ISSX Modeling and Simulation Focus Group Newsletter

JANUARY 2021

The ISSX Modeling and Simulation Focus Group (M&SFG) is chaired by Ping Zhao, Bill and Melinda Gates Foundation. 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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Professor Hartmut Derendorf

The ISSX M&SFG is a story of Professor Hartmut Derendorf.

A longtime advocate of applying quantitative methods to address pharmacological questions in drug development, regulation and clinical practice, Professor Derendorf became the founding chair of ISSX's M&SFG in 2017. With his vision to disseminate quantitative pharmacology concepts within the society of drug metabolism and transport, the M&SFG attracted many participants during pilot sessions at 2018 and 2019 annual meetings and ISSX webinar on biomarkers.

Professor Derendorf (1953-2020) had served as department chair of Pharmaceutics at University of Florida for many years, before retiring as a distinguished emeritus professor of pharmaceutics at the same university a few years ago. During his tenure, he mentored numerous graduate students, post doctorial fellows, and junior faculties both nationally and internationally, many of whom hold leading roles in various organizations in academic institutes, regulatory agencies and pharmaceutical industries around the world. Prof. Derendorf has published over 500 scientific publications with an h-index (Scopus) of 60 and given over 900 presentations at national or international meetings. He has published ten textbooks in English and German. He held leadership positions of scientific societies, and received numerous prestigious awards in the fields of clinical pharmacology, modeling and simulations, clinical pharmacy, and pharmacy education. In 2010, he was awarded the Volwiler Research Achievement Award from the American Association of Colleges of Pharmacy as well as the American College of Clinical Pharmacology, or ACCP, Distinguished Investigator Award — the highest research awards presented by both organizations. He was a fellow of ACCP and the American Association of Pharmaceutical Sciences and a former review panel member of the NASA Human Research Program.

He is considered one of the "fathers" of modern pharmacokinetics and pharmacometrics. The sudden passing of Professor Derendorf in November 2020 was a huge loss for our community.

In 2020, a few months before his passing, Professor Derendorf worked closely with the leadership of ISSX to formalize M&SFG. This included the establishment of a steering committee, organization of webinars, planning M&SFG sessions at the North American ISSX Meeting, and publishing M&SFG newsletters.

The members of the newly-established steering committee dedicate the inauguration newsletter in memory of Professor Derendorf. A webinar "Hartmut Derendorf: The Scientist, The Professor, The Human" is scheduled as we pay homage to Prof. Derendorf's many

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accomplishments on Tuesday, February 16, 2021. Please find details about the webinar on the next page of this newsletter.

Upcoming Webinar

Hartmut Derendorf: The Scientist, The Professor, The Human
Presenter: Dr. Amparo de la Peña, Eli Lilly and Company
Moderator: Dr. Nita Patel, Eli Lilly and Company
Time: February 16, 2021 at 11:00 am ET USA
Registration: https://www.issx.org/page/ISSXWebinar02162021

This Webinar is intended to salute Dr. Hartmut Derendorf for his immense contributions in the field of modeling and simulation through education and mentorship of his students and post-docs. This webinar will serve as a kick-off to future M&SFG-led ISSX webinars to follow.

Dr. Derendorf was a long-time advocator of using quantitative methods to address pharmacological questions in drug development, regulatory science, and clinical practice. While the original planned webinar was to be presented by Dr. Derendorf himself, his sudden demise leaves us with much sadness and we would like to commemorate his work by highlighting his deep commitment to educating and mentoring future scientists, many of whom hold leading positions in academia, regulatory agencies and pharmaceutical industries around the world. Dr. Amparo de la Peña, currently a leading scientist at Eli Lilly and Company, will provide the ISSX community with her personal and professional experiences not only while training on her doctoral work with Dr. Derendorf, but also thereafter. Dr. de la Peña will refer to selected highlights of Dr. Derendorf contributions to the scientific community. She will also highlight Dr. Derendorf's dedication and level of commitment to students, post-docs, and alumni who to this day benefit greatly in their careers as they continue to provide scientific contributions this field in academia and industry.

About the Speaker: Amparo de la Peña is an Asset Manager and Sr. Research Advisor for PK/PD at Chorus, Eli Lilly and Company. A native of Montevideo, Uruguay, she has degrees in Chemistry and Pharmacy from the University of the Republic, Uruguay. Amparo then earned a Ph.D. (2000) from the University of Florida, with Dr. Hartmut Derendorf as her advisor. She moved to Indianapolis after graduation, when she was hired as a PK/PD scientist by Eli Lilly and Company. Through her career, Amparo has provided her expertise to projects spanning several therapeutic areas, such as Anti-infectives, Neurosciences and Diabetes. In the Diabetes area, she led the PK/PD teams for the approval of Dulaglutide and Humalog U200 in several geographies. At Chorus, she manages assets from Lilly and partner companies, in diverse therapeutic areas. Amparo divides her time between work, her family and her involvement in scientific and community organizations, either as volunteer (AAPS/ACCP/ISSX), peer reviewer (several scientific journals), or Board member (Organization of Latinos at Lilly, Indianapolis Public Library Foundation).

ISSX M&SFG Steering Committee Members

Dr. Ping Zhao
ISSX M&SFG
Chair

Dr. Ping Zhao (Chair) 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.

Dr. Yuan Chen

Dr. Yuan Chen is a Principal Scientist 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.

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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 committe. 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 Institüt 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

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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 an Associate 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. Manthena Varma

Dr. Manthena 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. Manthena 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. He is member and ex-chair (2017-18) of North Jersey Drug Metabolism Discussion Group. 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

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published about 120 original articles/reviews/book chapters and presented over 75 presentations at the scientific conferences in these scientific areas.

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.

Update on ISSX M&SFG Activities

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 535 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 towards 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 a webinar in February 2021 in memory of Professor Derendorf.

ISSX M&SFG LinkedIn Group

We have established a LinkedIn page for this group and started inviting members. We have 130 members to ISSX M&SFG LinkedIn page. 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!

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.

Call for Ideas

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.