



Safety Pharmacology Society 10th Annual Meeting Program

Monday, September 20, 2010

8:00 AM – 6:00 PM **Continuing Education Courses**

AM 1: Safety Pharmacology: Introduction, Application, and Interpretation

8:00 AM-12:00 PM

Waterfront 3

Course Chairs: Tom Beck, PhD, Covance Laboratories, Inc., Madison, WI and Jay Gizzi, Data Sciences International, St. Paul, MN

Safety pharmacology is a relatively new and rapidly growing discipline. The primary regulatory documents governing safety pharmacology is the ICH Harmonised Tripartite Guidelines S7A and S7B. The stated goal of these documents is “To help protect clinical trial participants and patients receiving marketed products from potential adverse effects of pharmaceuticals”. These ICH documents serve as guidelines and provide recommendations regarding the approach to evaluate therapeutics with respect to core organ systems (cardiovascular, respiratory and central nervous systems), supplemental organ systems (e.g., GI and renal) and follow-up studies to describe effects and mechanisms of action. The objective of this course is to provide an overview of safety pharmacology, current regulations and how they relate to drug development. This course is a broad overview of the common test systems and is therefore a good prerequisite to the more advanced continuing education courses offered. The course will include presentations from principal scientists with emphasis on the regulatory environment and the current state-of-the-art methodologies specific to each of the core battery and supplemental organ systems assays. These didactic presentations will be followed by a presentation and group discussions on integrated risk assessment in safety pharmacology.

8:00-8:40 AM **Nonclinical Safety Pharmacology: Integrated Risk Assessment**

Tom Beck, PhD, Covance Laboratories, Inc., Madison, WI

8:40-9:20 AM **Intro to Cardiovascular Safety Pharmacology**

Brian Roche, PhD, Battelle Memorial Institute, Columbus, OH

9:20-10:00 AM **CNS Safety Pharmacology: S7A Guidelines and Beyond**

Paul Moser, PhD, Porsolt and Partners Pharmacology, Boulogne-Billancourt, France

10:00-10:30 AM **Break**

10:30-11:15 AM **Respiratory Safety Pharmacology: Current Strategy and Methodologies**

Dennis Murphy, PhD, DABT, GlaxoSmithKline, Philadelphia, PA



11:15-12:00 PM **Overview of Renal and GI Supplemental Studies**
Russell Bialecki, PhD, AstraZeneca Pharmaceuticals, Wilmington, DE

AM2: Intermediate Cardiovascular

8:00-12:00 PM
Cambridge

Course Chairs: Dusty Sarazan, DVM, PhD, Data Sciences International St. Paul, MN and Blake D. Anson, PhD, Cellular Dynamics International, Inc., Madison, WI

This Intermediate Cardiovascular course is intended for individuals with previous knowledge of cardiovascular safety pharmacology as well as those interested in learning more about cardiovascular safety studies. This is an “everything you want to know about cardiovascular system” course. With an over-arching leaning toward safety pharmacology applications, lectures covered in this course will include overviews of electrophysiology, electrocardiography, cardiovascular physiology-contractility, hemodynamics, the utility of stem cell technologies, and non-invasive measurements of cardiac function. Active participation from the attendees is highly encouraged.

- 8:00-8:10 AM** **Introduction**
- 8:10-9:05 AM** **hERG and Stem Cells: The Past, Present, and Future in Safety Pharmacology**
Blake D. Anson, PhD, Cellular Dynamics International, Inc., Madison, WI
- 9 :05-10 :00 AM** **Cardiovascular Physiology-Contractility and Hemodynamics**
Steve Swoap, PhD, Williams College, Williamstown, MA
- 10:00-10:30 AM** **Break**
- 10:30-11:15 AM** **The Role of In Vivo Models in Cardiovascular Safety Assessment**
Dusty Sarazan, DVM, PhD, Data Sciences International St. Paul, MN
- 11:15-12:00 PM** **Assessment of Cardiac Function in Laboratory Animals: "Images and Sounds"**
John Bonagura, DVM, MS, DACVIM, The Ohio State University, Columbus, OH



AM3: Safety Pharmacology Study Design and Data Analysis

8:00-12:00 PM

Beacon Hill 1

Course Chairs: George P. Thomas, MSc, PhD, Alcon Research, Ltd., Fort Worth, TX

Have you wondered about the right design for a Safety Pharmacology study? Is randomized Latin square design better than dose increment design in a telemetry study? Should I have male and female rats in my Irwin study? My data show statistical significance, but is it really a biologically relevant adverse effect? Should I use rats or guinea-pigs for my respiratory study? Which is the best QTc correction formula for telemetry monkey studies?

This course is designed to provide an overview of regulatory safety pharmacology study designs and analysis for NCEs and biologics. Basic questions arising from the practice of Safety Pharmacology will be addressed. The course will examine various study designs commonly utilized for ICH S7A- and S7B- guided studies such as Modified Irwin, Cardiovascular Telemetry, Pulmonary Function and hERG. Topics discussed will include appropriate test systems, different dosing paradigms, data analysis techniques, QT correction and importance of biological relevance. Specific questions/suggestions/cases from participants will be addressed / discussed during the last 30 minutes of the course.

8:00-8:10

Introduction

8:10-9:05 AM

Design of Safety Pharmacology Studies

Scott Mittelstadt, PhD, Abbott Laboratories, Abbott Park, IL

9:05-10:00 AM

The Use of Statistics in Safety Pharmacology

Dingzhou (Dean) Li, PhD, Pfizer Global Research and Development, Groton, CT

10:00-10:30 AM

Break

10:30-11:15 AM

Heart Rate Correction of the QT Interval

Henry Holzgrefe, PhD, F. Hoffmann-La Roche AG, Basel, Switzerland

11:15-12:00 PM

Strategy for Safety Pharmacology Evaluation for Biologics

Hugo Vargas, PhD, Amgen Inc., Thousand Oaks, CA

**8:00-12:00 PM
Beacon Hill 2-3**

AM4: Intermediate Central Nervous System Safety Pharmacology

Course Chairs: Wael M.Y. Mohamed, MBBCh, The Pennsylvania State University, State College, PA and Greet Teuns, DVM, Johnson & Johnson Research & Development, Beerse, Belgium



Animal models are essential to understand human disorders. In fact, in animals we can administer drugs in different doses and monitor the possible adverse effects and safety margins. For instance, using the rodent models has enabled us to identify some of the neurological changes underlying behavioral aspects of Attention Deficit Hyperactivity Disorder (ADHD). There are several animal models for studying ADHD, each of them has pros and cons; for example, some of these models have decreased in the extra-cellular dopamine (DA) concentration, while DA concentration has been increased in other models. Therefore, it is essential to study animal models to fully understand the neuropathology of ADHD. Moreover, using such animal models is useful in testing new compounds which might be useful in the alleviation of ADHD signs and symptoms.

Given the complex and diverse functions of the central nervous system, this course is designed to describe the validity of the different animal models used to study ADHD. This is followed by the use of multidisciplinary approaches including neurobiological, neurophysiological, neuropathological, and/or behavior techniques that is used. Examples of other models used to assess the potential for adverse neurological effects such as learning and memory deficits, seizure potential, abuse liability, and more will be discussed.

This course will explore some of the more advanced behavioral and electrophysiological techniques available for evaluation of key nervous system functions that are not adequately addressed by the animal models. These include assessment of abuse potential, EEG, net station and brain vision analyzer.

8:00-8:10 AM	Introduction
8:10-8:40 AM	Neurobiology of ADHD <i>Russell W. Brown, PhD, East Tennessee State University, Johnson City, TN</i>
8:40-9:20 AM	Clinical Assessment of ADHD: From Rating Scales to Neurophysiology <i>Gahan Pandina, PhD, Johnson & Johnson Pharmaceutical Research & Development, Titusville, NJ</i>
9:20-10:00 AM	Animal Models of ADHD <i>Richard M. Kostrzewa, PhD, East Tennessee State University, Johnson City, TN</i>
10:00-10:20 AM	Break
10:20-11:00 AM	Pharmacological Treatments of ADHD <i>Frank Tarazi, PhD, MBA, MBBS, Harvard Medical School & Mclean Hospital, Belmont, MA</i>
11:00-11:40 AM	Histamine H3 Receptor Antagonists in Preclinical Models of Cognition



Pascal Bonaventure, PhD, Johnson & Johnson Pharmaceutical Research & Development, San Diego, CA

11:40-12:00 PM Panel Discussion

12:00-2:00 PM Lunch Break

PM5: Pharmacokinetics / Dried Blood Spot Technologies

2:00-6:00 PM

Waterfont 3

Course Chairs: Lewis B. Kinter, PhD, AstraZeneca Pharmaceuticals, Unionville, PA and Stephen Ploch, PhD, DABT, Covance Laboratories, Madison, WI

Pharmacokinetic principles and technologies characterize and quantify exposure to parent drug and metabolites in preclinical studies (including Safety Pharmacology) and in clinical trials. Safety pharmacology studies are best interpreted, and potential drug effects on organ system functions mitigated in terms of assessment of human risk through comparative pharmacokinetics. However, while associations of drug-induced changes in organ functions and exposures in safety pharmacology studies are best accomplished when these measurements are collected coincidentally in the same animals, the blood collection procedures and necessary blood volumes have necessitated use of separate satellite groups or reliance on pharmacokinetic/toxicokinetic assessments in separate studies, especially when using small animals. Recent advances in microsampling and microanalysis technologies now permit safety pharmacology and pharmacokinetic endpoints in the same study animals without compromise, affording opportunities to improve study data quality, reduce animal study numbers (Refinement and Reduction improvements), and to identify biomarkers with which to mitigate risk in human clinical trials. This course will deliver general principles and technologies of modern pharmacokinetic sampling, data acquisition, manipulation and interpretation, and current status of microsampling/dried blood spot technologies for safety pharmacologists.

2:00-2:30 PM Assessing Test Article Exposure in Safety Pharmacology: Expectations & Challenges

Lewis B. Kinter, PhD, AstraZeneca Pharmaceuticals, Unionville, PA

2:30-3:00 PM General Presentation of Pharmacokinetic Principles and Practices for Safety Pharmacologists

Chengwei Fang, PhD, Pharmaron, Beijing, China

3:00-3:30 PM Break

3:30-4:15 PM Microsampling and Dried Blood Spot Technologies

Stephen Ploch, PhD, DABT, Covance Laboratories, Madison, WI



4:15-6:00 PM

Workshop on Dried Blood Spots

Lead by Stephen Ploch, PhD, DABT, Covance Laboratories, Madison, WI

'Hands on' experience with DBS, including videos of sampling and spotting procedures & techniques, opportunity to practice with surrogate materials, and discussions with staff who have operationalized DBS in their laboratories.

PM6: Safety Pharmacology in Early Drug Evaluation and Development: How Can Frontloading Save Time and Money?

2:00-6:00 PM

Cambridge

Course Chairs: Mary Jeanne Kallman, PhD, Covance Laboratories, Inc., Greenfield, IN and Pierre Morissette, PhD, Merck & Co., Inc., West Point, PA

This course examines the practice and philosophy of conducting studies designed to illuminate safety risk earlier in the drug development process (frontloading). Frontloading can be defined as those safety assessments conducted during lead optimization of compounds before selection as a candidate drug for development and before regulatory studies are performed. The goal of early safety assessment or frontloading is to provide quality safety data that can drive development decisions much earlier in the flow scheme. Such studies also save resources by reducing late stage attrition. The course will examine what methods and processes have been successfully applied at reducing attrition and to provide "no surprises" approach to later stage GLP safety studies. Various practices and philosophy will be discussed by the speakers with adequate time for class discussion.

2:00-2:15 PM

Introduction

Mary Jeanne Kallman, PhD, Covance Laboratories, Inc., Greenfield, IN

2:15-3:00 PM

Mitigation against Pharmacodynamic Toxicities in the Discovery

Alan Bass, PhD, Merck Research Laboratories, Kenilworth, NJ

3:00-3:30 PM

Break

3:30-4:15 PM

Pick the Best Compound Early- The Role of Safety Pharmacology

Silvana Lindgren, PhD, Safety Assessment, AstraZeneca R&D, Sodertalje, Sweden

4:15-6:00 PM

Workshop Exercise: Safety Pharmacology-It's Role in Early Research



Mark Holbrook, PhD, Pfizer Ltd., Kent, England and Derek Leishman, PhD, Lilly Research Laboratories, Indianapolis, IN

PM7: Drug Abuse Liability Testing
2:00-6:00 PM
Beacon Hill 1

Course Chairs: Greet Teuns, DVM, Johnson & Johnson Research & Development, Beerse, Belgium

Drug abuse liability testing has become a hot topic in drug development and in particular, within the nonclinical safety evaluation arena since the release of the EMEA guideline (March 2006), the ICH guideline (June 2009) and most recent U.S. FDA draft guidance (January 2010).

This course is meant to discuss the various topics within this field:

- The pathways responsible for development of potential abuse will be introduced to gain more understanding at the molecular level.
- The different aspects of drug abuse (physical dependence, conditioning and rewarding, reinforcing properties) and the various methods to investigate each of these dimensions will be discussed in detail. The impact of the GLP requirements as stated within the guidelines will also be assessed.
- For new molecular entities (NMEs) with novel mechanisms of action: what is a complete and robust nonclinical package on drug abuse potential for these compounds? What are possible variables in the test designs or within the package itself that might contribute to the identification of drug abuse potential if modified on a scientific basis?

Lastly the translational approach will be taken into account. What's the predictability of a preclinical package for drug abuse potential for NMEs in development and how will the next steps towards clinical evaluation be set?

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|---------------------|---|
| 2:00-2:30 PM | Drug Abuse and Pharmacological Pathways
<i>John R. Atack, PhD, Neuroscience Discovery, Johnson & Johnson PRD, Beerse, Belgium</i> |
| 2:30-3:00 PM | Preclinical Testing of Drug Abuse: Physical Dependence and Methods to Evaluate Withdrawal Effects in Rats
<i>Paul Moser, PhD, Porsolt and Partners Pharmacology, Boulogne-Billancourt, France</i> |
| 3:00-3:30 PM | Break |
| 3:30-4:10 PM | Preclinical Testing of Drug Abuse: Drug Discrimination Learning and Conditioned Place Preference in the Rat
<i>Karen Roels, DVM, Janssen Pharmaceutica NV, Beerse, Belgium</i> |
| 4:10-4:50 PM | Preclinical Testing of Drug Abuse Animal Models: The Self-administration Model
<i>Andy Mead, DPhil, Pfizer Inc., Sandwich, Kent, United Kingdom</i> |



4:50-5:30 PM **The Regulatory Aspects on Drug Abuse Liability Testing**
Carrie Markgraf, MD, PhD, Schering-Plough Research Institute, Lafayette, NJ

5:30-6:00 PM **Translational Approach for Abuse Liability Assessment**
Mary Jeanne Kallman, PhD, Covance Laboratories, Inc., Greenfield, IN

PM8: ECG Reading and Interpretation

2:00-6:00 PM
Beacon Hill 2-3

Course Chairs: Alfred Botchway, PhD, Xenometrics LLC, Stillwell, KS

This course will be taught by world leaders in the fields of human and veterinary Cardiology. This CE course is designed to help students, technicians and other allied health personnel acquire the skills to analyze and interpret fundamental changes in ECG morphology and identify common arrhythmias. The course will be a combined lecture & workshop, covering topics such as basic electrocardiography including a qualitative and quantitative assessment of the ECG. By the end of the day, attendees are expected to be able to:

1. Identify the components of a normal ECG
2. Recognize common arrhythmias
3. Perform quantitative measurement of PR, QRS and QT durations and intervals

Sample ECGs will be provided and, following practical, hands on instruction, attendees will be expected to read and interpret a test set. A passing grade will result in presentation of a certificate documenting proficiency and signed by the faculty.

Participation in the CE course, Intermediate Cardiovascular Safety Pharmacology, is strongly recommended prior to attending this class.

6:00-7:00 PM **Exhibit Opening & Welcome Reception**
Commonwealth Complex **10th Anniversary Celebration**
(Harbor Level)

Tuesday, September 21, 2010

9:00-9:15 AM
Amphitheatre **Welcome and Announcements**
Kristy D. Bruse, PhD, President of the Safety Pharmacology Society



9:15-10:00 AM
Amphitheatre

Plenary Session 1

Co-Chairs: Kristy D. Bruse, PhD, Lovelace Respiratory Research Institute, Albuquerque, NM and Donald Hodges Jr., PhD, Vertex Pharmaceuticals, Cambridge, MA

President's Keynote Address:

Biomaterials in Their Role in Creating New Approaches for the Delivery of Drugs, Proteins, Nucleic acids, and Mammalian cells

Keynote: Robert S. Langer, PhD Massachusetts Institute of Technology, Cambridge, MA

10:00-10:30 AM **Break**

A: Government, Regulatory, Academic and Societal Issues

Interactions between Academics and Industry: The Michigan State Experience

10:30-12:00 PM

Waterfront 1

Track Leader: Scott W. Mittelstadt, PhD, Abbott Laboratories, Abbott Park, IL

Co-Chairs: Scott W. Mittelstadt, PhD, Abbott Laboratories, Abbott Park, IL and Jason H. Gill, Ph.D., University of Bradford, West Yorkshire, UK

This is the first of two sessions, which will address key aspects in academic – industry interactions. This session will focus on what industry and academics can do to improve both communications and the business interactions and will focus on some of the experiences at Michigan State University.

The first presentation will focus on efforts at Michigan State to develop a Masters Degree Program in Integrative Pharmacology. This program has been developed with the goal of preparing students for careers in industry while focusing on non-traditional students who have already started their careers. The presentation will focus on how they have set out to design a curriculum that would educate students in a relevant way to help them meet their career goals. The presentation will also discuss potential ways that industry can help academic programs such as this.

The second presentation will focus on research interactions between industry and academics through Michigan State's In vivo Pharmacology Facility. This presentation will focus on expectations and needs from both an industry and academic perspective.

10:30-10:35 AM **Introduction**

10:35-11:15 AM **Understanding and Meeting the Educational Needs of Industry**

Joseph R. Haywood, PhD, Michigan State University, East Lansing, MI



11:15-12:00 PM

How to Develop Effective Private Sector Academic Interactions: "You want me to deliver what by when?!!"

Marc Bailie, DVM, PhD, Michigan State University, East Lansing, MI

B: Trends and Technical Advances

Early Prediction of Functional Liabilities

10:30-12:00 PM

Waterfront 2

Track Leader: Kathryn Bibeau, BSc, Intrinsik Health Sciences, Inc., Mississauga, ON, Canada

Co-Chairs: Andrew J. Sonderfan, PhD, DABT, Synta Pharmaceuticals Corp., Lexington, MA and Maxim Soloviev, MD, PhD, Incyte Corp., Wilmington, DE

It's well accepted that, since the 1980s, drug metabolism and pharmacokinetics (DMPK) has successfully and sharply reduced the rate of attrition for clinical candidates destined to fail because of PK issues. However nonclinical safety (Toxicology, Safety Pharmacology) has not fared nearly as well. We're somewhat more than ten years along with SP as a formally-recognized discipline; not coincidentally about a decade since the implementation of the ICHS7A ("Safety Pharmacology Studies for Human Pharmaceuticals") guideline. Are we making progress in successfully identifying, early, those compounds that would later fail for nonclinical safety reasons? This session will survey efforts to identify and implement early predictors of a clinical candidate's functional liabilities.

10:30-10:35 AM

Introduction

10:35-11:05 AM

Urinary Biomarkers of Drug-Induced Kidney Injury: Status and Future Opportunities

Lewis B. Kinter, PhD, AstraZeneca Pharmaceuticals, Unionville, PA

11:05-11:35 AM

Complementing S7A Safety Studies with Counter-Screens of Ion Channels and GPCRs

Arthur B. Brown, MD, PhD, ChanTest, Inc., Cleveland, OH

11:35-12:00 PM

Statistical Modeling of Telemetry Cross-Over Studies with Serial Correlation within Periods

Doris Damian, PhD, Vertex Pharmaceuticals, Cambridge, MA

C: Translational-Preclinical to Clinical

Oncology-Unique Challenges for Safety Pharmacology

10:30-12:00 PM



Waterfront 2

Track Leader: JoAnne Saye, PhD, AstraZeneca Pharmaceuticals, Wilmington, DE

Chair: Niels-Christian Ganderup, MSc, Ellegaard Göttingen Minipigs, Dalmose, Denmark and Claudio Arrigoni, DBiol, Accelera S.r.l., Nerviano, Italy

This session will focus on the ICH S9 Guideline (Nonclinical evaluation for anticancer pharmaceuticals) which became effective at the end of 2009. The session will provide a regulatory and industry perspective on the challenges of this Guideline with regards to preclinical development including Safety Pharmacology.

In addition, some case studies on Safety Pharmacology in oncology development will be presented as well. These cases will serve as examples of how Safety Pharmacology for preclinical oncology development was handled before the ICH S9 guideline became effective and how different approaches could be handled in the future.

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| 10:30-10:35 AM | Introduction |
| 10:35-11:05 AM | ICH S9 – A Regulator’s Perspective
<i>John Leighton, PhD, U.S. Food and Drug Administration, Silver Spring, MD</i> |
| 11:05-11:35 AM | Preclinical Development of Oncology Therapeutics
<i>Daniel Lapadula, PhD, Novartis, East Hanover, NJ</i> |
| 11:35-12:00 PM | Case Studies: Retrospective Analysis of Oncology Therapeutics Pre and Post ICH S9
<i>Rocio Lopez, PhD, Furiex Pharmaceuticals, Morrisville, NC</i> |
| 12:00-2:00 PM | LUNCH Break (Exhibit Hall) Stand-up Buffet Provided
<i>Visit Vendors and Poster Presentations</i> |
| 2:00-3:00 PM | Invited Oral Communications Session 1 |
| | 2:00-2:15 PM Invited Speaker 1 |
| | 2:15-2:30 PM Invited Speaker 2 |
| | 2:30-2:45 PM Invited Speaker 3 |
| | 2:45-3:00 PM Invited Speaker 4 |
| 2:00-3:00 PM | Invited Oral Communications Session 2 |
| | 2:00-2:15 PM Invited Speaker 5 |



2:15-2:30 PM	Invited Speaker 6
2:30-2:45 PM	Invited Speaker 7
2:45-3:00 PM	Invited Speaker 8

2:00-3:00 PM Invited Oral Communications Session 3

2:00-2:15 PM	Invited Speaker 9
2:15-2:30 PM	Invited Speaker 10
2:30-2:45 PM	Invited Speaker 11
2:45-3:00 PM	Invited Speaker 12

3:00-4:00 PM Invited Oral Communications Session 4

3:00-3:15 PM	Invited Speaker 13
3:15-3:30 PM	Invited Speaker 14
3:30-3:45 PM	Invited Speaker 15
3:45-4:00 PM	Invited Speaker 16

3:00-4:00 PM Invited Oral Communications Session 5

3:00-3:15 PM	Invited Speaker 17
3:15-3:30 PM	Invited Speaker 18
3:30-3:45 PM	Invited Speaker 19
3:45-4:00 PM	Invited Speaker 20

3:00-4:00 PM Invited Oral Communications Session 6

3:00-3:15 PM	Invited Speaker 21
3:15-3:30 PM	Invited Speaker 22
3:30-3:45 PM	Invited Speaker 23
3:45-4:00 PM	Invited Speaker 24

4:00-4:30 PM Break (Exhibit Hall)
Visit Vendor and Poster Presentations

A: Government, Regulatory, Academic and Societal Issues
 Case Studies of Start-up Companies: Transition of Technology from Academics to Industry

4:30-6:00 PM
Waterfront 1

Track Leader: Scott W. Mittelstadt, PhD, Abbott Laboratories, Abbott Park, IL
Co-Chairs: Franz J. Hock, PhD, CERB, Dieburg, Germany and Lothar Meister, MS., Ciba, Inc., Basel, Switzerland



This is the second of two sessions that will address key aspects in academic – industry interactions. Over the past 10 years many start-up companies were founded from technology that was initially discovered in academic institutions. This session will address a variety of case studies where technology was transferred from academics into product development. The speakers will present their different experiences in transferring technology from the university to industry. These will allow the audience to compare and contrast business models that have been used under the different scenarios presented. During the last part of this session, there will be a panel discussion allowing more in-depth questions across the three business models.

- 4:30-5:00 PM** **A Process for Identifying and Commercializing Novel Academic-based Technology**
Ronald Shebuski, PhD, MedElite, Inc., Ann Arbor, MI
- 5:00-5:30 PM** **Bringing VPM1002, a Genetically Modified Live Vaccine, from Bench into Man: Experiences of a Recent Collaboration between Private and Public Sectors**
Bernd Eisele, MD, Vakzine Projekt Management GmbH, Hannover, Germany
- 5:30-6:00 PM** **Genzyme Corporation's Initiative in Discovery of Antiparasitic Agents for Neglected Diseases of the Third World: A Case Study of the Exchange of Technology between Academia, Industry and Public Private Partnership**
Edmund J. Sybertz, PhD, Genzyme Corporation, Cambridge, MA

B: Trends and Technical Advances

Advances in CNS

4:30-6:00 PM

Waterfront 2

Track Leader: Kathryn Bibeau, BSc, Intrinsik Health Sciences Inc., Mississauga, ON, Canada

Co-Chairs: Mark A. Osinski, PhD, Covance Laboratories, Madison, WI and Tiffini K. Brabham, DVM, PhD, DABT, Pfizer Ltd., New York, NY

As Safety Pharmacology continues to mature as a distinct discipline within drug development, focus is expanding beyond cardiovascular liability screening. Integration of drug effects on the CNS no longer needs to be confined to an Irwin assay or functional observational battery.

Recent technological advances have made practical the translation of clinical approaches to the nonclinical realm. Neuroimaging techniques, including fMRI, PET, and SPECT in fully conscious animals, are increasingly being used to assess neurotoxicity. De-risking of seizure liability using higher throughput methods and fewer animals can occur much earlier in the drug discovery process. Come join us to hear



about these and other state-of-the-art methods for exploring test article effects on CNS function.

4:30-5:00 PM ***Using Awake Animal Imaging to Finger Print for CNS Liability: Risk of Suicide?***

Craig F. Ferris, PhD, Northeastern University, Boston, MA

5:00-5:30 PM ***Moving Beyond the FOB: A Snapshot of the CNS De-Risking Toolbox***

Keri E. Cannon, PhD, Pfizer Inc., Groton, CT

5:30-6:00 PM ***Preclinical Assessment of Seizure Liability***

Alison Easter, AstraZeneca Pharmaceuticals, Wilmington, DE

C: Translational-Preclinical to Clinical

Biologics

4:30-6:00 PM

Waterfront 3

Track Leader: JoAnne Saye, PhD, AstraZeneca Pharmaceuticals, Wilmington, DE

Co-Chairs: Hugo M. Vargas, PhD, Amgen Inc., Thousand Oaks, CA and Sarra Laycock, PhD, Aptuit, Riccarton, Scotland

Safety Pharmacology studies are a critical component of preclinical drug development, and the execution of these studies is described by the ICH S7A and S7B guidelines. While these guidelines have shaped the evaluation of small molecule therapeutics, the application of these studies to the safety assessment of protein or RNA-based therapeutics may not be straightforward and challenging. In addition, the pharmacokinetic characteristics of biologicals are unique and need to be considered in the dose selection and design of safety pharmacology, toxicology, and first-in-human studies. This session will cover topics of importance to safety pharmacologist's working with biotechnology-derived therapeutics, and the development of safety pharmacology strategy.

4:30-5:00 PM ***Alternative Animal Models for Species-specific Biopharmaceuticals: A Case Study***

James Murray, BS, LAT, Genzyme, Cambridge, MA

5:00-5:30 PM ***RNA Therapeutics: Preclinical Challenges in Safety Evaluation***



Christina Gamba-Vitalo, PhD, Alnylam Pharmaceuticals, Cambridge, MA

5:30-6:00 PM **PK of Biotherapeutics: Quantitative Dose Selection for Preclinical Safety and First-in-Human Studies.**
Jennifer Dong, PhD, Amgen Inc., Thousand Oaks, CA

6:00 PM **Adjourn SPS Annual Meeting Day 1**
Ancillary Events Begin

Wednesday, September 22, 2010

A: Government, Regulatory, Academic and Societal Issues

Drug Dependency (Non Human Primates vs. Rodents)

9:00-10:00 AM

Waterfront 1

Track Leader: Scott W. Mittelstadt, PhD, Abbott Laboratories, Abbott Park, IL
Co-Chairs: Philip Atterson, MSc, WIL Research Laboratories, Ashland, OH and
Paul Tarantino, PhD, Sepracor, Inc., Marlborough, MA

The recently issued U.S. FDA Guidance for Industry draft document entitled "Assessment of Abuse Potential of Drugs" discusses potentially useful animal behavioral pharmacology study designs. Within this section of the document, the use of several species is indicated (usually rodents and primates).

This session intends to address the potential issues surrounding appropriate species selection for abuse liability testing. The session will include a brief review of the models in each species with a focus on the strength and weaknesses of each approach. This will be followed by an open discussion of when a rodent or a nonhuman primate model would provide the most valid approach for successful evaluation of the abuse potential of novel medications in development.

9:00-9:30 AM **TITLE**
S. Stevens Negus, PhD, Virginia Commonwealth University, Richmond, VA

9:30-10:00 AM **TITLE**
Katherine L. Nicholson, DVM, PhD, Virginia Commonwealth University, Richmond, VA

10:00-10:30 AM **Break (Exhibit Hall)**



Visit Vendor and Poster Viewing

B: Trends and Technical Advances

Application of Stem Cell Technology for Identifying Cardiac Liabilities

9:00-10:00 AM

Waterfront 2

Track Leader: Kathryn Bibeau, BSc, Intrinsic Health Sciences Inc., Mississauga, ON, Canada

Co-Chairs: Anthony Bahinski, PhD, Wyss Institute for Biologically Inspired Engineering at Harvard University, Boston, MA and Khuram W. Chaudhary, PhD, GlaxoSmithKline, King of Prussia, PA

Muscular thin films (MTFs) are a biohybrid material that integrates a tissue engineered monolayer of cardiac muscle cells with a thin, elastic film (Feinberg et al, 2007). Dr. Parker has adapted the muscular thin film (MTF) technique to create microstructured tissues in vitro and directly measure stress generation as a function of structural, mechanical, electrical and pharmacological perturbation. The technology has been demonstrated to work with cultured rat neonatal ventricular cardiomyocytes and mouse ES derived cardiomyocytes. In this session, we will discuss the potential of this technology platform to offer a critical new tool to develop unique in vitro model systems for screening drugs in drug discovery and potentially predicting or anticipating cardiac adverse effects in humans.

9:00-10:00 AM ***In Vitro Cell and Tissue Engineering for Drug Safety and Efficacy Screening***

Kevin Kit Parker, PhD, Harvard University, Boston, MA

10:00-10:30 AM **Break (Exhibit Hall)**
Visit Vendor and Poster Viewing

C: Translational-Preclinical to Clinical

Medical Toxicology: Extension of Safety Pharmacology Principles to a Clinical Setting

9:00-10:00 AM

Waterfront 3

Track Leader: JoAnne Saye, PhD, AstraZeneca Pharmaceuticals, Wilmington, DE

Co-Chairs: Carrie Markgraf, MD, PhD, Merck Research Laboratories, Lafayette, NJ and JoAnne Saye, PhD, AstraZeneca Pharmaceuticals, Wilmington, DE



Nearly two million poisoning exposures are reported to Poison Control Centers every year, with an estimated two to three million cases unreported. Of the top ten most common categories of poisoning exposures that result in fatalities, five are prescription pharmaceuticals (#1 antidepressants, #2 analgesics, #3 sedatives, #5 cardiovascular drugs and #9 asthma medications).

Medical Toxicology is the multidisciplinary subspecialty of clinical medicine that focuses on the diagnosis, management and prevention of adverse health effects due to medications, or workplace/environmental chemical exposure. Medical Toxicology is a unique and complex specialty with ties to Emergency Medicine, Occupational Medicine and Pediatrics. As such, it shares scientific interests with the field of Safety Pharmacology. Life-threatening pharmacologic effects of medications on the CNS, respiratory and cardiovascular systems often confront the medical toxicologist treating a patient suffering acute poisoning or overdose. Investigating mechanisms of disease or poisoning caused by accidental or intentional overdose is a goal of medical toxicologists. This session will provide an overview of the field of Medical Toxicology and an understanding of its relationship to Safety Pharmacology endpoints. The relevance of Safety Pharmacology principles to the clinical overdose setting and the translation of preclinical data to the Medical Toxicology setting will be discussed.

- 9:00-9:30 AM** **Medical Toxicology: A "New" Specialty with Old Roots**
Erica Liebelt, MD, University of Alabama School of Medicine and President, American College of Medical Toxicology, Birmingham, AL
- 9:30-10:00 AM** **Drugs and Poisons: Medical Toxicology at the Bedside**
Paul Wax, MD, FACMT, University of Texas Southwestern Medical Center, Dallas, TX
- 10:00-10:30 AM** **Break (Exhibit Hall)**
Visit Vendor and Poster Viewing
- 10:30-11:30 AM** **Safety Pharmacology Society Annual Business Meeting and Awards**
Announcement of Poster Competition recipients, Jr. and Student Travel Award recipients
- 11:30-12:00 AM** **Distinguished Service Award Presentation**
Toxicologists and Safety Pharmacologists: Friends or Rivals?
Gerd Bode, MD, PhD, Consultant, Goettingen, Germany



**12:00-2:00 PM LUNCH Break (Exhibit Hall)
Visit Vendors and Poster Viewing**

A: Government, Regulatory, Academic and Societal Issues

Biodefense Talk

2:00-4:00 PM

Waterfront 1

*Track Leader: Scott W. Mittelstadt, PhD, Abbott Laboratories, Abbott Park, IL
Co-Chairs: Heather A. Manley, PhD, U.S. Department of Defense, Transformational Medical Technologies Initiative, Aberdeen Proving Ground, MD and Steve Hachtman, MA, Data Sciences International, St. Paul, MN*

This session will discuss challenges for both the Safety Pharmacology and Biodefense communities in determining the predictive value of preclinical models to observed effects or adverse events associated with drugs that have progressed into clinical trials. Both communities are interested in technologies enabling better identification of lead compounds to reduce attrition earlier in the pipeline.

All medical countermeasures developed for biodefense indications (e.g., anthrax, Ebola, smallpox) must go through the U.S. FDA regulatory process. An additional challenge is that for biodefense indications, it is anticipated that licensure of medical countermeasures will be conducted under the U.S. FDA Animal Rule (21 CFR Parts 314 and 601), due to ethical constraints surrounding efficacy testing.

The Biodefense community is especially concerned with investing in technologies (whether for whole animal models or for *in vitro* studies such as the Langendorff prep for cardiac safety studies) likely to yield near-term benefits and seeks to learn from the experience of the Safety Pharmacology Society in development of preclinical models.

2:00-2:30 PM

TITLE

Christopher P. Regan, PhD, Merck, West Point, PA

2:30-3:00 PM

TITLE

Lisa E. Hensley, PhD, US Army Medical Research Institute of Infectious Diseases, Frederick, MD

3:00-3:30 PM

TITLE

Frederic J. Marsik, PhD, ABMM, U.S. Food and Drug Administration, Silver Spring, MD

3:30-4:00 PM

TITLE

Chad Roy, PhD, Tulane National Primate Research Center, Covington, LA



B: Trends and Technical Advances

Emerging Methodologies for Evaluating Respiratory Function in Ambulatory Non-Rodent Animal Models

2:00-4:00 PM

Waterfront 2

Track Leader: Kathryn Bibeau, B Sc, Intrinsic Health Sciences Inc., Mississauga, ON, Canada

Co-Chairs: Dennis Murphy, PhD, GlaxoSmithKline, King of Prussia, PA and Philip Atterson, MS, WIL Research Laboratories, Ashland, OH

Symposium will focus on emerging new technologies that are being developed to monitor respiratory function continuously for extended periods of time in conscious, non-restrained (resting) dogs and monkeys. The theoretical basis, current uses, advantages and limitations of each methodology will be discussed. How these new methodologies expand our current capabilities in Safety Pharmacology will also be presented.

2:00-2:30 PM

Advantages of ambulatory monitoring of respiratory function in non-rodent models in Safety Pharmacology

Dennis J. Murphy, PhD, GlaxoSmithKline, King of Prussia, PA

2:30-3:00 PM

The Use of Respiratory Inductive Plethysmography for Non-Invasive Evaluation of Pulmonary Function in Unrestrained Dogs and Monkeys

Aidan Curran, PhD, Huntingdon Life Sciences, East Millstone, NJ

3:00-3:30 PM

Electromyographic Recordings from Respiratory Muscle as a Method for Evaluating Respiratory Function in Dogs and Monkeys

Stephane Milano, PhD, Ricera Biosciences, LLC, Lyon, France

3:30-4:00 PM

Thoracic Impedance as a Method for Evaluating Respiratory Function in Dogs and Monkeys

Boyce Moon, MS, Data Sciences International, New Brighton, MN

C: Translational-Preclinical to Clinical

Challenges and Controversies Associated with the Study of Cardiovascular Risks from Therapeutic for Type 2 Diabetes

2:00-4:00 PM

Waterfront 3

Track Leader: JoAnne Saye, PhD, AstraZeneca Pharmaceuticals, Wilmington, DE



Co-Chairs: Alan Bass, PhD, Merck Research Laboratories, Kenilworth, NJ and Peter Hoffmann, Ph.D., Novartis Pharma AG, Basel, Switzerland

Development of drugs for the treatment of type 2 diabetes has become more complex as a result of the experience with registered treatments that have demonstrated significant cardiovascular hemodynamic adverse events (e.g., congestive heart failure associated with PPAR γ agonists), as well as those events that have presented in various other forms (e.g., potential for cardiac arrhythmias and myocardial infarction associated, respectively, with certain sulfonylureas and PPAR γ agonists) and were only evident through a meta analysis of a body of clinical data.

In some cases, these concerns are not necessarily linked to known mechanisms of cardiovascular toxicity, but illustrate the unique challenges with which safety pharmacologists are faced in the current strategic discovery and development environment. In other words, the safety pharmacologist is being asked to identify potential cardiovascular toxicities of novel new agents at a very early stage of research, when little is known about the novel efficacy target, including those toxicities that may emerge after months, years or decades of exposure. It is clear from deliberations of this critical topic and related topics at recent conferences and workshops that the state of science is not yet complete to assume all of these challenges.

The intent of this session is to provide a broad background to the issues, state of science and identify those gaps that deserve the focus of the Safety Pharmacology community. To that end, the faculty will include individuals from Safety Pharmacology and toxicology/pathology, who will engage the audience in a debate of this important topic.

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|---------------------|--|
| 2:00-2:30 PM | Regulatory Expectations and Preclinical Study of the Cardiovascular Safety of Molecules in Development for T2D
<i>Alan S. Bass, PhD, Merck Research Laboratories, Kenilworth, NJ</i> |
| 2:30-3:00 PM | The Role of In-vitro Models in Predicting CV Risk (Cell systems, Cardiac Myocytes, Isolated Tissues and Organs)
<i>Peter Hoffmann, PhD, Novartis Pharma AG, Basel, Switzerland</i> |
| 3:00-3:30 PM | In-vivo Assays for Early Identification of Cardiovascular Toxicities during Drug Discovery
<i>Paul C. Levesque, PhD, Bristol-Myers Squibb, Princeton, NJ</i> |
| 3:30-4:00 PM | Assessment of Cardiovascular Safety in Repeat-Dose Toxicology Studies
<i>Brian R. Berridge, DVM, PhD, DACVP, GlaxoSmithKline, Research Triangle Park, NC</i> |
| 4:00-4:30 PM | Break (Exhibit Hall)
Visit Vendor and Poster Viewing |



Plenary Session 2: QT Prolongation – the issue of note at the inception of SPS, have we made a difference?

4:30-6:30 PM

Waterfront 2

Track Leader: Derek Leishman, PhD, Eli Lilly & Co., Indianapolis, IN

Co-chairs: Derek Leishman, PhD, Eli Lilly & Co., Indianapolis, IN and Steve Hachtman, MA, Data Science International, St. Paul, MN

It is a decade since the birth of the Safety Pharmacology Society, an event largely triggered by the emergence of the ICH S7 guidance. The “QT issue” is also largely credited as the subject which gave the emerging society its focus and foundation. There is also renewed scrutiny on the ICH S7b and E14 documents.

Now 10 years later, this session will examine what has changed and have we made a difference by examining the question through the eyes of speakers who were very much involved in the issue at the time.

4:30-5:15 PM

The Cardiologist’s View

Jeremy N. Ruskin, MD, Massachusetts General Hospital, Boston, MA

5:15-6:00 PM

The Regulator’s View

John Koerner, PhD, U.S. Food and Drug Administration, Silver Spring, MD

6:00-6:30 PM

Discussion

6:30 PM

Adjourn SPS Annual Meeting Day 2

Thursday, September 23, 2010

Plenary Session 3: Drug Safety, Development and Approval- Past, Present and Future

8:30-11:45 AM

Waterfront Rooms

Track Leader: Steve Hachtman, MA, Data Sciences International, St. Paul, MN

Co-Chairs: Steve Hachtman, MA, Data Sciences International, St. Paul, MN and Mary Jeanne Kallman, PhD, Director of Neuroscience, Covance Research Labs, Greenfield, IN



The closing morning Plenary Session will feature a speaker from a research organization, a speaker from a pharmaceutical company, and a speaker from the regulatory agency that approves new drugs. The session will discuss the place of Safety Pharmacology and Pharmaceutical Development in our time. The questions...“Where did we come from?” “Why are we here?” and “Where are we going?” will be addressed from different perspectives of market conditions, business strategy, and regulatory concerns. The session will provide a forum for looking carefully at the type, rate and direction of changes that are affecting our industry. Noted speakers offer us their unique experience and personal perspectives on the changes that so dramatically affect our work and the future of the pharmaceutical industry.

8:30-9:15 AM Drug Safety and the Current Climate for Pharmaceutical Innovation

Kenneth I. Kaitin, PhD, Tufts Center for the Study of Drug Development, Tufts University, Boston, MA

9:15-10:00 AM Strategic Sourcing of Pharmaceutical Research and Development: The Next Decade

Andrew M. Dahlem, PhD, Vice President and Chief Operating Officer of Lilly Research Laboratories, Indianapolis, IN

10:00-10:15 AM Break (Coffee available)

10:15- 11:00 AM Integrating Clinical and Non-Clinical Pharmacology in Drug Development

Douglas C. Throckmorton, MD, FDA Center for Drug Evaluation and Research, Rockville, MD

11:00-11:45 AM Discussion

11:45-1:00 PM Lunch Break

A HESI Symposium on Cross Disciplinary Perspectives in Cardiovascular Safety Assessment

1:00-4:00 PM

Waterfront Rooms

Cardiovascular safety issues in contemporary drug development span the spectrum of acute changes in function to chronic changes in structure to adverse clinical events. Ironically and unfortunately, safety assessment of these risks is often organizationally segregated and conducted in relative isolation. Current approaches to assessing drug-related cardiovascular effects in both the non-clinical and clinical settings are varied and include single-dose telemetered



animal studies, repeat-dose in vivo studies with more structural than functional evaluation, clinical ECGs and imaging. Integration of the range of data generated across these disciplines provides the potential for improved and early recognition of cardiovascular risk and the opportunity to mitigate that risk while progressing development of promising new medications. However, successful integration across different disciplines is often limited by technical, financial, or logistical constraints. This symposium will emphasize opportunities to overcome these constraints to the benefit of safety assessment. Speakers will be drawn from diverse areas of expertise (safety pharmacology, pathology, regulatory, and clinical) and will address opportunities for contemporary approaches within their discipline to add value as components of an integrated approach to cardiovascular safety. A panel discussion around best practices (and gaps) for integrated and translational cardiovascular safety assessment will conclude the session.

- 1:00-1:10 PM** **Integrative Approaches to CV Safety Assessment – A HESI Perspective**
Brian Berridge, DVM, PhD, GlaxoSmithKline, Research Triangle Park, NC
- 1:10-1:45 PM** **Safety Pharmacology Perspective – Opportunities and Challenges for Integration**
Scott Mittelstadt, PhD, Abbott Laboratories, Abbott Park, IL
- 1:45-2:30 PM** **Pathology Perspective – Opportunities and Challenges for Integration**
Brian Berridge, DVM, PhD, GlaxoSmithKline, Research Triangle Park, NC
- 2:30-3:05 PM** **Clinical Perspective – Opportunities and Challenges for Integration**
Frank Sellke, MD, Brown University Medical School, Boston, MA
- 3:05-3:40 PM** **Regulatory Perspective – Opportunities and Challenges for Integration**
Douglas C. Throckmorton MD, FDA Center for Drug Evaluation and Research, Rockville, MD
- 3:40-4:00 PM** **Panel Discussion**
- 4:00 PM** **Closing Remarks by incoming SPS President, Mary Jeanne Kallman, PhD**
- 5:00 PM** **SPS 10th Annual Meeting Adjourns**