and oversight the PBPK strategy and support to discovery and development projects at Genentech, including interactions with HA on MIDD and PBPK in drug labeling. In addition, Yuan has been active member on IQ PBPK expert working groups and contributed to several PBPK white papers.



*Dr. Oliver Hatley*

**Dr. Oliver Hatley** is a Principal Scientist who has been working at Certara UK Limited's Simcyp Division since 2013. He received his MSc in Drug Discovery Skills at the Kings College London in 2009. He went on to study Intestinal Metabolism with the University of Manchester (CAPKR) and AstraZeneca, focusing on in vitro to in vivo scaling factors, receiving his PhD in 2014. Oliver is part of the translational sciences in DMPK group within the Simcyp Division, and has lead development of the esterase organ and blood in vitro-in vivo scaling strategies. He currently leads the development of special adult populations within the Simcyp Population-based Simulator.



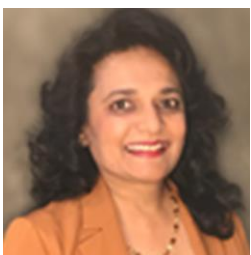
*Dr. Peter Kilford*

**Dr. Peter Kilford** is a Principal Scientist at Certara UK Limited (Simcyp Division). He received his PhD in the in vitro assessment and prediction of drug glucuronidation clearance from the University of Manchester. Following this Peter spent 10 years working at Covance Laboratories with roles in DMPK and later as a scientific lead in the development of IND and CTA enabling packages of work. During this time Peter was an active member of the DMDG Executive committee serving in the roles of Chairman, Treasurer and Secretary during his tenure on the committee. Since joining Simcyp in 2019, Peter has been working on projects to update the Simcyp compound library files and is currently leading the V20 project to develop new compound models.



*Dr. Yurong Lai*

**Dr. Yurong Lai** is a Sr. Director of Drug Metabolism at Gilead Sciences. He is a fellow of American Association of Pharmaceutical Scientists and Adjunct Faculty in the Department of Pharmacy of the University of Rhode Island. His current role in Gilead is to manage DMPK-drug disposition group and implement in vitro/in vivo preclinical and clinical strategies for compound advancement to regulatory filing. He received his M.D from Fujian Medical University in China and his Ph.D. (Toxicology) from Sapporo Medical University in Japan in 1998. Prior to joining Gilead Dr. Lai led research programs at Pfizer and BMS in transporter research and ADME-PK-Tox. He is the associate editor/editorial board member of top ranking DMPK journals including DMD, BDD, JPS and Frontier Pharmacology etc. He is a patent inventor and the author of a book, book chapters and over 160 original publications.



*Dr. Nita Patel*

**Dr. Nita Patel** is a Senior Research Advisor and Scientific Leader in the Drug Disposition group at Eli Lilly and Company and holds an Adjunct Professorship at UNC, Chapel Hill. She obtained her doctorate at the University of California, Los Angeles in 1990 in Pharmacology and completed her post-doctoral training in Pharmacology and Toxicology at the University of Rochester and Institut für Toxicologie, Universität Würzburg. She then joined the DMPK group at Pfizer Central Research, Groton CT. She returned to academia as a Research Assistant Professor to work on transporters at UNC, School of Pharmacy, Chapel Hill. In 2000, she decided to join Lilly Research Laboratories where she has supported and participated in many discovery and development projects over the past 20 years. Dr. Nita Patel is a twice recipient

of the LRL Presidents Recognition Award and has made several contributions to the discovery of clinical candidates in discovery and early development. Her interests have ranged from establishing and optimizing various experimental models to support PBPK predictions. She is actively involved in applying human PK predictions, including both translating in vitro systems to in vivo and applying understanding of clearance pathways to human PK projections in her teams. She has published and presented her work in about 60 original articles/reviews/book chapters and conferences to date.



*Dr. Venkatesh  
Pilla Reddy*

**Dr. Venkatesh Pilla Reddy** is a Director, Clinical Pharmacology and Quantitative Pharmacology function of AstraZeneca, Cambridge UK. He obtained his PhD in Pharmacometrics through a unique industry collaboration program between Pfizer, Janssen Pharmaceuticals and Merck via TI Pharma in the Netherlands. His PhD work was focused on PKPD M&S of antipsychotic drugs. He subsequently worked at Quantitative Pharmacology and Pharmacometrics group in Merck & Co before joining AstraZeneca Early Oncology function. Venkatesh provided Model-Informed Drug Development support to various oncology projects. He has been influential in gaining acceptance and addressing questions from regulatory agencies for Olaparib and Osimertinib programs. He has participated on MIDD related panel discussion with the European Medicines Agency and the US Food and Drug Administration (FDA). Venkatesh currently holds the Deputy Topic Leader position at the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Management Committee to work on the ICH M12 DDI guidelines, and co-leads various cross-industry working groups such as IQ TALG, ISOP and ISSX M&S. Over 15 years of his industry carrier, he has published > 40 peer review research articles, 2 book chapters. He presented >15 invited oral presentations at international quantitative clinical pharmacology, QSP and PKPD/PBPK events, and supervised a post-doc and 4 graduate students.



*Dr. Maria M.  
Posada*

**Dr. Maria M. Posada** is a Principal Research Scientist in the ADME group at Eli Lilly and Company. She received her bachelors in Pharmaceutical Chemistry from the National University of Colombia in 2004 and her Ph.D. in Pharmaceutical Sciences from the University of Michigan, Ann Arbor in 2012. Dr Posada worked as a Post-Doctoral Scientist at Eli Lilly and Company from 2012- 2014. In 2014, she joined the ADME group as a full-time employee working as a project leader and developing mechanistic pharmacokinetic (PBPK) models to support many projects in the portfolio, from discovery through regulatory submission. Since 2019, she has been leading the mechanistic pharmacokinetics group. Maria has co-led and implemented several strategies that have encouraged and extended the use of modeling and simulation to speed drug discovery and development and aid decision making. Maria is an advocate for diversity, equity, and inclusion and is passionate about mentoring.



*Dr. Jaydeep  
Yadav*

**Dr. Jaydeep Yadav** is a Senior Scientist at Merck Research Laboratories (MRL), Boston. Dr. Yadav received his B. Pharm. degree from the College of Pharmacy, Nashik, India in 2011, and an M.S. degree in Pharmacology and Toxicology from the National Institute of Pharmaceutical Education and research (NIPER), Punjab, India in 2013. Dr. Yadav obtained his Ph.D. from Temple University, Philadelphia in 2018. His Ph.D. work was focused on improving time dependent inhibition mediated drug-drug interaction predictions using numerical method. He joined the PKDM group at Amgen Inc, Boston in 2018 where he worked in developing in-vitro mathematical models to support drug discovery programs. Later, Dr. Yadav joined MRL, Boston in August 2020. He is a part of the PPDM ADME group at MRL. He is actively involved in applying translation mathematical models to improve IVIVE, improve drug-drug interaction predictions and understanding enzyme transporter interplay.



*Dr. Ping Zhao*

**Dr. Ping Zhao (M&SFG Chair 2020-2021)** obtained his BS in Pharmacy from Beijing Medical University in China in 1994, and his PhD in Pharmaceutics from University of Washington in Seattle, WA, USA in 2002. Since then, Ping worked as a DMPK scientist at Pfizer in La Jolla CA (2002-2005), a pharmacokineticist at Sonus Pharmaceuticals in Seattle (2005-2007), a clinical pharmacologist at Amgen in Seattle (2008), and the Scientific Lead of PBPK (physiologically-based pharmacokinetic modeling) Program and Expert Pharmacologist at the Office of Clinical Pharmacology, US FDA in Silver Spring, MD (2008-2017). At FDA, Ping led review of PBPK submissions in IND/NDA/BLAs, research in PBPK, and development of policy on PBPK, including authoring the agency's first draft PBPK guidance (2016) and updated in vitro and in vivo drug-drug interaction guidances (2017). He was responsible for the review of more than 200 PBPK analyses in IND, NDA, and BLA submissions. More than 40 of these submissions had simulation results being used in product labels to support optimal use of the drugs. In June 2017, Ping joined the Bill and Melinda Gates Foundation in Seattle, WA as a Senior Program Officer of Quantitative Sciences, where he applies pharmacology concepts and manages Model-informed Drug development (MiDD) efforts in programs funded by the foundation to academic centers, product development partners, and regulatory agencies around the world. He received many awards, published 79 articles in peer reviewed journals, and coauthored book chapters in 6 clinical pharmacology books. He is currently adjunct faculty of University of Florida and University of Washington, and an associate editor for the journal Clinical Pharmacology and Therapeutics-Pharmacometrics and Systems Pharmacology.

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## Update on ISSX M&SFG Activities

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*The ISSX M&SFG will engage ISSX members throughout the year via webinars and meeting planning.*

### **The members of ISSX M&SFG**

As of now, we have 732 members in the ISSX M&SFG. We would like to extend our warmest welcome to all existing and new members! We appreciate your support and hope you enjoy the programming, discussion, and networking opportunities! Please sign up on the ISSX Website if you are interested in joining the focus group. We look forward to hearing from you on proposals & ideas for the M&SFG to focus on (e.g., meetings/webinars & potential publication topics for the group to consider). To join, please visit

<https://www.issx.org/page/FG2>.

We will continue to organize FG events at annual meetings, offer regular webinars, and seek opportunities to network with other societies such as ISOP, ASCPT, and ACCP. Please plan to attend the webinar in February 2022, the joint DDI satellite session at ASCPT in April, the June virtual workshop, and the September in-person short course at the ISSX/MDO Meeting in Seattle.

### **ISSX M&SFG LinkedIn Group**

We have established a LinkedIn page for this group and started inviting members. This space was created to allow for discussions between members on scientific discussions, dissemination of recent publications of interest to the group, communications of related seminars and job opportunities, and connection with other members within our scientific community. We invite you to join the group. To do so, look us up as “ISSX Modeling & Simulation Focus Group” on [LinkedIn](#)! If you would like to start a discussion on a topic on the LinkedIn page, join “ISSX Modeling & Simulation Focus Group” on [LinkedIn](#). If you have a paper summary to submit for the next M&SFG newsletter, please submit your ideas through our community on LinkedIn.

### **Engagement and Programming**

The ISSX M&SFG is working to increase programming and engagement opportunities, including webinars and discussion content for the LinkedIn group. If you have a proposal for a seminar or a discussion topic, please reach out by sending a message through [LinkedIn](#) or by email to [information@issx.org](mailto:information@issx.org).