Tuesday
September 29

Welcome
8:15–8:30
Forum Hall

Keynote Plenary
8:30–9:30
Forum Hall
Impact of Inborn Error of Metabolisms on Brain Function
Prof. Dr. med. A.M. Das, Klinik für Pädiatrische Nieren-, Leber- und Stoffwechselerkrankungen, Zentrum Kinderheilkunde und Jugendmedizin, Medizinische Hochschule , Hannover, Germany

Exhibits/Posters Open
9:00–17:00
Exhibit and Poster Areas

Break
9:30–10:00
Exhibit and Poster Areas

Track A: Central Nervous System—Issue Resolution
10:00–12:00
Forum Hall
Co-Chairs: Amy Kim, PhD, DABT, H3 Biomedicine, Cambridge, MA, and Marie-Luce Rosseels, DVM, DSP, UCB Biopharma, Braine l’Alleud, Belgium
This session will focus on the central nervous system (CNS), identification of nonclinical and clinical safety pharmacology endpoints, and resolution or de-risking strategies of potential endpoints associated with adverse effects. An overview of voltage-gated sodium channel biology in relation to CNS safety pharmacology and disease will first be presented. This session will also highlight CNS safety pharmacology effects from an acute compared with chronic or longer-term dose administration regimen and how these differences in effects were evaluated and resolved. The clinical predictivity of CNS adverse outcomes such as drug-induced dyskinesia will then be discussed. Finally, the latest nonclinical models to assess cognition or cognitive function will be presented.

10:00–10:30 Voltage-Gated Sodium Channels: Disease-Causing Genes and Therapeutic Targets
Alan Goldin, PhD, MD, UC-Irvine, Irvine, CA, United States

10:30–11:00 Single versus Repeated Dosing in CNS Safety Pharmacology Studies
Karen Tse, PhD, AstraZeneca, Cambridge, United Kingdom

Track B: Cardiovascular—Cardiovascular Safety Assessment beyond the ECG
10:00–12:00
Meeting Hall V
Co-Chairs: Eric Martel, PhD, Boehringer Ingelheim Pharma GmbH, Biberach an der Riss, Germany, and Rob Kaiser, PhD, DABT, Charles River Laboratories, Reno, NV, United States
A proper cardiovascular safety assessment involves interrogation of multiple physiological and electrophysiological parameters to make the most educated predictions of clinical translation and ultimately, risk prediction. Oversimplification of CV safety assessment and accessibility of measurements has led to emphasizing of test article effects on ECG, but concomitantly de-emphasizing of more functional and performance endpoints. Increased attention has been placed on the latter due to novel pathways, atypical etiologies of cardiovascular effects, and late stage development findings. This session will present updates from the HESI initiative on left ventricular performance, and challenge the audience with atypical and program-specific endpoints and designs, considering evaluations over time, postural assessments, and custom CV study strategies.

10:00–10:30 HESI Update on Contractility Endpoints
Michael K. Pugsley, MSc, PhD, FBPharmS, DSP, Purdue Pharma, Cranbury, NJ, United States

10:30–11:00 Circadian Rhythms of the Cardiovascular Function: A Key Element of Cardiosafety Evaluation
Alexandra Basset, Sanofi--Aventis, Reuil-Malmaison, France

11:00–11:30 Evaluation of Drug-Induced Orthostatic Hypotension: From Animals to Humans and Back Again
Christophe Drieu La Rochelle, Biotrial, Rennes, France

11:30–12:00 Novel Comprehensive Cardiovascular Assessment
Tiffini Brabham, DVM, PhD, DABT, Pfizer, Andover, MA, United States

Lunch Break, Exhibits, Poster Presentations, and Poster Judging
12:00–14:00
Exhibit and Poster Areas
13:00–14:00 Even Poster Numbers Present
13:00–14:00 All Jr. Investigator Poster Contest Entries Present
Sponsored Presentations

12:30–13:30
See page 40

Oral Communications 1–2

Invited Oral Communications 1:
Follow up Approaches for Cardiovascular and Gastrointestinal Safety Assessments

14:00–15:00
Forum Hall
Co-Chairs: Tomas Mow, DVM, PhD, H. Lundbeck A/S, Copenhagen, Denmark, and Eric. J. Rossmann, PhD, GlaxoSmithKline, King of Prussia, PA, United States

14:00–14:15  Characterization of Canine Models of Heart Failure with Reduced and Preserved Ejection Fraction
Brad Youngblood, et al.

14:15–14:30  Echocardiography in a Toxicology Setting
Michael Engwall, et al.

14:30–14:45  Effect of a Prolyl Hydroxylase Inhibitor on Aortic Pressure, Heart Rate and Peak Right Ventricular Pressure in Rats Exposed to Acute Hypoxia
Loren Kohrs, et al.

14:45–15:00  A Platform for Cardiotoxicity Screening Based on Manufacturable Stretchable Microelectrodes Arrays (SMEAs)
Simon Authier, et al.

Invited Oral Communications 2:
Assessment of Acute, Drug-Induced Cardiotoxicity Using hIPS Derived Cardiomyocytes

14:00–15:00
Meeting Hall V
Co-Chairs: Khuram W. Chaudhary, PhD, GlaxoSmithKline, King of Prussia, PA, United States, and Ken Gibson, PhD, FAHA, Ionic Transport Assays, Inc., St. Louis, MO, United States

14:00–14:15  Electrophysiologic Actions of Diverse CIPA Compounds on Cor.4U Cardiomyocytes
Greg Luerman, et al.

14:15–14:30  Could In Vitro Animal Assays be Replaced by Human Stem Cell-Based Assays for Drug-Induced Cardiac Risks: Beyond QT-prolongation/CIPA?
Hua Rong Lu, et al.

14:30–14:45  Csahi Study: Evaluation of Med64 Multi-Electrode Array in Combination With Human Ips Cell-Derived Cardiomyocytes to Predict Drug-Induced Qt Prolongation and Arrhythmia
Takashi Kitagushi, et al.

14:45–15:00  In Silico Prediction of Drug Effects on Human Ventricular Electrophysiology Using the Virtual Assay Software and Comparison to In Vitro Data
Elisa Passini, et al.

Track A: Translational Safety Biomarkers—From Preclinical to Clinical

15:45–17:45
Forum Hall
Co-Chairs: Ahmad Al-Saffar, PhD, Associate Professor, Department of Medical Sciences, Faculty of Medicine, Uppsala University, Uppsala, Sweden, and Jean-Pierre Valentin, PhD, DSP, UCB Biopharma, Braine l’Alleud, Belgium

The session will provide insight into the latest knowledge and development in the field of translational safety biomarkers (from preclinical to clinical) with an emphasis on target organs of interest to the Safety Pharmacology community, namely cardiovascular and nervous systems. Experts will give presentation on Neurotox, Cardiotox, as well as two presentations focusing on approaches/technologies that support a better understanding of the translatability of safety biomarkers i.e., PK/PD and Imaging. Attendees of this track will have the opportunity to learn about best practice in translational safety biomarkers from pre-clinical to clinical directly relevant to practicing safety pharmacologist.

15:45–16:15  PKPD is Essential for Planning, Execution and Evaluation of Studies in Safety Pharmacology
Professor Johan Gabrielson, PhD, Swedish University of Agricultural Sciences, Division of Pharmacology and Toxicology, Uppsala, Sweden

16:15–16:45  Overview of Translational Biomarkers of Cardiovascular Injury and Dysfunction
Brian R. Berridge, DVM, DACVP, GlaxoSmithKline, Research Triangle Park, NC, United States

16:45–17:15  Cognitive Function and PET Signals of Activated Microglia: Non-invasive Translational Biomarkers of Neurotoxicity
Merle G. Paule, PhD, Fellow ATS, Director, Division of Neurotoxicology, National Center for Toxicological Research, US FDA, Jefferson, AR, United States

17:15–17:45  PET-Imaging in Drug Discovery and Development
Éva Lindström Böö, Global PET CoE Manager, AstraZeneca Translational Sciences Centre, Karolinska Institutet, Stockholm, Sweden
Track B: Integrative Pharmacology—Case Studies in Diabetes and Pulmonary Arterial Hypertension

15:45–17:45

Meeting Hall V

Co-Chairs: Bruce H. Morimoto, PhD, Applied Translational Medicine, Celerion, Inc., Redwood City, CA, United States, and Franz J. Hock, PhD, CorDynamics, Dieburg, Germany

This session will focus on two therapeutic indications, pulmonary arterial hypertension (PAH) and diabetes. Each topic will be represented by two talks and highlight how organ systems integrate and work together with examples translation from preclinical to the clinic.

PAH is an increase in pulmonary blood pressure which acutely results in shortness of breath, dizziness, and fainting. The long-term consequence of this change in respiratory physiology is a strain on the heart leading to congestive heart failure. PAH is an example of how closely the respiratory and cardiovascular systems are integrated.

Diabetes will be the second topic for the session on integrative pharmacology. It is estimated that worldwide over 387 million people have diabetes which is more than 8% of the adult population. Diabetes is dysregulation of blood glucose involving either a lack of insulin or insulin resistance. This change in insulin metabolism results in a plethora of metabolic and physiological changes including obesity and various neuropathies.

15:45–16:15

Advances in Pulmonary Vascular Medicine

Dr. med. Christian Nagel, Leitender Arzt des Lungenzentrums, Fachbereich Pneumologie, Klinikum Mittelbaden gGmbH, Baden-Baden, Germany

16:15–16:45

What is the Ideal Animal Model for Idiopathic Pulmonary Hypertension?

Kristy D. Bruse, PhD, DSP, Integrated Physiology & Pharmacology Consulting, LLC, Poughkeepsie, NY, United States

16:45–17:15

Emerging Treatment Options for Diabetes and Obesity

Christoffer Clemmensen, PhD, Division of Molecular Pharmacology, Institute for Diabetes and Obesity (IDO), Helmholtz Zentrum Munich, Garching Germany

17:15–17:45

Pharmacological Profiling of New Anti-Diabetic Drugs

Andreas Herling, DVM, PhD, Research & Translational Medicine R&D DIAB Division, Sanofi-Aventis Deutschland GmbH, Frankfurt, Germany

Sponsored Presentations

18:00–19:00

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Wednesday, September 30 continued

10:30–11:00 Hear Ye, Hear Ye - Preclinical Challenges in Bringing a Novel Gene Therapy for Hearing Loss to the Clinic
Tim MacLachlan, PhD, DABT, Global Head of Biologics Safety Assessment, Novartis, Cambridge, MA, United States

11:00–11:30 Methods for Detecting Adverse Effects on Visual Function
Willie Redfern, PhD, FRSB, FBPhS, DSP, AstraZeneca, Cambridge, United Kingdom

11:30–12:00 Models and Techniques Used for Determining Drug-Induced Olfactory and Gustatory Toxicity
Richard L. Doty, PhD, Professor and Director, Smell and Taste Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States

Track B: Cardiovascular—Translation of QT

10:00–12:00 Meeting Hall V
Co-Chairs: Joy Olbertz, PharmD, PhD, BioMarin, Novato, CA, United States, and Lorraine M. Rusch, PhD, Vince & Associates Clinical Research, Overland Park, KS, United States

The session aims to address the position and/or influence of Safety Pharmacology beyond the specific “Phase I preparation” paradigm. The needs of reducing attrition and improving safety translation in late stage drug development will be covered using specific population based risks or late emergent clinical safety findings. In particular, the session comprises four talks on different areas of late stage challenges: The importance of understanding and clinical management of seizure liability; cognitive impairment and the impact for the elderly patient population; chemotherapy-induced heart failure and the potential for stem cells in the mechanistic understanding of this; and, coronary microvascular dysfunction in CAD. We aim to demonstrate that in all these aspects, Safety Pharmacology can adapt itself to remain both proactive and reactive to face the safety assessment challenges.

10:00–10:30 Use of the hERG Assay to Predict QT Prolongation: In Pursuit of Perfection in an Imperfect World
Bernard Fermini, PhD, Global Safety Pharmacology, Pfizer, Groton, CT, United States

10:30–11:00 Using Multiple Ion Channel Screening to Predict QT Prolongation via In Silico Models: How Are We Doing?
Gary Mirams, PhD, University of Oxford, Oxford, United Kingdom

11:00–11:30 How Do the Preclinical Cardiac Safety Pharmacology Studies Inform Early Clinical Studies?
Corina Dana-Dota, MD, AstraZeneca, Gothenburg, Sweden

11:30–12:00 Panel Discussion

Lunch Break, Exhibits, and Poster Presentations

12:00–14:00

Exhibit and Poster Areas
13:00–14:00 Odd poster numbers present

Sponsored Presentations

12:30–13:30
See page 41

Oral Communications 3–4

Invited Oral Communications 3:
Neurotoxicity—From Single Cells to Behavioral Effects

14:00–15:00 Forum Hall

Co-Chairs: Greet Teuns, DVM, MSC, Janssen R&D, Beerse, Belgium and Martin Traebert, PhD, Novartis Pharma AG, Basel, Switzerland

14:00–14:15 Evaluation of Gross Behavioral and Physiological Status Following Administration of a Psychostimulant and Sedative Using a Functional Observational Battery Assessment Adapted for Trained Cynomolgus Monkeys
Joel Baublits, et al.

14:15–14:30 Utility of an In Vitro Platform to Assess Neuronal Toxicity Using Human iPSC-Derived Neurons
Dinah Misner, et al.

14:30–14:45 Kinetic image cytometry and High content Analysis Assay of Neurotoxicity
Patrick McDonough, et al.

14:45–15:00 Use of Stem Cell Derived Peripheral Neurons As a Model Of Chemotherapeutic Induced Peripheral Neuropathy
Eileen Dolan, et al.

Invited Oral Communications 4:
Integrated Risk Assessment—From Bench to Bedside

14:00–15:00 Meeting Hall V

Co-Chairs: Silke Schwengberg, PhD, Cells at Work Consulting & Services, Düren, Germany, and Mark Deurinck, DVM, Dr.med.vet, DABT, ERT, Novartis Pharma AG, Basel, Switzerland

14:00–14:15 Identifying Site-Specific Molecular Signatures for Sub-Acute Drug Induced Kidney Injury
Andre Da Costa, et al.

14:15–14:30 The Non-Invasive Translational Biomarker-Index of Cardiac Electrophysiological Balance (ICEB) Predicts Potential Risk of Cardiac Arrhythmias in Preclinical Models and in Patients: Superior to Current Biomarkers Such As QT?
Hua Rong Lu, et al.

14:30–14:45 An In Silico PBPK-PD Coupled Approach to Assess Zolpidem Effect on Pre-Clinically and Clinically Measured Cardiac Repolarisation Parameters in the Absence and Presence of a Circadian Model of Plasma Ion Concentration
Ben Small, et al.

14:45–15:00 Patient-Specific QT Risk Assessment: Case Study of An Oncology Agent and An Anti-Emetic
Chris Pollard, et al.

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Program

Wednesday, September 30 continued

**Exhibits, and Poster Presentations**

15:00–15:45
Exhibit and Poster Areas
15:00–15:45  Odd Poster Numbers Present

**Track A: Central Nervous System—Abuse Liability Potential: Current Advancements**

15:45–17:45
Forum Hall
Co-Chairs: Mary Jeanne Kallman, PhD, DSP, Kallman Preclinical Consulting, Greenfield, IN, United States, and Greet Teuns, DVM, MSc, Janssen R&D, Beerse, Belgium

A discussion of timely abuse potential topics will be the focus of this session. A summary of the clinical and non-clinical aspects of the April 2015 face-to-face meeting of the Cross Company Abuse Liability Consortium with the Food and Drug Administration (FDA)/Controlled Substance Staff (CSS) will be shared with a discussion of the future direction in abuse potential evaluations. A comparison of US and European expectancies for abuse potential reviews coupled with recent experiences with new registration compounds will provide current regulatory interaction. A final talk on the potential of screening approaches will focus on the value of a screening strategy for abuse liability and provide a discussion of the potential approaches to early screening that could be applied in drug development.

15:45–16:15  EMA Guideline on Non-Clinical Dependence Testing: The First Decade—Where Do We Go From Here?
Leon Van Aerts, PhD, Rijksinstituut voor Volksgezondheid en Milieu, Bilthoven, Netherlands

16:15–16:45  Update from the April Meeting with CSS/FDA
Carrie G. Markgraf, MD, PhD, Merck, Kenilworth, NJ, United States

16:45–17:15  Recent Experiences on Regulatory Abuse Potential Discussions
Thomas J. Hudzik, PhD, AbbVie, Chicago, IL, United States

17:15–17:45  Panel Discussion: Regulatory Expectations (FDA vs EMA)
Dr. Beatriz Silva-Lima, Dr. Michael Swedberg, Dr. Greet Teuns, Dr. Leon Van Aerts

**Track B: Novel In Vitro Models—From Stem Cells to Human Tissues**

15:45–17:45
Meeting Hall V
Co-Chairs: Silke Schwengberg, PhD, Cells at Work Consulting & Services, Düren, Germany, and Hua Rong Lu, PhD, Janssen Pharmaceutica NV, Beerse, Belgium

This session will focus on the use of human cells and tissue for safety and toxicity testing. The topics will include the generation and use of human iPS cells from individuals with disease phenotypes, the integration of human stem cell-derived cells into 3D models, and the use of fresh human tissue for the prediction of drug safety. The session will highlight the usefulness of human cells and tissues, either stem cell-derived or native, for safety and toxicity screening and should provide room for discussion about the pros and cons of these systems for safety screening.

15:45–16:15  Patient-Specific Induced Pluripotent Stem-Cells: Models for Long-QT Syndrome
Daniel Sinnecker, MD, Klinikum rechts der Isar der Technischen Universität München, München, Germany

16:15–16:45  Mechanical Characterization of hiPS-Cardiomyocytes: 2D vs 3D for Cardiotoxicity and Heart Failure Model
Matthias Goßmann, Axiogenesis AG, Cologne, Germany

16:45–17:15  3D Neural Tissues—In Vitro Models for Neurotoxicity Studies
Jenny Sandström von Tobel, PhD, Swiss Centre of Applied Human Toxicology, University of Lausanne, Lausanne, Switzerland

17:15–17:45  The Relevance of Functional Studies with Fresh Human Isolated Tissues for the Assessment of Safety and Efficacy
Keith Bowers, PhD, Bioppta Ltd., Glasgow, Scotland, United Kingdom

Poster Removal
17:00–19:00
Poster Areas

**Sponsored Presentations**

18:00 – 19:00
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**Thursday October 1**

**SPS Annual Member’s Meeting and Awards Ceremony**

8:30–9:15
Forum Hall

**Distinguished Service Award Presentation**

9:15–9:45
Forum Hall

Proposal for a New Target in Safety Pharmacology
Dennis J. Murphy, PhD, DABT, DSP, GlaxoSmithKline, King of Prussia, PA, United States
NC3Rs Workshop: Housing of Non-Rodents during Telemetry Recordings in Safety Pharmacology and Toxicology Studies

9:45–11:45  Forum Hall
Co-Chairs: Helen Prior, PhD, FSB, DSP, Regulatory Science Associates, Sandbach, United Kingdom, Anna Bottomley, PhD, NC3Rs, London, United Kingdom, and Jason Cordes, Pfizer, Inc., Groton, CT, United States

The NC3Rs, in collaboration with the Safety Pharmacology Society, has convened an international expert working group, including pharmaceutical and biotechnology companies and contract research organisations with the aim of sharing data on the housing of dogs, minipigs and non-human primates during the recording of cardiovascular telemetry data in safety pharmacology and toxicology studies. The group devised a questionnaire to collect information on study design, housing and current opinions on the risks/benefits of group housing non-rodents during the recording of cardiovascular telemetry data and this survey was then sent out to approximately 80 companies worldwide. The results from this survey will be presented and will provide an opportunity to make recommendations on best practice and discuss the current blocks preventing social housing of animals during telemetry recording on safety pharmacology or toxicology studies. This project is co-led on behalf of the SPS by Helen Prior and Jason Cordes, and by Anna Bottomley from the NC3Rs.

9:45–9:50  NC3Rs Introduction
Kathryn Chapman, PhD, NC3Rs, London, United Kingdom

9:50–10:10  Results from the Survey

10:10–10:40  A Debate (for and against) Group Housing of Non-Rodents
“For” Debate: Rob Kaiser, PhD, DABT, Charles River Laboratories, Reno, NV, United States, and Jason Cordes, Pfizer, Inc., Groton, CT, United States

“Agnist” Debate: Jean-Pierre Valentin, PhD, DSP, UCB Biopharma, Braine l’Alleud, Belgium and Eric Delpy, PhD, Biotrial, Rennes, France

10:40–11:40  Audience Discussion
Please participate in expressing concerns and/or asking questions about practicalities of group housing

11:40–11:45  Wrap Up

Lunch Break

11:45–12:15  Forum Hall Foyer

CiPA on Your Mind?

12:15–14:45  Forum Hall
Co-Chairs: Jean-Pierre Valentin, PhD, DSP, UCB Biopharma, Braine l’Alleud, Belgium, and Robert J. Austin-LaFrance, Groton, CT, United States

SPS will bring the debate to a more strategic level to discuss the impact of CiPA on drug discovery and development and how to work together as a community (service and technology providers, pharma, biotechs, regulators, academic institutions) in order to facilitate bringing innovative medicines, that have an acceptable risk/benefit, to patients in need. Updates on CiPA related activities across the globe will also be covered.

12:15–12:30  CiPA introduction—What is it? On-Going Activities (CiPA Steering Team), Next Steps and Timelines
Gary Gintant, PhD, AbbVie, North Chicago, IL, United States

12:30–12:45  Ion Channel Working Group Update and Next Steps
Bernard Fermini, PhD, Global Safety Pharmacology, Pfizer, Groton, CT, United States

12:45–13:00  In Silico Modeling update and Next Steps
Sara Dutta, PhD, US FDA, Silver Spring, MD, United States

13:00–13:15  Current situation and Future Plan in Japanese Activity of Kirishima Meeting
Atsushi Sugiyama, MD, PhD, Department of Pharmacology, School of Medicine, Faculty of Medicine, Toho University, Tokyo, Japan

13:15–13:30  Current Situation and Future Plan in Japan IPS Cardiac Safety Assessment (J-iCSA)
Yuko Sekino, PhD, Division of Pharmacology, National Institute of Health Sciences, Tokyo, Japan

13:30–13:45  A Case Study: How CiPA Would have impacted/Influenced Decision?
Marie-Luce Rosseels, DVM, DSB, UCB Biopharma, Braine l’Alleud, Belgium

13:45–14:00  CiPA, Ion Channels and Stem Cells—A Perspective from an Automated Electrophysiology Technology Provider
Rodolfo Haedo, Vice President USA, Nanion Technologies Inc, North Brunswick, NJ, United States

14:00–14:45  Panel Discussion
Gary Gintant, PhD, AbbVie, North Chicago, IL, United States, Bernard Fermini, PhD, Global Safety Pharmacology, Pfizer, Groton, CT, United States, Marie-Luce Rosseels, DVM, DSP, UCB Biopharma, Braine l’Alleud, Belgium, Blanca Rodriguez, PhD, University of Oxford, Oxford, United Kingdom, Derek Leishman, PhD, DSP, Eli Lilly & Co., Indianapolis, IN, United States, David Strauss, MD, PhD, US FDA, Silver Spring, MD, United States, Krishna Prasad, MD, MHRA, London, United Kingdom, Sara Dutta, US FDA, and Rodolfo Haedo, Vice President USA, Nanion Technologies Inc

President’s Summary and Closing Remarks

14:45–15:15  Forum Hall
Alfred Botchway, PhD, DSP, Xenometrics, LLC.

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