ISSX International Society for the Study of Xenobiotics

Volume 44 Issue 3, 2020

ISSX President's Message

By Ann Daly,
ISSX President

Welcome to the President's Message in this final issue of our Newsletter for 2020. As I discussed in my message in our previous issue, the COVID-19 pandemic has greatly impacted our normal program of activities for 2020 and early 2021. However, with the recent exciting results from vaccine trials run by BioNTech/Pfizer, Moderna, and AstraZeneca/Oxford with further announcements likely soon from other providers and good progress too on regulatory approvals, I think it's reasonable to end the year on a cautiously optimistic note.

We are currently doing a lot more virtual activities than in previous years. I hope many of you have already joined our webinars which, up to now, have been extremely varied and importantly have attracted large audiences. There is already a great webinar program lined up for early 2021. Details are available elsewhere in this Newsletter. I'm looking forward particularly to our Virtual Workshop: Translation of *in vitro* ADMET Science to *in vivo*: Current Perspectives and Challenges, scheduled for March 2–5 which is a joint event with the IQ Consortium with co-chairs Lei Zhang (FDA) and Christopher Gibson (Merck). I'm confident that it will be a great opportunity to listen to a range of wide-ranging presentations from academic, industrial, and regulatory speakers as well as offering panel discussions, poster sessions, and networking.

The 24th North American meeting is planned for Boston, Mass. September 12–15. The MOC for that meeting, led by Raymond Evers (J&J) and Joseph Balthazar (Buffalo), have now completed the program with registration due to open in early 2021. While we hope this will run as an in-person meeting, we will continue to explore virtual options if needed.

Ann Daly
ISSX President

I would like to acknowledge the efforts of all those who have generously given of their time and effort this past year to further the goals and activities of ISSX. The members of Council, regular committee members and their chairs, meeting organizing committees and their chairs, and leaders of the ISSX Focus Groups as well as the New Investigators Group have ensured that ISSX remained in communication with and in service to our members throughout the year. I would also like to thank our staff in the Washington DC office for all their efforts during this difficult year. In addition to all their other work including the expansion of our virtual activities, they have redesigned our website,

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Book Review

NANOTECHNOLOGY FOR ORAL DRUG DELIVERY
From Concept to Applications
Editors; J. Martins, H. Santos
Academic Press – Elsevier
534pp. ISBN: 978-0-128-18038-9 (2020).

As suspected, oral delivery is the most widely exploited and convenient route for the administration of therapeutic agents. For the treatment of gastrointestinal problems poor bioavailability may be beneficial but if the drug is to enter the systemic circulation and travel around the body a high bioavailability is desirable. This book considers the application of nanotechnology in assisting with this quest.

Forty-four authors from fourteen different countries have come together to write a comprehensive tome. The sixteen chapters presented are collected into four sections. The first entitled, "Biological aspects and properties of nanomaterials for oral drug delivery," details the composition of the intestinal mucosa and the barriers it presents for oral delivery including trans-buccal absorption. Nanomaterials, three-dimensional shape, and surface charge considerations are discussed together with the application of mucus-penetrating polymers and appraisal of current delivery platforms including modified drug release strategies. The second section, "Advanced technologies for oral delivery applications," mentions microdevices for oral delivery, synthesis methods for enteric drug carriers, spray drying in formulation processes and the exploitation of 3D-printing. This is followed by "Methods for evaluation of oral drug delivery systems," addressing ways of assessing suitability of nanoparticles and testing for their in vivo delivery after administration and the use of model systems to assist in designing delivery procedures. The final section, "Pharmaceutical industry perspective," is conclusory and contains one chapter discussing this aspect.

The volume includes many noteworthy details that readers will find interesting and useful. Once viewed as almost an accessory, the buccal route is becoming more popular and its usage is increasing to avoid the annoying "first pass metabolism" that may occur when a drug is swallowed. Improving the interaction of drug particles with mucins prolongs the length of time they stay within the oral cavity and enhances penetration to attain direct contact with the epithelial cell layer, thereby boosting the overall quantity absorbed at this site (Chapter 8). Standard laboratory testing using the common 2D-monocultures can be improved upon by employing 3D-structures such as scaffolds, hydrogels and "intestine-on-a-chip" technologies to give a closer approximation of the living situation. The mechanisms for exploiting these advances and the decrease in necessity for whole body studies are discussed (Chapter 13). One is informed also that the first delayed release products were invented in the 1880s (Chapter 6), that being long before Lipowski (1938) and his sustained release coated pellets.

As mentioned in the accompanying literature, the targeted readership is, "pharmaceutical scientists, researchers and advanced students in drug delivery, biomaterials and nanotechnology." Students studying in a variety of applied biochemical, pharmacological, pharmaceutical, and medically oriented courses may be interested also, as well as teachers, academics, and industrialist. In fact, the readership may be quite wide. A copy or two as a reference text would not go amiss.

Notified by

Steve Mitchell
Imperial College London, UK

Book Ordering Information

Elsevier Inc. (S&T Books and Cell Press)
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Cambridge, MA 02139, US

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ISSX Names Recipients of Prestigious Awards

Dr. K. Sandy Pang, Professor, Leslie Dan Faculty of Pharmacy at the University of Toronto is the 2020 recipient of the ISSX North American Scientific Achievement Award in Honor of Ron Estabrook.

Dr. Pang is an academic researcher with broad-reaching impact on both theoretical and experimental research, as well as mentoring scientists in her laboratory and in the field. It is clear that Dr. Pang has made transformational contributions to the understanding of drug absorption, metabolism, and elimination and significantly advanced the field of physiologically based pharmacokinetic (PBPK) modeling. These advances are evident in the summary below, the accompanying CV with bibliography of her highly cited publications, and the impact of her work as evidenced by the accompanying letters as well as the vast number of citations of her work across Pharmacokinetics textbooks and research articles.

Her seminal contributions to pharmacokinetics include the following:

Clearance Concepts: Dr. Pang has published on the fundamentals of drug clearance, a parameter critical to understanding drug disposition. Importantly, this work with Dr. Malcolm Rowland was seminal in establishing utility of the well-stirred model of the liver for predicting the hepatic clearance of drugs. Her experimental work in liver enzyme zonation and flow heterogeneity in this area have led to the development of other liver models. Much of the experimental and theoretical considerations have laid the foundations to Dr. Pang's early discoveries and research on liver drug clearance.

Metabolite Pharmacokinetics: Dr. Pang has led the field in understanding and modeling the disposition of circulating drug metabolites and metabolite elimination. Her group has developed methods and models to correctly quantitate the complexities within this important pharmaceutical science area. She has published extensively in this area and her research includes study on the formation of metabolite within an organ, its sequential metabolism, and modeling elimination of all drug-related metabolites along with parent drug; different fates of formed vs. preformed metabolites due to enzyme zonation or permeability barriers; futile cycling kinetics; and transporter-enzyme interplay.

Intestinal Drug Absorption and Metabolism: In addition to the transformational advances in improving our understanding of drug elimination in liver, Dr. Pang has contributed significantly to the area of drug absorption and intestinal metabolism. Dr. Pang modeled the intestine as a tissue receiving segregated blood flows to the enterocyte and serosal regions, namely the segregated flow model, SFM. This model has set the foundation for several key modeling frameworks widely used by modeling platforms today–specifically, the physiological framework for intestinal absorption and metabolism highlights a greater extent of intestinal removal for drugs given orally versus intravenously.

Critical Issues with Humanized Mouse Liver Models: Dr. Pang has published important work clearly showing that chimeric (humanized) mouse liver models generate toxic liver models due to persistence of murine bile acids, miscommunication between the mouse intestine and humanized liver, and disruptive handling of bile acids. This work has highly significant implications in the development of chimeric animal models to study disposition, and the interpretation of results obtained from such animal models.

Kinetics of 1α,25-Dihydroxyvitamin D3 (Calcitriol): Dr. Pang utilized the PBPK-PD model to describe the kinetics of calcitriol, active vitamin D receptor ligand, by properly including calcitriol-mediated CYP24A1 induction for calcitriol degradation and CYP27B1 inhibition for calcitriol synthesis. Dr. Pang uncovered calcitriol-mediated inhibition of SHP (small heterodimer partner), which increased CYP7A1 towards cholesterol degradation. Dr. Pang predicted the dynamics of calcitriol-mediated induction of CYP7A1 in cholesterol metabolism and lowering, the calcium channel TRPV6 in calcium absorption and P-glycoprotein in brain and kidney efflux.

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ISSX Names Recipients of Prestigious Awards

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In recognition of her outstanding scientific contribution developed over the span of a productive and successful scientific career, including many fundamental concepts and investigative approaches that are now commonly used in contemporary pharmacology research and drug development, ISSX proudly bestows Dr. K. Sandy Pang 2020 North American Scientific Achievement Award in Honor of Ron Estabrook.

Dr. Dhaval K. Shah has been named the winner of the 2020 ISSX New Investigator Award in Honor of James R. Gillette. Dr. Shah is Associate Professor at the Department of Pharmaceutical Sciences, School of Pharmacy and Pharmaceutical Sciences at the University of Buffalo.

Formerly with Pfizer Inc., Dr. Shah started a research program at the University of Buffalo that can transform the discovery, development, and preclinical-to-clinical translation of protein therapeutics. His goal is to develop a unique and impactful research program that can train future scientists in the field of protein engineering, drug development, and pharmacokinetics (PK) and pharmacodynamics (PD). His group has performed several pioneering investigations, including the development of quantitative structure pharmacokinetics relationships (QSPKR) for protein therapeutics, invention of the biodistribution coefficient concept, development of first-ever brain microdialysis system for antibodies, development of a novel microscopic system to study protein therapeutics disposition in mouse eye, development of first de novo 2-pore PBPK model, and development of systems PK-PD models and translational framework for bench-to-bedside translation of antibody-drug conjugates.

He has published 50 research papers and several book chapters. His research work has significantly impacted the development of protein therapeutics and many scientific principles and mathematical models developed by his group are routinely used by pharmaceutical companies for drug development and regulatory submissions. His research work has been highlighted at prestigious venues including The National Academies of Sciences, Engineering, and Medicine. He is deeply dedicated to mentoring the next generation of scientists. To date, Dr. Shah has mentored more than 75 individuals.

With the advancing field of protein therapeutics Dr. Shah's fundamental work on establishing the platform PBPK model for biologics and quantitative structure-PK relationship (QSPKR) for biologics is becoming increasingly significant. The premise for this work relies on the hypothesis that proteins with similar physicochemical properties demonstrate similar systemic and tissue disposition profiles, and the disposition profile of proteins in human can be predicted a priori based upon their PK in animals.

Dr. Shah's research has also contributed towards improving the discovery and development of ADCs, especially their preclinical-to-clinical translation. He has developed the first ever multi-scale systems PK/PD model for ADCs, which is able to integrate bio-measures and chemo-measures from all the stages of drug development to *a priori* predict preclinical and clinical PK of ADCs on cellular and tissue levels, and also predict the clinical responses of ADCs including their progression-free survival (PFS) and objective response rates (ORRs).

Recently, Dr. Shah has also made significant progress in understanding the disposition of protein therapeutics in anatomically peculiar tissues like brain, eye, and solid tumor. His group is the first one to use microdialysis technique to measure the distribution of antibody in different regions of brain. In addition, he has also developed an unprecedented systems PK model to characterize the disposition of protein therapeutics in the brain.

For his outstanding scientific contributions early in his career, ISSX awards the 2020 ISSX New Investigator Award in Honor of James R. Gillette to Dhaval K. Shah.

ISSX congratulates Dr. Edna Choo for being named the recipient of the 2020 North American Distinguished Accomplishments in Drug Discovery and Development Award.

Dr. Choo has a sustained body of scientific work in the ADME characterization, both non-clinical and clinical, across multiple projects and therapeutic areas. She has undertaken a sustained body of scientific work in the ADME characterization, both non-clinical and clinical, across multiple projects and therapeutic areas.

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Dr. Choo earned her PhD in pharmacokinetics from Monash University and completed a post-doctoral Fellowship in Clinical Pharmacology at Vanderbilt University. She joined Genentech after working at Pfizer in Groton, CT as principal scientist supporting multiple projects pre-IND to Phase 2. She joined Genentech in 2005 where, over time, she was appointed Associate Director in 2019. The group led by Dr. Choo (six PhD and five BS/MS) has responsibility for about half of the Genentech small molecule portfolio – both discovery and development.

Dr. Choo was a key contributor to the development of cobimetinib. She was Pharmacology Subteam Leader for this project, which handles all aspects during development related to DMPK, clinical pharmacology and nonclinical safety. As leader of this team, she played a key role in the development of this drug and the subsequent regulatory filings, including the ultimate NDA, and responses to questions from regulatory agencies. On the scientific front, her main contribution has been to integrate data from both preclinical and clinical studies to enhance our understanding of the cobimetinib pharmacokinetics, in particular the contribution of intestinal metabolism. Her data indicate that there is substantial contribution from intestinal metabolism for cobimetinib and this has also implications for drug-drug interactions. She confirmed the human finding with detailed studies with transgenic mice. This work and other cobimetinib related work has been published in several well-known journals including Drug Metabolism and Disposition, Molecular Pharmaceutics and Cancer Chemotherapy Pharmacology.

The second project that benefited in a major way from the contributions of Dr. Choo is venetoclax. In this collaboration with Abbvie, Dr. Choo focused on the absorption issues for venetoclax. Venetoclax is a BCS class IV compound, but absorption is still quite reasonable – both in preclinical species and in humans. Edna showed that this is due to a significant extent of lymphatic absorption, the importance of which has been overlooked for many lipophilic drugs. Edna performed *in vivo* experiments to support this and it was published in Drug Metabolism and Disposition in 2014. Beyond her contributions to many discovery and development projects, Edna has achieved a reputation for sophisticated PK-PD modeling, including modeling of efficacy following combo treatment (e.g., combining a MEK and a PI3K inhibitor).

As a scientist, Dr. Choo maintains an active presence in terms of publications and invited presentations. She is a strong proponent of the application of humanized animal models to address mechanistically DMPK-related questions at all stages of development. Her insight and approach are well described in her publication in Molecular Pharmaceutics (2014). Her work provided a robust characterization of the extent of CNS penetration and the influence of drug transporters (Choo, 2015 Drug Metabolism Disposition). Dr. Choo is a frequent reviewer for ADME related scientific journals including Current Drug Metabolism, AAPS Journal, Journal of Medicinal Chemistry and Xenobiotics.

Dr. Choo is a mentor and role model for multiple junior scientists and interns. She has built a broad and impactful career spanning the entire spectrum of drug discovery and development. She has made significant contributions to marketed products, discovery and development programs, ADME science, and the next generation of DMPK scientists through her work.

ISSX congratulates Dr. Edna Choo on winning the 2020 Distinguished Accomplishments in Drug Discovery and Development Award.

Invitation to Attend

Please join us for an exciting virtual workshop, "Translation of *in vitro* ADMET Science to *in vivo*: Current Perspectives and Challenges," jointly sponsored by **ISSX** and the **International Consortium for Innovation and Quality in Pharmaceutical Development (IQ).**

About the Workshop

This workshop has been organized through the efforts of the **Workshop Organizing Committee** under the leadership of the Workshop Chairs, Christopher Gibson and Lei Zhang.

This workshop will bring together scientists from academia, industry, and regulatory agencies in an interactive format to discuss contemporary topics in applied small molecule enzyme and transporter research. We are planning sessions covering not only laboratory and analytical challenges associated with studying enzymes and transporters *in vitro*, but also challenges and potential solutions/best practices in translation of *in vitro* ADMET data to *in vivo* drug disposition and clinical drug-drug interactions (DDIs).

There will be a mixture of presentations, including overview of the challenges in each research area, rapid-fire talks, followed by roundtable discussion sessions. In addition, interactive virtual poster sessions will be planned throughout the course of the workshop. This format will allow for the exchange of perspectives and ideas across regulatory, academic and industrial spaces to help address ADMET challenges in the discovery and development of tomorrow's medicines.

Workshop Organizers

Workshop Organizing Committee Chairs:

Christopher Gibson, Merck Research Laboratories, West Point, PA, USA and Lei Zhang, Silver Spring, MD, USA

Workshop Organizing Committee Members:

Adrian Fretland, Repare Therapeutics, Cambridge, MA, USA

Aleksandra Galetin, University of Manchester, United Kingdom

Yurong Lai, Gilead Sciences, Foster City, CA, USA

Laurent Salphati, Genentech Inc., South San Francisco, CA, USA

Kimio Tohyama, Takeda Pharmaceuticals, Cambridge, MA, USA

Jashvant Unadkat, University of Washington, Seattle, WA, USA

Call for Abstracts

This workshop will feature daily abstract presentations in virtual poster sessions. Additionally, selected abstract authors will have an opportunity to present in the daily lectures and panel discussions with invited speakers. Student and postdoc abstract authors will have an opportunity to compete for best poster presentations as well.

Don't delay! **Submit an abstract** by Monday, January 18, 2021.

Workshop Registration Fees

	EARLY 12/1/20–2/12/21	REGULAR 2/13/21–3/5/21
ISSX Member	$425	$495
Nonmember	$565	$615
Student/ PostdocMember	$99	$99
Student/Postdoc NonMember	$125	$125

Visit **https://www.issx.org/page/ISSXIQReg** to register to attend.

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ISSX and IQ Consortium Virtual Workshop

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Workshop Program*

Workshop Sessions

The sessions will cover laboratory and analytical challenges associated with studying enzymes and transporters *in vitro*, as well as challenges and potential solutions/best practices in translation of *in vitro* ADMET data to *in vivo* drug disposition and clinical drug-drug interactions (DDIs).

TUESDAY, MARCH 2, 2021
9:45 AM–3:00 PM ET (US)

Session 1: Biological, Experimental and Methodological Challenges Associated with the Study of Drug Metabolizing Enzymes
Chairs: Christopher Gibson, Merck & Co., Inc., West Point, Pennsylvania, USA and Adrian Fretland, Repare Therapeutics, Cambridge, Massachusetts, USA

9:45 am–10:00 am
Welcome with Workshop Chairs Christopher Gibson and Lei Zhang

10:00 am–10:30 am
Methods to Understand the Role of Gut and Liver CYP and UGT in Human PK Variability and DDI
Yingying Guo, Eli Lilly and Company, Indianapolis, Indiana, USA

10:30 am–11:00 am
Can we accurately measure free fraction of highly bound compounds for use in DDI risk assessment in the clinic?: IQ TALG Plasma Protein Binding Working Group
Faraz Kazmi, Janssen Research & Development, Spring House, Pennsylvania, USA

11:00 am–11:15 am
Break

11:15 am–11:25 am
Derivation of unbound Ki for metabolic enzymes: What have we learnt?
Renu Singh, GSK, Phoenixville, Pennsylvania, USA

11:25 am–11:35 am
Microphysiological Model to Investigate Ochratoxin A nephrotoxicity
Edward Kelly, University of Washington, Seattle, Washington, USA

11:35 am–11:45 am
Kinetics and *in vitro* Challenges with AO
Kanika Choughule, Merck & Co., Inc., Boston, Massachusetts, USA

11:45 am–11:55 am
Abstract Presentation
Author to be invited

11:55 am–12:30 pm
Panel Discussion with All Speakers

12:30 pm–1:00 pm
Break

1:00 pm–2:00 pm
Poster Session

2:00 pm–3:00 pm
Networking Hour

WEDNESDAY, MARCH 3, 2021
10:00 AM–3:00 PM ET (US)

Session 2: Biological, Experimental and Methodological Challenges Associated with the Study of Drug Transporters
Chairs: Aleksandra Galetin, University of Manchester, Manchester, England, United Kingdom and Laurent Salphati, Genentech Inc., South San Francisco, California, USA

10:00 am–10:30 am
Critical *in vitro* Factors to Consider when Conducting IVIVE of Transporter-based Drug Disposition
Jashvant Unadkat, University of Washington, Seattle, Washington, USA

10:30 am–10:50 am
Challenges in Translation of *in vitro* Transporter Data to Predict Unbound Tissue Concentrations
Xiaoyan Chu, Merck & Co., Inc., Rahway, New Jersey, USA

10:50 am–11:10 am
Challenges in Pharma Industry using *in vitro* and Preclinical Systems to Predict *in vivo* Clearance of Transporter Substrates
Yurong Lai, Gilead Sciences, Foster City, California, USA

11:10 am–11:25 am
Break

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11:25 am–11:35 am
Direct Transporter-Mediated Intestinal Secretion
Laurent Salphati, Genentech Inc., South San Francisco, California, USA

11:35 am–11:45 am
Abstract Presentation
Author to be invited

11:45 am–11:55 am
Abstract Presentation
Author to be invited

11:55 am–12:05 pm
Abstract Presentation
Author to be invited

12:05 pm–12:30 pm
Panel Discussion with All Speakers

12:30 pm–1:00 pm
Break

1:00 pm–2:00 pm
Poster Session

2:00 pm–3:00 pm
Networking Hour

THURSDAY, MARCH 4, 2021
10:00 AM–3:00 PM ET (US)

Session 3: Using *in vitro* Enzyme and Transporter Data in Translational Models of Human Pharmacokinetics, Dose and DDI
Chairs: Jashvant Unadkat, University of Washington, Seattle, Washington, USA and Kimio Tohyama, Takeda Pharmaceuticals International Co., Cambridge, Massachusetts, USA

10:00 am–10:20 am
Translation of *in vitro* and *in silico* Metabolic Data to Guide Drug Discovery and Development
Marcel Hop, Genentech Inc., South San Francisco, California, USA

10:20 am–10:40 am
PBPK Modelling and Simulation of Transporter-mediated PK and DDIs
Aleksandra Galetin, University of Manchester, Manchester, England, United Kingdom

10:40 am–11:00 am
Successes and Challenges Faced by Industry in IVIVE of Transporter-based Drug Disposition
Manthena Varma, Pfizer, Niantic, Connecticut, USA

11:00 am–11:15 am
Break

11:15 am–11:25 am
Application of PBPK using a Matrix Qualification Approach for Translational Predictions of OAT1/OAT3 Inhibition in the Clinic by Cabotegravir
Kunal Taskar, GSK, United Kingdom

11:25 am–11:35 am
Abstract Presentation
Author to be invited

11:35 am–11:45 am
Abstract Presentation
Author to be invited

11:45 am–11:55 am
Abstract Presentation
Author to be invited

11:55 am–12:30 pm
Panel Discussion with All Speakers

12:30 pm–1:00 pm
Break

1:00 pm–2:00 pm
Poster Session

2:00 pm–3:00 pm
Networking Hour

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ISSX and IQ Consortium Virtual Workshop

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FRIDAY, MARCH 5, 2021
10:00 AM–3:00 PM ET (US)

Session 4: Using *in vitro* Enzyme and Transporter Data in the Prediction of Drug-drug Interactions
Chairs: Lei Zhang, US Food and Drug Administration, Silver Spring, Maryland, USA and Yurong Lai, Gilead Sciences, Foster City, California, USA

10:00 am–10:15 am
A Comprehensive Review of Approaches and Recommendations for the Conduct and Analysis of Induction of CYP Enzymes *in vitro* for the Purpose of Human Drug-drug Interaction
Niresh Hariparsad, AstraZeneca, Boston, Massachusetts, USA

10:15 am - 10:30 am Industry Perspectives on Regulatory Guidance on Drug-drug Interactions
Venkatesh Pilla Reddy, AstraZeneca, Cambridget, United Kingdom

10:30 am - 10:45 am EMA Perspectives on Regulatory Guidance on Drug-drug Interactions
Elin Lindhagen, Medical Products Agency, Uppsala, Sweden

10:45 am - 11:00 am FDA Perspectives on Regulatory Guidance on Drug-drug Interactions
Xinning Yang, US Food and Drug Administration, Silver Spring, Maryland, USA

11:00 am–11:15 am
Break

11:15 am–11:25 am
Application of Transporter Biomarkers to DDI Risk Assessment
Hiroyuki Kusuhara, University of Tokyo, Tokyo, Japan

11:25 am–11:35 am
Lecture to be confirmed
Speaker to be confirmed

11:35 am–11:45 am
PBPK Modeling of Concomitant CYP3A Auto-induction and Time-dependent Inhibition of the Pharmacokinetics of the CYP3A Substrate Aprepitant
Tamara Cabalu, Merck & Co., Inc., Philadelphia, Pennsylvania, USA

11:45 am–11:55 am
Abstract Presentation
Author to be invited

11:55 am–12:30 pm
Panel Discussion with All Speakers

12:30 pm–1:00 pm
Break

1:00 pm–2:00 pm
Poster Session

2:00 pm–3:00 pm
Networking Hour

*Program subject to change.

Registration now open!

REGISTER NOW

Renew Your ISSX Membership for 2021

Thank you for your membership and support of ISSX this year!

We urge you to remain a part of the premier international association that advances research and education on the interplay of living systems with medicines and chemicals for the benefit of society worldwide by renewing your ISSX membership today.

We recognize that the COVID-19 epidemic continues to affect many in tragic ways and we are all trying to manage our work and home lives to the best of abilities under unusual circumstances. ISSX has not been immune to the impact of the epidemic and, unfortunately, we were forced to cancel our meetings in Switzerland and Hawai'i. This epidemic forced the society into a rethink of our offerings for our members. Consequently, the number of webinars has increased substantially as a way to connect with our members and offer both scientific content as well as educational material. The **ISSX Webinar Series** is a free benefit of Society membership. Some of the webinars were organized by the ISSX Focus Groups who have also stepped up their activities. The **ISSX Focus Groups** provide an excellent forum for scientific discourse and they will be more and more involved with organizing sessions at future ISSX meetings.

In addition, the **New Investigators Group** is very active and this group provides an excellent way to connect with fellow early career scientists to share experiences and tips. One immediate consequence of this group is the **ISSX Mentorship Program**, which connects early career scientists with experienced colleagues to provide career advice and discuss career options. Finally, ISSX members benefit from steep discounts to our highly-rated scientific meetings where they learn about the latest research developments, network with leaders in the field, and present their research in multiple forums.

2021 promises to be an exciting year for ISSX and we hope to be able to meet face-to-face with all of you again. The **Translation of *in vitro* ADMET Science to *in vivo*: Current Perspectives and Challenges Workshop**, which is organized jointly with the IQ Consortium, will take place from March 2–5, but will be virtual—a first for ISSX and a great opportunity to explore this medium as a means to connect with our members and gather experience for future meetings. We hope that the 24th North American ISSX Meeting in Boston in September will be a face-to-face venue. Please save the dates and make plans to join us! In addition, the ISSX Webinar Series, Focus Groups, New Investigator Group and Mentorship Program will continue with great energy—all free benefits from society membership.

Please follow the steps below to complete your renewal:

1. Visit **issx.org/renew**.

2. On the right-hand side of the page, log in with your ISSX username and password. If you do not know your username or password, you may re-set it by visiting **issx.org/password**.

3. Click RENEW YOUR MEMBERSHIP NOW in the blue box at the top of your profile page.

4. On the next screen, review and update your contact information to ensure uninterrupted communication from ISSX.

5. Once you verify your contact information, you will be directed to the payment screen, where you may view your renewal options, including instant payment online via credit card.

If you would like to pay by check, select "Bill Me" under Payment. You can access your invoice on the subsequent page and it will be automatically sent to you via email. Please print the invoice and submit it with your check to:
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ISSX members have access to a variety of exclusive benefits including:

- **Reduced registration fees** for all ISSX meetings and workshops;
- Access to join and engage with the four **ISSX Focus Groups**;
- **Online learning opportunities** such as the ISSX Webinar Series, which feature world-renowned speakers and cutting-edge science;

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ISSX President's Message

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www.issx.org. The refreshed site includes a lot of useful information and is very easy to navigate.

I would like to end by sending you my best wishes for the holiday season. I hope that you may all be able to enjoy a restful break after this challenging year. In particular, I would like to take this opportunity to wish you a happy and peaceful 2021 and hope that all of you and your loved ones stay safe and well.

Best regards,
Ann Daly

Renew Your ISSX Membership for 2021

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- **A subscription to the *ISSX Newsletter*** that highlights Society news, member spotlights, late-breaking scientific news, and much more;
- **The opportunity to submit and present scientific abstracts** at ISSX workshops and meetings;
- **Eligibility to apply for and receive travel grants** to attend ISSX meetings;
- **The chance to hold office, serve on a committee, and vote in ISSX elections**;
- **Free Enrollment into the ISSX Mentorship Program** that pairs new investigators with senior scientists with related interests;
- And more!

Your membership indicates support of our mission to advance research and education on the interplay of living systems with medicines and chemicals for the benefit of society worldwide and helps sustain our program of operations. **Visit issx.org/renew today!**

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Enroll in the ISSX Mentorship Program for 2021!

Calling all ISSX Members!
The ISSX Mentorship Program pairs young investigators with senior scientists within and across career pathways to discuss career options, review competencies for success, consider challenges and problems, and receive practical advice from experienced scientists. This program is an exclusive member benefit that has seen great success since its inception.

The 2021 mentorship cycle will run for 12 months and ISSX will begin making matches in January 2021. The program matches mentors and mentees based on an award-winning algorithm. From there, the pairs have the flexibility to define their conversation topics to best suit the needs of their relationship. Past participants noted their focus was individual and career development, collaboration, and leadership. Milestones are set along the way for participants to review their desired outcomes of the mentorship, set goals, and provide progress updates.

What did 2020 ISSX Mentorship Program participants say?
"I have learned a lot about alternate career paths and different ways that people can get to their current position. Talking with [my mentor] has also given me a lot of insight into how things are run in a larger company. During COVID19, I have felt really lucky to have a professional connection to discuss science and career paths with."

"It is an enriching opportunity to be mentored by J. in the framework of ISSX Mentorship Program. While being the mentee of [hers] I learned what areas of my technical expertise should be strengthened, she gave me the heads up on literature to look at and helped me enhance my organizational and leadership skills. The mentor encouraged me to engage proactively in my personal development and performance."

ISSX MENTORSHIP PROGRAM

"I highly appreciate inspiring discussions with [my mentor], sharing his experience and career path with me. He encouraged me to develop persistency in moving forward to meeting my career goals. [He] advised on the material to cover to foster my professional development. The mentor has also advised on the cover letter content, he gave me the heads up on how to prepare myself for the fruitful interview as well as provided me with some tips on individual development and research presentation."

ISSX thanks past participants for their work and dedication to this initiative and we invite you to re-enroll in the program so that you may continue growing personally and professionally.

Sign Up Today!
If you are interested in joining as a mentor or a mentee, please visit **www.issx.org/ISSXMentorship** to learn more.

ISSX will provide resources to help you launch and sustain effective mentoring relationships. Mentoring is a personal and professional development experience that challenges one to reflect on their own actions and behaviors over time. For those who have benefited from a helpful mentor in their lives or careers, there is often a strong drive to pay this forward to others by serving in the same role.

Finding a true mentor is not always easy. The ISSX Mentorship Program can help and we are proud to offer this valuable resource and opportunity for new relationships, skills, and conversations to develop.

Participate in the ISSX Webinar Series

About the ISSX Webinar Series
The ISSX Webinar Series is an engaging and innovative way to hear from and interact with speakers from around the world on a range of topics related to the metabolism and disposition of xenobiotics. Members can participate for free. Participate in regularly scheduled live webinars with an exciting range of speakers, as well as watch previous webinars on your own schedule.

ISSX webinars are presented by internationally recognized scientists on a variety of subjects relevant to the field. The ISSX Continuing Education Committee is charged with the responsibility for reviewing these educational offerings and setting the webinar schedule.

Mark Your Calendar for these Upcoming ISSX Webinars

JANUARY 2021
January 12 at 11:00 AM ET (15:00 UTC)
Glucuronide Metabolites, Why Bother?
Presented by Liam Evans, CEO, Hypha Discovery Limited

MARCH 2021
March 16 at 11:00 AM ET (15:00 UTC)
Inflammatory Regulation of P450 Enzymes: Implications for Drug Metabolism in the Time of COVID-19
Presented by Edward T. (Eddie) Morgan, Ph.D., Emory University School of Medicine

Additional webinars will be announced soon! Check the **ISSX webinar schedule** to stay in the know on upcoming scientific lectures and discussions.

Did you miss a recent webinar? Sign into your ISSX membership account and view all past webinars **here**.

SUBMIT A PROPOSAL TO PRESENT FOR THE ISSX WEBINAR SERIES

We invite proposal submissions for upcoming webinars.

Please note, the information presented in an ISSX Webinar must be balanced and provide the attendee with an objective viewpoint. Proposals for the ISSX Webinar will be evaluated by the ISSX Continuing Education Committee for the ability to provide educational content to ISSX members.

Click here to submit a proposal online today!

Changes to the ISSX Council

As we approach the end of 2020, we wish to thank two ISSX Council members for their terms of service with ISSX.

Eric Chun Yong Chan, National University of Singapore

Professor Eric Chan is a pharmaceutical scientist in the Department of Pharmacy, National University of Singapore (NUS) (2006–current). His research interests are (1) metabolism-driven systems biology modelling of diseases, pharmacology, toxicology and mammalian host-bacteria interactions and (2) xenobiotic-derived reactive metabolite research with specific focus on interaction with biological proteins and physiological-based pharmacokinetics-pharmacodynamics (PBPK-PD) modelling of pharmacology and toxicology.

Eric is currently Chair of Department Graduate Committee (2018–current), an affiliate member of the National University Cancer Institute, Singapore (NCIS) (2018–2021) and an adjunct principal investigator at the Singapore Institute for Clinical Sciences (SICS) (2016–2020). He is an editorial advisory board member of the Biochemical Pharmacology (Elsevier, 2018–current), Drug Metabolism and Disposition (American Society of Pharmacology and Experimental Therapeutics (ASPET), 2019–current), Journal of Chromatography B (Elsevier, 2008–current) and Asian Journal of the Scholarship of Teaching and Learning (NUS Centre for Development of Teaching and Learning, 2018–2020). He is a grant review board member for the Health and Medical Research Fund (HMRF) in Hong Kong (2013–current). He is a registered pharmacist under the Singapore Pharmacy Council, Ministry of Health (2001–current) and a member of the ASPET.

Eric was awarded the Dean's Chair Professorship in the Faculty of Science (2015–2018). He was five times a recipient of the Faculty of Science Teaching Excellence Award and four times the NUS Annual Teaching Excellence Award. He also received the Faculty of Science Young Scientist Award (2010) and Outstanding Scientist Award (2014). He was awarded the NUS Overseas Attachment Programme (OAP) and the National Medical Research Council (NMRC) research training fellowships at the Imperial College London (2008) and University of Washington (2012) respectively. Eric's academic career has been developed successfully based on his active participation in meetings and workshops organized by the International Society for the Study of Xenobiotics (ISSX) over the years. He also served previously as the Council Member of ISSX from 2019 to 2020 and Scientific Affairs Committee Member of the ISSX from 2016 to 2020.

Aleksandra Galetin, Centre for Applied Pharmacokinetic Research, University of Manchester, UK

Dr. Galetin is a Professor of Translational Pharmacokinetics in the School of Health Sciences, University of Manchester, UK and Deputy Director of the Centre for Applied Pharmacokinetic Research. She is the recipient of the 2012 ISSX European New Investigator Award and 2015 AAPS Meritorious Manuscript Award. Dr. Galetin is on expert panels such as International Transporter Consortium Steering Committee and is serving on the ISSX Council. Her research focuses on mechanistic *in vitro* characterisation of hepatic and renal transporters in 2D and 3D cellular systems and quantitative translation of such data using physiologically-based pharmacokinetic (PBPK) models. In addition, endogenous biomarkers for hepatic and renal transporters and development of PBPK models of renal impairment for model-based dose recommendations in such patients. As a result of her continuous international leading role in drug transporter area, she co-edited a special issue in Clin Pharmacol Ther Nov 2018 dedicated to 'Advances in the role of drug transporters in drug development' where she led or contributed to multiple white papers.

In 2016, Dr. Galetin completed a sabbatical in the US FDA Office of Clinical Pharmacology where she provided expert advice on the PBPK modelling of drug-drug interactions and special populations in new drug applications. She has published over 100 research papers in highly cited peer reviewed journals (H index 42) and supervised/mentored over 35 graduate students and postdoctoral research associates.

ISSX is thankful to each of these individuals for their service and commitment to the Society.

Save the Date: 24th North American ISSX Meeting: Broadening Our Horizons

September 12–15, 2021 | Westin Boston Waterfront Hotel | Boston, Massachusetts, USA

Meeting Organizing Committee
Meeting Chair: Raymond Evers, Janssen Pharmaceutica (J&J)

Meeting Co-Chair: Joseph Balthasar, University at Buffalo

Committee Members:
Ann Daly, Newcastle University
Xiaoyan Chu, Merck & Co.
Christine Fandozzi, Merck & Co.
Lucinda Hittle, Merck & Co.
Marcel Hop, Genentech
Amit Kalgutkar, Pfizer
Valerie Kramlinger, Novartis
Kaushik Mitra, Janssen Pharmaceutica
Bhagwat Prasad, Washington State University
Erin Schuetz, St. Jude Children's Research Hospital
Ping Zhao, Bill and Melinda Gates Foundation

Preliminary Program*

SUNDAY, SEPTEMBER 12, 2021

Short Course 1: Biotransformation, Mechanism, and Pathways Biotransformation Focus Group
Chair: Valerie Kramlinger, Novartis

Short Course 2: Application of Regulatory Guidances for Transporter Related DDIs
Chairs: Lei Zhang, Food and Drug Administration and Xiaoyan Chu, Merck & Co.

Short Course 3: PBPK Modeling in Drug Development Modeling and Simulation Focus Group
Chair: Ping Zhao, Bill and Melinda Gates Foundation

Short Course 4: Training Course: From Active Molecules to Approved Therapeutics: Navigating Drug Development and Regulatory Challenges
Chair: Christine Fandozzi, Merck & Co.

Opening Keynote Lecture: Discovery and Development of a COVID 19 Vaccine
Hanneke Schuitemaker, Janssen Vaccines & Prevention

Opening Welcome Reception with Exhibitors and Posters

MONDAY, SEPTEMBER 13, 2021

Plenary Lecture 1: The Economics of the Pharmaceutical Industry
Joseph DiMasi, Tufts University

Concurrent Symposia 1 & 2

Symposium 1: Latest Developments for Assessing the ADME of Biologics
Chairs: Dhaval K. Shah, University at Buffalo and Vittal Shivva, Genentech

Symposium 2: State of the Art Strategies to Enhance Brain Penetration of Small Molecules and Therapeutic Proteins
Chairs: Marilyn Morris, University at Buffalo and Xiaoyan Chu, Merck & Co.

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Save the Date: 24th North American ISSX Meeting

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Concurrent Symposia 3 & 4

Symposium 3: Driving Innovation in Qualitative and Quantitative Bioanalysis
Chairs: Lucinda Hittle, Merck & Co. and Valerie Kramlinger, Novartis

Symposium 4: Beyond Rule of 5
Chairs: Per Artursson, Uppsala University and Dehua Pei, The Ohio State University

New Investigators Session

TUESDAY, SEPTEMBER 14, 2021

Plenary Lecture 2: Membrane Protein Structure-function Analyses Using MS
Carol Robinson, University of Oxford

Concurrent Symposia 5 & 6

Symposium 5: ADME Success Stories
Chairs: Marcel Hop, Genentech and Dermot McGinnity, AstraZeneca

Symposium 6: New Strategies for Overcoming ADME Hurdles for Nucleic Acid
Chairs: Jessica Hawes, US Food and Drug Administration and Donglu Zhang, Genentech

ISSX Awards Presentations

ISSX Poster Award Finalist Competition Podium Presentations
Award finalists to be determined

ISSX 2020 European Scientific Achievement Award Lecture
Ulrich Zanger, Dr. Margarete Fischer-Bosch Institute of Clinical Pharmacology

ISSX 2021 North American Awards
Award finalists to be determined

ABSTRACT SUBMISSIONS

Poster presentations are an integral component of ISSX meetings. We encourage all those involved in the fields of metabolism, pharmacology, toxicology, molecular biology and other related disciplines to consider submitting an abstract for a poster presentation at the 24th North American ISSX Meeting. The abstract submission site opens soon! Visit **www.issx2021.org** for details.

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Save the Date: 24th North American ISSX Meeting

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WEDNESDAY, SEPTEMBER 15, 2021

Concurrent Symposia 7 & 8

Symposium 7: New Approaches to Improve the ADME Kinetics of Biologics
Chairs: Joseph Balthasar, Univesity at Buffalo and Greg Thurber, University of Michigan

Symposium 8: Non-invasive Approaches for Drug Disposition Prediction: Biomarkers, Liquid Biopsies and PBPK Modeling
Chairs: Bhagwat Prasad, Washington State University and David Rodrigues, Pfizer

Concurrent Symposia 9 & 10

Symposium 9: Identifying Biotransformations of Next Generation Biologics
Chairs: Mark Cancilla, Merck & Co. and Surinder Kaur, Genentech

Symposium 10: Epigenetics in Drug Disposition and Drug Therapy
Chair: Ann Daly, Newcastle University

Plenary Session: Predicting the Unpredictable – Idiosyncratic Drug Toxicity
Chairs: Amit S. Kalgutkar, Pfizer and Kaushik Mitra, Janssen Pharmaceutica

*Program subject to change.

REGISTRATION

Registration opens in 2021! Bookmark the meeting website, **www.issx2021**.org and check back for additional details in the new year.

Welcome New Members

The International Society for the Study of Xenobiotics proudly welcomes the following new members. We greatly appreciate their support and hope that each remains aligned and affiliated with ISSX for many years to come.

Deepak Ahire, Washington State University, Spokane, Washington, United States

Helena Andrade, Philip Morris International Science, Neuchâtel, Switzerland

Andrew Annalora, Oregon State University, Corvallis, Oregon, United States

Sophie Argon, University of Washington, Seattle, Washington, United States

Olivier Boutaud, Vanderbilt University, Franklin, Tennessee, United States

Soeren Buesker, University of Cologne, Cologne, Germany

Jingwei Cai, Genentech, South San Francisco, California, United States

Cathy Cantalloube, Sanofi, Chilly Mazarin, Batiment 11, France

Sagnik Chatterjee, Syngene International Ltd (BBRC), Bangalore, Karnataka, India

Mingqing Chen, Vertex Pharmaceuticals, Boston, Massachusetts, United States

Qiqing Chen, East China Normal University, Shanghai, Minhang District, China

Carol Collins, Beckman Coulter, Loveland, Ohio, United States

Filip Cuyckens, Janssen R&D, Beerse, Belgium

Danielle Drake, University of Toronto, Toronto, Ontario, Canada

Wojciech Dworakowski, Syros Pharmaceuticals, United States

Tracy Follansbee, Elsevier, South Deerfield, Massachusetts, United States

Ravindranath Reddy G, Syngene International Ltd (BBRC), Bangalore, Bommasandra, India

Sarah Glass, Vanderbilt University, Nashville, Tennessee, United States

Sree Gopal, Takeda Pharmaceuticals International Co., San Diego, California, United States

Jeffry Granados, UC San Diego, La Jolla, California, United States

Johanna Haglund, Admescope Sweden AB, Södertälje, Sweden

Oliver Hatley, Certara UK, Sheffield, South Yorkshire, United Kingdom

Simon Hauri, F. Hoffmann-La Roche Ltd., Basel, Basel-Stadt, Switzerland

Carley Heck, Pfizer, New London, Connecticut, United States

Chien-Ming Hsieh, Taipei Medical University School of Pharmacy, Taipei City, Taipei City, Taiwan

Ditte Iversen, University of Southern Denmark, Odense, Denmark

Megan Jackson, Vanderbilt University, Franklin, Tennessee, United States

Anand Joshi, Abbvie-Pharmacyclics, Sunnyvale, California, United States

Janneke Keemink, Roche, Basel, Switzerland

EunJeong Kim, Nextgen Bioscience, Seongnam, Gyeonggi-do, Korea

Prashant Kole, Biocon Bristol Myers Squibb R&D Centre, Bangalore, Karnataka, India

Laken Kruger, Washington State University, Pullman, Washington, United States

Chandandeep Kular, Philadelphia, Pennsylvania, United States

Laurent Laboureur, Servier, Orléans, France

Hans Lennernas, Uppsala University, Uppsala, Sweden

Christian Leung, Genentech, South San Francisco, California, United States

Louis Lin, University of British Columbia, Vancouver, British Columbia, Canada

Shuguang Ma, Genentech, South San Francisco, California, United States

Keiichi Morita, Chugai Pharmaceutical Co., Ltd., Kamakura, Kanagawa, Japan

William Murphy, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

Martina Navrátilová, Charles University, Prague, Czechia

Mikko Neuvonen, University of Helsinki, Helsinki, Finland

Continued on next page

Welcome New Members

Continued from previous page

James O'Neill, Charles River Laboratories, Tranent, United Kingdom

Boonsri Ongpipattanakul, Chulalongkorn University, Bangkok, Thailand

David Palmer, York Bioanalytical Solutions, Sandwich, Kent, United Kingdom

Venkatesh Pilla Reddy, AstraZeneca, Cambridge, United Kingdom

Sivaprasad Putlur, Syngene International Ltd, Bengaluru, Karnataka, India

Prabhakar Rajanna, Syngene International Limited, Bangalore, Karnataka, India

Karen Samy, Genentech, South San Francisco, California, United States

Rucha Sane, Genentech, Santa Clara, California, United States

Ilona Schreck, Daiichi Sankyo Europe GmbH, Martinsried, Bavaria, Germany

Carl Sennbro, LEO Pharma A/S, Ballerup, Copenhagen area, Denmark

Devang Shah, Syngene Intl (BBRC), Bangalore, Karnataka, India

Nina Shah, MyoKardia, Brisbane, California, United States

Jason Sherfey, Javelin Biotech, Woburn, Massachusetts, United States

Noora Sjöstedt, University of Helsinki, Helsinki, Finland

Eva Streekstra, Radboudumc, Nijmegen, Netherlands

Eeva Tarkiainen, HUS Helsinki University Hospital, Helsinki, Finland

Piet Swart, Nuvisan, Grafing, Munich, Germany

Surabhi Talele, University of Minnesota, Minneapolis, Minnesota, United States

Eugene Chen, Genentech, Inc., South San Francisco, California, United States

Simon Taylor, Pharmaron UK, Hoddesdon, Herts, United Kingdom

Brice Thompson, University of Washington, Seattle, Washington, United States

Yuen Ching To, The Chinese University of Hong Kong, Shatin, Hong Kong

Bo Tokarski, Charles River Laboratories, Ashland, Ohio, United States

Susanna Tse, Pfizer Inc, Groton, Connecticut, United States

K. Usmani, Gilead Sciences, San Diego, California, United States

Ron van Schaik, Erasmus MC, Rotterdam, ZH, Netherlands

Laurens Verscheijden, Radboud University Medical Center, Nijmegen, Netherlands

Markus Walles, Novartis, Basel, Switzerland

Yanran Wang, Genentech, Inc., South San Francisco, California, United States

Ruichao Xu, University of Pittsburgh, Pittsburgh, Pennsylvania, United States

Bing Yao, Ideaya Biosciences, South San Francisco, California, United States

Xu Zang, GBT, South San Francisco, California, United States

Ming Zheng, Daiichi Sankyo, Basking Ridge, New Jersey, United States

ISSX Focus Groups

ISSX Focus Groups provide ISSX members with a great opportunity to network with your colleagues while discussing topics relevant to the day. Your participation in the ISSX Focus Groups help us to enhance the exchange of the most current scientific research information and open doors to endless opportunities for collaboration and career advancement. View the latest from the ISSX Focus Groups by clicking on the titles below and join today!

BIOANALYSIS IN ADME SCIENCE

The aims of this group include: (a) to promote state-of-the-art analytical technologies to solve challenging issues faced in ADME studies and bioanalysis, (b) to enable industrial scientists to actively contribute to and participate at ISSX meetings and associated activities, and (c) to enhance synergy between industrial scientists and academic researchers.

BIOTRANSFORMATION, MECHANISMS, AND PATHWAYS

Points for discussion include: (a) metabolism-directed drug design (e.g., incorporation of D to reduce metabolic liability), (b) mechanisms underlying biotransformations that yield “unusual” metabolites and characterization of the metabolizing enzymes responsible for their formation, and (c) idiosyncratic immune-mediated toxicity via metabolism (e.g., reactive metabolites).

MODELING AND SIMULATION

This group focuses on the role of modeling and simulation in drug development in all stages, including topics such as (a) translational extrapolations from preclinical data to clinical expectations, (b) drug-drug interactions, (c) extrapolations of PK/PD data to special populations, (d) early dose optimization, and (e) selection of doses for clinical testing.

TRANSPORTERS

The goals of this focus group are to disseminate and promote state-of-the-art research and foster collaborations among ISSX members on the role of transporters in drug disposition, drug interactions, efficacy, and toxicity, and their impact on drug discovery, development, and regulatory decision making.

ISSX International Society for the Study of Xenobiotics

ISSX Newsletter is published quarterly in the spring, summer, autumn, and winter. For information concerning advertising in this publication, including rates and specifications, please visit **issx.org/advertising** or contact Scott Narug at **snarug@issx.org**.

Change of Address

If your mailing address, telephone, fax number, or e-mail has changed or will change, please let us know as soon as possible. You may update your contact information at any time using the online membership directory, which you can access in the Member Only section of the website. If you have forgotten your username and/or password, please contact **information@issx.org**.

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