



Safety Pharmacology Society 10th Annual Meeting Program

Tuesday, September 21, 2010

- 09:00 **Welcome and Announcements**
Kristy D. Bruse, PhD, President of the Safety Pharmacology Society
- 09:15 **Plenary Session 1:
President's Keynote Address**
Co-Chairs: Kristy D. Bruse, PhD, Lovelace Respiratory Research Institute and Donald Hodges, PhD, Vertex Pharmaceuticals
- Biomaterials in Their Role in Creating New Approaches for the Delivery of Drugs, Proteins, Nucleic acids, and Mammalian cells**
Keynote: Dr. Robert Langer, Massachusetts Institute of Technology
- 10:00 **Break**
- 10:30 **A: Government, Regulatory, Academic and Societal Issues**
Interactions between Academics and Industry: The Michigan State Experience
Track Leader and Chair: Scott W. Mittelstadt, PhD, Abbott Laboratories

Session Overview: 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.



Speakers:

Joseph R. Haywood, PhD, Michigan State University

Marc Bailie, DVM, PhD, Michigan State University

B: Trends and Technical Advances

Early Prediction of Functional Liabilities

Track Leader: Kathryn Bibeau

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

Session Overview: 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.

Speakers:

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

Lew Kinter, PhD, AstraZeneca Pharmaceuticals

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

Arthur Brown, MD, PhD, ChanTest, Inc.

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

Doris Damian, PhD, Vertex Pharmaceuticals

C: Translational-Preclinical to Clinical

Oncology-Unique Challenges for SP

Track Leader: JoAnne Saye, PhD, AstraZeneca Pharmaceuticals

Co-Chairs: Niels Christian-Ganderup, Ellegaard Göttingen Minipigs and Claudio Arrigoni, Accelera S.r.l.



Session Overview: Oncology, Unique Challenges for Safety Pharmacology: 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.

Speakers:

John Leighton, PhD, U.S. FDA

Daniel Lapadula, PhD, Novartis

Rocio Lopez, PhD, Pharmaceutical Product Development, Inc.

- 12:00 **LUNCH Break (Exhibit Hall) Stand-up Buffet Provided**
Visit Vendors and Poster Viewing
- 2:00 **Invited Oral Communications 1**
Invited Oral Communications 2
Invited Oral Communications 3
- 3:00 **Invited Oral Communications 4**
Invited Oral Communications 5
Invited Oral Communications 6
- 4:00 **Break (Exhibit Hall)**
Vendor and Poster Viewing
- 4:30 **A: Government, Regulatory, Academic and Societal Issues**
Case Studies of Start-up Companies: Transition of Technology from
Academics to Industry
Track Leader: Scott W. Mittelstadt, PhD, Abbott Laboratories
Co-Chairs: Franz J. Hock, CERB and Lothar Meister, Ciba, Inc.



Session Overview: 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.

Speakers:

Ronald Shebuski, PhD, MedElute, Inc.

Dr. med. Bernd Eisele, Vakzine Projekt Management GmbH

Edmund J. Sybertz, PhD, Genzyme Corporation

B: Trends and Technical Advances

Advances in CNS

Track Leader: Kathryn Bibeau, Intrinsik Health Sciences Inc.

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

Session Overview: 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.

Speakers:

Using Awake Animal Imaging to Finger Print for CNS Liability – Risk of Suicide?

Craig F. Ferris, PhD, Northeastern University

Moving Beyond the FOB: A Snapshot of the CNS De-Risking Toolbox

Keri E. Cannon, PhD, Pfizer Inc.



Preclinical Assessment of Seizure Liability

Alison Easter, AstraZeneca Pharmaceuticals

C: Translational-Preclinical to Clinical

Biologics

Track Leader: JoAnne Saye, PhD, AstraZeneca Pharmaceuticals

Co-Chairs: Hugo M. Vargas, PhD, Amgen Inc. and Sarra Laycock, PhD, Aptuit

Session Overview: 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 biologics 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.

Speakers:

Alternative Animal Models for Species-specific Biopharmaceuticals: A Case Study

Laura Andrews, PhD, Genzyme

RNA Therapeutics: Preclinical Challenges in Safety Evaluation

Christina Gamba-Vitalo, PhD, Alnylam Pharmaceuticals

PK of biotherapeutics: Quantitative dose selection for preclinical safety and first-in-human studies.

Jennifer Dong, PhD, Amgen Inc.

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



Wednesday, September 22, 2010

09:00 **A: Government, Regulatory, Academic and Societal Issues**
Drug Dependency (non human primates vs. rodents)
Track Leader: Scott W. Mittelstadt, PhD, Abbott Laboratories
Co-Chairs: Phil Atterson, WIL Research Laboratories and Paul Tarantino, Sepracor, Inc.

Session Overview:

The recently issued 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.

Speakers:

S. Stevens Negus, PhD, Virginia Commonwealth University

Katherine Nicholson, DVM, PhD, Virginia Commonwealth University

B: Trends and Technical Advances

Application of Stem Cell Technology for Identifying Cardiac Liabilities
Track Leader: Kathryn Bibeau, Intrinsik Health Sciences Inc.
Co-Chairs: Anthony Bahinski, PhD, Pfizer-Global Safety Pharmacology and Khuram Chaudhary, PhD, GlaxoSmithKline

Session Overview: 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.

Speakers:

In Vitro Cell and Tissue Engineering for Drug Safety and Efficacy Screening

Kevin Kit Parker, PhD, Harvard University

C: Translational-Preclinical to Clinical

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

Track Leader: JoAnne Saye, PhD, AstraZeneca Pharmaceuticals

Co-Chairs: Carrie Markgraf, MD, PhD, Schering-Plough Research Institute and JoAnne Saye, PhD, AstraZeneca Pharmaceuticals

Session Overview: 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.

Speakers:

Erica Liebelt, MD, University of Alabama School of Medicine and President, American College of Medical Toxicology

Paul Wax, MD, University of Texas Southwestern Medical Center



10:00 **Break (Exhibit Hall)**

Vendor and Poster Viewing

10:30 **Safety Pharmacology Society Annual Meeting & Awards-
EVERYONE INVITED!!!**

Announcement of Jr/Student Poster Competition winners, Jr/Student Travel Award Winners, and Distinguished Scientist Awardees' Presentation

12:00 **LUNCH Break (Exhibit Hall)**

Visit Vendors and Poster Viewing

2:00 **A: Government, Regulatory, Academic and Societal Issues**

Biodefense Talk

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

Co-Chairs: Heather Manley, US Department of Defense - Transformational Medical Technologies Initiative and Steve Hachtman, Data Sciences International

Session Overview: 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 FDA regulatory process. An additional challenge is that for biodefense indications, it is anticipated that licensure of medical countermeasures will be conducted under the 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.



Speakers:

Chris Doe, PhD, Almirall

Lisa Hensley, PhD, USAMRIID

Fred Marsik, PhD, U.S. FDA

Chad Roy, PhD, Tulane National Primate Research Center

B: Trends and Technical Advances

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

Track Leader: Kathryn Bibeau, Intrinsik Health Sciences Inc.

Co-Chairs: Dennis Murphy, GlaxoSmithKline and Phillip Atterson, WIL Research Laboratories

Session Overview: 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

Speakers:

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

Dennis J. Murphy, GlaxoSmithKline

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

Aidan Curran, Huntingdon Life Sciences

Electromyographic recordings from respiratory muscle as a method for evaluating respiratory function in dogs and monkeys

Stephane Milano, MDS Pharma Services

Thoracic Impedance as a method for evaluating respiratory function in dogs and monkeys

Boyce Moon, Data Sciences International



C: Translational-Preclinical to Clinical

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

Track Leader: JoAnne Saye, PhD, AstraZeneca Pharmaceuticals

Co-Chairs: Alan Bass, PhD, Merck Research Laboratories and Peter Hoffmann, Novartis Pharma AG

Session Overview: 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.

Speakers:

Regulatory Expectations and Preclinical Study of the Cardiovascular Safety of Molecules in Development for T2D

Alan S. Bass, PhD, Merck Research Laboratories

The Role of In-vitro Models in Predicting CV Risk (Cell systems, Cardiac Myocytes, Isolated Tissues and Organs)

Peter Hoffmann, Novartis Pharma AG

In-vivo Assays for Early Identification of Cardiovascular Toxicities during Drug Discovery



Paul C. Levesque, Bristol-Myers Squibb

Assessment of Cardiovascular Safety in Repeat-Dose Toxicology Studies

Brian Berridge, DVM, PhD, DACVP GlaxoSmithKline

4:00 Break (Exhibit Hall)

Vendor and Poster Viewing

4:30 Plenary Session 2:

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

Track Leader and Chair: Derek Leishman, PhD, Eli Lilly & Co.

Session Overview: 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 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.

Speakers:

The Cardiologist’s View

Jeremy Ruskin, MD, Massachusetts General Hospital

The Regulator’s View

John Koerner, PhD, U.S. FDA

18:30 Adjourn SPS Annual Meeting Day 2

Thursday, September 23, 2010

8:30 Plenary Session 3:

Drug Safety, Development and Approval- Past, Present and Future



Track Leader and Chair: Steve Hachtman, Data Sciences International
Session Overview: 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.

Speakers:

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

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

Douglas C. Throckmorton M.D., Deputy Director, FDA Center for Drug Evaluation and Research. Rockville, MD

- 10:00 **Break (Coffee available)**
- 10:15 **Drug Safety, Development and Approval- Past, Present and Future (Continued)**
Track Leader and Chair: Steve Hachtman, Data Sciences International
- 11:45 **Lunch Break**
- 1:00 **A HESI Symposium on Cross Disciplinary Perspectives in Cardiovascular Safety Assessment**
- 4:00 **Closing Remarks by incoming SPS President**
- 5:00 **SPS 10th Annual Meeting Adjourns**