Program Agenda

Tuesday, September 29

Morning

Keynote Plenary

Track A: Central Nervous System—Issue Resolution

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 manifestation of CNS adverse outcome such as effects on balance or locomotion 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, California, United States

10:30-11:00 Delayed Effects Acute versus Repeat Dosing
Karen Tse, AstraZeneca, Macclesfield, United Kingdom

11:00-11:30 Balance, Locomotor-effects
Tbd

11:30-12:00 Central Nervous System Safety Pharmacology: Additional Studies on Cognitive Functions
Christelle Froger-Colléaux, Porsolt S.A.S., Z.A. de Glatigné, France

Track B: Cardiovascular—Cardiovascular Safety Assessment beyond the ECG

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 concomitant 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, Whitehouse Station, NJ, United States

10:30-11:00 Circadian Rhythms of the Cardiovascular function: A Key Element of Cardiosafety Evaluation
Alexandra Bassett, 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
Afternoon

**Track A: Translational Safety Biomarkers—From Preclinical to Clinical**

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  **CVS Effort Overview/CV Biomarker**  
Brian R. Berridge, DVM, PhD, DACVP, GlaxoSmithKline, Research Triangle Park, NC, United States

16:15-16:45  **Neurotox Biomarker**  
FDA Speaker-TBD

16:45-17:15  **PET-imaging in Drug Discovery and Development**  
Éva Lindström Böö, Global PET CoE Manager, AstraZeneca Translational Sciences Centre, Karolinska Institutet, Stockholm, Sweden

17:15-17:45  **PKPD is Essential for Planning, Execution and Evaluation of Studies in Safety Pharmacology**  
Professor Johan Gabrielsson, PhD, Swedish University of Agricultural Sciences, Division of Pharmacology and Toxicology, Uppsala, Sweden

**Track B: Integrative Pharmacology—Case Studies in Diabetes and Pulmonary Arterial Hypertension**

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, Albuquerque, New Mexico

16:45-17:15  **Emerging Treatment Options for Diabetes and Obesity**  
Christoffer Ciemmensen, 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, Sanofi, Frankfurt, Germany
Wednesday, September 30

Morning

Keynote Plenary by Dr. David Sedmera

Track A: Central Nervous System—Sensory System Assessments in Safety Pharmacology
Loss of sight, hearing, smell, taste, or touch secondary to drug treatment dramatically diminishes a patient’s quality of life. There are many drugs that may affect our sensory systems and require specialized safety characterization during drug development. This session will cover the topic of sensory system assessments in Safety Pharmacology. Sensory system safety evaluations are conducted when the core battery is not sufficient to produce a comprehensive understanding of functional changes that occur following drug administration. The endpoints characterized on CNS assays, like the Functional Observational Battery and Irwin Test, provide information on behavior and somatosensory processing which may identify a potential effect, but lack the sensitivity to make definitive determinations concerning system safety. The objective of this session is for attendees to gain an understanding of relevant animal models and techniques used to determine drug safety for vision, hearing, taste, smell, and touch. Speakers will also address different approaches to drug development and study design when there are nonclinical and/or clinical data suggesting a sensory system liability.

10:00-10:30 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

10:30-11:00 Methods for Detecting Adverse Effects on Visual Function
Will S. Redfern, PhD, FBS, FBPharmacolS, DSP, AstraZeneca, Macclesfield, United Kingdom

11:00-11:30 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

11:30-12:00 Long-term Drug-induced Peripheral Neurotoxicity in Cancer Survivors
Prof. Guido Cavaletti, MD, PhD, Head, Experimental Neurology Unit - Director, PhD Program in Neuroscience, Dept. Surgery and Translational Medicine, University of Milano-Bicocca, Monza (MB), Italy

Track B: Cardiovascular—Translation of QT
Requirements for evaluating cardiac safety in drug development have been arguably narrowly focused over the last decade on arrhythmia assessment and even more specifically QTc prolongation. The objective of this session will be to discuss how well the current paradigm for preclinical testing translates to the clinic and informs early clinical development. Presentations will also review how the regulations in clinical development may evolve towards the ultimate goal of incorporating QT assessment in early clinical development with minimum patient risk.

10:00-10:30 How Well Does the hERG Assay Predict Clinical QT Prolongation and Torsades?
Bernard Fermini, PhD, Global Safety Pharmacology, Pfizer, Groton, CT, United States

10:30-11:00 How Do the Preclinical Cardiac Safety Pharmacology Studies Inform Early Clinical Studies?
Corina Dana-Dota, MD, AstraZeneca, Gothenburg, Sweden

11:00-11:30 Can Changes to the Preclinical Paradigm for Cardiac Safety Pharmacology Studies Change the Clinical Requirements for Arrhythmia Assessment?
Nenad Sarapa, MD, Bayer, Whippany, NJ, United States

11:30-12:00 Panel Discussion

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Afternoon

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

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

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**Track B: Novel In Vitro Models—From Stem Cells to Human Tissues**
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 iPSCs 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 Derived from Human Stem Cells as 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, Biopta Ltd., Glasgow, United Kingdom
Thursday, October 1

SPS Annual Members Meeting and Awards Ceremony

**Distinguished Service Award Presentation: Proposal for a New Target in Safety Pharmacology**

*Dr. Dennis Murphy, PhD, DABT, DSP*

**NC3Rs Workshop: Housing of Non-rodents during Telemetry Recordings in Safety Pharmacology and Toxicology Studies**

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.

**CIPA on Your Mind?**

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.

**President’s Summary**