Dear Colleagues:

On behalf of SOT Council, the SOT Committees, Regional Chapters, Special Interest Groups, Specialty Sections, SOT Supporters, exhibitors, and other partners, I invite you to join us in Baltimore, Maryland, March 12–16, 2017, for the SOT 56th Annual Meeting and ToxExpo.

Approximately 6,500 toxicologists from more than 50 countries are expected to share their research and expertise during the 160+ Scientific Sessions, featuring nearly 2,500 abstracts. This makes the SOT Annual Meeting an ideal place to expand your scientific knowledge, find new collaborators, and catch up on the latest techniques and initiatives.

Every year, networking is a key component of the meeting—from the Welcome Reception to Regional Chapter, Specialty Interest Group, and Specialty Section Receptions and all of the events in between. At this year’s meeting, plan to visit ToxExpo from 12:30 pm to 1:20 pm on Tuesday, March 14, for dedicated networking time, as only a limited number of Scientific Sessions are programmed during this time.

More than 350 exhibitors are expected in this year’s ToxExpo, where you can discover new products and technology, career and partnership opportunities, and more. ToxExpo is open Monday to Wednesday from 9:15 am to 4:30 pm, and I encourage all attendees to schedule time to visit our exhibitors.

SOT is pleased to be returning to Baltimore, the location of the 2009 Annual Meeting and ToxExpo. The Convention Center is located in downtown Baltimore, adjacent to the beautiful Inner Harbor and the historic Little Italy neighborhood. A short walk from the center is the National Aquarium, Port Discovery, the B&O Railroad Museum, and other attractions. And don’t forget the award-winning restaurants, where you can sample the famous Chesapeake Bay blue crabs.

I hope you join us in Baltimore for the 56th Annual Meeting and ToxExpo to help SOT fulfill its mission of creating a safer and healthier world by advancing the science and increasing the impact of toxicology.

Sincerely,

John B. Morris, PhD
2016–2017 SOT President
## Preliminary Program Contents

<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Annual Meeting Mobile Event App</td>
</tr>
<tr>
<td>5</td>
<td>Preliminary Program Content Reference Guide</td>
</tr>
<tr>
<td>6</td>
<td>Scientific Program Overview</td>
</tr>
<tr>
<td>12</td>
<td>Attend the Meeting</td>
</tr>
<tr>
<td>16</td>
<td>Hotel and Travel</td>
</tr>
<tr>
<td>22</td>
<td>Registration</td>
</tr>
<tr>
<td>28</td>
<td>General Information</td>
</tr>
<tr>
<td>42</td>
<td>Awards and Fellowships</td>
</tr>
<tr>
<td>48</td>
<td>Events and Activities</td>
</tr>
<tr>
<td>64</td>
<td>Continuing Education</td>
</tr>
<tr>
<td>74</td>
<td>Scientific Sessions</td>
</tr>
<tr>
<td>124</td>
<td>ToxExpo Exhibits</td>
</tr>
<tr>
<td>142</td>
<td>Support and Marketing Opportunities</td>
</tr>
</tbody>
</table>

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56th Annual Meeting and ToxExpo

2017 · Baltimore

March 12–16, 2017
SOT Mobile Event App!

Access information from the SOT Program, The Toxicologist, and ToxExpo Directory via your mobile device.

Available for download in February 2017 from the Apple and Google Play app store stores.

To purchase an advertisement on the SOT Mobile Event App, please go to www.toexpo.com.
Dear Colleagues,

I hope you are getting excited about the 2017 Annual Meeting to be held in Baltimore. The Scientific Program Committee has constructed the meeting with all of SOT’s members and partners in mind—gathering the best science from across a diverse spectrum of topic areas, research fields, and communities. The 2017 Symposia, Workshops, and Roundtables, and other sessions are timely and informative and represent the remarkable work conducted by our members and their colleagues.

We are pleased that the Daily Plenary Sessions are returning in 2017, so you should reserve each morning to attend these cross-disciplinary-focused lectures. During Monday’s Plenary Session Peter Sorger, Harvard Medical School, and Stephen Friend, Apple Inc., are sharing the latest in data science, while precision medicine is the focus on Tuesday morning when we will hear from Jun Yang, St. Jude Children’s Research Hospital, and Richard Barker, Oxford University. On Wednesday, Paul Elliott, Imperial College London, is discussing the exposome and metabolic profiling during the keynote Medical Research Council (MRC) lecture.

The statement “Toxicology Testing of Drug Combinations Does Not Add Significant Value to Human Risk Evaluation beyond What Is Known for the Individual Agents” is being argued during the SOT/EUROTOX debate on Monday afternoon, continuing the event’s tradition of addressing hot topics of high importance to toxicology and public health. In another partnership, the joint SOT and Japanese Society of Toxicology (JSOT) Symposium Session returns for the second year, focusing this year on drug-induced liver injury.

To discover award-winning research, plan on attending the 2017 SOT Award lectures. SOT Merit Award recipient Samuel Cohen, University of Nebraska Medical Center, is discussing his career-long contributions to toxicology, which include his current research into carcinogenesis with an emphasis on urinary bladder as a model system in rodents and extrapolation between rodent models and human diseases. The SOT Distinguished Toxicology Scholar Award recognizes substantial and seminal scientific contributions to the understanding of toxicology; this year’s recipient is Linda Birnbaum, NIEHS, whose research has focused on pharmacokinetic behavior of environmental chemicals, mechanisms of actions of toxicants, including endocrine disruption; and linking of real-world exposures to health effects during her career. The final 2017 Award Lecture is by Laura James, University of Arkansas for Medical Sciences, recipient of the SOT Translational Impact Award for her work involving mechanisms of liver repair in acetaminophen toxicity and clinical trials of drugs in children in order to gain dose and safety information.

While almost 2,500 abstracts are scheduled for presentation during the Annual Meeting, you can still add your science to the program by submitting a late-breaking abstract by January 12, 2017. The submission fee for late-breaking abstracts is $75. More information on submitting a late-breaking abstract is available on page 78 and online at www.toxicology.org/2017.

Please join me and the rest of the Scientific Program Committee in Baltimore for an enlightening and thought-provoking exploration of the latest research in toxicology.

Warmest regards,

Patricia E. Ganey, PhD
SOT Vice President and Scientific Program Committee Chairperson, 2016–2017
**Key Deadlines**

- **Late-Breaking Abstract Submission**  
  January 12, 2017
- **Early-Bird Registration**  
  January 13, 2017
- **Housing Reservation**  
  February 8, 2017
- **Standard Registration**  
  February 10, 2017
- **Registration Cancellation**  
  February 10, 2017

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**Important Program Information**

To conserve resources, the printed Program will be mailed ONLY by request—a selection available when you register. Attendees are encouraged to use the Online Planner, a tool to build your schedule for the meeting from your desktop in January and then synchronize it to the Mobile Event App in February.

*See page 2 for more details.*

**Registration Express**

Register by January 13, 2017, with full payment and you’ll receive your name badge and tickets in the mail before the meeting.
Preliminary Program Content Reference Guide

Maximize the value of your Annual Meeting attendance by familiarizing yourself with this reference guide for the Preliminary Program.

**Preliminary Program Overview**

<table>
<thead>
<tr>
<th>Section</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific Program Overview (pages 6–9)</td>
<td>Provides a daily listing of Annual Meeting sessions with their scheduled dates and times, including Symposia, Workshops, and Roundtables, special lectures, and Platform and Poster Presentations. Please refer to the final Program or Annual Meeting website for detailed information.</td>
</tr>
<tr>
<td>Events and Activities (pages 48–63)</td>
<td>The 56th Annual Meeting events and activities details are provided in this section—including the Regional Chapter, Special Interest Group, and Specialty Section reception schedules; and Student and Postdoctoral Scholar Events. This section includes the Undergraduate Diversity and Education Programs.</td>
</tr>
<tr>
<td>Continuing Education Courses (pages 64–72)</td>
<td>Continuing Education (CE) course descriptions and presenter information are located in this section. These courses have separate registration fees. Each participant in a CE course will receive a copy of the course booklet. Any remaining copies will be available for purchase to conference attendees on Monday, while supplies last.</td>
</tr>
<tr>
<td>Featured Sessions (pages 75–80)</td>
<td>This section lists the Daily Plenary Sessions and other special lectures and scientific sessions for the 2017 Annual Meeting. Detailed information for these sessions will be available in the final Program.</td>
</tr>
<tr>
<td>Scientific Sessions (pages 81–122)</td>
<td>The Preliminary Program layout is similar to that of the final Program. Specifically, this section lists the scientific sessions in date, time, and alphabetical order for Symposia, Workshops, Roundtables, Informational, Education-Career Development, and Historical Highlights sessions.</td>
</tr>
<tr>
<td>Exhibits (pages 124–138)</td>
<td>ToxExpo is the profession’s largest exposition and best resource for the latest information in technology, equipment, and services. This section contains the current list of exhibiting companies and Exhibitor-Hosted sessions.</td>
</tr>
</tbody>
</table>

**Session Types**

**Education-Career Development Sessions (80 minutes)**—Sessions that provide tools and resources to toxicologists that will enhance their professional and scientific development.

**Exhibitor-Hosted Sessions (60 minutes)**—Informative sessions developed by a ToxExpo Exhibitor or Annual Meeting Supporter (page 128).

**Featured Sessions**—Plenary, Keynote, and other special lectures (page 74).

**Historical Highlight Sessions (80 minutes)**—Sessions that provide a review of a historical body of science that has impacted toxicology.

**Informational Sessions (80 or 165 minutes)**—These present the latest science in toxicology or other learning opportunities that address the professional interests and needs of toxicologists in the areas of career development, general information, and planned scientific activities and are not based on the outcome of scientific research.

**Platform Sessions (165 minutes)**—Oral presentations that cover new areas, concepts, or data (see details in the final Program).

**Poster Sessions (195 minutes)**—Topic-specific presentations that cover new areas, concepts, or data (see details in the final Program).

**Roundtable Sessions (80 minutes)**—These provide an overview of controversial subjects, followed by questions and discussion.

**Symposium Sessions (165 minutes)**—Cutting-edge science, emphasizing new areas, concepts, and data. **Innovations in Toxicological Sciences Session**—This symposium subcategory will introduce new technologies or scientific disciplines to attendees.

**Workshop Sessions (165 minutes)**—Generally accepted, state-of-the-art knowledge in toxicology in informal interactive presentations with ample time for discussion.

You can build a customized schedule, mark your favorite abstracts and speakers for later reference, and more with the SOT Mobile Event App and Online Planner. See page 2 for details.
Sunday, March 12
7:00 AM to 7:45 AM
CONTINUING EDUCATION SUNRISE MINI-COURSE
SR01 Molecular Imaging for Toxicologists

8:15 AM to 12:00 Noon
CONTINUING EDUCATION MORNING COURSES
AM02 Adding Up Chemicals: Component-Based Risk Assessment of Chemical Mixtures
AM03 Current Principles for Nonclinical Chronic Toxicity/Carcinogenicity Testing of Environmental Chemicals
AM04 Navigating Drug-Induced Vascular Injury in Preclinical and Clinical Development of Novel Therapeutics
AM05 New Concepts and Technologies in Metals Toxicology
AM06 Reproductive Toxicity: Challenges and Practical Approaches to Determine Risk in Drug Development
AM07 Technologies and Applications of Stem Cells for Use in Toxicology

1:15 PM to 5:00 PM
CONTINUING EDUCATION AFTERNOON COURSES
PM08 Detecting Cancer Risk in Drugs: Design, Conduct, and Interpretation of Carcinogenicity Studies for Regulatory Approvals
PM09 Developmental and Reproductive Toxicology (DART) and Risk Assessment of Environmental Chemicals: Applications, Complexities, and Novel Approaches
PM10 Emerging Approaches in Genetic Toxicology for Product Development
PM11 Extrapolation in the Airways: Strategies to Incorporate In Vivo and In Vitro Data to Better Protect Human Health
PM12 Health-Based Limits for Toxicological Risk Assessment: Setting Acceptable Daily Exposures for Pharmaceutical and Chemical Safety
PM13 Read-Across: Case Studies, New Techniques, and Guidelines for Practical Application

Monday, March 13
8:00 AM to 9:20 AM
DAILY PLENARY SESSION
• Data Science
  Lecturers: Peter Sorger, Harvard Medical School; and Stephen Friend, Apple Inc.

9:30 AM to 12:15 PM
SYMPOSIUM SESSIONS
• Early-Life Inorganic Arsenic Exposures and Later-in-Life Effects
• Organs-on-a-Chip, Tissue Bioprinting, and 3D Cultures: Next Generation Models for Toxicology in the 21st Century
• Translational Control in Disease Progression and Xenobiotic-Mediated Toxicity

WORKSHOP SESSIONS
• Cross-Industry and Regulatory Approach for the Identification and/ or Qualification of Novel Safety Biomarkers of Drug-Induced Vascular Injury (DIVI)
• Fit for Purpose: Using Computational Models for Risk
• Scientific, Regulatory, and Safety Considerations for Probiotics and Microbiome Targeted Therapeutics

12:30 PM to 1:20 PM
MERIT AWARD LECTURE
• Lecturer: Samuel Cohen, University of Nebraska Medical Center

1:30 PM to 2:30 PM
MEET THE DIRECTORS
• A Conversation with Linda Birnbaum and Robert Kavlock
  Lecturers: Linda Birnbaum, NIEHS; and Robert Kavlock, US EPA

INFORMATIONAL SESSIONS
• Advances in Preclinical Safety Testing: Progress in Implementation of ICH Guidances
• Supporting Open Data in Toxicology

POSTER SESSIONS
• Carcinogenesis I
• Carcinogenesis II
• Developmental and Juvenile Toxicity
• Epidemiology and Public Health
• Epigenetics
• Liver: In Vitro and In Silico Approaches
• Mixtures
• Nanotoxicology: In Vivo
• Neurotoxicology: Metals—Cd, Pb, and Others
• Neurotoxicology: Metals—Mercury
• Receptors, Gene Regulation, and Signaling
• Reproductive Toxicology

9:30 AM to 4:30 PM
RESEARCH FUNDING INSIGHTS
• Network with Program Officers

12:30 PM to 1:50 PM
ROUNDTABLE SESSION
• Bias and Conflict of Interest in Conducting Research and Risk Assessments: Perspectives from Academia, Government, Industry, and Others

1:15 PM to 4:30 PM
POSTER SESSIONS
• Bioinformatics and Tox Databases
• Cytochrome P450
• Endocrine Toxicology
• Hepatotoxicity
• Nanotoxicology: In Vitro
• Neurodegenerative Diseases
• Neurotoxicology: Metals—Manganese
• Neurotoxicology: Microelectrode Arrays (MEAs)
• Pharmacogenomics
• Stem Cell Biology and Toxicology
2:00 PM to 4:45 PM
SYMPOSIUM SESSIONS
- Cell Health and Mechanistic Assays for the In Vitro Prediction of DILI
- Circadian Rhythms in Air Pollution-Induced Pulmonary and Cardiovascular Disorders: A Race against the Clocks
- Lifespan Neuroimmunotoxicology: Age-Dependent Neuroimmune Dyshomeostasis Caused by Pollutants, Pathogens, and Psychoactive Substances

WORKSHOP SESSIONS
- Bispecific Molecules: Nonclinical and Clinical Development Challenges
- Controversies in Pesticide Toxicology
- Improving Public Health through Innovations in Exposure Science
- Modernizing Toxicological Risk Assessment for Compounds Released from Pharmaceutical, Consumer, Medical Device and Combination Products: Alternative Tools and Methods

PLATFORM SESSIONS
- Multi-Omic Connections in Chemical Toxicity
- Reproductive Toxicology

4:45 PM to 6:00 PM
SOT/EUROTOX DEBATE
- Toxicology Testing of Drug Combinations Does Not Add Significant Value to Human Risk Evaluation Beyond What Is Known for the Individual Agents
Lecturers: Kenneth L. Hastings, Hastings Toxicology Consulting LLC; and Phil Bentley, Toxicodynamix International LLC

Tuesday, March 14
8:00 AM to 9:20 AM
DAILY PLENARY SESSION
- Precision Medicine
Lecturers: Jun J. Yang, St. Jude Children’s Research Hospital; and Richard Barker, University of Oxford

9:30 AM to 12:15 PM
SYMPOSIUM SESSIONS
- Cardiopulmonary Consequences of Gestational Toxicant Exposure: Getting to the Heart of the Matter
- Contribution of Gene Transcription to Spontaneous Mutation and Genotoxic Outcomes

WORKSHOP SESSIONS
- Incorporating In Vitro Reproductive and Developmental Assays into Regulatory Risk Assessment
- Opportunities for Read-Across Development and Application Using QSAR Approaches

INFORMATIONAL SESSION
- Thresholds of Toxicological Concern: 21st Century Safety Assessment

PLATFORM SESSIONS
- Chemical and Biological Weapons
- Endocrine Toxicology
- Mechanisms of Toxicity: SPC Highlights Emerging Scientists

9:30 AM to 12:45 PM
POSTER SESSIONS
- Dose-Response Assessment and Toxicity Reference Value Derivation
- Exposure Assessment and Biomonitoring
- Immunotoxicology
- Kidney
- Metals I: Arsenic and Lead
- Neurotoxicology: General Neurotoxicity
- Non-Pharmaceutical Safety Assessment
- Ocular Toxicology
- Oxidative Injury and Redox Biology
- Pharmaceutical Safety: Drug Development
- Pharmaceutical Safety: Drug Discovery
- Tobacco Products

9:30 AM to 12:45 PM
RESEARCH FUNDING INSIGHTS
- Network with Program Officers
- Biomarkers
- Biotransformation
- Cell Death Mechanisms
- Chemical and Biological Weapons
- Genetic Toxicity
- Medical Devices
- Metals II: Cadmium and Mercury
- Metals III: Various Metals and Mixtures
- Nanoparticle Exposure, Dosimetry, and In Silico Modeling
- Regulation and Policy
- Skin
- The Developmental Basis of Adult Disease

(continued on next page)
### Scientific Program Overview

**Wednesday, March 15**

**2:00 PM to 4:45 PM**

**SYMPOSIUM SESSIONS**
- Big Data, Meet Chemical Carcinogenesis! Are There New Solutions for an Old Problem?
- Chemically Induced Neuroinflammation and “Sickness Behavior” Disorders
- Emerging Concepts in Nonclinical Development of Immuno-Oncology Agents: Enabling Translation of Nonclinical Pharmacology and Safety Information to First-in-Human Clinical Trials
- Lost in Translation: Bringing the Real World to In Vitro Data
- MiRNAs As Translational Biomarkers of Kidney Injury

**WORKSHOP SESSIONS**
- Low Dose Non-Monotonic Responses
- Safety or Prediction? What is the Future of Regulatory Toxicity Testing?

**PLATFORM SESSIONS**
- Particulate Matter and Cardiovascular Impairment

**4:45 PM to 6:15 PM**

**SOT ANNUAL BUSINESS MEETING**

**5:00 PM to 6:20 PM**

**EDUCATION-CAREER DEVELOPMENT SESSION**
- Careers for Toxicologists at Primarily Undergraduate Institutions: Everything You Need to Know About the Job, Hiring Process, and Strategies for Success in Teaching and Research

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**8:00 AM to 9:20 AM**

**DAILY PLENARY SESSION—KEYNOTE MEDICAL RESEARCH COUNCIL (MRC) LECTURE**

- The Exposome: Challenges and Opportunities  
  *Lecturer: Paul Elliott, Imperial College*

**9:30 AM to 12:15 PM**

**SYMPOSIUM SESSIONS**
- Investigating Metabolic Diseases Using Integrated ‘Omic’ Approaches
- The Skin As A Metabolic and Immune-Competent Organ: Implications for Pharmaceutical Development and Safety Assessment

**WORKSHOP SESSIONS**
- 3D Cell Platforms to Advance Toxicological Sciences
- Challenges and Novel Approaches Evaluating Developmental and Reproductive Toxicity of Biotherapeutics
- Circulatory Mechanisms Underlying the Systemic Effects of Inhaled Nanoparticles and Complex Combustion Mixtures: Common Pathways for Diverse Toxicants
- Increasing the Utility and Acceptance of Chemical Specific Adjustment Factors—International Experience
- Measurement and Prediction of Chemicals in Consumer Products

**9:30 AM to 12:45 PM**

**POSTER SESSIONS**
- Air Pollution
- Air Pollution: Particulate Matter
- Animal Models
- Clinical and Translational Toxicology
- Developmental Neurotoxicity
- Disposition/Pharmacokinetics
- Food Safety and Nutrition
- Liver 1: Mechanisms and Translational Biomarkers
- Liver 2: Mechanisms and Translational Biomarkers
- Nanotoxicology: Carbon-Based Nanomaterials
- Natural Products
- Persistent Organic Pollutants
- Pesticides
- Respiratory Toxicology
- Stem Cells and ‘Omic’

**9:30 AM to 4:30 PM**

**RESEARCH FUNDING INSIGHTS**
- Network with Program Officers

**12:30 PM to 1:20 PM**

**DISTINGUISHED TOXICOLOGY SCHOLAR AWARD LECTURE**
- Dioxins and the Ah Receptor: Synergy of Discovery  
  *Lecturer: Linda Birnbaum, NIEHS-NTP*

**12:30 PM to 1:50 PM**

**ROUNDTABLE SESSIONS**
- Designing a Carcinogenic Mode-of-Action Research Program Useful for Regulatory Decision Making: Challenges and Lessons Learned
- Herbo-Metallic Mixtures in Traditional Medicines

**INFORMATIONAL SESSIONS**
- Communicating Toxicology to the Public
- Data Science to Generate Toxicity Signatures

**HISTORICAL HIGHLIGHTS SESSION**
- NIEHS Superfund Research Program: A History of Cutting-Edge Science and Innovative Technologies

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View featured speaker biographies, connect with other attendees, and create your own schedule using the SOT Mobile Event App or the Online Planner. See page 2 for details.
<table>
<thead>
<tr>
<th>Time</th>
<th>Session Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:15 PM to 4:30 PM</td>
<td>POSTER SESSIONS</td>
<td>- Alternatives to Mammalian Models I: Liver, Ocular, and Skin Alternatives</td>
</tr>
<tr>
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<td>- Alternatives to Mammalian Models II</td>
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<tr>
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<td>- Autoimmunity/Hypersensitivity</td>
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<td>- Cardiovascular and Hemodynamics Toxicity</td>
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<td>- Ecotoxicology</td>
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<td>- Education, Ethical, Legal, and Social Issues</td>
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<td>- General Toxicology</td>
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<td>- Inflammation in Disease</td>
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<td>- Inflammation: Methods and Mechanisms</td>
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<td>- Nanotoxicology: General</td>
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<td>- Neurotoxicology: Pesticides</td>
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<td>- Quantitative Systems Toxicology</td>
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<td></td>
<td>- Risk Assessment Strategies and Applications</td>
</tr>
<tr>
<td>2:00 PM to 4:45 PM</td>
<td>SYMPOSIUM SESSIONS</td>
<td>- Enhancing the Clinical Benefit of Cancer Drugs: Toxicity As a Therapeutic Target</td>
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<td>- Increasing Confidence in Safety Assessment Decisions: The Inclusion of Metabolism in Toxicity Testing Strategies</td>
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<td>- Novel In Vitro and In Silico Platforms for Modeling Developmental and Reproductive Toxicity</td>
</tr>
<tr>
<td></td>
<td>WORKSHOP SESSIONS</td>
<td>- Anesthetics, Analgesics, and Ionizing Radiation: Balancing Utility and Safety in Pregnant Women, Infants, and Children</td>
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<td>- Data Standardization Across ‘Omics Platforms in Regulatory Toxicology</td>
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<td>- Is There a Concern for Neurotoxicity from Replacement Organophosphorus Flame-Retardants?: Insights Using Molecular Approaches, Systems Biology, and Human Exposure</td>
</tr>
<tr>
<td>5:00 PM to 5:50 PM</td>
<td>TRANSLATIONAL IMPACT AWARD LECTURE</td>
<td>Lecturer: Laura James, University of Arkansas for Medical Sciences, Arkansas Children’s Hospital</td>
</tr>
<tr>
<td>5:00 PM to 6:20 PM</td>
<td>SOCIETY OF TOXICOLOGY AND JAPANESE SOCIETY OF TOXICOLOGY MINI-SYMPOSIUM</td>
<td>Immune Factors in Drug-Induced Liver Injury Lecturers: Robert A. Roth, Michigan State University; and Tetsushi Yokoi, Nagoya University Graduate School of Medicine</td>
</tr>
<tr>
<td>8:30 AM to 11:15 AM</td>
<td>SYMPOSIUM SESSIONS</td>
<td>- Evaluating the Reproductive and Developmental Effects of Botanical Dietary Supplements</td>
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<td>- In Vitro and Alternative Methods in Ocular Toxicology: The “Eyes” Have It</td>
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<td>- Quantitative Systems Toxicology for Chemical Safety Assessment</td>
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<td>- The Next Technology Wave: Biosensors, Extreme Computing, and Organ Chips for Predicting Cardiovascular Toxicity</td>
</tr>
<tr>
<td>8:30 AM to 11:45 AM</td>
<td>POSTER SESSIONS</td>
<td>- Alternatives to Mammalian Models III</td>
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<tr>
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<td>- Biological Modeling</td>
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<td>- Emerging Technologies</td>
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<td>- Systems Toxicology</td>
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<tr>
<td>8:30 AM to 11:15 AM</td>
<td>EDUCATION-CAREER DEVELOPMENT SESSION</td>
<td>Mastering Soft Skills to Advance Your Scientific Career</td>
</tr>
<tr>
<td>8:30 AM to 11:15 AM</td>
<td>LATE-BREAKING POSTER SESSION</td>
<td>See page 78 for submission information.</td>
</tr>
</tbody>
</table>

A Contemporary Concepts in Toxicology (CCT) Meeting on metabolic syndrome will be held prior to the start of the SOT Annual Meeting on Saturday, March 11. See page 20 for details.

See page 63 for details on additional Satellite Meetings or visit the SOT Annual Meeting website for the most up-to-date information.
SOT Undergraduate Student Affiliates

SOT Provides Access for Undergraduate Students to Explore Toxicology Training and Career Options

Sign up via www.toxicology.org
- Connect with SOT
- Participate in the Undergraduate ToXchange community
- Access CEd-Tox online courses for free
- Receive SOT publications

Mark Your Calendar

56th Annual Meeting and ToxExpo
Baltimore, Maryland † March 12–16, 2017

Share Your Research…
Connect with Collaborators!

Late-Breaking Abstract Submission Site Now Open

See details on page 78.

www.toxicology.org/2017
<table>
<thead>
<tr>
<th>Organization</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>AbbVie</td>
<td>North Chicago, Illinois</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>Mecclesfield, United Kingdom</td>
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<td>Princeton, New Jersey</td>
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<td>Summit, New Jersey</td>
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<td>Wilmington, Massachusetts</td>
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<td>San Ramon, California</td>
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<td>The DuPont Haskell Global Centers for Health and Environmental Sciences</td>
<td>Newark, Delaware</td>
</tr>
<tr>
<td>Eli Lilly and Company</td>
<td>Indianapolis, Indiana</td>
</tr>
<tr>
<td>Envigo</td>
<td>East Millstone, New Jersey</td>
</tr>
<tr>
<td>ExxonMobil Biomedical Sciences, Inc.</td>
<td>Annandale, New Jersey</td>
</tr>
<tr>
<td>Genentech, Inc.</td>
<td>South San Francisco, California</td>
</tr>
<tr>
<td>Gilead Sciences, Inc.</td>
<td>Foster City, California</td>
</tr>
<tr>
<td>Honeywell International, Inc.</td>
<td>Morristown, New Jersey</td>
</tr>
<tr>
<td>Janssen Pharmaceutical Companies of Johnson &amp; Johnson</td>
<td>Raritan, New Jersey</td>
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<tr>
<td>MPI Research</td>
<td>Mattawan, Michigan</td>
</tr>
<tr>
<td>Organovo, Inc.</td>
<td>San Diego, California</td>
</tr>
<tr>
<td>Oxford University Press</td>
<td>Oxford, United Kingdom</td>
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<tr>
<td>Pfizer, Inc.</td>
<td>Groton, Connecticut</td>
</tr>
<tr>
<td>Procter &amp; Gamble Company</td>
<td>Cincinnati, Ohio</td>
</tr>
<tr>
<td>Regeneron Pharmaceuticals, Inc.</td>
<td>Tarrytown, New York</td>
</tr>
<tr>
<td>Sanofi</td>
<td>Bridgewater, New Jersey</td>
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<tr>
<td>SNBL USA, Ltd.</td>
<td>Everett, Washington</td>
</tr>
<tr>
<td>Syngenta Crop Protection, Inc.</td>
<td>Greensboro, North Carolina</td>
</tr>
<tr>
<td>Takeda Pharmaceutical Company Limited</td>
<td>Cambridge, Massachusetts</td>
</tr>
<tr>
<td>TERA Center, University of Cincinnati</td>
<td>Cincinnati, Ohio</td>
</tr>
<tr>
<td>Western Slope Laboratory, LLC</td>
<td>Troy, Michigan</td>
</tr>
<tr>
<td>WIL Research Laboratories, LLC</td>
<td>Ashland, Ohio</td>
</tr>
<tr>
<td>XRpro Sciences, Inc.</td>
<td>Cambridge, Massachusetts</td>
</tr>
</tbody>
</table>

If your organization is interested in participating in the SOT Global Partner program, please contact Marcia Lawson at marcia@toxicology.org.
Attend the Meeting
Attend the Meeting

Reasons to Attend

The SOT Annual Meeting and ToxExpo is the largest meeting and exhibition dedicated to toxicology in the world. The Society anticipates that more than 6,500 toxicologists from more than 50 countries will attend, alongside 350 exhibitors.

Innovative Perspectives

The Annual Meeting provides the most complete and in-depth coverage of toxicology. It features a broad range of Scientific Sessions that provide participants with a unique opportunity to deepen their knowledge in topical areas and interact with leaders in their respective disciplines. The Scientific Program includes Plenary Lectures and other featured sessions, Continuing Education Sessions, Symposia, Workshops, Roundtables, and Informational Sessions, as well as Platform and Poster Sessions.

The meeting is the venue for toxicologists to learn about the scientific advances that have taken place during the past 12 months. The Scientific Program Committee reviews more than 2,500 abstracts to deliver the most comprehensive and up-to-date program imaginable.

ToxExpo: Access to Cutting-Edge Companies and Technology

ToxExpo features 350 exhibitors who lead the industry in developing cutting-edge products, services, and technology to benefit the toxicology community. Exhibitors also have the opportunity to demonstrate their products and educate attendees about their services via Exhibitor-Hosted Sessions throughout the week.

ToxExpo is accessible to attendees and exhibitors throughout the calendar year by visiting www.ToxExpo.com. ToxExpo is a valuable tool for the policymaker, scientist, student, or anyone who is looking for the latest that toxicology has to offer.

Global Networking Opportunities

Thousands of networking moments take place during the Annual Meeting and ToxExpo. From exhibits to posters and Scientific Sessions to receptions, you have the opportunity to network with colleagues and leading scientists from around the world.

More than 20 percent of the attendees come from outside North America, some from as far away as Australia, Egypt, China, Latin America, and Africa.

Affordability and Value

The meeting is one of the most cost-effective ones you can attend. For example, you pay $320 for early-bird registration, compared to an average cost of $461 for other toxicology society meetings. That registration gives you access to more than 160 Scientific Sessions and 2,500 abstracts, representing latest scientific insights and discoveries.

SOT has arranged air carrier discounts and has reserved SOT meeting attendee discount-rated rooms at various hotels in the Baltimore area through the SOT hotel room block.
Accessibility for Persons with Disabilities

The Baltimore Convention Center and most of the SOT hotels are accessible to persons with disabilities. If you require special services, please let SOT know by indicating your needs while registering or by contacting Heidi Prange (heidi@toxicology.org; 703.438.3115 ext. 1424).

To arrange special services, SOT recommends the following two providers for language and mobility needs.

**LSA Interpretation Services**

800.305.9673 | www.lsaweb.com

Language Services Associates (LSA) is a nationwide full-service firm providing translators and interpreters in 180 languages.

**Scoot Around**

888.441.7575 | www.scootaround.com

Scootaround Inc. is North America’s #1 source for wheelchair, scooter, and powerchair rentals.

Attire

Business casual. No coat or tie required! Bring comfortable clothing and shoes and dress in layers, as meeting rooms sometimes fluctuate in temperature.

Badges and Event Tickets

If you register by January 13, 2017, you will receive your badge, event tickets, and other requested registration materials in the mail. Please remember to bring these items with you to Baltimore, as your badge is your admission to the meeting, sessions, and events. Tickets for CE Courses and other events also may be required and are issued with your meeting badge.

If you register after January 13, 2017—or did not receive your badge or misplaced it—go to the “BADGE PICK UP” registration counter on-site to pick up your badge. You will be asked to show a photo ID.

Badge holders, the printed Program, and ToxExpo Directory will be available on-site near registration. If you ordered a printed copy of The Toxicologist, it can be acquired at a special registration counter.

If you have not registered for the meeting before you arrive in Baltimore, please complete the on-site registration form found at the kiosks in the registration area and proceed to the appropriate registration line.

*Additional registration information is available on page 22.*
**Safety and Security**

Baltimore’s Inner Harbor area is a safe, beautiful, vibrant entertainment and retail district. As with all SOT Annual Meeting and ToxExpo locations, we encourage attendees to walk “smart” when you leave the Baltimore Convention Center:

- Know your destination and the best way to reach it.
- Travel along sidewalks in lighted areas at night, and don’t walk alone.
- Establish a “buddy” system with another meeting attendee.
- Share schedules and check on each other periodically.
- Build your awareness of unknown surroundings by reviewing local information.
- Laptop computers are attractive, easy targets for thieves. Be sure your laptop is in a secure place.
- Jackets with pockets provide a convenient alternative for women to reduce the chance for lost or stolen handbags.

Baltimore also has Hospitality Guides available to escort you while walking to your hotel or waiting for a taxi after dark:

- Guides are available everyday from 10:00 am to 10:30 pm for areas north and east of the Inner Harbor. Anyone wishing to receive an escort should call 410.244.1030 during business hours or 410.802.9631 after hours.
- Additional guides are available along the waterfront from 8:00 am to 8:30 pm by calling 443.278.4701. They will meet you at your location and walk with you to your Inner Harbor/ Harbor East destination.

---

**Visa Information**

**Tips for applying for a visa:**

- **Start Early**—The US is advising visa applicants to apply at least three to four months in advance of their travel date. Also, additional reviews may be required. This could add an additional four to six weeks to the processing time.
- **Gathering Your Application Materials**—Organize your passport; necessary applications; and supporting documents, including information on employment, reason for travel, and financial status; and proof of payment of fees. For more detailed information on visa requirements, consult the US Department of State’s visa site (www.travel.state.gov/content/visas/en.html) and the International Visitors Office of The National Academies (www.sites.nationalacademies.org/PGA/biso/visas/index.htm).
- **Submitting Your Application**—Make an appointment to visit your US Embassy or Consulate. Make sure you ask if there are any fees required. Most fees must be paid before your appointment. Wait times for appointments may be longer than in the past. Schedule the appointment as soon as possible. Information on visa wait times can be found at the US Department of State website (www.travel.state.gov/content/visas/en/business.html).

If you need additional visa assistance, contact the International Visitors Office of The National Academies (www.nationalacademies.org/visas).

If you need a formal invitation letter for visa purposes, you may request an invitation by sending your name, address, and other contact information to the SOT Registration Department (jimd@toxicology.org; 703.438.3115). If you have been accepted to make a presentation at the meeting, please include the name and date of your presentation. You will need to make your own hotel reservations and register for the meeting.
Housing
The Society of Toxicology has reserved and arranged for discounted room rates at various Baltimore hotels—known as the SOT hotel room block. Booking a room in the room block is an important way to support the Society and keep overall meeting costs as low as possible. Your patronage of these official meeting hotels makes it possible for SOT to secure the space necessary for this event at a greatly reduced cost. The hotels not only offer discounted rates and the best networking opportunities, but staying in the group blocks helps the Society meet its obligation to the hotel, avoid penalties, and keeps meeting registration prices down. Please assist the Society by making your hotel reservation using the Connections Housing online housing reservation system.

Hotel Reservation Information
All reservations for housing must be made through Connections Housing and not with the hotels directly. The deadline date for housing reservations is February 8, 2017. Please choose only one option to make your reservation. For best availability and immediate confirmation, make your hotel reservation via Internet or by telephone. Faxed and mailed housing requests will take longer to process and your hotel selections may not be available.

- [www.toxicology.org/housing](http://www.toxicology.org/housing)
- **Mail Housing Form to:**
  Connections Housing
  950 Scales Road, Building 200
  Suwanee, GA 30024 United States
- **Tel:** 800.262.9974 (USA) or 404.842.0000 (Domestic and International)
- **Fax:** 404.601.7441 (Domestic and International)
- **Hours of Operation:**
  8:30 AM–7:00 PM (EST) Monday–Friday

Hotel Acknowledgment
A reservation acknowledgment will be emailed, faxed, or mailed via Connections Housing to you once your reservation has been booked. (You will not receive a confirmation from your hotel.) If you do not receive an acknowledgment within three business days, please call Connections Housing.

Changes and Cancellations
You can make changes and/or cancellations online or by contacting Connections Housing at 404.842.0000 or 800.262.9974. All cancellations made within 72 hours prior to the day of arrival and no shows will be charged the first night’s room and tax by the hotel. Early departures are subject to penalty fees set by the hotel.

Room-Share Program
The Society is pleased to provide a room-share program to those registered for the Annual Meeting. It is available to each meeting registrant who voluntarily enrolls in the program and accepts the terms of the legal disclaimer. This program allows SOT Annual Meeting registrants to identify others with whom a room might be shared. For more information on this program and to sign up, visit the SOT Annual Meeting website.

Transportation
Air Transportation
Baltimore is serviced by Baltimore/Washington International Thurgood Marshall Airport (BWI), which is a 20-minute drive from the Baltimore Convention Center and the SOT hotel area. The airport offers 650 flights daily on 15 different carriers. For more information visit [www.bwiairport.com](http://www.bwiairport.com).

Preferred Carrier Airfare Discounts
SOT has established discounted rates through Southwest and United Airlines on select routes to Baltimore. Be sure to use the appropriate reference numbers when making your reservation. You may purchase your ticket online, call the airline directly using the toll-free numbers, or provide your travel agent with the reference/discard numbers listed below to receive the discount.

**Southwest Airlines**
Tel: 800.435.9792 | [www.swabiz.com](http://www.swabiz.com)
SOT Discount Code: 99150833

Book through our SWABIZ® account to receive discounts and bonus Rapid Reward points:
- 8% discount off Anytime and Business Select® fares
- 2% discount off select Wanna Get Away® fares
- 50% bonus Rapid Reward points for your travel to and from the convention with Rapid Rewards # added to your reservation. To enroll in the Rapid Rewards program, visit [www.southwest.com/corporaterapidrewards](http://www.southwest.com/corporaterapidrewards).


**United Airlines**
Tel: 800.426.1122 (a service fee will apply) | [www.united.com](http://www.united.com) (no service fees)
SOT Discount Code: ZXBX204806

Use offer code ZXBX204806 to receive a discount up to 10%. Discount is valid for travel March 7–20, 2017.

International attendees should call their local United Airlines reservations office or email groupmeetings@united.com with their preferred itinerary and discount codes.

If you are booking through a travel professional, please give them the following information to receive a discount: Agreement Code: 204806, Z Code: ZXBX.

Baltimore is home to many interesting attractions, neighborhoods, and activities.

See the Discover Baltimore section, starting on page 35, for more information.
# Hotel & Travel

**Hotel Map**

<table>
<thead>
<tr>
<th>Hotel Name</th>
<th>Map Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baltimore Marriott Inner Harbor at Camden Yards</td>
<td>1</td>
</tr>
<tr>
<td>Baltimore Marriott Waterfront</td>
<td>2</td>
</tr>
<tr>
<td>Days Inn Inner Harbor</td>
<td>3</td>
</tr>
<tr>
<td>Embassy Suites Baltimore Downtown</td>
<td>4</td>
</tr>
<tr>
<td>Hampton Inn Baltimore-Downtown/Convention Center</td>
<td>5</td>
</tr>
<tr>
<td>Hilton Baltimore, SOT Headquarters Hotel</td>
<td>6</td>
</tr>
<tr>
<td>Baltimore Marriott Waterfront</td>
<td>7</td>
</tr>
<tr>
<td>Hotel Monaco Baltimore, A Kimpton Hotel</td>
<td>8</td>
</tr>
<tr>
<td>Hyatt Regency Baltimore Inner Harbor</td>
<td>9</td>
</tr>
<tr>
<td>Lord Baltimore Hotel</td>
<td>10</td>
</tr>
<tr>
<td>Renaissance Baltimore Harborplace Hotel</td>
<td>11</td>
</tr>
<tr>
<td>Royal Sonesta Harbor Court Hotel</td>
<td>12</td>
</tr>
<tr>
<td>Sheraton Inner Harbor</td>
<td>13</td>
</tr>
</tbody>
</table>

**Baltimore Convention Center**

![Hotel Map Image]
<table>
<thead>
<tr>
<th>Hotel Services</th>
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<tbody>
<tr>
<td><strong>Hotel</strong></td>
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<tr>
<td><strong>1) Baltimore Marriott Inner Harbor at Camden Yards</strong></td>
</tr>
<tr>
<td><strong>2) Baltimore Marriott Waterfront</strong></td>
</tr>
<tr>
<td><strong>3) Days Inn Inner Harbor</strong></td>
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<tr>
<td><strong>4) Embassy Suites Baltimore Downtown</strong></td>
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<tr>
<td><strong>5) Hampton Inn Baltimore-Downtown/Convention Center</strong></td>
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<tr>
<td><strong>6) Hilton Baltimore SOT Headquarters Hotel</strong></td>
</tr>
<tr>
<td><strong>7) Holiday Inn Inner Harbor-Downtown Baltimore</strong></td>
</tr>
<tr>
<td><strong>8) Hotel Monaco Baltimore, A Kimpton Hotel</strong></td>
</tr>
<tr>
<td><strong>9) Hyatt Regency Baltimore Inner Harbor</strong></td>
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<tr>
<td><strong>10) Lord Baltimore Hotel</strong></td>
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<tr>
<td><strong>11) Renaissance Baltimore Harborplace Hotel</strong></td>
</tr>
<tr>
<td><strong>12) Royal Sonesta Harbor Court Hotel</strong></td>
</tr>
<tr>
<td><strong>13) Sheraton Inner Harbor</strong></td>
</tr>
</tbody>
</table>

*Subject to Change

All hotel accommodations, rates, Internet access, and parking pricing are subject to change. Early departures are subject to penalty fees set by the hotels. Although making your reservations outside of the SOT hotel block can sometimes be more economical, it decreases the money available to the Society to carry out its strategic goals and may cause the Society to pay attrition fees for unutilized hotel rooms. In addition, the Society is unable to assist you if you have any difficulties with your room reservation, such as the hotel over-booking or misplacing your reservation. SOT depends on the Annual Meeting revenue (hotel room commissions and rebates) to fund other programs throughout the year and to keep future registration fees low. Please assist the Society by making your hotel room reservation through SOT Housing Bureau. Rates shown are for single and double occupancy; additional fees may apply for additional guests. Please note: services offered, taxes, and fees associated with hotel services are subject to change and availability; tax rate 14.75%. Information listed is complete and accurate as of July 1, 2016. Note: Checkout times usually are between 11:00 am–1:00 pm; Check-in times usually are between 2:00 pm–4:00 pm.
Global Gallery of Toxicology

A Worldwide Vision for Toxicology

Opportunity to Learn About Toxicology Societies Around the World

- Accomplishments
- Initiatives
- Vision

Posters will be displayed prominently in the ToxExpo Exhibit Hall.

UPCOMING MEETING

SOT | Contemporary Concepts in Toxicology

METABOLIC SYNDROME

bench to clinic

March 11, 2017
Baltimore, Maryland

Satellite Meeting

WWW.TOXICOLOGY.ORG/METABOLIC
SOT Air Travel Provider—ATC Travel Management
ATC Travel is the official travel management firm for the SOT 56th Annual Meeting and ToxExpo.
Tel: 800.458.9383 | www.atcmeetings.com/sot
Email: reservations@atcmeetings.com
Hours of Operation: 8:30 AM–7:00 PM (ET) Monday–Friday

Please note that depending on your reservation method, ATC Travel Management charges a $10 online service fee or a live agent reservation fee.

To obtain the maximum discounted fares, call at least 60 days prior to departure and identify yourself as a Society of Toxicology meeting attendee. ATC Travel Management will find the best fare for you and email you an itinerary.

Before contacting ATC Travel Management, please gather the following information:

- Your name as it appears on your ID and your date of birth
- The desired dates of arrival to and departure from Baltimore
- Your home city or originating airport
- Your approximate time of departure from the originating airport
- The number of persons traveling (adults/children)
- Your method of payment, either credit card or check
- Your airline frequent flyer number(s)

Identify yourself as a Society of Toxicology attendee. ATC Travel Management will find the best fare for you and email you an itinerary.

Ground Transportation from the Airport
Ground transportation is located curbside outside the baggage claim area.

Car Rental
Passengers arriving on flights should take the free shuttle from the lower level terminal for a 10-minute ride to the rental car facility.

The 11 different car rental agencies that service the airport can be found on the BWI website at bwiairport.com/en/travel/ground-transportation/trans/carrental.

Shuttle Services
SuperShuttle and Execucar provide the most cost-effective ground transportation service between BWI Airport and major hotels in the downtown area. Shuttle service is operated from 8:00 am to 12:00 midnight daily. A discount for each service is available by using the discount code ZG7TC:

- 10% off all Execucar private airport sedans and SUVs
- $3.50 off all SuperShuttle round trips

These discounts are available online at SuperShuttle (www.supershuttle.com/default.aspx?GC=EA58G) and Execucar (www.execucar.com), as well as over the phone (SuperShuttle: 602.244.9000; Execucar: 800.410.4444).

Taxi Cabs
The taxi stand is located just outside of the baggage claim area of the Lower Level of the terminal. Taxicabs are prohibited from charging flat rates. For more information, call 410.859.1100 or visit www.bwiairporttaxi.com.

Train Transportation
AMTRAK
Tel: 800.872.7245 | www.amtrak.com

Amtrak operates out of Penn Station, which is a 20-minute drive from the Baltimore Convention Center and the SOT hotel area. There are always taxis ready and waiting outside the station.

Ride-Share Program
SOT is offering a ride-share program in conjunction with the Annual Meeting. For those who live close enough to the Baltimore area or those who do not wish to fly, you may want to consider the ride-share program. Avoid airport hassles by driving and make it easier for other scientists to attend by sharing rides. Students especially appreciate ways to make the meeting even more economical.

Once you have registered for the Annual Meeting, you can access the ride-share program. You can indicate whether you want to drive or be a passenger, and then see a list of others who have signed up. It will be up to you to match your plans with someone else who is registered, and then to remove your name when you have travel plans in place.

Getting around Town
Baltimore Convention Center Location and Parking
Baltimore Convention Center
One West Pratt Street
Baltimore, MD 21201

Ample public parking is available in close proximity to the convention center for an hourly/daily fee. Check the Baltimore Convention Center website for more information about parking.

Please review the SOT Hotel Services chart on page 19 for valet and self-parking rates for your hotel.

Public Transportation
The Maryland Transit Administration (MTA) operates bus, Metro Subway, Light Rail, and MARC train services. For fares and schedules, please call 888.218.2267 or 410.539.5000 or visit www.mta.maryland.gov.

The Charm City Circulator is a free transportation service with four routes that intersect downtown Baltimore, including a route to Fort McHenry National Monument and Historic Shrine. The routes also connect to other forms of transit such as the Light Rail, MARC, the Metro Subway, and the Baltimore Water Taxi.
Registration
Registration Deadlines
Registration for the Annual Meeting is open now. Register by January 13 to obtain the Early-Bird rate and to ensure that you receive your registration materials before the meeting. You can register online, via fax, or by mail to SOT Headquarters.
- Early-Bird Registration: January 13, 2017
- Standard Registration: February 10, 2017
- Final Registration after: February 10, 2017

How to Register

Online Registration
SOT members and nonmembers are invited to register for the 2017 SOT Annual Meeting using the SOT Online Registration System. The system is designed for those who will be paying their registration fee by credit card.

Registration information can be accessed via the SOT website at www.toxicology.org/register. After registering, you will receive an electronic confirmation. If you do not, please send an email to jimd@toxicology.org. The online registration system will be open throughout the meeting, and if you register online after March 9, 2017, you can easily pick up your badge at the “BADGE PICK UP” registration counter.

Confirmation
Online registrants will receive an electronic confirmation following registration. All registrants will be mailed a registration confirmation, name badge, and Continuing Education and/or event ticket(s) before the meeting if your registration form is received by January 13, 2017. If your registration is received after January 13, you can pick up your badge and tickets at the “BADGE PICK UP” registration counters on-site. You do not need to enter the regular registration line.

Mail or Fax Registration
Registrants may fax or mail their registration payments using the registration form located on pages 24–25. No phone registrations will be accepted.

Please type or print clearly.

Please send registration forms to:
SOT Headquarters
1821 Michael Faraday Dr, Suite 300
Reston, VA 20190
(Faxes require credit card payment)
Fax: 703.438.3113

Forms will be date-stamped as they arrive. This is your date of registration. Fax registrations will be accepted by SOT Headquarters only if a credit card number is clearly listed in the appropriate area. SOT needs only one copy for processing.

DO NOT mail your registration form to SOT if it will arrive after March 9, 2017. SOT will accept Annual Meeting registrations until March 9. After March 9, registrations not processed online will only be accepted on-site at the Annual Meeting.

Payment
Registration forms must be accompanied by one of the following methods of payment:
- Check (company or personal), United States currency only
  Please list all registrants on check memo or check stub.
- Government Purchase Order (Check must be drawn from the US Department of Treasury.)
- Money Order
- Visa, MasterCard, Discover, Diner’s Club, or American Express

Exhibitor Registration
To register exhibitor booth staff, please visit www.ToxExpo.com and log into the Exhibitor Service Center using your company password, which was provided in your booth confirmation email. For more information, please email sot_exhibits@toxicology.org.

Guest/Spouse Registration
If a non-scientist is accompanying you to the meeting, Guest Registration is available. You may register your guest while registering for the meeting. If you have already registered for the meeting, complete the Registration Form, marking the appropriate sections for Guest Registration and send it to SOT Headquarters along with a copy of your registration confirmation.

The SOT Guest/Spouse Hospitality Room, located in the Armistead Room at the Hilton Baltimore, provides guest registrants with a place to meet and socialize. The room will be open Sunday through Thursday.

Reminder: Guest registrants and children under the age of 15 are not permitted in the ToxExpo Exhibit Hall at any time or in Scientific Sessions. Only the Scientific Session Chairs can give permission for attendance for sessions held outside the Exhibit Hall.

Cancellation Refund Policy
All requests for cancellations and/or refunds must be received in writing at SOT Headquarters by February 10, 2017. These refunds will be processed, less a $50 cancellation fee, following the Annual Meeting. Refund requests received after February 10, 2017, will not be processed.

Nonmember Attendee Offer
JOIN SOT AND SAVE!

Special offer to nonmember 2017 Annual Meeting attendees: Submit your application for the May review cycle (deadline is May 1, 2017), and, upon acceptance, SOT will waive your 2017 membership dues.

More information can be found on the SOT website.
### Attendee Registration Form

**SOT 56th Annual Meeting • March 12–16, 2017**

(Required: Please check the appropriate box)

**PLEASE PRINT CLEARLY OR TYPE**

- SOT Member
- Nonmember
- Badge Name: ____________________________

| First Name/Middle Initial: | ____________________________ |
| Last Name: | ____________________________ |
| Professional Degree(s): | ____________________________ |
| Organization/University: | ____________________________ |
| (Is this a new employer and/or new address? Yes No) | ____________________________ |
| Company (second line): | ____________________________ |
| Department: | ____________________________ |
| Street Address: | ____________________________ |
| City/Region: | ____________________________ |
| State/Prov: | ____________________________ |
| Postal Code: | ____________________________ |
| Country: | ____________________________ |
| Area Code/Telephone Number: | ____________________________ |
| Fax Number: | ____________________________ |
| Email Address: | ____________________________ |

**Special Accessibility Requirements:**

- Postdoc
- Graduate Student
- Undergraduate Student (Fax or mail a copy of Student ID with the form)

**Institution:** ____________________________

**Advisor’s Name:** ____________________________

**Advisor’s Telephone Number:** ____________________________

**Advisor’s Email:** ____________________________

**Institution:** ____________________________

**Advisor’s Name:** ____________________________

**Advisor’s Telephone Number:** ____________________________

**Advisor’s Email:** ____________________________

**Registration Fee(s):**

<table>
<thead>
<tr>
<th>Early-Bird Registration (Received by Jan. 13)</th>
<th>Standard Registration (Jan. 14 to Feb. 10)</th>
<th>Final Registration (After Feb. 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOT Member</td>
<td>$320</td>
<td>$380</td>
</tr>
<tr>
<td>Nonmember**</td>
<td>$680</td>
<td>$740</td>
</tr>
<tr>
<td>SOT Retired/Emeritus Member</td>
<td>$70</td>
<td>$135</td>
</tr>
<tr>
<td>Postdoctoral SOT Member</td>
<td>$85</td>
<td>$135</td>
</tr>
<tr>
<td>Postdoctoral Nonmember**</td>
<td>$170</td>
<td>$220</td>
</tr>
<tr>
<td>Graduate Student Member</td>
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<td>$115</td>
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<tr>
<td>Graduate Student Nonmember**</td>
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<td>$180</td>
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<tr>
<td>Undergraduate Student (Copy of Student ID Required)</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>High School Student (Copy of Student ID Required)</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>SOT Global Partner</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>Press</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>Guest/Spouse (Nonscientist/No access to the scientific sessions or ToxExpo)</td>
<td>$70</td>
<td>$85</td>
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</tbody>
</table>

**Guest/Spouse Name:** ____________________________

**METHOD OF PAYMENT:**

All registrations submitted by hard copy or fax will be processed online by SOT staff.

- Check or Money Order # ____________________________ (PAYABLE TO “SOCIETY OF TOXICOLOGY”)
- Government Purchase Order # ____________________________ (US GOVERNMENT PO FORM MUST BE ATTACHED)
- American Express
- Diner’s Club
- Discover
- MasterCard
- Visa

**Credit Card #:** ____________________________

**Expiration Date:** ____________________________

**Signature:** ____________________________

**Cardholder’s Printed Name:** ____________________________

By registering for the SOT Annual Meeting you agree to the terms and conditions outlined in the registration policies on page 26.

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**RETURN THIS TWO-PAGE FORM WITH PAYMENT TO:**

SOT Headquarters Registration Dept., 1821 Michael Faraday Drive, Suite 300, Reston, VA 20190

Fax form to: 703.438.3113.

**Questions? Contact SOT • Tel: 703.438.3115 • Email: sothq@toxicology.org**

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* After February 10, Final Registration rates apply. SOT will accept faxed registration forms until March 9. Online registration will be open until March 16. On-Site registration forms will be available at the Annual Meeting Registration Desk.

** Special offer to nonmember 2017 Annual Meeting attendees: submit your completed application for the May review cycle (deadline May 1, 2017) and, upon acceptance, SOT will waive your 2017 membership dues.
CONTINUING EDUCATION COURSES:

Yes, I would like to attend the following CE courses. (Only meeting registrants may enroll in a CE course.)

<table>
<thead>
<tr>
<th></th>
<th>AM #</th>
<th>PM #</th>
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</thead>
<tbody>
<tr>
<td>Early-Bird Registration (Jan. 14 to Feb. 10)</td>
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<tr>
<td>Standard Registration (Jan. 14 to Feb. 10)</td>
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<tr>
<td>Final Registration (After Feb. 10)</td>
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<tr>
<td># of Courses</td>
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</tbody>
</table>

SOT Member/Global Partner
- $150 each
- $185 each
- $220 each
- $_______________

SOT Retired/Emeritus Member
- $110 each
- $145 each
- $180 each
- $_______________

Nonmember
- $300 each
- $335 each
- $370 each
- $_______________

Postdoctoral (SOT Member/Nonmember)
- $90 each
- $125 each
- $160 each
- $_______________

Graduate or Undergraduate Student (SOT Member/Nonmember)
- $45 each
- $80 each
- $115 each
- $_______________

Press
- $0 each
- $0 each
- $0 each
- $_______________

Yes, I would like to attend the Sunrise CE Mini-Course (includes continental breakfast)

SOT Member/Global Partner
- $55 each
- $90 each
- $125 each
- $_______________

SOT Retired/Emeritus Member
- $55 each
- $90 each
- $125 each
- $_______________

Nonmember
- $75 each
- $110 each
- $145 each
- $_______________

Postdoctoral (SOT Member/Nonmember)
- $55 each
- $90 each
- $125 each
- $_______________

Graduate or Undergraduate Student (SOT Member/Nonmember)
- $25 each
- $60 each
- $95 each
- $_______________

Press
- $0 each
- $0 each
- $0 each
- $_______________

STUDENT AND POSTDOCTORAL FUNCTIONS:

Yes, I am an undergraduate student and would like to attend the Sunday Undergraduate Education Program. (Limited seating and ticket required)

Yes, I am a student or postdoctoral registrant and would like to attend the complimentary Student/Postdoctoral Mixer on Sunday, 7:30 pm - 9:00 pm. (Ticket required)

Yes, I would like to attend the Complimentary Trainee Discussion with Daily Plenary Speakers:
- Monday, 9:45 am - 10:45 am: Peter Sorger and Stephen Friend
- Tuesday, 9:45 am - 10:45 am: Jun J. Yang and Richard Barker
- Wednesday, 9:45 am - 10:45 am: Paul Elliott

Yes, I am a graduate student or postdoctoral member registrant and would like to attend the complimentary Trainee Discussion with Daily Plenary Speakers:
- Monday, 9:45 am - 10:45 am: Peter Sorger and Stephen Friend
- Tuesday, 9:45 am - 10:45 am: Jun J. Yang and Richard Barker
- Wednesday, 9:45 am - 10:45 am: Paul Elliott

PRINT MATERIALS:

In an effort to conserve resources, the printed Program will be mailed ONLY by request (in the US and Canada only). If you wish to receive your printed Program via the SOT website, please mark this checkbox and it will be mailed to you in early March (in the US and Canada only). The Program will be available for download via the SOT website in January and for pick up on site.

Yes, I want to receive the printed Program in the mail (option not available after February 10, 2017).

2017 Annual Meeting registrant fees include access to the abstracts as a downloadable PDF of The Toxicologist via the SOT website.

Yes, I want to purchase the printed version of The Toxicologist (available for pick up on site while supplies last).

REGISTRANT — CIRCLE ALL THAT APPLY: (YOU MUST MAKE ONE SELECTION/CATEGORY)

A. Type of Organization:
- Academia
- Consultant
- Contract Research
- Government
- Military
- Private Industry
- Other

B. Job Function:
- Analytical
- Financial/Purch.
- Computer/Statistics
- Health and Safety
- Mgmt. Corporate
- Mgmt. Facilities
- Mgmt. Personnel
- Marketing/Sales
- Quality Assurance
- Regulatory

C. Field of Work:
- Biological Modeling
- Biotechnology
- Carcinogenesis
- Cardiovascular
- Clinical & Transl. Tox.
- Comparative and Vet.
- Dermal Tox.
- Drug Discovery Tox.
- Epidemiology
- Ethical, Legal, and Social Issues
- Food Safety
- General Tox.
- Genetic Tox.
- Immunotoxicology
- Infusion Tox.
- Inhalation Tox.
- In Vivo and In Vitro Methods
- Mechanisms
- Medical Devices
- Metals
- Methods
- Mixtures
- Molecular Biology
- Mutagenicity
- Nanotoxicology
- Neurotoxicology
- Occupational and Public Health
- Ocular Tox.
- Pathology
- Pharmacokinetics
- Pharmacology
- Risk Assessment
- Reg. and Safety Eval.
- Repro. and Develop. Tox.
- Stem Cells
- Other

D. Product Interest:
- Analytical
- Aquatic Tox.
- Clinical Tox.
- Computer
- In Vivo
- In Vitro
- Analytical
- Pathology
- Preclinical Tox.
- Quality Assurance
- Wildlife Tox.

E. Purchasing Responsibilities:
- a. I make purchasing decisions
- b. I influence purchasing decisions
- c. I do not participate in purchasing decisions

There will be no refunds for cancellations received at SOT Headquarters after February 10, 2017.
Registration Materials

Badges

Badges and event tickets will be mailed in advance if you register by January 13, 2017. If you need to register or have not received your badge, assistance will be available on-site in the registration area.

NOTE: If you are registered and have your badge, you do not need to enter the registration line.

Program

The printed Program will be mailed ONLY by request (in the US and Canada only). If you wish to receive your printed Program before the meeting, please select the appropriate box on the registration form.

Submission must occur by February 10. The Program will be mailed to you in early March (in the US and Canada only). The Program also will be available for download via the SOT website in early February and for pick up on-site. See page 34 for more details about the Program and The Toxicologist.

2017 SOT Annual Meeting Policies

By registering for the 2017 SOT Annual Meeting, you are agreeing to the following terms and conditions:

For individuals who are not members of SOT, participation in SOT’s Annual Meeting and ToxExpo is available only to bona fide individuals who are engaged in or promote the field of toxicology or biotechnology research and support the growth and development of the toxicology field.

For organizations, participation in SOT’s Annual Meeting and ToxExpo is available only to bona fide organizations with public policy positions and business practices that are generally consistent with SOT’s mission, goals, reputation, and its policies and principles as determined by SOT.

SOT reserves the right to review applications for participation at SOT’s Annual Meeting and ToxExpo to confirm that the applicant meets these criteria and may, at SOT’s sole discretion, reject a registration by any individual or organization or withdraw registration privileges at any time if any individual or organization is found to be inconsistent with SOT’s principles and interests.

Unless written notification by the registrant, stating otherwise, is submitted to SOT Headquarters prior to the Annual Meeting or while registering on-site, SOT Annual Meeting registrants grant SOT permission:

• To reproduce, copy, and publish image, voice, and any or all media taken at the Annual Meeting.

• To share registrant contact information with organizations that we believe might have a product or service of interest to you. Limited data provided to third parties include name, affiliation, and business address. Your telephone and fax numbers, and email will not be disclosed to third parties.

• To share registrant name and affiliation with SOT exhibiting companies.

• To be included in the attendee listing accessible to meeting registrants using the Mobile Event App—registrant name and affiliation shared.

SOT Annual Meeting registrants are prohibited from:

• Inviting children under the age of 15 and guest/spouse registrants into the ToxExpo Exhibit Hall. (Session chairs must provide consent for the guest/spouse or child to attend sessions.)

• Soliciting in the ToxExpo Exhibit Hall unless they are a current exhibitor. SOT retains the right to have removed from the exposition any company that has not duly contracted for exhibit space.

• Taking photographs or other electronic capture of scientific sessions in meeting rooms or the ToxExpo without the consent of the session chair and the presenter(s)/author(s).

• Photographing colleagues against the backdrop of scientific posters on display without the express consent of the presenting author(s).

• Photographing exhibit booths.

• Speaking on a cell phone while attending scientific sessions.

The Toxicologist

The Toxicologist contains the abstracts for the meeting. A printed copy of The Toxicologist may be purchased by selecting the appropriate box on the registration form. Printed copies will be available on-site in the registration area. A PDF version will be available for download via the SOT website.

Tickets

Tickets are required for Continuing Education (CE) courses and some other events. If you have these events on your registration form, your tickets will be issued with your meeting badge. Annual Meeting registration is required to participate in CE and other activities.

ToxExpo Directory

The ToxExpo Directory provides an outline of each exhibiting organization along with their contact information and area of expertise. Use the directory to plan your ToxExpo experience and learn about emerging organizations and developing technology.

Advertising opportunities are available in the ToxExpo Directory! Visit our website at www.ToxExpo.com for details or contact Tonja Morrow at tmorrow@toxicology.org.
Join SOT and Save!

Special Offer for Nonmember 2017 Annual Meeting Attendees:
Submit your completed application for the May review cycle and, upon acceptance, SOT will waive your 2017 membership dues.

Member Benefits Include:

- Discounted registration rates for SOT-hosted meetings.
- Ability to communicate and collaborate with colleagues from industry, government, and academia.
- Access to Toxicological Sciences, the official journal of the Society.
- Connecting with Regional Chapters, Special Interest Groups, and Specialty Sections.
- Qualifying for more than 45 SOT Awards.
- Career and education resources.

Choose the membership level that’s right for you:
Full • Associate • Postdoctoral • Graduate Student

Reduced dues available to members from developing countries.

8,100 members from more than 70 countries
Join the SOT community by completing the online membership application at www.toxicology.org.
General Information
The SOT 56th Annual Meeting and ToxExpo will be held at the Baltimore Convention Center located at 1 West Pratt Street in downtown Baltimore. For things to do in Baltimore, see page 35 or visit the SOT Discover Baltimore website, www.baltimore.org/sot.

**Business Center**

**Tel:** 410.649.7194  
**Email:** baltimore.cc@abcimaging.com

The Baltimore Convention Center ABC Imaging Business Center is located in the Pratt Street Lobby across from Room 334. The Business Center offers services such as shipping via FedEx, DHL or UPS; common office supplies; and high-quality full color and black and white copying, printing, and uploading of documents from a memory stick or CD.

- **Business Center Hours:**
  - Saturday–Sunday: Closed
  - Monday–Tuesday: 8:30 AM–4:30 PM
  - Wednesday: 8:30 AM–7:00 PM
  - Thursday–Friday: 8:30 AM–4:30 PM

**Child Care Services**

Child care services are not provided during the Annual Meeting. Arrangements may be made by contacting the concierge desk at your hotel. Children are not permitted in session rooms, the Exhibit Hall, or the poster area.

**Coat/Luggage Check**

For your convenience, a coat/luggage check will be available near the Pratt Street lobby. The coat/luggage check will be open Sunday, March 12, through Thursday, March 16. There will be a fee of $3 per item checked. Laptops, cameras, and other electronics will not be accepted.

- **Hours of Operation:**
  - Sunday: 7:00 AM–8:00 PM
  - Monday: 7:00 AM–6:00 PM
  - Tuesday: 7:00 AM–6:00 PM
  - Wednesday: 7:00 AM–6:00 PM
  - Thursday: 7:00 AM–12:00 Noon

Coat/Luggage Check hours are subject to change.

**Maps of the Baltimore Convention Center, as well as room information for sessions and services, are available on the SOT Mobile Event App. See page 2 for details.**

(continued on page 31)
Why do you love toxicology?

Tell the world on social media using #YouTox. 📱💡

Initiative spearheaded by the Graduate Student Leadership Committee (GSLC) Communications Subcommittee

Calling All Contestants!

**TOX SHOWDOWN**

An evening of tox trivia and fun as three teams compete to see who knows the most when it comes to toxicological fact and fancy. To participate, contact sothq@toxicology.org.

Tuesday, March 14 | 7:30 PM | Baltimore Hilton Hotel
First Aid and Emergency Services at the Convention Center

If an emergency should occur while at the Baltimore Convention Center, use any beige house phone located around the facility to contact the Public Safety Office or call 410.649.7055. You will be connected directly to the 24-hour manned public safety dispatcher at the convention center.

A First Aid room will be located in the Pratt Street East Show Office.

Hours of Operation:

- Saturday: 12:00 Noon–7:00 PM
- Sunday: 6:00 AM–8:00 PM
- Monday: 7:00 AM–6:00 PM
- Tuesday: 7:00 AM–6:00 PM
- Wednesday: 7:00 AM–6:00 PM
- Thursday: 7:00 AM–12:00 Noon

Please note that in accordance with regulations, the first aid administrator is not permitted to dispense any medication.

Guest/Spouse Hospitality Room

The SOT Guest/Spouse Hospitality Room will be located in the Hilton Baltimore in the Armistead Room. The Hospitality Room provides guest registrants (nonscientists) with a place to meet and socialize with other guests. The room will be open Sunday through Thursday, and information on local attractions will be available. Guests and spouses must be registered for the Annual Meeting to access the Hospitality Room. Guests must register for the Annual Meeting with the person they are accompanying. Registration information is available on page 23.

Internet Access at the Convention Center

SOT knows the importance of staying connected to your daily activities while attending the Annual Meeting and provides several ways for you to access the Internet while in the Baltimore Convention Center.

@SOT Center—Internet Access

SOT will provide computers you can use to access the Internet. These computers are available to attendees in the @SOT Center, located near the Registration Desk.

Free Wireless Internet Access

As a service to Annual Meeting attendees, SOT will be providing free wireless Internet access in designated areas of the Baltimore Convention Center.

Lost and Found

Lost and found articles should be taken to the SOT Headquarters Office in the convention center. Any items left in the office after 12:00 noon, Thursday, March 16, will be returned to SOT Headquarters. If you do not remove your poster at the end of your session, you will find it on the “Poster Retrieval Tables” located in the Exhibit Hall. Any posters left behind at 4:30 pm on Wednesday will be taken to SOT Headquarters Office, Thursday morning, March 16. All posters not claimed by 12:00 noon on Thursday, March 16, will be recycled.

Any items that are left behind in any of the rooms should be taken to the SOT Headquarters Office.

If you have any questions regarding these policies, please contact the SOT Headquarters Office.

Media Support Services

SOT welcomes accredited representatives of media organizations to its Annual Meeting. Attending media representatives receive complimentary registration for the meeting, and interviews can be arranged with SOT Council members, meeting speakers and presenters, and SOT general members. For more information, please contact Michelle Werts (Tel: 703.438.3115; michelle@toxicology.org).

Scientific Poster Printing Services

SOT is pleased to offer poster presenters a convenient printing service through Shepard Exposition Services, the official general service contractor for the SOT Annual Meeting and ToxExpo. Shepard will produce your poster for a reasonable price (rates available on the Poster Printing Order Form), which will include transportation and storage for the show. Preordered posters should be picked up on-site at the Exhibitor Service Center in the ToxExpo Exhibit Hall.

The deadline to take advantage of this service is February 20, 2017. To place an order for poster printing, complete the Poster Printing Order Form available in the Presenters section of the SOT Annual Meeting website (www.toxicology.org/2017) and email (abarker@shepards.com) or fax (410.737.9270) it to Shepard Exposition Services. For further information, contact Shepard at 410.737.9270, Monday–Friday 8:00 am–5:00 pm (ET).

Viewing Abstracts

All abstracts are available through the SOT Mobile Event App beginning in February. The Toxicologist and The Toxicologist: Late-Breaking Abstracts Supplement will be available to download as PDFs via the SOT website in March. Printed copies of The Toxicologist are available for a fee at Registration.

(Please see complete details on page 78.)
51 Ways to Enhance Your Annual Meeting Experience

Regional Chapters
Participate in the reception of your hometown chapter while you are in Baltimore—Attend the local events during the year.

Special Interest Groups
Participate in events that bring together scientists who share a common interest in issues germane to their communities.

Specialty Sections
Participate in meetings and network with individuals who share common scientific interests, join in recognition of Award Recipients, and have some fun!

Get Involved—You’ll be glad you did!
Become an active Regional Chapter, Special Interest Group, or Specialty Section member! Their events are held throughout the Annual Meeting and are open to those who are interested in joining. If you’re a component group member, you know these events are the perfect opportunity to connect with existing friends and colleagues, and create new relationships.

See page 55 for the schedule component group events.
On-Site Services

SOT Headquarters Office
The SOT Headquarters Office is located in the Baltimore Convention Center. SOT leadership and staff utilize this office to conduct SOT business while on-site. Attendees are encouraged to visit the office to receive assistance with the Mobile Event App or for general inquiries and assistance.

 процедура
Sunday _______ 7:00 AM–8:00 PM
Monday _______ 7:00 AM–6:00 PM
Tuesday _______ 7:00 AM–6:00 PM
Wednesday _______ 7:00 AM–6:00 PM
Thursday _______ 7:00 AM–12:00 Noon

SOT Pavilion
Stop by the SOT Pavilion anytime during ToxExpo hours. Get answers to SOT questions and catch up with friends and colleagues. You can:
• Chat with Toxicological Sciences Editor-in-Chief Gary Miller and Managing Editor Virginia Hawkins.
• Share your Annual Meeting, SOT, and toxicology experiences in our social media corner.
• Receive guidance on communicating your science more effectively.
• Learn about SOT activities, programs, and membership.

You always are welcome at the SOT Pavilion. See you there!

SOT has the Numbers Exhibitors Want
6,500 scientists and industry experts attend the SOT Annual Meeting and ToxExpo. Take the opportunity to…
• meet face-to-face,
• build relationships with new prospects, and
• network with exhibiting companies.

Highly Influential Audience
Over 70 percent of ToxExpo attendees are involved in purchasing decisions.

Online Marketplace at ToxExpo.com
ToxExpo exhibitors are a year-round resource online at ToxExpo.com, which provides a robust search feature allowing you to locate an exhibitor by name, service, or product. ToxExpo.com is a resource for all the products and services necessary to toxicologists throughout the year.

A Global Audience
Nearly 20 percent of SOT’s Annual Meeting and ToxExpo attendees represent scientists from countries outside the United States.

ToxExpo Attendees Are Engaged in One or More of the Following Areas of Research
• Biological Modeling
• Biomarkers
• Biotechnology
• Carcinogenesis
• Cardiovascular Toxicology
• Clinical and Translational Toxicology
• Comparative and Veterinary
• Dermal Toxicology
• Drug Discovery Toxicology
• Epigenetics
• Ethical, Legal, and Social Issues
• Food Safety
• Immunotoxicology
• In Vitro and Alternative Methods
• Inflammation and Disease
• Inhalation and Respiratory
• Mechanisms
• Medical Device and Combination Product
• Metals
• Mixtures
• Molecular Biology
• Nanotoxicology
• Neurodegenerative Disease
• Neurotoxicology
• Occupational and Public Health
• Ocular Toxicology
• Pharmacology
• Regulatory and Safety Evaluation
• Reproductive and Developmental Toxicology
• Risk Assessment
• Stem Cells
• Toxicologic and Exploratory Pathology

For more information about exhibiting at the largest toxicology exposition in the world, please visit ToxExpo.com, or contact Tonja Morrow at 703.438.3115 or email at tmorrow@toxicology.org.
The Program
The Program is the official guide to all the activities of the 2017 Annual Meeting and ToxExpo. The Program includes detailed information on the Scientific Sessions, including an overview for these sessions, with the exception of the Poster and Platform Sessions. The Program includes the Poster Session schedule and a map of the Poster Sessions, as well as an overview of all the Continuing Education course offerings.

Copies of the Program can be picked up on-site. The printed Program will be mailed ONLY by request (within the US and Canada only). If you wish to receive your printed Program before the meeting (request made by February 10), please select the “I want to receive the printed Program before the meeting by mail” checkbox on the registration form, and the Program will be mailed in late February (in the US and Canada only). The Program PDF is available for download via the SOT website in February.

All of the information available in the Program also is available in the SOT Mobile Event App (see page 2 for details).

Scientific ePosters
SOT is pleased to offer our poster presenters the opportunity to share their research electronically as well as in their assigned Poster Sessions. Poster presenters will be able to upload their ePosters beginning in mid-February. ePosters will be available to meeting attendees exclusively through the SOT Mobile Event App until May 11, 2017.

The Toxicologist: The Official Record of the 2017 Annual Meeting Abstracts
The Toxicologist is an important scientific resource, as it is the official compilation of all accepted abstracts for the 56th Annual Meeting of the Society of Toxicology. With nearly 2,500 abstracts for the meeting, this supplementary issue of Toxicological Sciences is a critical publication to access the latest findings in toxicology.

• A copy of the printed version of The Toxicologist may be purchased for $50 by preordering via the registration form or on-site while supplies last.
• The Toxicologist PDF is available for download via the SOT website.
• Full abstracts can be accessed via the Mobile Event App or Online Planner.
• Late-breaking abstracts are available in the The Toxicologist: Late-Breaking Supplement, available in March as a PDF only.

ToxExpo Directory
The ToxExpo Directory provides an outline of each exhibiting organization along with their contact information and area of expertise. Use the directory to plan your ToxExpo experience and learn about emerging organizations and developing technology.

Advertising opportunities are available in the ToxExpo Directory! Visit our website at www.ToxExpo.com for details or contact Tonja Morrow at tmorrow@toxicology.org.
Discover Baltimore, Maryland

Baltimore offers the perfect combination of history, culture, fun, and excitement, with a touch of hometown hospitality. Known as Charm City, Baltimore is easy to get to and easy to get around, and nearly everything is within walking distance from the spacious Baltimore Convention Center and the world-famous Inner Harbor.

A variety of first-class hotels and outstanding restaurants, one-of-a-kind attractions and museums, great sports venues, and more are part of the city’s compact, convenient “convention campus.”

But if the Inner Harbor is Baltimore’s heart, its diverse neighborhoods are its soul. Neighborhoods—from trendy Harbor East and kitschy Hampden to the cultural hub of Mount Vernon and the historic Federal Hill and Fell’s Point—are great places for you to explore and discover fantastic shopping, a diverse culinary scene, fascinating history and heritage, and much more while enjoying the SOT Annual Meeting.

Fun Facts

- Baltimore is the hometown of the most decorated Olympian of all time, Michael Phelps, and baseball great Babe Ruth.
- Baltimore’s waterfront neighborhood of Fell’s Point was the second largest point of immigration after Ellis Island in New York.
- Baltimore is home to The Lacrosse Museum and National Hall of Fame where visitors can discover and relive the origins of America’s oldest sport.
- Baltimoreans take pride in the fact that their doorsteps are made from the same beautiful white marble used for the construction of the famous Washington Monument located in Washington, DC.
- Popular TV shows filmed in Baltimore include HBO’s The Wire and Netflix’s House of Cards.
- The first dental school was founded in Baltimore in 1830.
- “The Star-Spangled Banner,” the US national anthem penned by Francis Scott Key, was inspired by the events at the Battle of Baltimore during the War of 1812.

Green Baltimore

Visit Baltimore, the Maryland Office of Tourism Development, the Baltimore Convention Center (BCC), and hospitality businesses are working closely with meeting professionals to provide greener experiences for attendees. A number of initiatives are already in place to help offset the carbon footprint and foster green meetings. The Baltimore Convention Center has “gone green” on a number of fronts. Examples include:

- The center takes trash to the “Wheelabrator Incinerator,” which converts trash to electricity.
- The BCC is the first convention center in the country to operate SOMAT, a two-part waste reduction system that reduces solid waste up to 90 percent and produces a useable soil product.
- Completed in August 2010, the center’s 27,000-square-foot Outdoor Terrace Green Roof, featuring drought-resistant vegetative roofing, doubles as space for receptions or relaxation. The beds are maintained with material produced from the SOMAT system.
- Eighty percent of the cleaning products used at the center are certified as “Green Seal” or “Designed for the Environment,” including paper products used in the restrooms.
- The center’s VIP Suites, Board Room, and East Side restrooms have been renovated to incorporate fixtures that reduce annual water consumption by 25 percent.
- A performance contract with Constellation Energy has re-lamped the entire facility with energy-efficient bulbs that provide financial savings as well as reduce carbon, sulfur, nitrogen dioxide, and mercury.
- Visit Baltimore became the first CVB in the Northeast to achieve a new international sustainability standard, the Level One certification to the ASTM Standard pertaining to the Evaluation and Selection of Destinations for Environmentally Sustainable Meetings, Events, Trade Shows, and Conferences (APEX/ASTM).

Weather

Baltimore in March.

54°F to 34°F

For an up-to-date, detailed weather forecast, visit the National Weather Service Forecast Office at www.weather.gov/lwx.
SOT FDA Colloquia on Emerging Toxicological Science: Challenges in Food and Ingredient Safety

Organized by Society of Toxicology and the US FDA Center for Food Safety and Applied Nutrition

Toxicological Training
- High quality
- Cutting-edge
- Future-oriented
- Accessible at no cost
  o Attend on-site
  o Receive webcast
  o Review recordings and materials on SOT website

✈ Upcoming Colloquia ✈

- December 1: Application of In Vitro to In Vivo Extrapolation in Safety Assessment
- March: Clarifying “Adversity” in Food Safety
- May/June: Watch for topic announcement

Wiley Auditorium
US FDA, Center for Food Safety and Applied Nutrition
5001 Campus Drive, College Park, Maryland 20740

Also Webcast

✈ Previous Colloquia ✈

- State of the Science in Developmental Neurotoxicology
- Safety Assessment in Young Children
- State of the Art in the Cramer Classification Scheme and Threshold of Toxicological Concern
- Role of Mode of Action in Dose-Response Assessment for Carcinogens
- A Path Forward for Using Computational and In Vitro Methods for Food Ingredient Assessments
- Contemporary Issues in Risk Assessment
- Immunotoxicology in Food and Ingredient Safety Assessment: Approaches and Case Studies
- Application of ADME/PK Studies to Improve Safety Assessments for Foods and Cosmetics
- Complexities in Evaluating Human Clinical and Observational Data for Ingredient Safety Assessment: Partially Hydrogenated Oils As a Case Study

Find details and recordings at www.toxicology.org/fda
Green Baltimore (continued)

• Maryland Green Travel, launched by the State of Maryland, encourages environmentally friendly practices in all aspects of the state’s tourism industry and promotes Maryland as a green destination. Visit www.visitmaryland.org/green to find information about the state’s green programs and listings of certified members of the hospitality industry actively involved, including LEED-certified hotels in Baltimore.

• In an effort to keep Baltimore green and easy to navigate, the city introduced the Charm City Circulator—a fleet of free bus shuttles that travel four routes throughout the city. The shuttle is intended to reduce congestion and greenhouse gas pollution by offering a convenient, reliable, and eco-friendly form of public transportation. The fleet of shuttles is composed of 21 hybrid electric vehicles, the first fleet of this type in a major metropolitan area.

• The Waterfront Partnership of Baltimore’s Healthy Harbor initiative installed the world’s first solar and hydro-powered Water Wheel trash interceptor located in the harbor. It uses a combination of old and new technology to harness the power of water and sunlight to pick up litter and debris flowing down the Jones Falls River and has removed hundreds of tons of trash and debris from the harbor. The initiative also introduced Floating Wetlands in the Inner Harbor, 2,000 square feet of floating islands planted with native species that provide habitat for marine life and help clean the water.

• In the past few years, the Downtown Partnership of Baltimore has established and grown a Green Team to improve and maintain open spaces throughout the city. Their efforts have included planting thousands of seasonal plants throughout the downtown area, removing garbage from city streets, creating curbside cafes and other outdoor public spaces, re-landscaping, installing new trees and water runoff control zones, and more.

Baltimore-Area Activities

For more information about things to do in Baltimore, go to www.baltimore.org/sot.

American Visionary Art Museum
800 Key Highway | Tel: 410.244.1900

This one-of-a-kind national museum and education center presents outstanding original works by intuitive, self-taught artists.

Baltimore Museum of Industry
1415 Key Highway | Tel: 410.727.4808

Explore industries of yesterday, today, and tomorrow, from canning oysters to making video games. The museum also offers family tours and free on-site parking.

Babe Ruth Birthplace Museum
216 Emory Street | Tel: 410.727.1539

Located two blocks from Camden Yards, this National Historic Site is Babe Ruth’s birthplace and features rare artifacts, photos, videos, and more.

Baltimore Museum of Art
10 Art Museum Drive | Tel: 443.573.1700

Maryland’s largest art museum showcases a dazzling collection, from ancient mosaics to contemporary art, and offers free admission. The museum also features the world’s most extensive collection of works by famed artist Henri Matisse.

B&O Railroad Museum
901 W. Pratt Street | Tel: 410.752.2490

The “birthplace of American railroading” features the most comprehensive collection of 18th- and 19th-century railroad artifacts, plus America’s first mile of commercial railroad track.
Meet the Editor-in-Chief of Toxicological Sciences

Gary W. Miller

SOT Pavilion
Monday–Wednesday
March 13–15
2:00 PM–4:00 PM


Tell the stories of the science and events at the 2017 meeting.

Become an SOT Reporter.

Contact michelle@toxicology.org to sign up and for more information.
Fort McHenry National Monument and Historic Shrine  
2400 E. Fort Avenue | Tel: 410.962.4290

This 18th-century brick fort defended the Baltimore Harbor during the War of 1812 and is the birthplace of the United States’ National Anthem. Park rangers offer visitor programs and special events that highlight the park’s history.

Geppi’s Entertainment Museum  
301 W. Camden Street | Tel: 410.625.7060

Journey through American history with a focus on pop culture in media, toys, and comic characters at this museum that offers a magical blend of entertainment and education.

Historic Ships in Baltimore  
Pier 1, 301 E. Pratt Street | Tel: 410.539.1797

Historic Ships in Baltimore encompasses four ships and a lighthouse—the USS Constellation, USS Torsk, USCGC Taney, Lightship 116 Chesapeake, and Seven Foot Knoll Lighthouse. Enjoy “hands-on encounters with history,” demonstrations, activities, overnight adventures and tours, and more.

Jewish Museum of Maryland  
15 Lloyd Street | Tel: 410.732.6400

The museum features multiple exhibition galleries, two historic synagogues—Lloyd Street (1845) and Bnai Israel (1876)—a research library, archives, and a gift shop.

Maryland Historical Society  
201 W. Monument Street | Tel: 410.685.3750

The historical society is one of the nation’s oldest cultural institutions, founded in 1844. Its many treasures include the original, only-surviving manuscript of “The Star-Spangled Banner.”

Oriole Park at Camden Yards  
333 W. Camden Street | Tel: 410.685.9800

Home of Major League Baseball’s Baltimore Orioles, Oriole Park at Camden Yards was the first of the downtown retro ballparks to be built.

Power Plant Live!  
34 Market Place | Tel: 410.727.LIVE

Power Plant Live! features entertainment, restaurants, and nightclubs, all spilling out into a common plaza with outdoor seating.
General Information

Discover Baltimore

Reginald F. Lewis Museum of Maryland African American History & Culture
830 E. Pratt Street | Tel: 443.263.1800
This museum highlights the history and accomplishments of Maryland’s African-American community through an extensive permanent collection and exhibition galleries.

Ripley’s Believe it or Not! Baltimore
301 Light Street, Light Street Pavilion | Tel: 443.615.7878
Ripley’s features hundreds of unbelievable interactive exhibits, a 4D moving theater, and the Marvelous Mirror Maze.

Top of the World Observation Level
401 E. Pratt Street, World Trade Center, 27th Floor | Tel: 410.837.VIEW
A spectacular and unforgettable view of Baltimore awaits you from the top of the world’s tallest pentagonal building. New exhibits about local landmarks, famous people and “firsts,” and historic events will engage and inspire you to explore more of Charm City!

The Walters Art Museum
600 N. Charles Street | Tel: 410.547.9000
This free museum features 55 centuries of art, including Egyptian mummies, medieval armor, illustrated manuscripts, and Asian art and European masterpieces.

Washington Monument
699 N. Charles Street | Tel: 410.962.5070
Recently renovated, this is the nation’s first monument dedicated to the United States’ first president, George Washington. Check out interactive digital exhibits inside, or take the 227-step climb to the top for breathtaking views of the city.

Science-Based Attractions

Carrie Murray Nature Center
1901 Ridgetop Road | Tel: 410.396.0808
www.carriemurrarnaturecenter.org
This nature center is located inside Baltimore’s 1,216-acre historic Gwynns Falls/Leakin Park. The nature center features a rehabilitation center to care for injured and orphaned wildlife, a one-of-a-kind Rainforest Room, program area, a hawk house, live reptiles and amphibians, and more.

Cylburn Aboretum
4915 Greenspring Avenue | Tel: 410.367.2217
www.cylburn.org
The aboretum is a public garden/nature preserve of 200+ acres, featuring trails through a piedmont forest, man-made wetlands, and a historic mansion. There are multiple indoor and outdoor activities available, including walking along three miles of wooded trails; taking a free, self-guided cell phone tour; visiting the Nature Museum; and more.
Howard Peter Rawlings Conservatory and Botanic Gardens
3100 Swann Drive | Tel: 410.396.0008
www.rawlingsconservatory.org

The historic Rawlings Conservatory features year-round displays of plants in five distinct greenhouse rooms—the 1888 Palm House, the Orchid Room, the Mediterranean House, the Tropical House, and the Desert House.

Maryland Science Center
601 Light Street | Tel: 410.685.5225
www.mdsci.org

The science center overlooks the Inner Harbor and features three levels of hands-on exhibits—including “Dinosaur Mysteries,” which features a dozen full-size dinosaurs—an IMAX theater, and Planetarium.

Maryland Zoo in Baltimore
1876 Mansion House Drive, Druid Hill Park | Tel: 410.396.7102
www.marylandzoo.org

The zoo is home to more than 1,500 exotic mammals, birds, and reptiles in a wooded, 180-acre setting. Visit the newest exhibit, Penguin Coast, home to one of the largest and most successful African penguin breeding colonies in all of North America. Enjoy daily activities like training demos, chats with animal keepers, feedings, and more.

National Aquarium
501 E. Pratt Street | Tel: 410.576.3800
www.aqua.org

Located in the heart of the Inner Harbor, the aquarium features more than 20,000 animals in award-winning habitats. The newest exhibit, Living Seashore, is an interactive exhibit replicating the Mid-Atlantic seashore that features two touchpools and a variety of hands-on experiences, like feeling Atlantic stingrays, moon jellies, horseshoe crabs, and other animals.

National Museum of Dentistry
31 S. Greene Street | Tel: 410.706.0600
www.dental.umaryland.edu/museum/index.html

The museum is designated as the official museum of the dental profession in the US. Its extensive 40,000 object collection of dental instruments, furniture, and artwork is one of the most important and oldest in the world, tracing its roots to the Baltimore College of Dental Surgery, the world’s first college of dentistry, founded in Baltimore in 1840.
AWARDS CEREMONY
Sunday, March 12, 2017 • 5:15 PM to 6:30 PM
Music Starting at 4:45 PM
Awards and Fellowships

**Awards Ceremony Music**

**Sunday, March 12, 4:45 PM to 5:15 PM**

*Performed by Luke Brindley*

Luke Brindley is a critically acclaimed singer/songwriter and fingerstyle guitarist. He tours nationally and has a dynamic live show. Along with his brothers, he owns Jammin Java, a premier music venue in Virginia presenting the finest local, regional, and nationally touring acts.

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**Awards Ceremony**

**Sunday, March 12, 5:15 PM to 6:30 PM**

Please join the Awards Committee, in conjunction with SOT Council, the Board of Publications, and the Education Committee, as we honor distinguished scientists at our prestigious SOT Awards Ceremony (pages 44–47). At the ceremony, SOT Awards are presented, as well as a number of grants, fellowships, and other honors for cutting-edge and novel research. Please refer to the Awards and Fellowships section of the SOT website for complete details at [www.toxicology.org/awards](http://www.toxicology.org/awards).

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**Endowment Fund 2016 Awards**

The Endowment Fund Awards are conferred throughout the Annual Meeting. SOT Endowment Award recipients are recognized through picture displays during the Awards Ceremony Music. SOT Endowment Funds have a mission of assisting in advancing the science of toxicology by providing financial support for the Society’s programs. The vision for the SOT Endowment Fund is to establish and increase in net worth a set of Endowment Funds that will provide significant, stable, long-term financial support to aid in achieving the Society’s strategic objectives. To learn more, visit [www.toxicology.org/endowment](http://www.toxicology.org/endowment).

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**Upcoming Award Announcements**

**Regional Chapter, Special Interest Group, and Specialty Section Awards**

Regional Chapters, Special Interest Groups, and Specialty Sections offer awards throughout the year. Recognition and presentation of these awards will occur during their respective meetings and receptions in Baltimore. Visit the SOT website for full details at [www.toxicology.org/awards](http://www.toxicology.org/awards).

**SOT Developing Country Travel Awards**

The SOT/SOT Endowment Fund/IUTOX Travel Awards for several individuals from countries where toxicology is underrepresented will be honored during the Awards Ceremony.

**Outstanding Graduate Student Leadership Committee Award**

The Outstanding Graduate Student Leadership Committee Award recognizes a student representative who has contributed to the Society in a significant manner (i.e., above and beyond the normal expected basic service as a representative). Academic achievements are not considered for the award. Representative nominations and support letters should be submitted by February 1. The recipients will be honored during the Student/Postdoctoral Scholar Mixer on Sunday, March 12.
Awards and Fellowships

SOT Honors and Awards

Honorary Membership
George D. Leikauf, PhD
University of Pittsburgh, Pittsburgh, PA

Founders Award
Meryl Karol, PhD, ATS
University of Pittsburgh, Pittsburgh, PA

Honorary Membership
Jonathan M. Samet, MD
University of Southern California, Los Angeles, CA

Merit Award
Samuel Cohen, MD, PhD, ATS
University of Nebraska Medical Center, Omaha, NE
Merit Award Lecture—
Monday, March 13, 12:30 PM to 1:20 PM

Achievement Award
Jason Richardson, PhD, DABT
Northeast Ohio Medical University, Rootstown, OH

Public Communications Award
Bernard Goldstein, MD
University of Pittsburgh, Pittsburgh, PA

Arnold J. Lehman Award
Lorenz Rhomberg, PhD, ATS
Gradient, Cambridge, MA

Translational Impact Award
Laura James, MD
University of Arkansas for Medical Sciences, Arkansas Children’s Hospital, Little Rock, AR
Translational Impact Award Lecture—
Wednesday, March 15, 5:00 PM to 5:50 PM

Distinguished Toxicology Scholar Award
Linda Birnbaum, PhD, DABT, ATS
NIEHS-NTP, Research Triangle Park, NC
Distinguished Toxicology Scholar Award Lecture—
Wednesday, March 15, 12:30 PM to 1:20 PM

Translational/Bridging Travel Award
Jayanta Das, PhD
Florida International University, Miami, FL

Education Award
Debra Laskin, PhD
Rutgers University, Piscataway, NJ

Undergraduate Educator Award
Karen Stine, PhD
Auburn University at Montgomery, Montgomery, AL

Enhancement of Animal Welfare Award
David Allen, PhD
ILS-NICEATM, Research Triangle Park, NC
**Toxicological Sciences Paper of the Year Award**

Ethanol Attenuates Histiotrophic Nutrition Pathways and Alters the Intracellular Redox Environment and Thiol Proteome During Rat Organogenesis

*Toxicological Sciences, 2015, 147(2), 475–489*

Joseph L. Jilek, Karilyn E. Sant, Katherine H. Cho, Matthew S. Reed, Jan Pohl, Jason M. Hansen, and Craig Harris

**Global Senior Scholar Exchange Program**

**Scholar:**

Olufunke Eunice Ola-Davies, DVM, PhD  
University of Ibadan, Ibadan, Nigeria

**Host:**

Augustine Arukwe, BS, DSc  
Norwegian University of Science and Technology, Trondheim, Norway

**Scholar:**

Ansam F. Sawalha, PhD  
An-Najah National University, Nablus, Palestine

**Hosts:**

Stephen G. Gilbert, PhD, DABT  
David L. Eaton, PhD, ATS  
Elaine Faustman, PhD, DABT  
University of Washington, Seattle, Washington

**Best Postdoctoral Publication Awards**

**Presented at the Postdoctoral Assembly Luncheon on Tuesday.**

**Fabian Grimm,** PhD  
Texas A&M University, College Station, TX


**Sascha C.T. Nicklisch,** PhD  
University of California, San Diego, CA


**Mira Pavkovic,** PhD  
Harvard Medical School, Boston, MA


**Perry J. Gehring Diversity Student Travel Award**

**Presented at the Committee on Diversity Initiatives Reunion**  
7:30 pm Saturday.

Kaylin M. White,  
Spelman College, Atlanta, GA
Awards and Fellowships

Pfizer SOT Undergraduate Student Travel Awards

Keegan Krick
University of Massachusetts Boston, Cambridge, MA
Institution where research was conducted:
Woods Hole Oceanographic Institution

Jesse Leissa
Ohio State University, Columbus, OH
Institution where research was conducted:
US Food and Drug Administration - White Oak Campus

Michael McLawhorn
Mars Hill University, Marshall, NC

Mariella A. Mestres-Villanueva
University of Puerto Rico Rio Piedras, Rio Piedras, PR
Institution where the research was conducted:
Purdue University

Isabella Reichardt
University of Wisconsin-Madison, Madison WI
Institution where the research was conducted:
Michigan State University

Samantha Saunders
Virginia Commonwealth University, Richmond, VA

Rachel Schafer
Kenyon College, Gambier, OH

Stacy Schkoda
California State University Fullerton, Fullerton, CA
Institution where the research was conducted:
Oregon State University

Hannah J. Smith
University of North Carolina Chapel Hill, Chapel Hill, NC

Mary F. Stofan
New Mexico State University, Las Cruces, NM
Institution where the research was conducted:
Rutgers, The State University of New Jersey

Kaylin White
Spelman College, Atlanta, GA
Institution where the research was conducted:
University of North Carolina at Chapel Hill

Veronika Yakovishina
John Jay College of Criminal Justice, Brooklyn, NY

Hollie Adejumo
University of Maryland Baltimore County, Baltimore, MD

Katrina Borofski
University of Massachusetts Amherst, Amherst, MA

Jeliyah Clark
University of North Carolina Chapel Hill, Chapel Hill, NC
Institution where research was conducted:
Gillings School of Global Public Health

Itaevia Curry-Chisolm
North Carolina Central University, Durham, NC
Institution where research was conducted:
Environmental Protection Agency

Chantel V. Duscent
Claflin University, Orangeburg, SC

Jellisa Ewan
Claflin University, Orangeburg, SC

Alexandra Folcik
Florida Institute of Technology, Melbourne, FL
Institution where research was conducted:
National Center for Toxicological Research

Julian Freedland
University at Albany, Albany, NY

Danielle Germundson
University of North Dakota, Grand Forks, ND

Alondra Harris
University of Arizona, Tucson, AZ

Lauren Heine
University of New Mexico, Albuquerque, NM
Institution where the research was conducted:
Oregon State University

Jessica Hoffman
University of North Carolina Chapel Hill, Chapel Hill, NC

Find up-to-date information at www.toxicology.org/2017
Awards and Fellowships

Colgate-Palmolive Grant for Alternative Research

Hao Zhu, PhD
Rutgers University, Camden, NJ

Almudena Veiga-Lopez, DVM, PhD
Michigan State University, East Lansing, MI

Colgate-Palmolive Award for Student Research Training in Alternative Methods

Emily Martell, BS
University of Rhode Island, Ashaway, RI

Colgate-Palmolive Postdoctoral Fellowship Award in In Vitro Toxicology

Peer Karmaus, PhD
St. Jude Children’s Research Hospital, Memphis, TN

Syngenta Fellowship Award in Human Health Applications of New Technologies

Fabian Grimm, PhD
Texas A&M University, College Station, TX

Call for 2018 Nominations

More than 200 distinguished toxicologists, postdoctoral researchers, and students are honored each year.

View award descriptions, requirements, and details at www.toxicology.org/awards

Submit your nominations by October 9, 2017

Society of Toxicology
1821 Michael Faraday Drive, Suite 300 | Reston, VA 20190 | T: 703.438.3115 | F: 703.438.3113 | Email: sothq@toxicology.org | Website: www.toxicology.org
Events and Activities
All activities will be held at the Baltimore Convention Center in Baltimore, Maryland, unless otherwise noted.

Welcome Reception
Sunday, March 13, 6:30 PM to 7:30 PM

The Welcome Reception is a great opportunity to renew friendships and to make new acquaintances. Please join the Society in this kick-off of the Annual Meeting.

Global Gallery of Toxicology
Monday, March 13 to Wednesday, March 15, 9:15 AM to 4:30 PM

Toxicology societies from around the world are invited to participate in the Global Gallery of Toxicology. Now in its sixth year, posters of these sister societies will be prominently displayed during the meeting, showcasing their formation, key accomplishments, strategic initiatives, and activities. Meet representatives of these organizations from 11:45 am to 12:15 pm on Monday, March 13. Posters will be available for viewing during the ToxExpo hours. The goal of SOT and of all these societies is to increase the reliance of international decision-makers on the science of toxicology and to advance human health and disease prevention. For more information about participating in the Global Gallery, please contact Kevin Meritt at 703.438.3115 by January 6, 2017.

Regional Chapter, Special Interest Group, and Specialty Section Posters
Monday, March 13 to Wednesday, March 15, 9:15 AM to 4:30 PM

Dedicated poster space is available for the SOT Regional Chapters, Special Interest Groups, and Specialty Sections during the 2017 SOT Annual Meeting. The poster area will be located adjacent to the SOT Pavilion in the ToxExpo Exhibit Hall. Come meet representatives on Monday, March 13, from 11:45 am to 12:15 pm. Posters will be available for viewing during the ToxExpo hours.

Meeting Requests:
Hospitality Suites and Ancillary Meetings

All requests for hospitality suites and ancillary meetings are approved by SOT Headquarters. Ancillary functions may be hosted only by SOT Global Partners, exhibitors, supporters, or organizations otherwise associated with SOT. All ancillary functions are held outside of the convention center in nearby hotels. Only meeting requests received by January 4, 2017, will be listed in the Program.
Global Collaboration Coffee

Monday, March 13, 9:30 AM to 11:30 AM

IUTOX invites all Global Gallery participants and representatives of societies from around the world to the Global Collaboration Coffee hosted by SOT. This event offers an opportunity for scientific leaders to connect and gain a better understanding of the initiatives of societies around the world. Following the coffee, attendees will adjourn together to the Global Gallery, where presenters will share their posters in a “Representative Attended” poster time from 11:45 am to 12:15 pm on Monday, March 13. Please see page 12 for additional information about the poster display. Please contact Kevin Merritt (kevin@toxicology.org) for participation information in the Global Collaboration Coffee and Global Gallery.

Past Presidents’ 5K Fun Run/Walk

Tuesday, March 14, 7:00 AM
Inner Harbor

Supported by: IDEXX Laboratories, Inc.

When you pack for the meeting, don’t forget your running shoes so you can join us for the seventh annual Past Presidents’ 5K Fun Run/Walk! Open to anyone interested, this event is a great opportunity to meet old friends and make new acquaintances in a casual environment, joining SOT’s Past Presidents in showing support for SOT. Whether you’re in it for some friendly competition or would rather take a leisurely stroll, this event’s emphasis is on camaraderie and will bring together runners and walkers of all levels and paces. Come join us—we look forward to seeing you!

Register by February 17 to receive a complimentary souvenir t-shirt; visit the Program section of the SOT Annual Meeting website to register. Registration is only $25, and all proceeds support the SOT Endowment Fund.

SOT Annual Business Meeting

Tuesday, March 14, 4:45 PM to 6:15 PM

SOT Members are invited and encouraged to attend the 56th SOT Annual Business Meeting. The agenda includes discussion of plans for next year, a financial summary, and a review of the 2016–2017 accomplishments.

Tox ShowDown

Tuesday, March 14, 7:30 PM to 9:00 PM
Hilton Baltimore Hotel

Chairperson(s): Phil Wexler, NIH-NLM, Bethesda, MD.

This is the sixth year of the Tox ShowDown, the toxicological quiz game par excellence. Three teams of three contestants each—the Endocrine Disruptors, the Free Radicals, and the Toxic Metabolites—battle each other to answer questions wholly, partially, or remotely related to toxicology. Topics cover the gamut, including the role of toxicology in history, current events, arts, culture, and society, not to mention science. The event features a cash bar and is a great opportunity to see how many questions you can answer correctly, while enjoying a good laugh. As always, there will be prizes for all participants and audience door prizes.

Undergraduate Educator Network Meeting

Visit Website for Date/Time

Chairperson(s): Kristine Willett, University of Mississippi, University, MS.

Endorser(s):
Education Committee
Undergraduate Education Subcommittee

The Education Committee and the Undergraduate Education Subcommittee are hosting the Undergraduate Educator Network Meeting for all faculty involved in the teaching of toxicology to undergraduates, trainees thinking about teaching, and those interested in including toxicology at the undergraduate level. Hear an update on initiatives for undergraduate faculty, provide your input, and discuss shared interests. The hour-long meeting will be followed with networking time.
Undergraduate Diversity Program

Saturday, March 11 to Monday, March 13
Hilton Baltimore Hotel

Chairperson(s): Judy Zelikoff, New York University School of Medicine, Tuxedo Park, NY.

Hosted by: Committee for Diversity Initiatives (CDI)

Recipients of the Undergraduate Diversity Program Student and Advisor Travel Awards participate in a three-day program to learn more about toxicology and careers in biomedical research. The program begins Saturday evening with networking within mentor groups, an introduction to toxicology, and the CDI Reunion, a celebration including current and past program participants and organizers. See the description below for the Sunday program. On Monday, these students participate in Scientific Sessions, visit Poster Sessions, attend the In Vitro Lecture and Luncheon; continue to network with graduate students, postdoctoral scholars, and career toxicologists; and conclude this concentrated exposure to the discipline of toxicology and possibilities inherent in the pursuit of graduate studies in the biomedical sciences. For schedule details go to www.toxicology.org/am-undergraduates.

Sunday Undergraduate Education Program

Sunday, March 12, 8:00 AM to 5:00 PM
Hilton Baltimore Hotel

Chairperson(s): Judy Zelikoff, New York University School of Medicine, Tuxedo Park, NY.

Hosted by: Committee for Diversity Initiatives (CDI)

Endorser(s): Education Committee
Undergraduate Education Subcommittee

Any undergraduate student who attends the Annual Meeting is invited to register for the Sunday Undergraduate Education Program. The schedule for the day includes introductory lectures in different areas of toxicology, including an opportunity to explore and interpret data. Students discuss with graduate students and academic program directors how to submit strong graduate school applications and succeed in graduate school, as well as learning the merits of specific graduate programs. They also network with SOT mentors and toxicologists in various employment sectors to become more familiar with different career paths in toxicology. For schedule details go to www.toxicology.org/am-undergraduates.

Student/Postdoctoral Scholar Mixer

Sunday, March 12, 7:30 PM to 9:00 PM
Hilton Baltimore Hotel

(Ticket Required)

Hosted by: Graduate Student Leadership Committee (GSLC)

This opportunity for all students and postdoctoral scholars to gather, meet new colleagues, and reestablish relationships in an informal atmosphere at the beginning of the meeting. Learn about being involved in SOT by speaking with student leaders at the SOT component group posters. The GSLC Outstanding Leadership Award is presented during this event. Tickets are obtained at no cost by registering for the Mixer on the Annual Meeting Registration Form. Ticket and meeting badge are required. Complimentary refreshments and a cash bar will be available.

Committee on Diversity Initiatives Reunion

Saturday, March 11, 7:30 PM to 8:30 PM
Hilton Baltimore Hotel

Hosted by: Committee for Diversity Initiatives (CDI)

Join the Committee on Diversity Initiatives as we celebrate the Undergraduate Diversity Program and the people who make it successful. The CDI Reunion is a great opportunity for former students, organizers of the program, and volunteers to gather and celebrate 28 years of success in encouraging the next generation of scientists. Please welcome and network with this year’s undergraduate student participants. The program will include the presentation of the 2017 Perry J. Gehring Diversity Student Travel Award. Dessert, coffee, and tea will be served, so please mark your calendars and start the 56th Annual Meeting with a fun and interactive evening at the CDI Reunion.
In Vitro Toxicology Lecture and Luncheon

Human Organs-on-Chips Testing—Strengths and Challenges

Monday, March 13, 11:30 AM to 1:00 PM
Hilton Baltimore Hotel
(Ticket Required)

Chairperson(s): Barbara L. Kaplan, Mississippi State University, Mississippi State; Mindy Reynolds, Washington College, Chestertown, MD; Deb Hoivik, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT; and Alison Sanders, Icahn School of Medicine at Mount Sinai, New York, NY.

Lecturer: Anthony Bahinski, GlaxoSmithKline, King of Prussia, PA.

Supported by:
An Educational Grant from the Colgate-Palmolive Company

Hosted by:
Education Committee

The goal of the In Vitro Toxicology Lecture series is to feature important research using in vitro and alternative techniques to study basic mechanisms and to illustrate how these test methods benefit animal welfare by refining, reducing, and replacing animal use whenever it is feasible. Undergraduate students, graduate students, postdoctoral scholars, and recipients of Colgate-Palmolive awards are among the guests at the In Vitro Toxicology Lecture and Luncheon. Students and postdoctoral scholars register for $10 (nonrefundable) via the Annual Meeting registration process.

Dr. Bahinski will discuss the potential for human organs-on-chips to provide better predictive power over existing preclinical animal models that often lead to failure of drug compounds late in their development. Organs-on-chips are microfluidic cell culture devices that contain hollow micrometer-sized chambers inhabited by living cells that recreate the specialized multicellular architectures, tissue-tissue interfaces, physicochemical microenvironments, and vascular perfusion necessary to recapitulate organ-level physiology in vitro. These biomimetic devices provide a window on human physiology as they enable real-time, high-resolution microscopic imaging as well as analysis of biochemical, genetic, and metabolic activities of living cells when they are positioned within the context of functional tissue and organ units. These microsystems could potentially further our understanding of disease etiology and fill the critical need for improved model systems to predict efficacy, safety, bioavailability, and toxicology outcomes for candidate compounds. Luncheon participants will discuss a case study involving this new approach.

Postdoctoral Assembly Luncheon

Tuesday, March 14, 12:00 Noon to 1:15 PM
(Ticket Required)

Chairperson(s): Gabriel Knudsen, National Cancer Institute at NIEHS, Research Triangle Park, NC.

Hosted by:
Postdoctoral Assembly (PDA)

The Postdoctoral Assembly Luncheon is a casual event that encourages engagement and networking among postdoctoral scholars. Finishing up a discussion from your morning poster session? Leaving early to set up a poster or attend another meeting? That’s no problem; stop in when you can! Enjoy a buffet lunch while networking with others, including PDA officers, Postdoctoral Representatives, and SOT Councilors. This is the time for postdocs to relax, celebrate achievements, and have fun. At 12:45 pm there will be a short program which will include recognition of the Best Postdoctoral Publication Award recipients and the welcoming of the 2017–2018 PDA officers. Door prizes add even more fun to this lively event. Postdocs should reserve a ticket for $10 when registering for the Annual Meeting.

Book your hotel reservation today!
Go to www.toxicology.org/housing or call SOT’s official housing company: Connections Housing, 800.262.9974 or 404.842.0000.
The deadline is February 10, 2017.
See details on page 16.
Career Exploration through Speed Informational Interviews

Tuesday, March 14, 1:20 PM to 2:40 PM
(Ticket Required)

Chairperson(s): Natasha Caitlin, NIEHS-NTP, Research Triangle Park, NC; and Alexandra Noël, Louisiana State University, Baton Rouge, LA.

Co-Chairperson(s): Gabriel Knudsen, NCI, Research Triangle Park, NC; Samantha McNeal, University of South Carolina, Columbia, SC; Daniel Spade, Brown University, Providence, RI; Christopher Stewart, MPI Research, Mattawan, MI.

Hosted by:
Postdoctoral Assembly
Toxicologists of African Origin

Do you find yourself wondering what your career options are in the field of toxicology? Then this is the event for you! This career development special event is designed for graduate students and postdocs who want to gain insight into the different career sectors in toxicology. Groups of three trainees will rotate through a series of approximately eight-minute discussions with career representatives from academia, government, and industry. Trainees can ask the career representatives questions about their background, career path, the hiring process in their company/sector, and other aspects of identifying and pursuing career interests. This session will provide an informal opportunity to gain insight about different employment sectors in toxicology through candid discussions in a casual setting. Graduate students and postdocs are encouraged to register early, as registration will be limited to maximize the opportunity for small group discussion with career representatives.

Scientific Sessions of Note for Students and Postdoctoral Scholars

Symposium

Investigating Metabolic Diseases Using Integrated ‘Omics Approaches

Organized by the Postdoctoral Assembly and Graduate Student Leadership Committee

Wednesday, March 15, 9:30 AM to 12:15 PM
See full description on page 102.

Education-Career Development Sessions

Careers for Toxicologists at Primarily Undergraduate Institutions: Everything You Need to Know about the Job, Hiring Process, and Strategies for Success in Teaching and Research

Tuesday, March 14, 5:00 PM to 6:20 PM
See full description on page 101.

Mastering Soft Skills to Advance Your Scientific Career

Wednesday, March 15, 5:00 PM to 6:20 PM
See full description on page 117.

Undergraduate Student Meeting

Visit Website for Date/Time

Chairperson(s): Kristine L. Willett, University of Mississippi, University, MS.

Hosted by:
Education Committee
Undergraduate Education Subcommittee

Undergraduate students are encouraged to participate in an informal meeting to talk about shared interests related to career paths in toxicology, discuss undergraduate tox-related activities, and provide feedback to the Undergraduate Education Subcommittee. Most of the meeting will be devoted to small group interaction with graduate students and postdoctoral scholars who can provide perspective and answer questions about toxicology graduate programs, getting started in a toxicology job, and career options available to those with toxicology degrees.
**Education-Career Development Opportunities**

**Chat with an Expert**

**Monday, March 13 to Thursday, March 16**

**Time Varies by Group**

(Meet at the Chat with an Expert Poster Board in the Pratt Street Lobby near Registration)

**Hosted by:**

Graduate Student Leadership Committee

The purpose of Chat with an Expert is to provide graduate students and postdoctoral scholars with the opportunity to network informally with well-established toxicologists while obtaining career advice and meeting new colleagues. Small groups are composed by matching research interests of students and postdocs with those of an expert. The expert for each group identifies a time and a place for an informal meeting, and the group meets at the Chat with an Expert Poster before proceeding to the meeting location. This program also includes opportunities for postdocs to host informal meetings with graduate students. Expert registration generally opens in December; Graduate student/postdoc registration will open in early 2017. Details for each group meeting will be sent to participants in advance of the meeting.

**Poster Tours for Trainees**

**Monday, March 13 to Wednesday, March 15**

**Time Varies by Group**

(Meet at the Poster Tour Board in the Pratt Street Lobby near Registration)

**Hosted by:**

Postdoctoral Assembly

The Postdoctoral Assembly organizes Poster Tours for Trainees for graduate students and postdoctoral scientists to participate in a one-hour guided poster tour with an expert toxicologist. These small group tours provide the opportunity for trainees to take part in critical evaluation of cutting-edge toxicology methods and research findings and network with an expert toxicologist. Recruitment of individuals interested in being poster tour guides will begin in early December. Graduate student and postdoctoral scholars sign-up will open in early 2017. Details for each group will be distributed to the participants in advance of the meeting.

**Trainee Discussion with Plenary Session**

Presenters: Peter Sorger and Stephen Friend

**Monday, March 13, 9:45 AM to 10:45 AM**

(Ticket Required; Limited Seating)

**Lecturers:** Peter Sorger, Harvard Medical School, Boston MA; and Stephen Friend, Apple Inc., Cupertino, CA.

Drs. Sorger and Friend will meet informally for discussion with graduate students and postdoctoral scholars after their Plenary Session (see page 75). Registration is limited to SOT student and postdoctoral members.

**Trainee Discussion with Plenary Session**

Presenters: Drs. Jun Yang and Richard Barker

**Tuesday, March 14, 9:45 AM to 10:45 AM**

(Ticket Required; Limited Seating)

**Lecturers:** Jun Yang, St. Jude Children’s Research Hospital, Memphis, TN; and Richard Barker, University of Oxford, Oxford, United Kingdom.

Drs. Yang and Barker will meet informally for discussion with graduate students and postdoctoral scholars after their Plenary Session (see page 75). Registration is limited to SOT student and postdoctoral members.

**Trainee Discussion with Medical Research Council (MRC) Lecturer: Dr. Paul Elliott**

**Wednesday, March 15, 9:45 AM to 10:45 AM**

(Ticket Required; Limited Seating)

**Lecturer:** Paul Elliott, Imperial College, London, United Kingdom.

Dr. Elliott will meet informally for discussion with graduate students and postdoctoral scholars after his Keynote MRC Lecture (see page 77). Registration is limited to SOT student and postdoctoral members.
Regional Chapter Meetings/Luncheons or Receptions

Monday, March 13, through Wednesday, March 15, Various Times and Locations

(Refer to the Annual Meeting Program, Mobile Event App, or Online Planner for up-to-date details.)

Many of the SOT Regional Chapters meet during the SOT Annual Meeting. All current and prospective SOT Regional Chapter members are encouraged to attend.

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allegheny-Erie, Michigan, and Lake Ontario Regional Chapters Joint Reception</td>
<td>Monday, March 13</td>
<td>4:45 PM to 6:15 PM</td>
</tr>
<tr>
<td>Lone Star and South Central Regional Chapters Joint Mixer</td>
<td>Tuesday, March 14</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Mid-Atlantic Regional Chapter Business Meeting and Networking Luncheon</td>
<td>Monday, March 13</td>
<td>12:15 PM to 2:00 PM</td>
</tr>
<tr>
<td>National Capital Area Regional Chapter Reception</td>
<td>Tuesday, March 14</td>
<td>6:30 PM to 9:00 PM</td>
</tr>
<tr>
<td>Northeast Regional Chapter Student Luncheon</td>
<td>Tuesday, March 14</td>
<td>12:00 Noon to 2:00 PM</td>
</tr>
<tr>
<td>Pacific Northwest Regional Chapter Reception</td>
<td>Monday, March 13</td>
<td>5:30 PM to 7:30 PM</td>
</tr>
<tr>
<td>Southeastern Regional Chapter Reception</td>
<td>Monday, March 13</td>
<td>6:00 PM to 10:00 PM</td>
</tr>
</tbody>
</table>
Special Interest Group Meetings/Luncheons or Receptions

(Refer to the Annual Meeting Program, Mobile Event App, or Online Planner for up-to-date details.)

Each of the six Special Interest Groups will hold a meeting/reception during the 2017 SOT Annual Meeting at various local locations. All current and prospective SOT Special Interest Group members are encouraged to attend.

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
<th>Time</th>
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<tbody>
<tr>
<td>American Association of Chinese in Toxicology Distinguished Special</td>
<td>Monday, March 13</td>
<td>5:00 PM to 9:00 PM</td>
</tr>
<tr>
<td>Group Chinese Toxicologist Lectureship Award and Reception</td>
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<tr>
<td>American Association of Chinese in Toxicology Special Interest Group</td>
<td>Tuesday, March 14</td>
<td>12:15 PM to 1:45 PM</td>
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<tr>
<td>Career Development Workshop</td>
<td></td>
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<tr>
<td>Association of Scientists of Indian Origin Special Interest Group</td>
<td>Monday, March 13</td>
<td>7:00 PM to 9:30 PM</td>
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<tr>
<td>Reception</td>
<td></td>
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<tr>
<td>Association of Scientists of Indian Origin Special Interest Group</td>
<td>Tuesday, March 14</td>
<td>12:15 PM to 1:15 PM</td>
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<tr>
<td>Lunch and Learn</td>
<td></td>
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<tr>
<td>Hispanic Organization of Toxicology Special Interest Group Mentoring</td>
<td>Tuesday, March 14</td>
<td>12:15 PM to 1:15 PM</td>
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<tr>
<td>Activity</td>
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<tr>
<td>Hispanic Organization of Toxicology Special Interest Group Reception</td>
<td>Tuesday, March 14</td>
<td>6:30 PM to 8:30 PM</td>
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<tr>
<td>and Awards Ceremony</td>
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<tr>
<td>Korean Toxicologists Association in America Special Interest Group</td>
<td>Monday, March 13</td>
<td>6:30 PM to 8:30 PM</td>
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<tr>
<td>Meeting/Reception</td>
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<tr>
<td>Toxicologist of African Origin Special Interest Group Annual Reception</td>
<td>Monday, March 13</td>
<td>5:30 PM to 8:00 PM</td>
</tr>
<tr>
<td>Women in Toxicology Special Interest Group Executive Committee Meeting</td>
<td>Monday, March 13</td>
<td>6:45 AM to 7:45 AM</td>
</tr>
<tr>
<td>Women in Toxicology Special Interest Group Reception</td>
<td>Wednesday, March 15</td>
<td>5:00 PM to 7:00 PM</td>
</tr>
</tbody>
</table>
**Specialty Section Meetings/Luncheons or Receptions**

*Monday, March 13, through Wednesday, March 15, Various Times and Locations*

(Refer to the Annual Meeting Program, Mobile Event App, or Online Planner for up-to-date details.)

Each of the 27 SOT Specialty Sections will hold either a luncheon or early evening meeting/reception during the 2017 SOT Annual Meeting. All current and prospective SOT Specialty Section members are encouraged to attend.

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
<th>TIME</th>
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</thead>
<tbody>
<tr>
<td>Biological Modeling Specialty Section Meeting/Reception</td>
<td>Tuesday, March 14</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Biotechnology Specialty Section Meeting/Reception</td>
<td>Tuesday, March 14</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Carcinogenesis Specialty Section Meeting/Reception</td>
<td>Wednesday, March 15</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Cardiovascular Toxicology Specialty Section Meeting/Luncheon</td>
<td>Wednesday, March 15</td>
<td>12:15 PM to 1:45 PM</td>
</tr>
<tr>
<td>Clinical and Translational Toxicology Specialty Section Meeting/Reception</td>
<td>Wednesday, March 15</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Comparative and Veterinary Specialty Section Meeting/Luncheon</td>
<td>Monday, March 13</td>
<td>12:15 PM to 1:45 PM</td>
</tr>
<tr>
<td>Dermal Toxicology Specialty Section Meeting/Reception</td>
<td>Tuesday, March 14</td>
<td>6:00 PM to 7:30 PM</td>
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<tr>
<td>Drug Discovery Toxicology Specialty Section Meeting/Reception</td>
<td>Monday, March 13</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Ethical, Legal, and Social Issues Specialty Section Meeting/Luncheon</td>
<td>Tuesday, March 14</td>
<td>12:15 PM to 1:45 PM</td>
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<tr>
<td>Food Safety Specialty Section Officers Meeting</td>
<td>Monday, March 13</td>
<td>7:00 AM to 8:00 AM</td>
</tr>
<tr>
<td>Food Safety Specialty Section Meeting/Reception</td>
<td>Monday, March 13</td>
<td>6:00 PM to 8:00 PM</td>
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</table>

(continued on next page)
### Specialty Sections

#### Specialty Section Meetings/Luncheons or Receptions (continued)

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
<th>Time</th>
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<tbody>
<tr>
<td>Immunotoxicology Specialty Section Meeting/Reception</td>
<td>Monday, March 13</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>In Vitro and Alternative Methods Specialty Section Meeting/Luncheon</td>
<td>Tuesday, March 14</td>
<td>12:15 PM to 1:45 PM</td>
</tr>
<tr>
<td>Inhalation and Respiratory Specialty Section Meeting/Reception</td>
<td>Wednesday, March 15</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Mechanisms Specialty Section Meeting/Reception</td>
<td>Tuesday, March 14</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Medical Device and Combination Product Specialty Section Meeting/Reception</td>
<td>Monday, March 13</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Metals Specialty Section Meeting/Reception</td>
<td>Monday, March 13</td>
<td>6:00 PM to 7:30 PM</td>
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<tr>
<td>Mixtures Specialty Section Meeting/Reception</td>
<td>Wednesday, March 15</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Molecular and Systems Biology Specialty Section Meeting/Reception</td>
<td>Wednesday, March 15</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Nanotoxicology Specialty Section Meeting/Reception</td>
<td>Monday, March 13</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Neurotoxicology Specialty Section Meeting/Reception</td>
<td>Monday, March 13</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Occupational and Public Health Specialty Section Meeting/Luncheon</td>
<td>Wednesday, March 15</td>
<td>6:00 PM to 7:30 PM</td>
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<tr>
<td>Ocular Toxicology Specialty Section Meeting/Reception</td>
<td>Wednesday, March 15</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Regulatory and Safety Evaluation Specialty Section Meeting/Reception</td>
<td>Tuesday, March 14</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Reproductive and Developmental Toxicology Specialty Section Meeting/Reception</td>
<td>Tuesday, March 14</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Risk Assessment Specialty Section Meeting/Reception</td>
<td>Monday, March 13</td>
<td>6:00 PM to 7:30 PM</td>
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<tr>
<td>Stem Cells Specialty Section Meeting/Reception</td>
<td>Tuesday, March 14</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
<tr>
<td>Toxicologic and Exploratory Pathology Specialty Section Meeting/Reception</td>
<td>Wednesday, March 15</td>
<td>6:00 PM to 7:30 PM</td>
</tr>
</tbody>
</table>
Council

John B. Morris ................................................. President
Patricia E. Ganey ........................................... Vice President
Leigh Ann Burns Naas .............................. Vice President-Elect
Ruth A. Roberts ........................................... Secretary
George P. Daston ..................................... Treasurer
Michael Aschner ..................................... Treasurer-Elect
Peter L. Goering .................................... Past President

Aaron Barchowsky ........................................ Councilor
Rosonal R. Bell ............................................ Councilor
Paul M. D. Foster ........................................ Councilor
Mary Beth Genter ........................................ Councilor
Ofelia A. Olivero ....................................... Councilor
Tao Wang ................................................ Councilor

Continuing Education Committee

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Cynthia V. Rider .......................................... Co-Chair
Niranjan S. Goud ......................................... Member
Rhiannon N. Hardwick .......................... Member
Michael F. Hughes ................................ Member
Bette Meek ................................................ Member

Anthony M. Ndifor .................................... Member
Robert Roy ................................................ Member
James G. Wagner ....................................... Member
Joe Cichocki ............................................ Postdoctoral Representative
Jie Luo .................................................. Student Representative

Scientific Program Committee

Patricia E. Ganey ........................................... Chair
Leigh Ann Burns Naas ......................... Co-Chair
Lauren M. Aleksunes ................................. Member
William D. Atchison ........................... Member
Jeanine L. Bussiere ................................ Member
Brian J. Day ............................................... Member
Jennifer L. Freeman ............................... Member

Saber M. Hussain ....................................... Member
Matthew J. LeBaron ................................. Member
Barry S. McIntyre ................................... Member
Sean E. Ottinger .................................... Member
Lisa M. Sweeney ..................................... Member
Vishal S. Vaidy .......................................... Member
Heather M. Wallace ............................... Member

Thank You
Job bank
Online Job Search and Recruiting Service

Job Seekers
- Find Your Next Career Opportunity
- SOT Members Post Resumes and Search Positions Free

Employers
- Focus Your Hiring Efforts
- Recruit Highly Qualified Candidates

Academia ⬤ Government ⬤ Industry

www.toxicology.org/jobbank
Research Funding Insights

Monday, March 13 to Wednesday, March 15, 9:30 AM to 4:30 PM

Hosted by:
Career Resource and Development Committee

Representatives from federal agencies will be available in the Research Funding Room for individual conversations. Make an appointment with your program officer in advance or at their exhibit booth or check the posted schedule to meet with a staff member who can discuss aspects of scientific review or specific grant opportunities. New investigators are especially encouraged to meet with program staff.

Job Bank

Job Bank access will be available, as always, through your computer or mobile device and at the Annual Meeting @SOT Center. Visit the Job Bank at www.toxicology.org/jobbank. For additional information, contact Kim von Brook at SOT Headquarters: 703.438.3115 ext. 1600 or careerresources@toxicology.org.

Mentor Match

The objective of the Mentor Match online database is to connect mentees with potential mentors from the SOT membership to provide advice on career path selection, professional development, and work/life balance topics. SOT members are encouraged to share their professional knowledge and experience by serving as mentors for colleagues and for the next generation of toxicologists.

The SOT Annual Meeting provides a great opportunity for the mentor and mentee to meet in person. We strongly encourage members of the Society to visit the Mentor Match site and register online as mentors and/or mentees. The Mentor Match program is free to all active SOT members. Visit www.toxicology.org/mentormatch.

SOT Mentoring Breakfast

Monday, March 13, 6:15 AM to 7:45 AM

(Registration Required)

Endorser(s):
Career Resource and Development Committee
Postdoctoral Assembly
Graduate Student Leadership Committee

The Society of Toxicology recognizes the importance of mentoring in the scientific and professional development of its members. As such, we are pleased to announce the sixth annual Mentoring Breakfast.

The Mentoring Breakfast is for SOT members at any career stage—from students and scholars to senior scientists—who are seeking a mentor. Trained facilitators will lead small group discussions to determine each individual’s wants and needs in a mentor and then will use this information to connect the participant with an appropriate mentor. Please note that mentor information will be provided after the Annual Meeting, and mentors do not attend the breakfast.

A limit of 55 mentees will be accepted on a first-come, first-served basis at a cost of $10/person, which includes a continental breakfast.

Education-Career Development Sessions

Careers for Toxicologists at Primarily Undergraduate Institutions: Everything You Need to Know about the Job, Hiring Process, and Strategies for Success in Teaching and Research

Tuesday, March 14, 5:00 PM to 6:20 PM
See full description on page 101.

Mastering Soft Skills to Advance Your Scientific Career

Wednesday, March 15, 5:00 PM to 6:20 PM
See full description on page 117.
Contemporary Concepts in Toxicology (CCT)
Submit a CCT Meeting Proposal
...It’s Easy and Rewarding

Your Idea
Include:
• Scientific Topic
• Proposed Speakers
• Potential Audience

Approval
CCT Committee:
• Reviews Proposals
• Provides Feedback
• Recommends Logistics

Development
SOT Manages:
• Venue and Housing
• Registration
• Speaker Communication
• Promotional Materials
You Manage:
• Scientific Program

The CCT Meeting
Content delivered to scientists via face-to-face meeting or webinar

Shared Benefit
• SOT Provides $25,000 in Seed Money to CCT Meeting
• Regional Chapters, Specialty Sections, and Special Interest Groups Share in Profits

SOT | Society of Toxicology
www.toxicology.org/cct
Satellite Meetings

Each year, SOT endorses several Satellite Meetings that are held in conjunction with the Annual Meeting. Satellite Meetings are organized around scientific topics related to toxicology and will be held in and around the Baltimore area. See more at: www.toxicology.org/am-satellite.

Proposing a Satellite Meeting

Proposals for a satellite meeting should be sent by email to heidi@toxicology.org to the attention of Patricia E. Ganey, SOT Vice President and Scientific Program Committee Chair. Requests approved by January 4, 2017, will be published in the Program. All requests must be received by January 19, 2017.

Metabolic Syndrome and Associated Diseases: From the Bench to the Clinic
(SOT Contemporary Concepts in Toxicology [CCT] meeting)

Saturday, March 11, 8:45 AM to 5:30 PM
Baltimore Convention Center
(Separate Registration Required)

Hosted by: SOT Metabolic Syndrome CCT Organizing Committee.

This conference will examine current knowledge on metabolic diseases, including developmental aspects and challenges in therapeutic strategies for associated diseases. It also will include a poster session and time devoted to a discussion of mechanisms thought to play important roles in the syndrome/diseases and provide insight into drugs and environmental agents thought to influence them.

Visit the SOT website to register for this CCT meeting, view the agenda, and find abstract submission information.

Horizons and Challenges in Organotypic Culture Models for Predictive Toxicology

Saturday, March 11, 9:00 AM to 5:00 PM
Baltimore Convention Center

Hosted by: Elaine Faustman, University of Washington, Seattle, WA; and Barbara Klieforth, US EPA, Washington, DC.

The ability to create microphysiological organotypic culture models provides an opportunity for a paradigm shift and the advancement of alternative, more public health relevant, and efficient chemical toxicity testing methods. These Organotypic Culture Models for Predictive Toxicology (OCM-PTs) will be faster, less costly, and more scientifically robust than many currently available toxicity assessment methodologies. The successes and challenges in these OCM-PTs systems are complicated by the highly interdisciplinary nature of their development. Refined assessment models of how organs and tissues respond to environmental chemicals, coupled with the rigorous requirements of contemporary toxicity screening, are critical to informing implementation of the Frank R. Lautenberg Chemical Safety for the 21st Century Act, the amended Toxic Substances Control Act.
Continuing Education

SR—Sunrise (7:00 AM–7:45 AM)
AM—Morning (8:15 AM–12:00 Noon)
PM—Afternoon (1:15 PM–5:00 PM)
Continuing Education Courses

The Continuing Education (CE) Program offers a wide range of courses that cover established knowledge in toxicology, as well as advanced techniques or approaches for those with experience in the field. Courses can be applied toward certifying and licensing board requirements and may also be used for recertification with the American Board of Toxicology (ABT). General courses are intended to provide a broad overview of an area or to assist individuals in learning new techniques or approaches, while courses based on more specialized topics are intended to be of interest to individuals with previous knowledge of the subject or already working in the field.

All courses will be held on Sunday, March 12, 2017, at the Baltimore Convention Center. Please check the signage in the registration area and at the CE booth for room assignments. Note: Your course materials will be available in the room immediately prior to the course (they will not be available at the registration area). If you have your course ticket, go directly to the assigned room. If you have not received your course ticket or have not registered, please go to the Registration on Saturday afternoon/evening or on Sunday morning. If you have misplaced your ticket, please go to a Continuing Education booth in the convention center on Sunday. The booths will be open from 6:30 am–5:30 pm.

Please Note: Each Continuing Education Course is offered in one of three time blocks:

- SR—Sunrise (7:00 AM–7:45 AM)
- AM—Morning (8:15 AM–12:00 Noon)
- PM—Afternoon (1:15 PM–5:00 PM)

Registration for the Annual Meeting and a separate CE course ticket are required.

SUNDAY

Molecular Imaging for Toxicologists

Sunday, March 12, 7:00 AM to 7:45 AM
SR01 | SUNRISE MINI-COURSE

Chairperson(s): Aurore Varela, Charles River Laboratories, Senneville, QC; and David L. Hutto, Charles River Laboratories, Wilmington, MA.

Endorser(s):
Toxicologic and Exploratory Pathology Specialty Section

Advanced in vivo imaging techniques such as magnetic resonance and nuclear and tomographic imaging are the gold standard in several areas of clinical medicine for diagnosis and guided therapy and play an increasing role in clinical trials, being an integral part of the drug development process. Imaging sciences have known an incredible development, and many techniques, such as MRI, PET, SPECT, and X-ray-computed tomography, have become indispensable. The applications of in vivo translational imaging are now extending further into drug discovery and development and have the potential to considerably accelerate the process, reduce the cost, significantly affect the drug development process, and comply with the 3R. It is important to understand the technologies and their applications and limitations. Imaging technology includes a range of modalities such as magnetic resonance imaging (MRI), positron emission tomography (PET), single photon emission computed tomography (SPECT), computed tomography (CT), in vivo optical imaging, and ultrasound. These noninvasive and quantitative techniques provide not only anatomical evaluation but also functional and molecular information that can access the mechanisms of drug action or its toxicity. The future trends will certainly be in multimodality imaging, combining high sensitivity and molecular techniques with high spatial resolution and morphological techniques. Imaging stands out as one of the most promising translational techniques that can significantly improve decision-making in early phase, to kill compounds that are destined to fail in later phase, and the go/no go decisions can be made earlier based on pertinent information. Imaging technologies can improve the drug development process, not only with the development of safer and effective drugs but also with reducing timelines. Better prediction of toxicology in an earlier stage will certainly limit the large contribution of drug failure for adverse effect in later stage development. Although, imaging has not yet a major place in safety pharmacology and toxicology studies, several applications exist in cardiovascular, neurology, teratology, and reproductive toxicity. The same technologies and the same physiological and pathoanatological parameters can be quantified for both pharmacology and toxicology applications, confirming the role of in vivo imaging as a translational biomarker for both efficacy and safety assessment. This overview provides the opportunity to review fundamentals of molecular imaging, review important applications of imaging in different therapeutic areas, opportunities for decision-making in preclinical phase and challenges of GLP validation, and to actually integrate imaging approaches into safety assessment in drug development.

The Wonderful World of Molecular Imaging: Understand the Technology. Roger Lecomte, Université de Sherbrooke, Sherbrooke, QC.

Imaging Biomarkers for Decision Making in Drug Discovery. Paul J. McCracken, Eisai AiM Institute, Andover, MA.
Adding Up Chemicals: Component-Based Risk Assessment of Chemical Mixtures
Sunday, March 12, 8:15 AM to 12:00 Noon
AM02 | MORNING COURSE

Chairperson(s): Jane Ellen Simmons, US EPA, Research Triangle Park, NC; and Richard Hertzberg, Biomathematics Consulting, Atlanta, GA.

Endorser(s):
Mixtures Specialty Section
Occupational and Public Health Specialty Section
Risk Assessment Specialty Section

Component-based methods, while least preferred, are most frequently used to conduct mixtures risk assessments (RA), needing only toxicological information on the individual chemicals or pairs. Inherent in component-based methods are assumptions regarding: toxicological similarity (e.g., dose addition) or independent action; the likelihood or relevance of nonadditive interactions; and the appropriate combined action model. This course covers underlying concepts, inherent assumptions, and uncertainties for mixture assessments. Topics include: guidance from regulatory and advisory bodies for component-based mixtures RA; empirical support and biological understanding for concepts of toxicological similarity and independence; existing and emerging methods, such as grouping chemicals for mixtures RA; influence of study design and data analysis on choice of a combined action model; uncertainties from extrapolation of models to untested dose ranges; conceptual differences of individual risk vs population fraction; consequences of forcing effect measures into a pseudo-risk construct; a rubric of criteria for evaluating usefulness of existing interaction studies; and approaches for reducing the uncertainty of, or incorporating nonadditive interactions into the RA. Three types of component-based methods are considered, based on: toxicological similarity, independent action, and more complex and hybrid concepts. Step-by-step case studies with different mixtures allow the attendee to work through examples with the instructor. A case study is presented that includes toxicological experimentation and environmental RA for an intentional mixed mixture of insecticidal proteins that have been commercialized to enhance efficacy against agricultural pests and combat insect resistance by targeting multiple modes of action. The course will help those who conduct component-based mixtures RA for occupational health and safety, product safety, public health protection, or regulatory decision-making and will appeal to toxicologists who conduct component-based mixtures experiments. Attendees will be equipped to use component-based mixture RA methods and understand their assumptions, advantages, and limitations.

Grouping Chemicals for Assessment and Conducting Assessments with the Hazard Index and Related Methods. Jane Ellen Simmons, US EPA, Research Triangle Park, NC.


The Flip Side: Methods for Independent Action, and Hybrid Methods for Interactions and for Mixed Modes. Richard C. Hertzberg, Biomathematics Consulting, Atlanta, GA.

A Case Study: How Mixture Data are Used in Risk Assessments for Genetically-Engineered Crops Expressing Multiple Insecticidal Traits. Steven L. Levine, Monsanto Company, St. Louis, MO.

Current Principles for Nonclinical Chronic Toxicity/Carcinogenicity Testing of Environmental Chemicals
Sunday, March 12, 8:15 AM to 12:00 Noon
AM03 | MORNING COURSE

Chairperson(s): Kristen Ryan, National Toxicology Program/NIEHS, Durham, NC; and Lynea Murphy, The Dow Chemical Company, Midland, MI.

Endorser(s):
Carcinogenesis Specialty Section
Regulatory and Safety Evaluation Specialty Section

Chronic toxicity and carcinogenicity testing in rodents is considered the “gold-standard” approach for identifying potential hazards of chemicals and is necessary to inform risk assessment or risk management. The objectives of this course are to provide the basic tools for toxicologists who desire a better understanding of how to assess chemical-related toxicity associated with chronic exposure and subsequent potential risk(s) to humans. The course will begin with an overview of the current practices for conducting chronic toxicity and carcinogenicity studies and provide examples for how integrated testing strategies may aid in refinement of study design/conduct. The next presentation of this course will focus on evaluating rodent pathology in long-term toxicity studies (i.e., what to expect, pathology peer review, and differentiating between age-related or strain-specific findings and chemical-mediated toxicity). Next, an overview of the regulatory requirements for chronic toxicity/carcinogenicity studies will be presented with a discussion of how data inform regulatory decisions with a focus on environmental chemicals. The final presentation in this course will highlight recent advances in identifying and classifying carcinogens, with an emphasis on the development and application of novel approaches and high-throughput data streams in human health hazard assessments. The expected audience includes toxicologists who work in regulated product development (e.g., chemical industries), scientists who may be responsible for monitoring or directing contracted chronic toxicity/carcinogenicity studies, as well as regulators of chemicals in commerce or environmental contaminants.

Introduction and Course Goals. Kristen Ryan, National Toxicology Program/NIEHS, Durham, NC.

Design, Conduct, and Interpretation of Chronic Toxicity/Carcinogenicity Studies: Where We’ve Been and Where We’re Going. Lynea Murphy, The Dow Chemical Company, Midland, MI.

Overview of Pathology for Chronic Toxicity and Carcinogenicity Studies in Rodents. Mark Cesta, Division of the National Toxicology Program/NIEHS, Durham, NC.


Navigating Drug-Induced Vascular Injury in Preclinical and Clinical Development of Novel Therapeutics

Sunday, March 12, 8:15 AM to 12:00 Noon

AM04 | MORNING COURSE

Chairperson(s): Hong Wang, Genentech, South San Francisco, CA; and Bradley Enerson, Pfizer, Groton, CT.

Endorser(s):
- Cardiovascular Toxicology Specialty Section
- Regulatory and Safety Evaluation Specialty Section

Drug induced vascular injury (DIVI) can cause significant delays in or even halt the development of promising new drugs due to the uncertainty in the predictivity of preclinical findings to humans and the lack of validated safety biomarkers for DIVI. Increasing numbers of cross-industry collaboration to explore and validate novel safety biomarkers and imaging technologies are being carried out in preclinical and clinical studies to better enable the development of novel drugs associated with DIVI. When encountering DIVI in preclinical studies, it is important that the toxicologists and pathologists work together to understand the mechanisms, species translatability, and to engage early discussions with the clinicians and Regulatory Agencies to evaluate potential path forward. This CE course is dedicated to provide a systematic training on DIVI. The first presenter will provide an overview on the different mechanisms of DIVI, pathology lesions, clinical manifestation, different tools and novel safety biomarkers available to investigate DIVI, and regulatory consideration. The second and the third presenters will use case examples to discuss common mechanisms of pharmaceuticals- and biotherapeutics-induced DIVI, respectively. Presenters will illustrate common tools and novel technologies that can be used to investigate the mechanisms and preclinical to clinical translation, how to use these data to inform go/no-go decisions, and to support clinical development and registration. Lastly, the final speaker will utilize a fun, interactive working session to challenge the audience to solve DIVI findings real-time, and to engage the audience to consider alternative strategies to enable the development of novel safe and efficacious drugs. The course will be wrapped up with pragmatic points for considerations for the toxicologists when DIVI is observed in preclinical studies.

- Drug Induced Vascular Injury: From PDEs to Proteins, How Little Holes Cause Big Problems. James Weaver, US FDA, Silver Spring, MD.
- Vascular Injury Associated with Biotherapeutics: Mechanisms of Toxicity and Consideration for Risk Assessment. Hong Wang, Development Toxicology, Safety Assessment, Genentech, South San Francisco, CA.
- Drug-Induced Vascular Injury: Practical Exercises. Tanja Zabka, Pathology, Safety Assessment, Genentech, South San Francisco, CA.

New Concepts and Technologies in Metals Toxicology

Sunday, March 12, 8:15 AM to 12:00 Noon

AM05 | MORNING COURSE

Chairperson(s): Wei Zheng, Purdue University, West Lafayette, IN; and Michael Hughes, US EPA, Research Triangle Park, NC.

Endorser(s):
- Mechanisms Specialty Section
- Metals Specialty Section
- Neurotoxicology Specialty Section

Metals have provided unique challenges to toxicologists because of difficulties in methods of their detection, limited understanding of their mechanisms of action, means of medical intervention, and the connections between human health, animal health, and the ecosystem. A recent incident of drinking water lead exposure in Flint, Michigan bespeaks the social, economic, and ethnic impacts of metal toxicity in general populations. This basic course is intended to introduce the audience with the novel concepts and technologies in metal toxicological research, from mechanistic interpretation to therapeutic intervention, and from innovative technologies in diagnosis and quantification of metal body burden to the concept of “One Health” that integrates ecology, animal health, and human health as a whole system. The Introduction will briefly review the current state of metal-induced toxicities due to worldwide environmental and occupational exposure and state the purposes of this course (Dr. Zheng). The first lecture will introduce the integrative concept of “One Health” that embraces the factors from ecology and the environment to animal and human susceptibility to interpret metal toxicity (Dr. Wise). The second lecture will further extend the concept by providing a concise overview of general disposition (e.g., absorption) and mechanisms of metal toxicity (e.g., direct interaction with functional groups of critical proteins, generation of reactive oxygen species, and alteration of cell signaling pathway) and the integrating these factors on the impact of metals on epigenetics and cancer stem cells (Dr. Hughes). The third lecture will provide an overview of advanced medical imaging modalities such as MRI/MRS, PET, and XRF and their applications. The speaker will use manganese (Mn) as an example to showcase how imaging can be used for early diagnosis of metal toxicities and monitoring of disease progression and therapy (Dr. Dydak). The final lecture will discuss new concepts in clinical treatment of metal toxicities within and beyond the traditional chelation therapy (Dr. Smith). Speakers will discuss these concepts and technologies in the context of metal toxicology with details specific to metals having particular human environmental health relevance, such as lead (Pb), manganese (Mn), cadmium (Cd), arsenic (As) and mercury (Hg). The course will benefit those who desire knowledge on novel mechanistic interpretation of metal toxicities, theories on metal toxicity treatment and intervention, and technical approaches in utilizing widely available imaging technologies that can be used to support research in metal toxicology. As the course introduces concepts and techniques that are equally applicable to other fields, researchers engaged in wider aspects of metal toxicology, such as neurotoxicology, nanotoxicology, carcinogenesis, risk assessment, and occupational health will benefit by attending this course.

- Introduction: Current State of Metal Toxicities. Wei Zheng, Purdue University, West Lafayette, IN.
- Metals Specialty Section
- Mechanisms Specialty Section
- Neurotoxicology Specialty Section
Reproductive Toxicity: Challenges and Practical Approaches to Determine Risk in Drug Development

Sunday, March 12, 8:15 AM to 12:00 Noon
AM06 | MORNING COURSE

Chairperson(s): Jeffrey Moffit, Alnylam Pharmaceuticals, Cambridge, MA; and Edward Dere, Brown University, Providence, RI.

Endorser(s):
Regulatory and Safety Evaluation Specialty Section
Reproductive and Developmental Toxicology Specialty Section

The goal of this course is intended to provide an overview of reproductive biology, typical mechanisms of toxicity, and provide a path forward to critically evaluate reproductive liabilities for risk/benefit in humans. This course is primarily intended for toxicologists who encounter reproductive toxicity in a drug development setting, but these tools and approaches are equally applicable to assessing consumer products or environmental chemicals. Reproductive toxicity is a major source of compound attrition, representing one of the most difficult toxicities to predict or monitor in humans. The broad description of reproductive toxicity can arise from direct adverse effects on specific reproductive cell types, perturbations in hormonal signaling cascades, or toxicities that may only become evident from adverse effects on the conceptus. Mechanistic insight into reproductive toxicities is often difficult to ascertain, as reproductive tracts are exceedingly complex with many biological unknowns and species-specific differences in biology or maturation. The first two presentations will focus on male and female reproductive toxicity, respectively. These sessions will cover basic reproductive biology, typical types of reproductive toxicity findings, and case studies that provide real-world approaches to developing decision making criteria for evaluating reproductive liabilities. The third talk will describe various in vitro techniques to profile early development candidates for reproductive liabilities or mechanistically investigate toxicities identified in vivo. A final presentation will cover the unique ways in which biologics can cause reproductive toxicities and alternative approaches to investigating these modalities, which differ from small molecules. In summary, this course will give attendees an appreciation for the complexities of reproductive biology, challenges associated with understanding the mechanistic basis of reproductive findings, and provide practical approaches to determining the risk/benefit relationship of these reproductive toxicities.

Introduction. Edward Dere, Brown University, Providence, RI.

Failure to Launch—Challenges and Strategies to Assess Risk in Male Reproductive Toxicity. Jeffrey Moffit, Alnylam Pharmaceuticals, Cambridge, MA.

Female Reproductive Toxicology—Evaluating Toxicity and Assessing Risk. Kimberly Hatfield, US FDA, Silver Spring, MD.

In Vitro Approaches to Assessing Reproductive Toxicology. Sarah Campion, Pfizer Inc., Groton, CT.

Reproductive Safety Assessment for Biopharmaceuticals. Wendy Halpern, Genentech, South San Francisco, CA.

Technologies and Applications of Stem Cells for Use in Toxicology

Sunday, March 12, 8:15 AM to 12:00 Noon
AM07 | MORNING COURSE

Chairperson(s): Erik Tokar, NTP, NIEHS, Durham, NC; and Aaron Bowman, Vanderbilt University Medical Center, Nashville, TN.

Endorser(s):
In Vitro and Alternative Methods Specialty Section
Neurotoxicology Specialty Section
Stem Cells Specialty Section

Stem cells (SCs) biology has been one of the most active areas of research over the last decade. Advances in SC technology are providing exciting opportunities for in vitro modeling in a physiologically-relevant environment that is both consistent and replicable. Indeed, SCs are revolutionizing toxicological research and continue to be an area with tremendous potential for areas including toxicity screening, drug development, and disease pathogenesis. In order to remain at the forefront of these important areas of research, toxicologists must continue to learn and integrate these cutting-edge technologies and applications of SCs into their research. In this course, speakers representing academia, government, and industry will provide diverse viewpoints on the use of SCs in toxicology in both broad and specific contexts. Technologies and potential applications for assorted types of stem cell models (i.e. embryonic, induced pluripotent, multipotent, cancer stem cells, etc.) for various research purposes, including disease modeling, regenerative therapies, drug discovery, and toxicity testing will be described. The first speaker, Dr. Tokar, will provide an updated summary of available SC technology platforms and current protocols. The second speaker, Dr. Moore, will provide examples of how SC resources can be sourced or generated for studies with specific emphasis on genome modifying technology. The third speaker, Dr. Bowman, will provide specific examples of how SC models enable gene x environment interaction and translational environmental health studies with special emphasis the potential for clinical applications. The final speaker, Dr. Kolaja, will close out the session with new microphysiological applications of SC platforms for safety assessment. Overall, this important and timely course will highlight the history, nomenclature, properties, regulation, and derivation of SCs, and the key roles these cells play in the genesis of various human diseases.

The Fundamentals of Stem Cells for Use in Toxicological Research. Erik Tokar, NTP, NIEHS, Durham, NC.

Strategies for Building Better iPSC Models of Human Disease and Development. Jennifer Moore, Rutgers University, Piscataway, NJ.

Patient-Derived Stem Cells As a Translational Model for Molecular Neurotoxicology and Environmental Health Research. Aaron B. Bowman, Vanderbilt University Medical Center, Nashville, TN.
Applications of Microphysiological Systems and Induced Pluripotent Stem Cell Derived Tissues in Safety Assessment. Kyle L. Kolaja, Celgene, Summit, NJ.

Detecting Cancer Risk in Drugs: Design, Conduct, and Interpretation of Carcinogenicity Studies for Regulatory Approvals
Sunday, March 12, 1:15 PM to 5:00 PM
PM08 | AFTERNOON COURSE

Chairperson(s): Owen McMaster, US FDA Center for Drug Evaluation and Research, Silver Spring, MD; and James Popp, Stratoxon LLC, Morgantown, PA.

Endorser(s):
Carcinogenesis Specialty Section
Regulatory and Safety Evaluation Specialty Section

Evaluation of the carcinogenic potential of therapeutic agents is a very complex, multi-step process that is conducted only for drugs which meet certain criteria. Recently, International Council for Harmonisation (ICH) has issued a regulatory notice document regarding proposed changes to rodent carcinogenicity testing of pharmaceuticals. This course is designed to provide an overview of the practical aspects of the design, conduct, and interpretation of the US FDA-required carcinogenicity assessments. This course will be useful for students and investigators who have not had recent, hands-on experience conducting such studies, or who would like to update their knowledge of recent advancements in carcinogenicity assessment. The first talk will provide an overview of the current procedures for evaluating the potential carcinogenicity of a drug to be marketed in the US. The second talk will go into the review of the carcinogenicity assessments from the perspective of an US FDA reviewer. This reviewer will describe the point of view of the Pharmacology/Toxicology review, the review division, and that of CDER’s Executive Carcinogenicity Assessment Committee. The third talk will detail the planning, conduct, and interpretation of the two-year rat carcinogenicity study, the cornerstone of many carcinogenicity assessments. The fourth talk will detail the planning, conduct, and interpretation of studies using the TgrasH2 mouse model to assess cancer risk. The TgrasH2 has become the most widely used alternative to the two-year mouse carcinogenicity study. This talk also will include a discussion of other alternatives to the two-year bioassay and will end with a case study of a TgrasH2 study. The fifth talk will discuss an initiative by the ICH S1 Expert Working Group to assess the feasibility of a weight-of-evidence approach as a possible future option for the carcinogenicity testing of pharmaceuticals.

Essentials of Carcinogenicity Testing. Owen McMaster, US FDA Center for Drug Evaluation and Research, Silver Spring, MD.
The TgrasH2 Assay. Mark Morse, Charles River, Spencerville, OH.
Evaluating Carcinogenicity: The Reviewer’s Perspective. Timothy McGovern, US FDA Center for Drug Evaluation and Research, Silver Spring, MD.

Developmental and Reproductive Toxicology (DART) and Risk Assessment of Environmental Chemicals: Applications, Complexities, and Novel Approaches
Sunday, March 12, 1:15 PM to 5:00 PM
PM09 | AFTERNOON COURSE

Chairperson(s): Heather Lynch, Gradient, Cambridge, MA; and Natasha Catlin, National Toxicology Program, Durham, NC.

Endorser(s):
Reproductive and Developmental Toxicology Specialty Section
Risk Assessment Specialty Section

The potential for developmental and reproductive toxicity (DART) is a unique and critical consideration for product safety as well as for the derivation of environmental health criteria and occupational exposure levels (OELs) for chemicals. The establishment of safe levels of exposure that protect against DART effects remains a major challenge, due to factors such as the complexity of human reproductive and developmental processes, unique routes of exposure (e.g., breast milk), sensitive subpopulations (e.g., the fetus and pregnant women), and short duration windows of susceptibility (e.g., the period of organogenesis). The goal of this course is to provide the participant with an introduction to traditional and emerging DART assessment approaches, with a focus on their practical application in safety assessment and policy-making. The first presentation will provide an overview of the biology of the mammalian reproductive system and prenatal/early life development, focusing on physiological and timing-specific vulnerabilities of critical importance to risk assessment (RA). The second presentation will describe standard testing protocols for DART and provide information regarding requirements for industry. The third presentation will expand beyond traditional experimental approaches to assays designed to elucidate the mechanistic aspects of DART effects, including novel in vitro assays, and will discuss key considerations in the interpretation of the biological relevance of DART effects. The fourth presentation will then review the application of DART data to human health risk assessment of environmental chemicals, focusing on the consideration of these data in the derivation of toxicity criteria by US agencies. The final presentation will demonstrate the use of DART RA in industry, describing several practical screening approaches for assessing the potential for DART effects in the workplace. This course will be of broad interest to testing laboratories, general toxicologists, risk assessors, risk managers, industrial hygienists, and others seeking a better understanding of how DART data are generated and applied in hazard and risk assessment.

DART Testing Protocols and Applications Within Industry. Reza Rasoulpour, Dow AgroSciences, Indianapolis, IN.
Targeted Approaches for DART Adverse Outcome Hypothesis Testing. John Rogers, US EPA, Research Triangle Park, NC.
Application of DART Risk Assessment: Protecting Workers from Chemical Exposures. Heather Lynch, Gradient, Cambridge, MA.
Emerging Approaches in Genetic Toxicology for Product Development
Sunday, March 12, 1:15 PM to 5:00 PM
PM10 | AFTERNOON COURSE

Chairperson(s): Jeffrey C. Bemis, Litron Laboratories, Rochester, NY; and Krista L. Dobo, Pfizer Worldwide R&D, Groton, CT.

Endorser(s):
- Carcinogenesis Specialty Section
- Drug Discovery Toxicology Specialty Section

Genetic toxicology is a well-established part of safety testing for product development. Recent advances in methods and technologies, as well as the emergence of new challenges for product development, are changing the type of data that are generated and the way that genetic toxicology data are utilized. The goal of this continuing education course is to highlight the development and application of novel methods and approaches that have the potential to improve well-established safety studies and risk assessment. The focus will be on in vitro/in vivo systems and computational approaches which can be used to support and enhance data required for regulatory submissions and improve human health risk assessment.

The topics covered will be of interest to both genetic toxicology experts, as well as other toxicologists who want to learn about emerging developments in genetic toxicology testing, risk assessment approaches, and how they can be utilized to make informed decisions. The course content will also speak to the importance of in vitro studies in addressing 3R’s initiatives and their increasing role in genotox testing and human risk assessment. The Course Chair, Jeff Bemis, chaired a similar SOT CE course back in 2011 covering new technologies in genetic toxicology. This will provide an opportunity to revisit some of the forward-looking statements made in that course and where genetic toxicology actually is six years later. Overall, the CE course will deliver comprehensive information on new technologies along with practical examples, so attendees will come away with an understanding of how state-of-the-art approaches can be integrated to benefit their product development activities.

Introduction to Genetic Toxicology in Drug Development.
Krista L. Dobo, Pfizer Worldwide R&D, Groton, CT.

Emerging and Established Mutagenicity Assays to Support and Enhance Regulatory Evaluations.
Paul White, Health Canada, Ottawa, ON, Canada.

Maik Schuler, Pfizer PGRD, Groton—New London, CT.

Multiplexed In Vitro Assays for the Determination of Genotoxic Mode of Action.
Steven M. Bryce, Litron Laboratories, Rochester, NY.

Application of 3D Models and Other Advancements for the Determination of Genotoxicity in Consumer Products.
Stefan Pfuhler, Procter & Gamble, Cincinnati, OH.

Contribution of Genotoxicity Information and Point of Departure Metrics to Improve Decision Making and Risk Assessment in Drug Development.
George Johnson, Swansea University, Swansea, United Kingdom.

Extrapolation in the Airways: Strategies to Incorporate In Vivo and In Vitro Data to Better Protect Human Health
Sunday, March 12, 1:15 PM to 5:00 PM
PM11 | AFTERNOON COURSE

Chairperson(s): Marie Fortin, Colgate-Palmolive, Piscataway, NJ; and Madhuri Singal, Reckitt Benkinser, Montvale, NJ.

Endorser(s):
- In Vitro and Alternative Methods Specialty Section
- Regulatory and Safety Evaluation Specialty Section
- Risk Assessment Specialty Section

The science of safety and risk assessment relies primarily upon the use of data generated with in vivo or in vitro models that significantly differ physiologically from humans. While tremendous leaps have been made in the extrapolation of animal-to-human data for the oral route of exposure, significant gaps remain with respect to the inhalation route. The intrinsic differences between animals and humans are such that even dosimetry is complicated by the intrinsic differences between humans and other animals with respect to anatomy, breathing rate, depth of deposition, gas exchange capacity, and in situ metabolism. While a variety of assumptions are routinely used to provide rough estimates, a greater level of understanding is necessary to ensure that risk is not underestimated. In recent years, financial and ethical concerns have driven substantial efforts to substitute in vitro approaches for animal models; however, this transition comes with greater challenges in developing scientifically sound extrapolations for risk assessment. The fluid mechanics and cellular diversity within the airways has made it difficult to model, and it has become increasingly more difficult for safety and risk assessors to perform their evaluations with a high degree of confidence because they lack robust extrapolation strategies.

The aim of this advanced CE Course is to review the critical differences between humans and common surrogate species and explain approaches to strengthen safety evaluation and risk assessment by integrating complementary in vitro data and leveraging novel in vitro models when in vivo data is not available. While alternative airway models have been previously described, this session will focus on the extrapolation from these models to inform risk assessment. Consideration will be given to gas/vapor and particulate/droplets to provide the breadth necessary to address the different types of exposure that can occur via inhalation and strategies to incorporate the outcomes of alternative testing methods into risk assessment will be presented. By the end of this advanced CE Course, attendees will have a better understanding of how to integrate and utilize in vitro and in vivo data to support the safety evaluation of their products, or for the risk assessment of environmental and occupational exposures that occur via the inhalation route.

Laboried Extrapolation: From Data Gasps to a Sigh of Relief.
Marie C. Fortin, Colgate-Palmolive, Piscataway, NJ.

Review and Analysis of Species Differences in Respiratory Anatomy.
Kent E. Pinkerton, University of California—Davis, Davis, CA.

Using Physiologically Based Pharmacokinetic Modeling and In Vitro Metabolism Data to Conduct Animal-to-Human Extrapolation in Inhalation Dosimetry.
Harvey J. Clewell, ScitoVation, LLC, Research Triangle Park, NC.
Health-Based Limits for Toxicological Risk Assessment: Setting Acceptable Daily Exposures for Pharmaceutical and Chemical Safety

Sunday, March 12, 1:15 PM to 5:00 PM
PM12 | AFTERNOON COURSE

Chairperson(s): Patricia Weideman, Sakari Consultants LLC, Stratham, NH; and Andrew Maier, University of Cincinnati, Cincinnati, OH.

Endorser(s):
Occupational and Public Health Specialty Section
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

Health-based exposure limits (HBELs) have been used for many years to assure safety or assess risks from potential adverse health-related effects arising from exposures to xenobiotics. Acceptable Daily Exposure (ADE) and Permitted Daily Exposure (PDE) are terms referencing assessments that can be considered as the bases for a variety of health-based assessments associated with the development and manufacture of chemicals and pharmaceuticals, industrial and specialty chemicals, consumer products, and other environmental contaminants, including active ingredients and products, process/product impurities, chemical intermediates, extractables, and leachables. ADEs/PDEs have similar overall intent and definition as other HBELs and may also have regulatory implications. Generally the numerous specific HBELs, including ADEs, are based on robust hazard assessments that can be used as the basis for subsequent risk assessments for a variety of situations, including further derivation of occupational exposure limits (OELs) to protect workers who manufacture or process chemicals and pharmaceuticals and the derivation of limits for cleaning validation processes. As an example, the transition to the use of HBELs (i.e. ADEs) to protect product quality of pharmaceuticals has gained industry and regulatory interest and created much effort in the implementation of HBEL concepts on a large scale. In addition, recent regulatory scrutiny and international guidelines have focused attention on prevention of cross-contamination in equipment or facilities for which HBELs and industrial hygiene principles have significant impact. Various traditional default approaches (e.g. 10 ppm) have been used historically to manage cross-contamination issues and good manufacturing procedures (GMPs); however, these default approaches have not been based on current health-based risk assessment methods. In contrast to the default approaches, derivation of ADEs includes the use of robust datasets such as those in the pharmaceutical industry. These datasets are generally more complete than those for chemical manufacturing and often include information about mechanism of action, pharmacodynamics, and kinetics, bioavailability, and application of appropriate adjustment factors to better inform hazard and risk decisions. Although toxicological information about industrial chemicals may not be based on human experience and the datasets are constructed differently, these data often offer additional information based on use and experience that are not available for pharmaceuticals. Use of data and methods parallels many aspects of the evolving methods in deriving HBELs for either industrial chemicals or pharmaceuticals. Although ADEs are a step toward better informed science- and health risk-based decisions, the methods used to derive ADEs are complex and are not harmonized among various regulatory constituencies and practitioners. The unique aspects of ADE derivation and application will be highlighted. Using pharmaceuticals as the example, this session will provide background and tools for toxicologists and regulators to better understand the basis, derivation, and application of these unique assessments for protection of human safety as an attempt to provide more consistency in approach and outcomes.


Application of Data-Derived Health Limits Versus Default Limits. Brad Stanan, MedImmune, Gaithersburg, MD.

The Point of Departure As a Central Aspect of ADE Derivation. Joel Bercu, Gilead Sciences, Foster City, CA.

Fine-Tuning the Health-Based Assessment: Applying Adjustment Factors and Use of Pharmacokinetic Data. Bruce D. Naumann, Merck and Co., Inc., Kenilworth, NJ.

Read-Across: Case Studies, New Techniques, and Guidelines for Practical Application

Sunday, March 12, 1:15 PM to 5:00 PM
PM13 | AFTERNOON COURSE

Chairperson(s): Kristie Sullivan, Physicians Committee for Responsible Medicine, Oakland, CA; and Mark Cronin, Liverpool John Moores University, Liverpool, United Kingdom.

Endorser(s):
Biological Modeling Specialty Section
In Vitro and Alternative Methods Specialty Section
Regulatory and Safety Evaluation Specialty Section

The relationship between structure and activity has been exploited in the hazard characterization of chemicals for several decades, including specifically the practice of “reading across” or applying toxicity data from one or more chemicals to another with a similar structure to fill a data gap. Read-across is currently a useful strategy to increase our understanding of chemical hazard without de novo testing. However, expertise, application, and acceptance of the results of a particular read-across vary within and among organizations and geographical regions. There are a number of reasons for this, including regulatory or legislative drivers, an increasing motivation to expand the use of non-testing strategies, and minimal consensus around how to weigh evidence and address and express uncertainty. Recently, multiple stakeholder organizations have contributed to active and robust discussions on read-across in a variety of venues in an effort to build consensus around these issues. This course will update participants on those efforts and provide practical guidance for conducting read-across for regulatory use, including across different regulatory regions. Speakers will present experience-driven case studies to share best practices and communi-
cate the state-of-the-art for structure-based read-across, while looking ahead at how results from New Approach Methodologies including in vitro, “omics,” and high throughput/content methods may be incorporated into a read-across to improve its outcome.

**The Regulatory Landscape for Read-Across.** Kristie Sullivan, Physicians Committee for Responsible Medicine, Washington, DC.

**Setting the Stage: Forming a Category Using Chemical Structures to Read Across Toxicological Data.** Mark Cronin, Liverpool John Moores University, Liverpool, United Kingdom.

**Improving Read-Across Using Biological Data and Quality Assessment.** Nicole Kleinstreuer, National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), Research Triangle Park, NC.

**A Framework to Build Scientific Confidence in Read-Across Results.** Grace Patlewicz, US EPA, Research Triangle Park, NC.


**Applying the Read-Across Assessment Framework to Identify and Address Uncertainty.** Andrea Richarz, European Commission, Joint Research Centre, Ispra (VA), Italy.

**Building a Read-Across from the Ground Up.** Sharon Buring Stuard, The Procter & Gamble Company, Cincinnati, OH.

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### Daily Plenary Sessions

#### Data Science

- **Monday, March 13, 8:00 AM to 9:20 AM**
  - Lecturers: Peter Sorger, Harvard Medical School, Boston, MA; and Stephen Friend, Apple Inc., Cupertino, CA.

#### Precision Medicine

- **Tuesday, March 14, 8:00 AM to 9:20 AM**
  - Lecturers: Jun J. Yang, St. Jude Children’s Research Hospital, Memphis, TN; and Richard Barker, University of Oxford, Oxford, United Kingdom.

#### Daily Plenary Session—Keynote Medical Research Council (MRC) Lecture

- **The Exposome: Challenges and Opportunities**
  - Wednesday, March 15, 8:00 AM to 9:20 AM
  - Lecturer: Paul Elliott, Imperial College, London, United Kingdom.

*See full descriptions on pages 75–77.*
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Daily Plenary Session: Data Science

Monday, March 13, 8:00 AM to 9:20 AM

Systems Approaches to Drug Efficacy and Toxicity in an Era of Big Data

Lecturer: Peter Sorger, Harvard Medical School, Boston, MA.

The development of new therapeutic drugs is fundamental to improving human health but the process is challenged by rising costs and a high rate of failure. New and better technology and big data are often put forward as the solutions to these problems. However, I will discuss laboratory and clinical studies showing that some of the fundamental concepts in pharmacology and toxicology are ripe for reinvention. Increasing data on the impact of cell-to-cell variability and temporal variation in cellular physiology motivates new ways of thinking about seemingly simple concepts such as drug dose-response. Better understanding of sources of variation in laboratory and clinical data should also improve our ability to identify robust biomarkers of therapeutic and adverse effects.

I will argue that big data and data science are essential but insufficient: correct interpretation of empirical data in biomedicine hinges on theories about mechanism. I will discuss these theories with reference to cytotoxic and targeted anti-cancer therapies and studies of drug response in cell culture, animal models and human clinical trials. New pharmacological principles derived from such studies are being developed into practical algorithms and open-source software as a means to improve target qualification, lead molecule optimization and early phase clinical trials. The hoped for outcome: better drugs at a cost society can afford.

How Sensor-Based Reporting of Adverse Side Effects Might Replace Patient-Reported Outcomes

Lecturer: Stephen Friend, Apple Inc., Cupertino, CA.

The presentation will address how data is captured today and look at alternatives if one could take sensor based approaches. Extrapolating from the efforts the community has shown feasible using various Research Kit Apps it is worth considering tracking of adverse effects.

Daily Plenary Session: Precision Medicine

Tuesday, March 14, 8:00 AM to 9:20 AM

Pharmacogenomics of Drug Toxicity in Cancer: Making the Case for Precision Medicine

Lecturer: Jun J. Yang, St. Jude Children’s Research Hospital, Memphis, TN.

Elucidation of the genetic basis for inter-patient variability in drug toxicity not only reveals important biology of a drug’s mechanism of action but also provides critical knowledge that enables risk-adapted treatment individualization. This is particularly relevant in cancer where chemotherapy is often associated with severe acute toxicities and debilitating long-term side effects. Therefore, the narrow therapeutic index of anti-leukemic drugs provides a compelling rationale for improvements in evidence-based precision medicine approaches. Focusing on acute lymphoblastic leukemia as a model disease, our pharmacogenomics research identifies genetic factors associated with response and toxicity of a wide range of common anti-cancer drugs, from which we then develop genetics-guided individualized therapy. For example, inherited deficiency in detoxification enzymes TPMT and NUDT15 predisposes children with leukemia to severe thiopurine-induced myelosuppression and preemptive dose adjustment based on gene genotype effectively minimizes host toxicity without compromising anti-cancer efficacy of this class of drugs. In fact, there is a rapidly-growing number of medications for which pharmacogenomic variants can directly guide treatment choice and/or dosing strategy. At the forefront of precision medicine, pharmacogenomics hold particularly great promise to transform medical practice with more efficacious and safer therapies across diseases.

The Role of Precision Medicine in Closing the Innovation Gap

Lecturer: Richard Barker, University of Oxford, Oxford, United Kingdom.

The tremendous recent advances in basic bioscience are not translating as effectively and affordably as they should into health benefit for patients and positive change in healthcare delivery. The presentation will analyze and illustrate this phenomenon and the threat it represents to the long-term sustainability of biomedical innovation. It also will propose changes to both the innovation process and the environment in which it operates, highlighting the golden thread of precision medicine—vital to the potential to make major changes in innovation productivity. The talk will draw on the speaker’s recent experience launching the UK’s Precision Medicine Catapult.

(continued on page 77)
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Contributors to the SOT Endowment Fund are helping to build for the future of toxicology through long-term financial support that generates critical resources to enable the Society to fulfill its mission, now and in the years to come. Please help SOT continue to make a difference by becoming a contributor to the SOT Endowment Fund.

Visit www.toxicology.org/endowment.
Daily Plenary Session: Keynote Medical Research Council (MRC) Lecture

Wednesday, March 15, 8:00 AM to 9:20 AM

The Exposome: Challenges and Opportunities

Lecturer: Paul Elliott, Imperial College, London, United Kingdom.

Professor Paul Elliott, MBBS, PhD, FMedSci, trained in clinical medicine and epidemiology as a Wellcome Trust Clinical Fellow at St. Mary’s Hospital London and the London School of Hygiene & Tropical Medicine. He heads what is now the Department of Epidemiology and Biostatistics in the School of Public Health. The Department has expanded significantly during recent years to encompass a wide-ranging program of health research and extensive collaborations with honorary and visiting staff. Dr. Elliott also is Director of the MRC-PHE Centre for Environment and Health which sits within the Department and includes the Small Area Health Statistics Unit (SAHSU). He also is an honorary consultant in public health medicine in the Directorate of Primary Care and Public Health of the Imperial College Healthcare NHS Trust and the academic lead for the Biobanking research theme for the Imperial NIHR Biomedical Research Centre. He was recently appointed as the Academic Health Sciences Centre’s (AHSC) Director of Information Governance.

MEET THE DIRECTORS

A Conversation with Linda Birnbaum and Robert Kavlock

Monday, March 13, 1:30 PM to 2:30 PM

Chairperson(s): Patricia E. Ganey, Society of Toxicology Vice President; Michigan State University, East Lansing, MI.

Lecturers: Linda Birnbaum, NIEHS, Research Triangle Park, NC; and Robert Kavlock, US EPA, Washington, DC.

This important session will provide an informal venue for meeting attendees to have a candid and open discussion with two key leaders of federal organizations with missions to protect and improve public health: Dr. Linda Birnbaum, Director, National Institute of Environmental Health Sciences (NIEHS), NIH, and Dr. Robert Kavlock, Deputy Assistant Administrator for Science at the Office of Research and Development for the US EPA. The entire session will be devoted to a question-and-answer format concerning scientific directions and priorities for NIEHS and US EPA including funding priorities and outlooks, and training opportunities.

SOT/EUROTOX DEBATE

Toxicology Testing of Drug Combinations Does Not Add Significant Value to Human Risk Evaluation Beyond What Is Known for the Individual Agents

Monday, March 13, 4:45 PM to 6:00 PM

Chairperson(s): Leigh Ann Burns Naas, Gilead Sciences Inc., Foster City, CA; and Heather Wallace, University of Aberdeen, Aberdeen, United Kingdom.

SOT Debater: Kenneth L. Hastings, Hastings Toxicology Consulting LLC, Mount Airy, MD.

EUROTOX Debater: Phil Bentley, Toxicodynamix International LLC, Hendersonville, NC, and Basel, Switzerland.

Endorser(s):
Society of Toxicology (SOT)
European Societies of Toxicology (EUROTOX)

The use of innovative drug combinations—both large and small molecule—in clinical development is increasing. The objective is often to increase efficacy by targeting multiple pathways for the same disease, to improve safety by being able to lower doses of one or more drugs, or to provide more convenient/acceptable therapies to patients. As the number of these clinical combinations rises, there is an increasing need to evaluate their nonclinical safety. At the heart of this evaluation is the question regarding the need for actual animal testing. Global regulatory guidance has provided a framework for the nonclinical safety evaluation of combination products, which considers the need for testing based on such things as the potential for PK or PD interactions, overlapping toxicity profiles, extent of toxicity characterization of the individual agents and their margins of safety, human clinical experience with the individual agents, and the stage of clinical development of each agent. The guidance applies not only to fixed dose combinations but co-packaged and co-use as well. Unless there is clinical experience with the combination and that combination involves two late stage (Phase 3, Marketed) entities, toxicity studies up to 90 days are recommended. This broad recommendation is inconsistent with the principles of the 3Rs for reduction, refinement, and replacement in animal experimentation. Conversely, the potential for unexpected safety events with novel, targeted therapies is a clear clinical concern. Regardless of framework differences and personal convictions, each delegate will discuss the evidence regarding whether the information gathered in nonclinical combination studies provides clear benefit in the overall risk evaluation for clinical combinations in order to obtain audience approval or rejection of the motion. In addition to being a featured session at the SOT Annual Meeting in Baltimore, Maryland, this debate will again take place (with the debaters taking the reverse positions) in Bratislava, Slovak Republic during the 53rd Congress of the European Societies of Toxicology (2017 EUROTOX Annual Congress), September 10-13, 2017.
Final Chance to Submit Your Research to the 2017 Meeting

Late-Breaking Abstract Submission Phase

December 5, 2016–January 12, 2017

Cost: $75 per abstract

Important Reminders:

Late-breaking abstracts should represent new research—not a revision of a previously submitted abstract. They should describe high-impact, original research that could not be completed prior to the original abstract deadline.

Late-breaking abstracts will be programmed on Thursday, March 16. They are reviewed by the Scientific Program Committee and evaluated by the same standards as abstracts submitted for the original deadline.

Accepted late-breaking abstracts will be provided as a PDF addendum to The Toxicologist and are accessible through the SOT Mobile Event App and Online Planner.

Take advantage of this opportunity to present your research to a global audience.
Reactions arise, evidence in people and animal models points to an activation of immune system as critical to the pathogenesis. For several drugs, specific HLA polymorphisms are associated with risk for IDILI in human patients. For other drugs, animal models based on immune system activation have provided evidence of a role for inflammatory cytokines. For example, a murine model in which mice were sensitized and challenged with halothane resulted in hepatitis associated with interferon-gamma (IFNg) production. Similarly, in mice undergoing an acute inflammatory episode, trovafloxacin enhanced the appearance of tumor necrosis factor-alpha (TNF) and IFNg in the plasma. In vitro, trovafloxacin amplified the production of TNF in macrophages activated by LPS. In addition, in a human hepatocyte cell line (HepG2), TNF interacted with trovafloxacin to cause cell death, and IFNg enhanced this response. Likewise, in rats, chlorpromazine interacted with an inflammatory episode caused by LPS, resulting in liver injury, and in vitro, TNF interacted with chlorpromazine to cause cytotoxicity. Similar results were found with diclofenac, a nonsteroidal anti-inflammatory drug that has caused IDILI in humans. These drugs cause nonlethal cell stress of various sorts that resulted in activation of mitogen-activated protein kinases (MAPKs). Indeed, each of the above-mentioned drug-TNF interactions was associated with activation of C-jun N-terminal kinase (JNK), and JNK inhibition abolished the drug-TNF interaction. Moreover, the cytotoxic drug-TNF interactions were enhanced by IFNg exposure. These and other results suggest that drug-induced cell stress and its interaction with cytokines such as TNF and IFNg can lead to prolonged activation of JNK and perhaps other MAPKs, resulting in death of hepatocytes. Such cytotoxic drug-cytokine interaction could provide the basis for an assay to aid in preclinical identification of drug candidates with IDILI potential.
AWARD LECTURES

Award lecture titles and descriptions will be available in the Program and SOT Mobile Event App.

Merit Award Lecture

Monday, March 13, 12:30 PM to 1:20 PM

Lecturer: Samuel Cohen, University of Nebraska Medical Center, Omaha, NE.

Distinguished Toxicology Scholar Award Lecture

Wednesday, March 15, 12:30 PM to 1:20 PM

Lecturer: Linda Birnbaum, NIEHS, Research Triangle Park, NC.

Translational Impact Award Lecture

Wednesday, March 15, 5:00 PM to 5:50 PM

Lecturer: Laura James, University of Arkansas for Medical Sciences, Arkansas Children’s Hospital, Little Rock, AR.

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Adverse Pregnancy Outcomes Associated with Arsenic Exposure. Margaret Karagas, Geisel School of Medicine at Dartmouth, Lebanon, NH.

Building AOPs for Arsenic-Induced Developmental Outcomes for Improved Risk Assessment. Rebecca Fry, University of North Carolina Chapel Hill, Chapel Hill, NC.

Organs-on-a-Chip, Tissue Bioprinting, and 3D Cultures: Next Generation Models for Toxicology in the 21st Century

Monday, March 13, 9:30 AM to 12:15 PM

Chairperson(s): Shaun McCullough, US EPA, Chapel Hill, NC, and Emma Bowers, University of North Carolina, Chapel Hill, NC.

Endorser(s):
In Vitro and Alternative Methods Specialty Section
Mechanisms Specialty Section
Molecular and Systems Biology Specialty Section

Toxicity testing is a cornerstone for risk assessment in applications ranging from product development to the regulation of environmental pollutants; however, the vast majority of toxicity data has been collected in animal models. While the extrapolation of toxicity data from animal models to humans is imperfect due to differences in anatomy and physiology, these traditional models are used because they represent whole-organism biology that is not well replicated by in vitro methods. In recent years, concerns over high cost, long study duration, and ethical considerations have led to increasing pressure to Replace, Reduce, and Refine the use of animal models in toxicity testing. Institution of the “Three Rs” has propelled the use of in vitro systems to characterize the cellular and molecular mechanisms underlying biological changes associated with toxicant exposure. While cell lines have been the workhorses of in vitro toxicology studies for decades, their utility comes at the cost of concerns about their ability to reliably mirror the responses of their in vivo counterparts. The increased availability of primary cells and the ability to generate induced pluripotent stem cells (iPSC) has opened the door to the development of the next generation of in vitro models. The combination of these newly available cell types and advances in cell culture methods has led to the establishment of three-dimensional organoids, bioprinted tissues, and microphysiological systems (“organs-on-a-chip”) that all have great potential to revolutionize the role of in vitro models in toxicity testing. By incorporating features that are absent from current cell culture models, such as cell-cell interactions, three-dimensional architecture, and mechanophysiological cues, these systems provide greater physiological relevance for the future of molecular, mechanistic, and high-throughput toxicology studies. By incorporating these aspects of the native environment within parent tissues, these next generation in vitro systems have the potential to reduce the reliance on animal models by dramatically increasing the relevance of in vitro models in toxicity research. The goal of this workshop is to examine applications of next generation in vitro models in molecular and mechanistic toxicology studies. To achieve this, the experts will discuss the development of these models and their current use in toxicity studies. The session will answer questions such as: What are the benefits and challenges facing the use of next generation in vitro
models in toxicology research? Can iPSC-derived mini-brains effectively model neurotoxicity in pesticide exposures? How can heart-on-a-chip and 3D bioprinted liver tissue be used as screening tools for the toxicity of pharmacologic agents? Does the incorporation of multicellular architecture and mechanophysiologic cues impact toxicity of tobacco and e-cigarette exposures in vitro? What are the perspectives from government and industry on the integration of these models in toxicology and drug discovery research? Following the session attendees will have a better understanding for the benefits, challenges, and applications of next generation in vitro models, and how both government and industry envision their role in the future of toxicity testing.

Introduction. Shaun McCullough, US EPA, Chapel Hill, NC.

21st Century Cell Culture for 21st Century Toxicology. Thomas Hartung, Johns Hopkins University, Baltimore, MD.

Organs-on-a-Chip: Microphysiological Platforms as In Vitro Models of Cardiac and Adipose Tissue. Peter Loskill, Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB, Stuttgart, Germany.

Human Small Airway-on-a-Chip: Applications in Comparing Tobacco and E-Cigarette Exposures. Kambez Benam, Harvard University, Boston, MA.

Utilization of Bioprinted Human Liver Tissues for Toxicology Applications and Disease Modeling. Rhiannon Hardwick, Organovo, San Diego, CA.

Adopting Microphysiological Systems (MPS), or Tissue Chips, as a Research Tool for Drug Development. Kristin Fabre, AstraZeneca, Waltham, MA.

Translational Control in Disease Progression and Xenobiotic-Mediated Toxicity

Monday, March 13, 9:30 AM to 12:15 PM

Chairperson(s): Thomas Baker, Eli Lilly, Indianapolis, IN; and James Stevens, Eli Lilly, Indianapolis, IN.

Endorser(s):

Molecular and Systems Biology Specialty Section

Proper translational control of mRNA to protein has shown to play an essential role for a variety of physiological functions, including development, regulation of cell growth, and metabolic function. Currently, two major regulatory pathways have been described to control the rate of protein synthesis: one via the mammalian target of rapamycin (mTOR); and a second through eukaryotic initiation factor 2 (eIF2) kinases. While the mTOR pathway responds primarily to growth signals and changes in nutrient content, eIF2 kinases respond to an array of cellular stresses, including ultraviolet irradiation and misfolded proteins in the endoplasmic reticulum. Both the mTOR and eIF2 kinase pathways directly affect translational control through modulating distinct components involved in translational initiation. However, this same translational machinery, which maintains homeostasis, is often aberrant during the disease pathogenesis, resulting in abnormalities such as enhanced oncogenic potential, neurodegeneration, and metabolic dysfunction. Translational inhibitors are currently being investigated for therapeutic intervention, but modulation of biological pathways that control translation initiation have been implicated in toxicities associated with a variety of xenobiotics. To better apply novel techniques and approaches toward mechanistic toxicity, systems biology, and drug discovery, it is critical to understand the key intracellular signaling events and pathologic consequences of modulating translation. The session will provide an overview of groundbreaking advances in the understanding of how mTOR and eIF2 kinases, key regulators of translational control, play a role in health and disease at the molecular level, and bridge this knowledge to current applications of risk assessment and translational toxicology. The speakers, representing perspectives from industry to academia, will provide mechanistic insight into the pathogenesis of disease and drug-induced toxicities associated with altered translational control as well as provide guidance toward drug safety. The session will briefly introduce translational control’s relationship to toxicity and pathogenesis of disease, followed by a discussion on novel mechanistic insights into differential signaling pathways, which activate mTORC1 through unique amino acid sensing. Presentations will address mTOR inhibition and the signaling cascade resulting from reactive oxygen species (ROS) toxicity as an adaptive response to control redox homeostasis through selective autophagy of peroxosomes. The presenters will transition from translational control by mTOR to eIF2 kinases. Translational control by eIF2 kinases have been identified in numerous disease states and drug related toxicities. With this, The presenters will discuss novel translation mechanisms of GCN2 activation as an adaptive response in the skin following UV irradiation, and the role of ER stress in the progression of liver disease, such as nonalcoholic steatohepatitis and drug induced liver injury, linking hepatocellular death to inflammation for approaches of risk management. At the conclusion of this symposium, participants will have a good understanding of the role translational control plays in various disease states as well as approaches for elucidating mechanism of toxicity for various drugs and xenobiotics.

Introduction. Thomas Baker, Eli Lilly, Indianapolis, IN.

Differential Regulation of mTORC1 by Amino Acids. Jenna Jewell, University of Texas Southwestern Medical Center, Dallas, TX.

A New Look at an Old Machine: New Cellular Targets for the Cell’s Translational Machinery. Cheryl Walker, Baylor College of Medicine, Houston, TX.

Translational Control and the eIF2 Kinase Pathway in Health and Disease. Ronald Wek, Indiana University School of Medicine, Indianapolis, IN.

ER Stress Regulates a Biological Network Driving the Pathogenesis of Liver Disease. Jeffrey Willy, Eli Lilly, Indianapolis, IN.

The Role of ER Stress in Progression of NAFLD to NASH. Randal Kaufman, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, CA.
WORKSHOP SESSIONS

Cross-Industry and Regulatory Approach for the Identification and/or Qualification of Novel Safety Biomarkers of Drug-Induced Vascular Injury (DIVI)

Monday, March 13, 9:30 AM to 12:15 PM

Chairperson(s): Deidre Dalmas, GlaxoSmithKline, King of Prussia, PA; and Nicholas King, Critical Path Institute, Predictive Safety Testing Consortium, Tucson, AZ.

Endorser(s):
- Cardiovascular Toxicology Specialty Section
- Clinical and Translational Toxicology Specialty Section
- Regulatory and Safety Evaluation Specialty Section

Drug-induced vascular injury (DIVI) in nonclinical toxicology studies is a challenging safety issue that can lead to significant delays in the drug development process and/or result in project termination due to lack of sensitive, specific, and/or effective translational biomarkers, and an incomplete understanding of predictivity of nonclinical models for clinical risk. In nonclinical species, DIVI has been observed with numerous structurally and pharmacologically diverse compounds. Despite individual efforts across industry, mechanisms by which DIVI damage occurs to blood vessels is still not completely understood. Because the issue is too complex to be solved by individual companies working in isolation and with limited resources, the Predictive Safety Testing Consortium’s (PSTC) Vascular Injury Working Group (VIWG), and the Safer and Faster Evidence-based Translation (SAFE-T) Consortium, have been working individually and jointly to identify non-invasive translational biomarkers of DIVI. This will address the question of human relevance using panels of nonclinical and clinical biomarkers that underpin histomorphologic features (endothelial damage, smooth muscle damage, and inflammation) common across species, including humans that can detect the onset, progression, and reversibility of DIVI irrespective of the mechanism of injury. A panel of circulating candidate protein biomarkers that can differentiate rodents with evidence of DIVI from vehicle-treated rats has been developed by the PSTC VIWG. Similarly, the SAFE-T consortium has demonstrated a panel of circulating protein biomarkers that are shared or have shared biology to those identified by the VIWG and may distinguish between patients with vascular disease/injury and healthy volunteers. In addition, the PSTC VIWG and SAFE-T Consortium have developed key outputs required for the qualification of clinical and nonclinical safety biomarkers, and have jointly developed a translational approach to qualify new vascular safety biomarkers for use in clinical drug development research. This session will highlight the industry and regulatory perspective on nonclinical DIVI, its impact on the drug development process, and evolution of the regulatory processes for biomarker qualification. It will showcase the progress of each consortium toward development of novel assays for vascular injury, the collaborative, cross-industry translational approach developed by the PSTC VIWG and SAFE-T Consortium towards qualification of the candidate DIVI biomarkers, and innovative in vitro and non-invasive approaches currently being utilized to assist in the identification/prediction of DIVI.


Novel Integration of Off-Target Screening, Genomic, and Cardiovascular Risk Assessment Strategies for Prediction of Nonclinical Drug-Induced Vascular Injury. Deidre Dalmas, GlaxoSmithKline, King of Prussia, PA.


Panel Discussion. Deidre Dalmas, GlaxoSmithKline, King of Prussia, PA.

Fit for Purpose: Using Computational Models for Risk

Monday, March 13, 9:30 AM to 12:15 PM

Chairperson(s): John Wambaugh, US EPA, Research Triangle Park, NC; and Nisha Sipes, NTP/NIEHS, Research Triangle Park, NC.

Endorser(s):
- Biological Modeling Specialty Section
- In Vitro and Alternative Methods Specialty Section
- Molecular and Systems Biology Specialty Section

The aim of this workshop is to discuss the development, acceptance, and use of fit for purpose computational models for risk assessment applications. In fields ranging from chemical toxicology to health and property reinsurance, decision makers frequently face data gaps when analyzing risk. Some critical data gaps can be successfully bridged using fit for purpose computational models, which are defined as much by what is omitted as what is included in the model. Examples of these models include quantitative structure activity (QSAR) models for specific hazards and environmental fate, pharmacokinetic models of chemical disposition, toxidynamic models for effect, and exposure models. This workshop brings together a panel of experts with first-hand experience ranging from constructing computational models included in screening-level tools, such as EPI Suite, to risk-based decision making using predictive models. Presenters will provide examples of the application of fit for purpose models in the environmental and pharmaceutical arenas, how uncertainties are defined in these models, and what are the strengths and limitations of the models in the particular decision context. Discussions will encompass a broad range of computational models (from physico-chemical properties to human population risk assessment) and chemicals (including pharmaceuticals.
and environmental exposures) in risk applications. Presenters also will discuss objectives, approaches, technologies, knowledge gaps, and suggestions for future research, with an emphasis on lessons learned. The last presentation will provide unique commentary on the use of computational models and risk in corporate reinsurance. This workshop is designed to appeal to a broad audience interested in using or understanding computational methods to elucidate and predict toxicological outcomes for risk assessment. The workshop concludes with a panel discussion on new computational tools that could or should be used for the study of chemical risk.


Development and Application of Computational Tools to Support Chemical Exposure and Risk Assessment. Jon Arnot, ARC Arnot Research and Consulting, University of Toronto Scarborough, Toronto, ON, Canada.

Population Based Risk Assessment. Lesa Aylward, Summit Toxicology, Falls Church, VA.

Drug Development in the 21st Century. Hugh Barton, Pfizer, Groton, CT.

An Intuitive Approach toward Predicting Human Risk with the Tox21 10k Library. Nisha Sipes, NTP/NIEHS, Research Triangle Park, NC.

Calculating Risk on the Really Large Scale with Less than Ideal Information. Ryan Hansen, Gen Re (General Reinsurance Corporation), Stamford, CT.

### Scientific, Regulatory, and Safety Considerations for Probiotics and Microbiome Targeted Therapeutics

**Monday, March 13, 9:30 AM to 12:15 PM**

**Chairperson(s):** Lois Haighton, Intertek Scientific and Regulatory Consultancy, Mississauga, ON, Canada; and Andrea Wong, Council for Responsible Nutrition, Washington, DC.

**Endorser(s):**
- Food Safety Specialty Section
- Regulatory and Safety Evaluation Specialty Section

Advances in the understanding of relationships between gastrointestinal microbiota and human health outcomes have stimulated much research in the field of probiotics and therapeutics that target the microbiome. The global demand for this product class has seen significant recent growth due largely to genomic advances that have made it possible to more accurately characterize individual microbial strains and the gut microbiome as a whole. Probiotics are being proposed for use as functional ingredients in foods and beverages, dietary supplements, animal feed, medical foods, and drug products, with each category subjected to different regulatory requirements for the demonstration of safety. The guidelines are not harmonized, neither across the different product categories, nor between different jurisdictions; thus, the relevant regulatory path can be difficult to navigate. Similar to probiotics, the required regulatory path and associated safety requirements for microbiome targeted therapeutics, such as Fecal Microbiota Transplants, single strain commensal therapies, or small molecule approaches, differ greatly by product type. The safety assessment of microbials for use as live probiotic cultures requires additional hazard characterization beyond that which can be provided by the standard battery of toxicity testing studies applied to chemicals, since the physiological and pathological interactions between microorganisms and their “hosts” are often highly species-specific. Advances in genome sequencing techniques have allowed for vast improvements in the regulatory oversight of consumer products containing microbial ingredients and have highlighted the importance of understanding strain level genomic differences. Just as the probiotic or microbiota-modulating effects of two closely related strains may differ, so too will their safety profiles. Recommended safety evaluation procedures for probiotics have been discussed in general terms with a number of guidance documents available from different authoritative and regulatory bodies (e.g., US FDA, EFSA, FAO/WHO). Recently, however, a more comprehensive safety decision tree has been proposed, which aims to aid in the harmonization of these guidelines and promote the continued development of safe microbial cultures intended for human consumption. The objectives of this workshop are to discuss and highlight the following:

1. Current regulations in the US and other global jurisdictions that apply to the use of probiotics and provide clarity regarding acceptable claims for such products;
2. Health Canada’s model approach to streamlining the regulation of probiotics as Natural Health Products;
3. The recent development of a decision tree to assist in the safety evaluation of novel microbial cultures intended for consumption by humans and animals;
4. The US FDA’s genomic science-based approach to improve the safety and regulatory oversight of foods and dietary supplements containing live microbial ingredients; and
5. Approaches utilized to target and improve the health of the microbiome, including Fecal Microbiota Transplants, and the regulatory challenges associated with microbiome targeted therapeutics. All speakers will participate in a panel discussion following the last presentation.

**Understanding the Safety Requirements and Regulatory Hurdles of Different Product Classes Containing Probiotics.**

Alexandra Lobach, Intertek Scientific & Regulatory Consultancy, Mississauga, ON, Canada.

**Health Canada’s Natural Health Product Monograph for Probiotics: A Streamlined Model.**

Solange Henoud, Lallemand Health Solutions Inc., Montreal, QC, Canada.

**Development and Application of a Safety Decision Tree to Assess the Safety of Probiotics.**

Michael Pariza, University of Wisconsin-Madison, Madison, WI.

**Genomic Approaches to Characterizing Live Microbial Ingredients in Foods for Improved Safety and Regulatory Oversight.**

Christopher Elkins, US FDA, Laurel, MD.

**Scientific and Regulatory Challenges to Measuring the Health of the Microbiome and in the Development of Targeted Therapeutic Agents.**

John Eid, Whole Biome, Inc., San Francisco, CA.
ROUND TABLE SESSION

Bias and Conflict of Interest in Conducting Research and Risk Assessments: Perspectives from Academia, Government, Industry, and Others

Monday, March 13, 12:30 PM to 1:50 PM

Chairperson(s): Kun Yi, Syngenta Crop Protection, LLC, Greensboro, NC, and Jaqueline Patterson, University of Cincinnati, Cincinnati, OH.

Endorser(s):
- Ethical, Legal and Social Issues Specialty Section
- Regulatory and Safety Evaluation Specialty Section

Charges or claims of conflict of interest (COI) are made with increasing frequency with regard to suspicion that personal employment, associations, or funding sources will interfere with the ability of a scientist to objectively conduct or interpret studies, and/or serve on peer review or advisory panels. A frequent concern is funding sources. As public funding for scientific research decreases and becomes more competitive, researchers are seeking funding from other sources (e.g., non-profit organizations, special interest groups, industry, foundations, and advocacy groups). How can we address these concerns in a way that makes best use of the data and talents of all? COI is generally defined as a personal financial interest that interferes with the individual's ability to perform objectively. The National Academies (2003) define conflict of interest as "any financial or other interest which conflicts with the service of the individual because it (1) could significantly impair the individual’s objectivity, or (2) could create an unfair competitive advantage for any person or organization....The term ‘conflict of interest’ means something more than individual bias. There must be an interest, ordinarily financial, that could be directly affected...." In addition, “questions of lack of objectivity and bias ordinarily relate to views stated or positions taken that are largely intellectually motivated or that arise from the close identification or association of an individual with a particular point of view or the positions or perspectives of a particular group. Some potential sources of bias, however, may be so substantial... (e.g., where one is totally committed to a particular point of view, and unwilling, or reasonably perceived to be unwilling, to consider other perspectives or relevant evidence to the contrary).” SOT has developed definitions and guidance for members regarding COI, bias, and advocacy (www.toxicology.org/about/vp/coi.asp). This roundtable session will begin with a philosopher of science examining three philosophical criteria for objectivity in science: transparency, reproducibility, and critical review. This will be followed by scientists from various sectors (government, contract research organization (CRO), academia, private sector, and scientific society) who will reflect upon COI and potential for bias in their professional work (e.g. interpretation and application of their work), and how one might mitigate or manage biases and conflicts of interest. Speakers will address questions such as: How are affiliation (e.g., industry, NGO, consultant) and funding source (e.g., government, foundation, industry) viewed when evaluating potential conflicts of interest and bias? Do (or how might?) funding sources influence study design, reporting of data, and interpretation? How can concerns regarding COI and bias on peer review and advisory panels be managed with reviewers, editors, and publishers? How can bias and conflict of interests be minimized? Can systematic review approaches help to minimize effects of bias/COI? Is GLP an effective tool to address consistency and transparency? Do standardized/validated test guidelines provide solutions to address consistency, reproducibility, and transparency? Can transparency be satisfied with requirements for raw data availability? Is it practical to call for blinding or double-blinding experimental studies? How do we deal with publication bias? Conflict of interest and bias are on-going issues in toxicology research and use of study results. It is important to recognize possible sources of COI and bias and develop ways to mitigate the potential effects. This session will provide an opportunity for participants to discuss openly issues around conflict of interest, and how COI and bias might affect scientists’ work, as well as their integrity and credibility.

Introduction. Kun Yi, Syngenta Crop Protection, LLC, Greensboro, NC.

Key Philosophical Criteria for Objectivity in Science: Transparency, Reproducibility, and Critical Review. Kevin Elliott, Michigan State University, East Lansing, MI.

Bias and Funding Sources: A Perspective from the Private Sector. Richard Becker. American Chemistry Council, Washington, DC.

An Academic’s Perspective on COI and Bias. Norbert Kaminski, Michigan State University, East Lansing, MI.

Managing COI and Bias in a CRO Setting. Pragati Sawhney Coder, Charles River Laboratories, Ashland, OH.

Inherent and Acquired Biases in Interpreting Toxicological Data for Regulatory Risk Assessment. Rita Schoeny, US EPA (Retired), Washington, DC.
INFORMATIONAL SESSIONS

Advances in Preclinical Safety Testing: Progress in Implementation of ICH Guidances

**Monday, March 13, 12:30 PM to 1:50 PM**

**Chairperson(s):** Kenneth Loveday, Biogen, Cambridge, MA; and Michael Graziano, Bristol-Myers Squibb, Princeton, NJ.

**Endorser(s):**
- Carcinogenesis Specialty Section
- Regulatory and Safety Evaluation Specialty Section
- Reproductive and Developmental Toxicology Specialty Section

New strategies and approaches for preclinical safety testing are progressing at a rapid pace. The International Conference on Harmonisation (ICH), which consists of drug regulatory authorities from Europe, Japan, United States, Switzerland, and Canada, along with regional pharmaceutical trade associations, is responsible for generating standardized scientific and technical aspects of pharmaceutical product development and registration. ICH has clearly recognized a need to revise several existing safety guidelines and develop new ones based on evolving science. The Preclinical Safety Leadership Committee (DruSafe) in the International Consortium for Innovation and Quality in Pharmaceutical Development (IQ) provides technical and scientific support in the development of these safety guidelines. DruSafe also promotes an awareness of, and facilitates discussions on, implementation issues. This session will feature speakers from EMA and pharmaceutical companies to review progress, implementation issues, and scientific considerations and contributions for several new and revised ICH Guidelines including: ICH S1 — Rodent Carcinogenicity Studies for Human Pharmaceuticals. In 2013, ICH initiated a project to evaluate the ability of sponsors and drug regulatory authorities (DRAs) to use a weight-of-evidence approach for carcinogenicity assessments as an alternative to conducting 2-year rat studies, when appropriate. This presentation will review the status of the project, and provide a DRA assessment on opportunities to build better alignment on the predictions between sponsors and DRAs, with a focus on the value of pharmacology data. Successful implementation of this approach will result in a reduction in unnecessary rat carcinogenicity studies; ICH M7 — Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk. This guideline focuses on potential mutagenic impurities, which are classified into one of five risk categories. This presentation will describe key elements of the guideline and highlight areas where issues in implementation may arise; Update on Proposed Revisions to ICH S5(R3)—Correlation of In Vitro and In Vivo Assays of Developmental Toxicity. The objectives of this revision are to align ICH S5 with recommendations in other safety guidelines, to provide better rationale for species and dose selection (including human exposure data), and to offer recommendations on integrating in vitro teratogenicity and non-mammalian in vivo testing strategies with in vivo mammalian embryo-fetal development (EFD) studies; ICH S11 — Nonclinical Safety Testing in Support of Development of Pediatric Medicines. An ICH Expert Working Group has been convened to develop a harmonized guidance document for nonclinical development of pediatric medicines. In this session, aspects of juvenile animal studies that proved to be of most value for clinical development will be identified, with a goal of achieving world-wide harmonization on when juvenile animal studies are needed, and provide value for safe use of pharmaceuticals in pediatric populations.

**Supporting Open Data in Toxicology**

**Monday, March 13, 12:30 PM to 1:50 PM**

**Chairperson(s):** George Woodall, US EPA, Research Triangle Park, NC; and Gary Miller, Emory University, Atlanta, GA.

**Endorser(s):**
- Regulatory and Safety Evaluation Specialty Section
- Risk Assessment Specialty Section
- Specialty Section Collaboration and Communication Group

The goals of the session are to provide basic conceptual frameworks to increase open access to toxicological data, encourage cross-discipline collaboration, link existing toxicological research data with computational toxicology and Tox21, and ensure long-term sustainability for toxicological data resources into the future. The move toward open data has increased across all scientific disciplines for several years. In Toxicity Testing in the 21st Century, the NAS recommended development of data management infrastructure “to enable broad data-sharing across academic, government, industry, and NGO sectors and institutions.” A February 2013 Memorandum from the Office of Science and Technology Policy (Executive Office of the President of the United States) ordered Federal Agencies to make data they create publicly available. SOT has made several forays into this topic, including a CCT Session in May 2012, “Building for Better Decisions,” and a roundtable session at SOT 2015 discussing the barriers to sharing toxicological data. In this session, presentations will move beyond the barriers to investigate what resources have been built, what needs to be developed to accommodate all subdisciplines of toxicology, and ensure sustainability into the future. The session will address areas of common cause with other sciences, strategies to tap existing open data infrastructure, leverage across knowledge domains, and identify strategies to avoid redundancy. Key aspects also include developing authoritative reference standards (a common lexicon) to ensure clarity and avoid ambiguity in communicating complex datasets across disciplines; common metadata and data format standards to ensure efficient interoperability; moving beyond chemical-specific toxicity models (e.g., Adverse Outcome Pathways) as a strategy to protect proprietary data and still contribute to the open data model; ensuring existing legacy data are not lost; and planning for long range data curation. Speakers and panelists have
been recruited to represent a broad range of disciplines (policy-makers, information scientists, journal editors, and toxicologists) and types of organizations (government, academia, industry, and NGOs). Likewise, this session is relevant to the full range of subdisciplines within toxicology, as represented by the Specialty Sections within SOT, which generate toxicological data (dose-response, hazard ID, mechanistic, etc.) and those which use such data in cross-discipline analysis, regulatory decisions, or risk assessments. Outcomes expected from the session are a set of recommendations for basic conceptual frameworks to increase open access to toxicological data; strategies to encourage cross-discipline collaboration; approaches for linking legacy study data to computational toxicology and the Tox21 initiative; and methods to ensure longterm sustainability and access to toxicological data. Note: The views expressed in this abstract are those of the authors and do not necessarily represent the views or policies of the US EPA.

Introduction. George Woodall, US EPA, Research Triangle Park, NC.

Open Data in Biomedical Science: Policy Drivers and Recent Progress. Allen Dearry, NIEHS, Research Triangle Park, NC.

Creating a Common Vocabulary to Enable Data Sharing and Integration. Carolyn Mattingly, North Carolina State University, Raleigh, NC.

Building Infrastructure to Support Data Sharing and Interoperability. Lynn Yarmey, Research Data Alliance/US, Boulder, CO.

Hidden in Plain Sight: The Value and Importance of Unpublished Data. Timothy Pastoor, Pastoor Science Communications, Greensboro, NC.


SYMPOSIUM SESSIONS
Cell Health and Mechanistic Assays for the In Vitro Prediction of DILI

Monday, March 13, 2:00 PM to 4:45 PM

Chairperson(s): Yvonne Will, Pfizer, Groton, CT; and Dominic Williams, AstraZeneca, Cambridge, United Kingdom.

Endorser(s):
Drug Discovery Toxicology Specialty Section
Mechanisms Specialty Section
Risk Assessment Specialty Section

The current test systems employed by the pharmaceutical industry are poorly predictive of drug-induced liver injury (DILI); in particular, idiosyncratic DILI cannot be predicted in animal systems. This session seeks to address this issue through outlining liver cell heath assays that are fit for purpose, and also outline the development of innovative preclinical test systems, which are both mechanism-based and of physiological, pharmacological, and pathological relevance to DILI in humans. An iterative, tiered approach with respect to test compounds, test systems, bioanalysis, and mathematical systems analysis has been adopted to evaluate existing models, and develop new models that can provide validated test systems, with respect to the prediction of specific forms of DILI and further elucidation of mechanisms that relate to idiosyncratic DILI. The approach encompasses completely characterised cell lines, well-defined, and physiologically stable hepatocytes, multicell type in vitro models and animal models. Triangulation of human, in vitro and animal data is providing a fundamental understanding of how drugs can harm the liver, and how this relates to the idiosyncratic response. The objectives of this symposium: 1. Define the application and limitations of current and novel test systems and provide an improved panel of in vitro “best practice assays” for predicting DILI in the human population during drug development; 2. Explore and understand the relationship between in vitro assay signals and DILI in vivo, in preclinical test species, and in man; 3. Enhance shared understanding, between academia, pharma, and regulatory agencies, of the value and limitations of new and existing approaches for DILI hazard identification and risk assessment.

Introduction. Dominic Williams, AstraZeneca, Cambridge, United Kingdom.

The Importance of Defining the Physiological, Pharmacological, and Toxicological Phenotype of In Vitro Test Systems. Kevin Park, University of Liverpool, Liverpool, United Kingdom.


Systems Microscopy Approaches in Unraveling and Predicting DILI. Bob van der Water, Leiden University, Leiden, Netherlands.

Circadian Rhythms in Air Pollution-Induced Pulmonary and Cardiovascular Disorders: A Race against the Clocks

Monday, March 13, 2:00 PM to 4:45 PM

Chairperson(s): Petra Haberzettl, University of Louisville, Louisville, KY; and Martin Young, University of Alabama at Birmingham, Birmingham, AL.

Endorser(s):
- Cardiovascular Toxicology Specialty Section
- Inhalation and Respiratory Specialty Section
- Neurotoxicology Specialty Section
- Immunotoxicology Specialty Section

Exposure to air pollution has emerged as one of the leading causes of death world-wide. The World Health Organization (WHO) estimates that every year exposure to air pollution causes 7 million premature deaths. Extensive epidemiological studies have shown that exposure to polluted air increases the risk of pulmonary and cardiovascular diseases as well as metabolic disorders; however, the underlying pathophysiological mechanisms have remained elusive. Air pollution exposure affects pulmonary, cardiac, and vascular functions that follow circadian rhythmicity and increases the risk for pulmonary and cardiovascular events that follow diurnal patterns. Recent studies have shown that exposures to air pollution disrupt pulmonary and cardiovascular molecular circadian clocks, changes circadian blood pressure pattern, and exacerbates the cardiometabolic effects of dysynchrony (misaligned circadian rhythm). This symposium will highlight this research, identifying the circadian clocks and rhythms as a novel target of air pollution exposure, and will compare the effects of air pollution on circadian rhythmicity with circadian rhythm disruption induced by other stressors such as ischemia, virus infections and diabetes. The circadian rhythm—defined as physiological, mental, and behavioral changes following a 24 hour cycle—controls fundamental physiology, cellular, and molecular processes, such as blood pressure, cell division, and DNA-repair that regulate physiological homeostasis. Circadian rhythmicity is regulated by external signals such as light, temperature, food, or physical activity, called Zeitgeber. However, the normal circadian rhythmicities of these environmental factors are disrupted by our modern lifestyle choices. Recent reports suggest that urbanization, accompanied by migration to more polluted areas (with light and air pollution), and our modern 24 hour lifestyle (35% adults sleep less than the recommended 7-8 hours) contributes to the development of pulmonary, cardiovascular, and metabolic disorders. For instance, circadian dysynchrony, the misalignment between the central clock (supra chiasmatic nucleus, SCN) in the hypothalamus and peripheral clocks by the disturbing the light cycle (e.g. due to changes in sleep/wake pattern, jet lag, or shift work) has been described to increase the risk of developing metabolic and cardiovascular disease. Although the central pacemaker, the SCN has long been considered the primary regulator of circadian rhythm the discovery of clock gene expression, and function in peripheral tissues has challenged this dogma. Peripheral circadian clocks play a critical role in optimizing the organization of cellular function in the lungs, and are directly involved in metabolic homeostasis and cardiovascular function. The studies presented in this symposium will illustrate the importance of different peripheral circadian clocks in the development of pulmonary, cardiovascular, and metabolic disorders, and will provide evidence that exposure to different air pollution disrupt peripheral circadian clocks and circadian rhythm in pulmonary and cardiovascular tissues similar to the circadian misalignment induced by other stressors such as ischemia, virus infections, and diabetes. The specific presentations of this symposium will show that: 1) Peripheral circadian clocks in cardiomyocytes modulate the responsiveness of the heart to physiologic stimuli (e.g., insulin) and pathologic stresses (e.g., ischemia/reperfusion); 2) Peripheral circadian clock disruption in the lungs by environmental tobacco smoke exposure or influenza infection contributes to the pathophysiology and toxicology of chronic airway diseases and their exacerbation in mice; 3) Peripheral circadian clocks in vascular smooth muscle cells contribute to the disruption of blood pressure circadian rhythm in diabetic db/db mice; 4) Circadian blood pressure pattern are altered by exposure to second hand tobacco smoke and its constituent benzo-a-pyrene (BaP) in rats; and 5) Peripheral circadian clocks in the lungs and aorta are disrupted by the exposure to fine particulate air pollution, and that fine particulate air pollution exposure exacerbates metabolic injury in circadian dysynchrony. In summary, this symposium will provide novel aspects and new mechanistic insights to understand the adverse health effects originating from air pollutant exposure, and our modern lifestyle in association with circadian clock and rhythm disturbances.

Introduction. Petra Haberzettl, University of Louisville, Louisville, KY.

Clock Control of Cardiovascular Physiology and Pathophysiology. Martin Young, University of Alabama at Birmingham, Birmingham, AL.

Inhaled Toxins and Influenza Virus-Mediated Molecular Clock Disruption in Lung Toxicology or Pathobiology. Irfan Rahman, University of Rochester Medical Center, Rochester, NY.

Blood Pressure Circadian Rhythm. Ming Gong, University of Kentucky, Lexington, KY.

Second Hand Tobacco Smoke and Benzo-a-pyrene Increase Arterial Stiffness and Alter Circadian Blood Pressure Patterns Associated with Systemic Inflammation and Oxidative Stress. Lynn Weber, University of Saskatchewan, Saskatoon, SK, Canada.

Fine Particulate Matter (PM2.5) Exposure-Induced Clock Disruption and Its Possible Contribution to the Cardiometabolic Effects of Dysynchrony. Petra Haberzettl, University of Louisville, Louisville, KY.

Lifespan Neuroimmunotoxicology: Age-Dependent Neuroimmune Dyshomeostasis Caused by Pollutants, Pathogens, and Psychoactive Substances

Monday, March 13, 2:00 PM to 4:45 PM

Chairperson(s): Nick Filipov, University of Georgia, Athens, GA; and Vic Johnson, Burleson Research Technologies, Inc., Morrisville, NC.

Endorser(s):
- Immunotoxicology Specialty Section
- Neurotoxicology Specialty Section

Interactions between the immune and nervous systems are critical to overall health and wellness. These interactions are dynamic and vary throughout life, in part due to the age-dependent plasticity of these two complex and dispersed organ systems. In addition, early in development, the maternal immune system contributes to both normal and
Abnormal brain development of the offspring. Perturbation of neuroimmune interactions and cross talk underlies a deluge of neurological disorders and diseases, ranging from neurodevelopmental disorders, such as Autism Spectrum Disorder, to neurodegenerative diseases like Parkinson’s, Multiple Sclerosis, and Alzheimer’s, the latter considered a disease of the elderly. Evidence indicates that exogenous exposures to a variety of pressures such as stress, xenobiotics, including psychoactive substances, and infection can result in neuroimmune dyshomeostasis that is a core component in the etiology of many neurological disorders. Age and developmental stage are already recognized as key toxicity modifiers due to age-dependent differences in metabolism or barrier, i.e., blood-brain barrier, presence, and structure. However, perturbation of the integrity of the neuro-immune axis by environmental factors within the context of age is only a recent focus of investigation, and is largely underestimated by the toxicology community. The goal of this symposium is to highlight the importance of considering age and developmental stage in neuroimmunotoxicology by providing examples of neuroimmune dyshomeostasis caused by pollutants, pathogens, and psychoactive substances when exposures take place at different stages of life.

An Introduction to Neuroimmune Dyshomeostasis: The Game Changes as We Develop and Age. Vic Johnson, Burleson Research Technologies, Inc., Morrisville, NC.

Environmental Influences Early in Life Impact the Neuroimmune Axis: Focus on Autism-Like Neurodevelopmental Disorders. David Lawrence, Wadsworth Center, New York State Department of Health, Albany, NY.

Neuroimmune Interactions and Drugs of Abuse: Overview of Marijuana Compounds with a Focus on Critical Exposure Windows. Barbara Kaplan, Mississippi State University, Mississippi State, MS.

Microglia and the Neuroinflammation Hypothesis of Air Pollution in Adult Mice and Rats. Michelle Block, Indiana University School of Medicine/Stark Neuroscience Research Institute, Indianapolis, IN.

Neuroimmunology of the Aged: Interactions with Pathogens Contributing to Neuroimmune Dyshomeostasis. Rodney Johnson, University of Illinois, Urbana, IL.

Bispecific antibodies combine antigen-recognizing elements into a single molecule and are able to bind to two or more targets. This design was described more than 30 years ago, and it addresses the fact that more than one pathway is often present in many diseases. Initial challenges in the development of bispecific antibodies included inefficient designs, manufacturing problems, immunogenicity, undesirable toxicity liabilities, and shorter half-life that hampered their development but provided many lessons learned. New molecular engineering technologies that incorporates high-throughput methods for quantitative analysis are generating alternatives for selection of bispecific antibodies formats that can be grouped as 1) bispecific fragments, 2) bispecific IgG (BsIgG), 3) appended IgG, 4) bispecific fusion proteins, and 5) bispecific antibodies conjugates. Discussion of engineering strategies for the production of a large matrix of bispecific antibodies will illustrate the technological developments in manufacturing that have occurred in recent years. Bispecific antibodies are being developed for treatment of solid tumors and hematologic malignancies, for virus neutralization, for treatment of inflammatory diseases, gene mediated therapy, and for immunodiagnostic applications. While different bispecific antibodies formats widened the potential therapeutic applications of the molecules, they also introduced hurdles for nonclinical toxicology programs to characterize toxicity liabilities and identify target organs of toxicity to enable clinical trials. For example, both targets are often not present in healthy animals or they are not present in a manner similar to humans. That is the case of blinatumomab, the first bispecific antibody approved in the US. It is a bispecific T cell-engaging (BiTE®) format against CD3xCD19 composed only of the variable regions of antibodies that are connected by flexible linker peptides. Blinatumomab lacks an Fc region resulting in a smaller size molecule relative to a mAb, leading to enhanced tissue penetration but conferring short serum half-life that requires administration by continuous infusion. No neurological toxicities were observed in non-terminal toxicology studies, still life-threatening neurological toxicities occurred in patients. The current generation of BiTE® constructs is fully human in sequence and cross-reacts with NHPs. Discussion of strategies for nonclinical assessment, including target liability assessment for defining a safe clinical starting dose and for mimicking the clinical dosing regimen for various BiTE® constructs, will explain the challenges faced during the development of this type of bispecific antibody. BsIgGs retain Fc-mediated effector functions such as antibody-dependent cell mediated cytotoxicity, complement-dependent cytotoxicity, and antibody-dependent cellular phagocytosis. Modifications to the Fc to minimize those effector functions can also be incorporated depending on the intended target; some bispecific antibodies are designed for membrane bound targets; for
example, to bring T or natural killer cells in close proximity to malignant cells promoting activation of immune effector cells for tumor cell destruction. Others are being designed to interact with two different disease mediators neutralizing two different signaling cascades through inactivation either on the level of the receptor or on the ligands, proliferation, or inflammatory processes. In most cases of bispecific antibodies redirecting T cells to tumor cells, integrated safety assessments relies on MABEL approaches for defining a FIH starting dose. Though MABEL approaches based on in vitro assays can define a safe starting dose for a FIH trial, it may take a long time to define a therapeutic dose to be tested in subsequent trials. A retrospective analysis of available data is important to understand limitations of current paradigms for FIH. When one of the targets is not present in animal models, safety pharmacology assessments provided limited information of undesirable pharmacodynamic properties. Generation of bispecific constructs that cross-react with animal models would be important to understand bispecific antibodies attributes such as mechanism of action, pharmacokinetics, and immunogenicity that influence nonclinical development strategies. The talks in this workshop are designed to spark discussion about the nonclinical programs for the development of different bispecific antibodies formats, the hurdles encountered for toxicity testing, and how toxicologists sorted them out to advance bispecific antibodies successfully in clinical development, and the regulatory challenges the Agency faces. This workshop will aid toxicologists with a better understanding of bispecific antibodies applications, the characteristics of different bispecific formats and their toxicity liabilities, and alternative strategies for toxicity testing to adequately assess the safety profile for patients.

**Historical Perspectives of Bispecific Antibodies.** Pedro Del Valle, US FDA, Silver Spring, MD.

**Bispecific Antibodies: Strategies, Considerations, and Challenges.** Christoph Spiess, Genentech, Inc., San Francisco, CA.

**Nonclinical Characterization of Blinatumomab and Its Translation into the Clinic.** Benno Rattel, AMGEN Research (Munich) GmbH, Munich, Germany.

**Strategies for Nonclinical Safety Assessment of Bispecific mAbs.** Cliff Sachs, MedImmune, LLC, Gaithersburg, MD.

**Bispecific Antibody Constructs: A Retrospective Examination of Nonclinical Data.** Haleh Saber, US FDA, Silver Spring, MD.

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### Controversies in Pesticide Toxicology

**Monday, March 13, 2:00 PM to 4:45 PM**

**Chairperson(s):** Allister Vale, School of Biosciences, University of Birmingham, Birmingham, United Kingdom; and Martin Wilks, Swiss Centre for Applied Human Toxicology, University of Basel, Basel, Switzerland.

**Endorser(s):**
- Clinical and Translational Toxicology Specialty Section
- Neurotoxicology Specialty Section
- Occupational and Public Health Specialty Section

Neonicotinoids block postsynaptic nicotinic acetylcholine receptors (nAChRs) and their specificity for insect nAChR is several hundred times greater than for vertebrate nAChR. It would be expected, therefore, that the features of human neonicotinoid poisoning would be less severe than nicotine poisoning, but after a substantial ingestion this is not the case. Bees can be exposed to neonicotinoids when foraging on seed treated crops and as a result of dust expelled into the environment from drilling machines. Both laboratory studies and semifield experiments have shown that sublethal neonicotinoid exposure can affect many aspects of pollinator behavior and physiology, though responses vary between bee species and by type of exposure. For another class of insecticides, the organophosphorus chemicals, there is substantial controversy as to whether neurobehavioral changes can occur in humans as a consequence of acute poisoning and after low level exposure to these insecticides. The evidence base is relatively scarce for the former and extensive for the latter, but in both cases the results are not convincing and are conflicting. In most studies, assessment of exposure is vague and, given the variability of farmer exposures, chemicals other than anticholinesterases might account for the observed effects. Severe cholinergic overstimulation causing hypoxia and convulsions may lead to permanent neurobehavioral deficits, but such conditions are often unreported. The choice of controls also is critical when deficits on visual attention, visuomotor speed, and motor dexterity are detected in those workers previously poisoned when compared with those never poisoned. Also measurements of red cell AChE activity are rarely performed, hampering the understanding of the underlying mechanism(s). While the variable presence of more susceptible individuals, possibly due to polymorphisms of metabolic profiles, may account for these differing results, it is unclear what the potential mechanisms could be. Another controversy that has been debated for many years is whether pesticide exposure is a causative factor in neurodegenerative disease. So far, possible underlying mechanisms are not well understood, and epidemiological evidence linking its etiology with long-term/low-dose exposure to specific pesticides is limited. A potential source of bias in many epidemiological studies that rely on self reports is the absence of specific exposure assessments since pesticides are often grouped together in questionnaires, despite the fact that their mechanisms of action are very different. The European Food Safety Authority (EFSA) has proposed the concept of the OECD Adverse Outcome Pathways to describe different putative mechanisms underlying Parkinson’s Disease that may be linked ultimately to specific pesticides. Although this provides a scientific rationale for the processes that may lead to a final outcome of neurodegeneration, it is not yet clear that it will allow the establishment of cause-effect relationships since it relies on heterogeneous data from different sources (human
epidemiology, animal, *in vitro* and of different quality. The final controversy in this session concerns glyphosate, a broad spectrum herbicide currently with the highest production volumes of all pesticides. It is used in more than 750 different products for agriculture, forestry, urban, and home applications. The International Agency for Research on Cancer (IARC) Working Group classified glyphosate as “probably carcinogenic to humans” (Group 2A) in 2015. In making this overall evaluation, the Working Group noted that mechanistic and other relevant data support the classification of glyphosate in Group 2A. In addition to limited evidence for the carcinogenicity of glyphosate in humans and sufficient evidence for the carcinogenicity of glyphosate in experimental animals, the Working Group were of the view that there is strong evidence that glyphosate can operate through two key characteristics of known human carcinogens, and that these can be operative in humans. The European registration renewal assessment, published by EFSA in October 2015, was the first comprehensive regulatory scientific evaluation. The Working Group noted that mechanistic and other relevant data support the classification of glyphosate in Group 2A. In addition to limited evidence for the carcinogenicity of glyphosate in humans and sufficient evidence for the carcinogenicity of glyphosate in experimental animals, the Working Group were of the view that there is strong evidence that glyphosate can operate through two key characteristics of known human carcinogens, and that these can be operative in humans. The European registration renewal assessment, published by EFSA in October 2015, was the first comprehensive regulatory scientific assessment conducted after the publication of the IARC monograph, and used the classification criteria for chemicals adopted under the United Nation Globally Harmonised System (UNGHS). Based on the same evidence base regarding epidemiological studies, and broader evidence regarding carcinogenicity in animals and genotoxicity, EFSA has concluded that glyphosate is unlikely to be genotoxic or pose a carcinogenic threat to humans.

**Introduction.** Allister Vale, University of Birmingham, Birmingham, United Kingdom.

**Neonicotinoid Insecticides: Safe for Humans, but Toxic to Bees?** Allister Vale, University of Birmingham, Birmingham, United Kingdom.

**Do Neurobehavioral Changes Occur in Humans as Long-lasting Consequences of Acute Poisoning with Organophosphorus Insecticides and after Low Level Exposures to Anticholinesterase Agents?** Marcello Lotti, Università degli Studi di Padova, Padova, Italy.

**Pesticides and Neurodegenerative Disease: Is There a Causal Link?** Martin Wilks, University of Basel, Basel, Switzerland.

**Is Glyphosate a Probable Human Carcinogen? Yes!** Christopher Portier, US National Center for Environmental Health and US Agency for Toxic Substances and Disease Registry, Atlanta, GA.

**Is Glyphosate a Probable Human Carcinogen? No!** Jose Tarazona, European Food Safety Authority (EFSA) Pesticides Unit, Parma, Italy.

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**Is Glyphosate a Probable Human Carcinogen? Yes!** Christopher Portier, US National Center for Environmental Health and US Agency for Toxic Substances and Disease Registry, Atlanta, GA.

**Is Glyphosate a Probable Human Carcinogen? No!** Jose Tarazona, European Food Safety Authority (EFSA) Pesticides Unit, Parma, Italy.
Innovative Screening Methods to Identify Chemical Exposure Signatures and Linkages to Toxicity: Case Study with House Dust. Julia Rager, ToxStrategies, Austin, TX.

Uncovering Prenatal and Early Childhood Windows of Susceptibility to Environmental Chemicals Using Teeth. Manish Arora, Icahn School of Medicine at Mount Sinai, New York, NY.

Understanding of Air Pollution-Related Health Impacts Using Sensor Technologies. Edmundo Seto, University of Washington, Seattle, WA.

Aggregate Exposures and Adverse Outcome Pathways for Estrogen Mimics: Can the Frameworks and Emerging Exposure Data Help Focus Public Health Research on the Most Relevant Exposures? Justin Teeguarden, Pacific Northwest National Laboratory, Richland, WA.


Modernizing Toxicological Risk Assessment for Compounds Released from Pharmaceutical, Consumer, Medical Device and Combination Products: Alternative Tools and Methods

Monday, March 13, 2:00 PM to 4:45 PM

Chairperson(s): Richard Hutchinson, Johnson & Johnson, Somerville, NJ; and Alan Hood, US FDA, Silver Spring, MD.

Endorser(s):
In Vitro and Alternative Methods Specialty Section
Medical Device and Combination Product Specialty Section
Regulatory and Safety Evaluation Specialty Section

The potential toxicological effects of compounds released from medical devices and combination products are a patient safety concern for both device manufacturers and regulatory stakeholders. This session will address the need to advance methods for the toxicological risk assessment of compounds released from medical devices and combination products, and will explore opportunities for modernizing the risk assessment approaches for these compounds. This session is intended to generate a dialogue for recent advancements from a variety of industry and non-industry initiates in the development, acceptance, and application of alternative tools that complement or replace in vivo testing. The session focuses on two areas of toxicological risk assessment: hazard assessment, and risk characterization. The session begins with modernizing hazard assessment through systematic review using objective, reproducible methods that transparently document scientific judgments and the scientific basis of hazard identification conclusions. Then, recent insights on assigning Cramer classification to compounds that can be used as guidance and improvement of in silico tools will be presented. Computational tools, such as QSAR models and Read-Across, to predict the toxicity of compounds lacking experimentally-derived toxicity data and the use of these predicted toxicity values will be discussed. The final topic is a semi-quantitative risk evaluation matrix to determine the amount and rigor of component testing that may be necessary and appropriate to establish that the component is suitable for its intended use. Academic/industry/consulting toxicological risk assessors and regulatory affairs representatives who have an interest in recent advancements in toxicological risk assessment in medical devices, combination, and consumer products should consider attending this workshop.

Introduction. Alan Hood, US FDA, Silver Spring, MD.

Evaluation of the Potential Immunotoxicity Associated with Exposure to Perfluorooctanoic Acid (PFOA) with a Systematic Review Framework. Andrew Rooney, NIEHS-NTP, Research Triangle Park, NC.


Modernizing Toxicological Risk Assessment for Medical Devices Using ISO 10993 Standards. Ron Brown, US FDA, Silver Spring, MD.

Development and Justification of a Risk Evaluation Matrix to Guide Chemical Testing Necessary to Select and Qualify Plastic Components Used in Production Systems for Medical Device and Combination Products. Dennis Jenke, Baxter International, Deerfield, IL.

Daily Plenary Session

Precision Medicine

Tuesday, March 14, 8:00 AM to 9:20 AM

Lecturers: Jun J. Yang, St. Jude Children’s Research Hospital, Memphis, TN; and Richard Barker, University of Oxford, Oxford, United Kingdom.

See full descriptions on page 75.
**SYMPOSIUM SESSIONS**

**Cardiopulmonary Consequences of Gestational Toxicant Exposure: Getting to the Heart of the Matter**

**Tuesday, March 14, 9:30 AM to 12:15 PM**

**Chairperson(s):** Lynette Rogers, The Ohio State University, Columbus, OH; and Phoebe Stapleton, Rutgers University, Piscataway, NJ.

**Endorser(s):**
- Cardiovascular Toxicology Specialty Section
- Reproductive and Developmental Toxicology Specialty Section
- Women in Toxicology Special Interest Group

Xenobiotic exposures affect the maternal and/or *in utero* environment resulting in impairments in fetal development. During the period of rapid fetal growth, underdeveloped cardiovascular systems are especially vulnerable to their environment. Furthermore, fetal exposures can evoke changes in epigenetic signatures that result in permanent modifications in gene expression. This symposium will focus on the intersection between maternal and fetal exposure and the developing cardiovascular system. Speakers will provide data from three common exposures: nanomaterials; particulate matter or air pollution (PM 2.5); and nicotine. The current findings related to susceptible gestational windows for cardiovascular development and epigenetic, transcriptional, and toxicokinetics changes in vascular physiology and cardiac function will be presented. The impact of these exposures is of major concern for regulatory agencies, as the developing fetus is more susceptible to environmental or personal exposures than are adults. In response to these concerns, new concepts in predictive modeling and risk assessment associated with fetal exposures will be presented as future avenues of research within developmental toxicology. Finally, current applications using the adverse outcome pathway framework (ToxCast library) for risk assessment in embryonic vascular disruption and developmental defects will be presented. The topics discussed will provide the state of the art information on effects of maternal toxicant exposure on cardiovascular deficits in the offspring which are of concern to clinicians and basic scientists, as well as government and pharmaceutical regulatory agencies. In summary, this symposium seeks to address the significant threats to cardiovascular health that are associated with fetal/perinatal exposures, and offer new insights into the predictive, mechanistic, and risk assessment strategies in developmental toxicology.

**Introduction.** Lynette Rogers, The Ohio State University, Columbus, OH.

**Altered Maternal and Placental Vascular Responses following Acute Nanomaterial Administration.** Christopher Wingard, Brody School of Medicine at East Carolina University, Greenville, NC.

**Alterations in the Cardiovascular Epigenome after Prenatal Engineered Nanomaterial Exposures.** Timothy Nurkiewicz, West Virginia University, Morgantown, WV.

**Fetal Cardiac Function and Related Health Parameters are Altered by Maternal Exposure to Ambient Particulate Matter during Specific Gestational Exposure Windows in a Mouse Model.** Judith Zelikoff, New York University School of Medicine, Tuxedo, NY.

**Cardiovascular Risk Factors following Fetal and Neonatal Exposure to Nicotine.** Alison Holloway, McMaster University, Hamilton, ON, Canada.

**Advancements in Cardiopulmonary Toxicology and Developmental Risk Assessment for Product Safety Assessment.** Reza Rasoulipour, Dow AgroSciences, Indianapolis, IN.

**Adverse Outcome Pathway (AOP) Framework for Embryonic Vascular Disruption and Developmental Defects.** Thomas Knudsen, US EPA, Research Triangle Park, NC.

**ITS Contribution of Gene Transcription to Spontaneous Mutation and Genotoxic Outcomes**

**Tuesday, March 14, 9:30 AM to 12:15 PM**

**Chairperson(s):** Robert Schiestl, University of California Los Angeles, Los Angeles, CA; and Joanna Klapacz, The Dow Chemical Company, Midland, MI.

**Endorser(s):**
- Carcinogenesis Specialty Section

All organisms sustain a certain number of background mutations as a result of cellular processes or interactions with their environment. The significant source of spontaneous mutation, arising from normal DNA metabolism, is contributed by mispairing of bases during DNA replication. As DNA metabolic processes of transcription, replication, and repair are not temporally separated, one process has the potential to influence the occurrence and outcome of another. In fact, recent research in the area of genetic instability has demonstrated that the process of gene transcription alone can elevate DNA damage load and genetic modifications. Transcription unwinds DNA strands, potentially sensitizing the untranscribed strand to react with endogenous and exogenous agents. Thus, the understanding of background spontaneous mutation, including that arising from transcription, can be a critical aspect of understanding point-of-departure metrics of DNA-reactive agents. Genetic instability also is a hallmark of carcinogenesis, and cells from patients carrying mutations conferring cancer prone phenotypes show a higher level of genetic instability. To better understand how transcription influences genetic instability, various researchers have constructed
and validated different genetic assays in model organisms, including, bacteria, yeast, human culture cells, and even in vivo mouse models, to study the generality and occurrence of transcription-associated mutagenesis (TAM). Using the highly inducible promoter systems in model organisms, it has been documented that high levels of transcription are associated with elevated mutation and recombination rates. In the case of TAM, the level of mutagenesis was shown to be directly proportional to the level of transcription, and the direction of replication fork movement relative to that of RNA polymerase. Molecular mechanisms have also been elucidated by which cells can solve transcription-replication conflicts to prevent genome instability and will be discussed during the symposium. The role of RNA-DNA hybrids in these conflicts, their role in modulating chromatin structure, and epigenetic modifications also will be addressed to explain how they can lead to chromosome breakage, fragility, and contribute to background DNA damage levels and even disease.

**Introduction.** Robert Schiestl, University of California Los Angeles, Los Angeles, CA.

**Transcription-Associated Mutagenesis Contributes to Background Gene Mutation.** Joanna Klapacz, The Dow Chemical Company, Midland, MI.

**Ames Assay Negative Carcinogens Cause DNA Deletions Preferentially in Transcribed DNA.** Robert Schiestl, University of California Los Angeles, Los Angeles, CA.

**Proceed with Caution: Removal of Transcription-Associated Supercoils Can Be Hazardous to Genome Integrity.** Sue Jinks-Robertson, Duke University Medical Center, Durham, NC.

**Coordinated Action of RNA-Binding Factors and Chromatin Remodeling to Prevent Genome Instability.** Andres Aguillera, CABIMER-Universidad de Sevilla, Sevilla, Spain.

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**WORKSHOP SESSIONS**

**Incorporating In Vitro Reproductive and Developmental Assays into Regulatory Risk Assessment**

**Tuesday, March 14, 9:30 AM to 12:15 PM**

**Chairperson(s):** Suzanne Fitzpatrick, US FDA, College Park, MD; and Elaine Faustman, University of Washington, Seattle, WA.

**Endorser(s):**

- *In Vitro and Alternative Methods Specialty Section*
- *Regulatory and Safety Evaluation Specialty Section*
- *Reproductive and Developmental Toxicology Specialty Section*

Reproductive and developmental hazards are an important public health risk. Toxicology testing plays a fundamental role in characterizing these potential risks. However, most of the toxicology tools used for regulatory assessment of potential reproductive and developmental toxicants rely on high-dose animal studies and default extrapolation procedures and have remained relatively unchanged for decades, despite the scientific revolutions of the past half century. New predictive models are needed to gain a better understanding of reproductive and developmental toxicity mechanisms at multiple levels of biological organization, including genes, proteins, pathways, and cell/organ function. Assessing safety is particularly challenging in the reproductive/developmental toxicology field due to the reproductive cycle’s complexity and unusually long time frame for testing. Several promising new *in vitro* assays for reproductive and developmental endpoints have been developed that could address important questions such as species-specific toxicity and endocrine effects, while promising faster and more efficient toxicity testing with the use of less animals. Regulatory toxicologists must decide how these methods can be used for regulatory assessment. This workshop will be an opportunity for all stakeholders to discuss how to gain confidence in the results of these new models for reproductive and developmental testing. The workshop will discuss some new promising *in vitro* models and proposals on how these new tests can be incorporated into regulatory risk assessment. A panel of the speakers and additional federal regulatory scientists will then review challenges presented in the talks, and outline how to move forward to use these models in regulatory assessments.

**Introduction.** Suzanne Fitzpatrick, US FDA, College Park, MD.

**A Review of In Vitro Developmental Toxicology Assays and Potential Applications in Regulatory Developmental Toxicology Testing.** Karen Augustine, Bristol-Myers Squibb Company, Pennington, NJ.

**Testicular Cells Co-Culture as an Alternative Model for Male Reproductive Toxicity.** Elaine Faustman, University of Washington, Seattle, WA.

**Qualifying New In Vitro Tools for Use in a Regulatory Risk Assessment.** Suzanne Fitzpatrick, US FDA, College Park, MD.

**Reimagining Evaluation of Human Pharmaceutical Reproductive Risk.** Christopher Bowman, Pfizer Inc, Groton, CT.

**An Integrated European Program Driving Mechanism-Based Toxicity Testing and Risk Assessment for the 21st Century.** Marcel Leist, University of Konstanz, Konstanz, Germany.

**Panel Discussion.** Suzanne Fitzpatrick, US FDA, College Park, MD.
Opportunities for Read-Across Development and Application Using QSAR Approaches

Tuesday, March 14, 9:30 AM to 12:15 PM

Chairperson(s): Richard Becker, American Chemistry Council, Washington, DC; and Grace Patlewicz, US EPA, Research Triangle Park, NC.

Endorser(s):
In Vitro and Alternative Methods Specialty Section
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

Read-across is a data gap filling technique used within analogue and category approaches for regulatory purposes. Although there has been considerable experience applying these techniques for regulatory programs, acceptance remains context dependent and reliant on expert assessment. Recent activities, including those led by Cosmetics Europe, and separately by the European Chemicals Agency (ECHA), have developed conceptual frameworks to identify and document sources of uncertainty. Addressing uncertainties using mechanistic information within Adverse Outcome Pathways (AOPs) is still in its infancy; although several case studies have been developed, their success and uptake remains dependent on subjective assessment. Currently, there are no objective metrics to evaluate the performance or quantify the uncertainties in read-across predictions. This is in sharp contrast to (Q)SARs (which are underpinned by the same principles), where measures of performance are specified as one of the (Q)SAR validation principles. This raises the question of whether there are learnings and approaches that can be drawn from this related field that could be exploited to enhance read-across, and in doing so, transition away from expert assessment. Research to develop read-across predictions of toxicity (qualitatively or quantitatively, e.g. benchmark dose or NOAELs) using similarity weighted activity of nearest neighbors based on chemistry and/or bioactivity descriptors (akin to a local QSAR model) are being investigated. Opportunities also exist to derive read-across predictions within local domains using other chemoinformatics techniques, from systematically identifying and evaluating source analogues, characterizing analogues with relevant mechanistic information to using machine learning techniques. This workshop will discuss opportunities of moving from expert-driven approaches to systematic read-across prediction by exploiting informatics. Methods to quantify uncertainty, combine different types of information, and thereby to reduce the uncertainty, also will be discussed. The workshop will comprise a series of highly focused presentations that will provide an update of the state of the science for traditional read-across, and demonstrate opportunities for using informatics approaches in selecting and characterizing analogues, objectively evaluating read-across predictions, and assessing performance. The session is intended to foster discussion between practitioners of read-across and other modeling approaches, and investigators and regulators across environmental, industrial, consumer products, and pharmaceutical toxicology at the same time as articulating the practical value of the read-across methodologies being developed in enhancing human and environmental risk assessment.

Read-Across at the Crossroads of Chemoinformatics and Regulatory Science. Chihae Yang, Altamira and Molecular Networks, Columbus, OH.
Reproducible Read-Across Evaluations Based on SAR Information. Emilio Benfenati, Mario Negri Institute, Milan, Italy.
Using Quantitative Predictions of Continuous Toxicity Values in Read-Across. Jessica Wignall, ICF International, Fairfax, VA.
Focused Discussion and Wrap-Up. Richard Becker, American Chemistry Council, Washington, DC.
INFORMATIONAL SESSION

Thresholds of Toxicological Concern: 21st Century Safety Assessment

Tuesday, March 14, 9:30 AM to 12:15 PM

Chairperson(s): Heli Hollnagel, Dow Europe GmbH, Horgen, Switzerland; and Kristi Muldoon-Jacobs, US FDA, College Park, MD.

Endorser(s):
Regulatory and Safety Evaluation Specialty Section

Safety assessment is the evaluation of a chemical to ensure that exposure from its use is acceptable within the current risk analysis paradigm. Typically, this involves an evaluation of chemical-specific toxicity data from animal studies, to derive acceptable levels of exposure. As analytical methods improve, more and more chemicals are detected in our environment for which chemical specific exposure levels can be estimated, but toxicology data is lacking. The Concept of the Threshold of Toxicological Concern (TTC) uses the principles of chemical grouping and read-across to screen chemicals at low levels of exposure for prioritization of follow-up testing. The approach considers chemical structure, metabolism, and animal toxicity data to establish generic chronic exposure thresholds below which there is no appreciable health risk. At the same time, scientists are striving to identify methods and approaches capable of achieving the NAS vision to Refine, Replace and Reduce animal testing, while improving the efficiency of low tier evaluations. Within that context, the TTC approach should be evaluated against emerging methods such as: computational approaches, in vitro methods, and individual chemical read-across, to predict systemic repeat-dose toxicity. This session is laid out to review the scientific basis of the TTC concept and the areas of ongoing improvements, such as database updates, the derivation of internal TTCs, and updates to the structural groupings used in TTC. This status quo also will be challenged by looking at if, and how, the TTC approach can be advanced into the 21st century. Sufficiently large databases with information from in vivo toxicity studies are a crucial foundation for the TTC concept. The thresholds for potential carcinogens were derived from a dataset originally build in the 1980s from the UC Berkeley Cancer Potency Database. The thresholds for non-cancer endpoints were developed in the 1990s from the Munro dataset of repeated dose studies. Since then, different smaller projects have confirmed the robustness of the thresholds in general, and for specific endpoints, by demonstrating that updates to study subsets or addition of new data did not result in relevant changes. However, the datasets serving as the basis of the current TTC values are partly outdated and do not necessarily represent all types of chemical structures. One major effort to expand the structural domain of the TTC dataset for non-cancer endpoints with chemicals related to cosmetics has just been concluded by the COSMOS/ILSI Europe project. For the cancer potency TTC dataset, an ILSI Europe Expert Group is developing a framework for evaluation of cancer bioassay and genotoxicity data, to lay out how the cancer TTC thresholds could be refined despite the challenges of predicting cancer mechanism of action, human relevance of tumor findings, and potency based on often scant data. The current TTCs are representative of external oral exposures. Recently, the development of TTCs based on internal exposure, such as chemical concentration in blood, has been proposed, with the particular advantage that they could be used in risk assessment for non-oral routes of exposure. Examples will be presented of the use of PBPK modeling to derive internal concentrations for chemicals in the existing TTC database, which is the first step towards developing internal TTCs. The TTC approach relies on grouping chemicals using the Cramer et al. 1978 Decision Tree (DT), which was developed 40 years ago to provide a tool to prioritize orally ingested substances based on their chemical structure. Combining knowledge of structure, metabolism, and toxicity, a sequence of yes/no questions were devised that leads to the assignment of a substance to one of three classes of toxic concern. Given the scientific knowledge accumulated since 1978, the DT is overdue for an update. The session will discuss current work to develop more refined DT questions, which leads to an increased number of six classes of toxic concern, aimed at more accurate allocation of a broad range of structures to toxicity classes with appropriate thresholds. Rapid progress in the development of in vitro and in silico methods is giving rise to alternative approaches, which could make the current TTC approach redundant. The volume of data being generated by Tox21 methods, allied with the development of adverse outcome pathways and their respective molecular initiating and other key events, is providing opportunities for molecular read-across, including QSAR, which should be more accurate that conventional approaches based on in vivo toxicity data. The session will examine whether Tox21 data could be used to develop TTCs, and if abandoning the TTC approach would result in an unnecessary limitation in available risk assessment strategies.


Updating the TTC Cancer Potency Database and the Cosmetic-Related Substance Database. Heli Hollnagel, Dow Europe GmbH, Horgen, Switzerland.

The Application of Physiologically Based Pharmacokinetic (PBPK) Modeling to Support the Derivation of Internal Thresholds of Toxicological Concern (TTCs). Harvey Clewell, ScitoVation, Research Triangle Park, NC.

The Application of an Updated Cramer Decision Tree to Food Ingredient Safety Assessment. Szabina Stice, US FDA, College Park, MD.

The ability of chemicals to cause cancer is a highly relevant end point with a significant public health impact. Determining the mechanisms by which chemicals modulate normal cellular pathways to induce neoplastic transformation and growth is central to the discipline of toxicology. New data obtained via development of new animal models combined with high-throughput ‘omics technologies has revolutionized the way we identify modes of action (MOA). These new “Big Data”-assisted technologies have highlighted several novel molecular targets involved in chemical carcinogenesis and changed our understanding of MOA. Development of molecular networking tools has revealed novel gene networks that regulate neoplastic growth secondary to chemical exposure. A completely unbiased adverse outcome pathway analysis is yet another approach that can revolutionize understanding the mechanisms of chemical carcinogenesis. Despite several key advances, major challenges remain in employing the new systems biology based big data techniques to chemical carcinogenesis research. This symposium will bring together scientists bringing “Big Data” methodologies to the chemical carcinogenesis field. The new frontiers of using data analytics to study chemical carcinogenesis and the challenges ahead will be discussed.

**Introduction.** James Klaunig, Indiana University, Bloomington, IN.

**Mode of Action in Chemical Carcinogens: Setting the Baseline.** James Klaunig, Indiana University, Bloomington, IN.

**Integrating Toxicogenomics Data into Adverse Outcome Pathways for Cancer.** Chris Corton, US EPA, Research Triangle Park, NC.

**Warburg-Like Differential Gene Expression and Metabolic Reprogramming during Progression of Cancer Pathogenesis: Lesson Learned from Liver Cancer Studies.** Timothy Zacharewski, Michigan State University, East Lansing, MI.

**NGS Reveals Novel Targets and MOA in Chemical Carcinogenesis.** Udayan Apte, University of Kansas Medical Center, Kansas City, KS.

**Chemically Induced Neuroinflammation and “Sickness Behavior” Disorders**

**Tuesday, March 14, 2:00 PM to 4:45 PM**

**Chairperson(s):** James O’Callaghan, CDC-NIOSH, Morgantown, WV; and G. Jean Harry, NIEHS/NIH, Research Triangle Park, NC

**Endorser(s):**
- Immunotoxicology Specialty Section
- Neurotoxicology Specialty Section

Neuroinflammation is a dominant theme in contemporary neuroscience. This is not surprising given the number of neurological disease states, e.g. Alzheimer’s Disease, Parkinson’s Disease, Huntington’s Disease, where neuroinflammation has been implicated. Thus, a clear association has emerged among neurodegenerative disorders, and the elaboration of proinflammatory cytokines and chemokines in the CNS, the core feature of the neuroinflammatory condition. While neuroinflammation often occurs in association with damage to neurons and glia, it also can occur in the absence of neurodegeneration, e.g. where elevated concentrations of proinflammatory cytokines are seen with systemic infection. In these circumstances, neuroinflammation is associated with sickness behavior, i.e. a constellation of symptoms manifested in loss of appetite, fever, muscle pain, fatigue, and cognitive problems. Typically, sickness behavior accompanies an inflammatory response that resolves with time, with gradual restoration to homeostasis. However, chronic sickness behavior syndromes can also occur, and may be instigated or exacerbated by chemical exposures, both from the environment and pharmaceuticals. In this symposium, we bring together two junior investigators and two senior investigators to provide an overview of the central/peripheral immune system interactions that can contribute to the sickness behavior condition, and present recent preclinical and clinical data, as well as data from experimental models, on three sickness behavior disorders: Chemobrain, Gulf War Illness, and Chronic Fatigue. These presentations serve as examples of the chronic neuroinflammatory condition as an important chemical exposure issue, with implications beyond the disorders and exposures to be presented. The goal of the symposium is to provide a framework for considering alterations in the normal inflammatory response of the nervous system as a basis for complex neurological and physiological disorders that can be initiated or exacerbated by chemical or pharmaceutical exposure.

**Introduction.** G. Jean Harry, NIEHS/NIH, Research Triangle Park, NC.

**Overview of Neuroinflammation and Sickness Behavior.** Christopher McPherson, NIEHS/NIH, Research Triangle Park, NC.

**Chemobrain.** Cobi Heijnen, University of Texas MD Anderson Cancer Center, Houston, TX.

**Gulf War Illness.** Lindsay Michalovicz, CDC-NIOSH, Morgantown, WV.

**Chronic Fatigue.** Nancy Klimas, Nova Southeastern University, Fort Lauderdale, FL.

**Panel Discussion.** James O’Callaghan, CDC-NIOSH, Morgantown, WV.
Emerging Concepts in Nonclinical Development of Immuno-Oncology Agents: Enabling Translation of Nonclinical Pharmacology and Safety Information to First-in-Human Clinical Trials

Tuesday, March 14, 2:00 PM to 4:45 PM

Chairperson(s): Vijayapal Reddy, Eli Lilly and Company, Indianapolis, IN; and Jacqueline Kinyamu-Akunda, Novartis Institute for Biomedical Research, East Hanover, NJ.

Endorser(s):
- Comparative and Veterinary Specialty Section
- Immunotoxicology Specialty Section
- Toxicologic and Exploratory Pathology Specialty Section

Immunotherapy is a fast growing area of new pharmaceuticals in oncology, the success of which is evidenced by the recent approval of a number of immune modulators and numerous others in development. Immuno-oncology (IO) agents target suppressive signals that prevent the development of an immune response and activate the immune system to help fight cancer. The breadth of immune targets is expanding rapidly; consequently, new challenges in nonclinical assessment have emerged, including a lack of appropriate animal models to assess efficacy and safety; differences in sensitivities of various animal species to immune modulators; safety issues in humans not predicted by nonclinical testing; and limited knowledge of the translatability of data from nonclinical species to humans. This session will provide attendees with practical knowledge for approaches to evaluate the safety of novel immune modulatory agents, with an emphasis on assessments to support first-in-human clinical trials. The first speaker will give an overview of nonclinical assessment of immune therapies, discuss considerations for target safety, challenges in identifying the right models for nonclinical studies, and considerations for the starting dose in first-in-human studies based on nonclinical safety and efficacy studies. The fourth speaker will highlight the challenges in translating nonclinical information to first-in-human and early clinical trials with respect to pharmacology and safety. Finally, the last speaker will discuss regulatory aspects and considerations of the safety evaluation to support human clinical trials.

Introduction. Vijayapal Reddy, Eli Lilly and Company, Indianapolis, IN.


Looking Beyond Cytokines: A Pathology Perspective on Humanized Immune System Models. Sunish Mohanan, Eli Lilly and Company, Indianapolis, IN.

Critical Endpoints in Safety Studies Supporting Immuno-Oncology Agents. Rakesh Dixit, Medimmune (a member of AstraZeneca Group), Gaithersburg, MD.

Translating Preclinical Data for Immunotherapeutic Agents to the Design of First in Human Oncology Trials—Challenges and Opportunities. Randi Isaacs, Novartis Institute for Biomedical Research, East Hanover, NJ.


Lost in Translation: Bringing the Real World to In Vitro Data

Tuesday, March 14, 2:00 PM to 4:45 PM

Chairperson(s): Michelle Embry, ILSI Health and Environmental Sciences Institute, Washington, DC; and Todd Gouin, Unilever, Milton Keynes, United Kingdom.

Endorser(s):
- In Vitro and Alternative Methods Specialty Section
- Regulatory and Safety Evaluation Specialty Section
- Risk Assessment Specialty Section

Recent advances in high-throughput in vitro assays provide opportunities for improved mechanistic understanding of toxicity for chemical safety assessment, and ultimately for reduced animal testing. In order to expand the utility of in vitro bioassay data for human and environmental systems, a “translation” of information obtained in vitro to in vivo systems, commonly referred to as in vitro to in vivo extrapolation (IVIVE), is required. Methods that more explicitly and quantitatively translate information from in vitro test systems to in vivo systems, as well as reliable approaches that quantifiably link external exposures to internal exposures corresponding to target sites, will foster confidence in the acceptance of the emerging high-throughput data streams for applications in hazard and risk assessment. Despite the advances in IVIVE, toxicokinetic (TK) models, and understanding of key processes such as absorption, distribution, metabolism, and excretion (ADME) processes, there are still outstanding issues that must be addressed before these in vitro methods can reliably be applied for hazard-based and risk-based assessment. Recent developments have improved characterization of exposure in vitro, including the development of modelling tools that calculate the concentration of chemicals in various test and environmental systems (e.g., humans), based on system and chemical-specific properties. Advances in analytical chemistry, such as passive dosing, solid phase micro-extraction (SPME), gas and liquid chromatography, and mass spectrometry, provide tools that could be applied to in vitro systems to better understand and control in vitro exposure of both the parent chemical and metabolites. Improved quantification of in vitro exposure-response relationships, in combination with better understanding of the physiological mode of action of a chemical, represent better quality input data for use within mechanistic toxicokinetic and physiologically-based pharmacokinetic models. This session will communicate cross-disciplinary advances in the development, evaluation, and application of quantitative tools that help link the external and internal exposures with exposure-response relationships, allowing for a more robust real world translation, application, and acceptance of emerging high-throughput data streams for hazard and risk assessment.

Introduction. Todd Gouin, Unilever, Milton Keynes, United Kingdom.
**Dosemetrics in In Vitro Repeated Dosing Toxicity Assays and Other Complex Assays.** Nynke Kramer, Utrecht University, Utrecht, Netherlands.

**Utilizing Mass Balance Modeling for the Assessment of Internal Exposure in Cell-Based Bioassays.** Beate Escher, UFZ-Helmholtz Centre for Environmental Research, Leipzig, Germany.

**QVIVE Approaches to Evaluate Interindividual Toxicokinetic Variability.** Barbara Wetmore, US EPA, Research Triangle Park, NC.


**Evaluation of Pharmacokinetic Models for In Vitro to In Vivo Extrapolation (IVIVE) of High-Throughput Toxicity Screening Data.** Lisa Sweeney, Naval Medical Research Unit Dayton, Wright Patterson AFB, OH.

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MiRNAs As Translational Biomarkers of Kidney Injury

**Tuesday, March 14, 2:00 PM to 4:45 PM**

**Chairperson(s):** Jean-Charles Gautier, Sanofi, Alfortville, France; and Rounak Nassirpour, Momenta Pharmaceuticals Inc., Cambridge, MA.

**Endorser(s):**
- Drug Discovery Toxicology Specialty Section
- Molecular and Systems Biology Specialty Section
- Toxicologic and Exploratory Pathology Specialty Section

Biomarker monitoring for kidney injury remains a challenge in both preclinical and clinical settings. There is a critical need for sensitive, specific, translatable, and non-invasive biomarkers of renal toxicity to diagnose nephron segment specific injury. MicroRNAs (miRNAs) are attractive biomarker candidates for kidney injury because they are stable in urine, are conserved across species, and relatively easy to measure. Additionally, due to their proposed tissue-specific or at least kidney-enriched expression, miRNAs released into the urine could indicate the specific location of cellular damage. Thus, miRNAs may constitute an attractive alternative to proteins as kidney safety biomarkers. Several efforts are currently underway to identify tissue-specific or pathology-specific miRNA patterns for drug-induced kidney injury from urine samples across species in the context of consortia—namely the Health and Environmental Sciences Institute (HESI) and the Predictive Safety Testing Consortium (PSTC). The goal of this symposium is to provide an overview of the methodology and best practices, together with the most recent results obtained to assess cellular specificity of urinary miRNA biomarkers along with identification of cross-species concordance. Information also will be provided on how the miRNA urinary biomarkers compare with other novel kidney protein biomarkers that have already been discovered. The symposium will begin with a detailed background on miRNA biogenesis and function and how they relate to kidney injury. This will be followed by presentation of original data showing identification of sensitive, specific, and mechanistic miRNAs to detect acute kidney injury and chronic kidney disease in humans. The third presentation will address site specificity aspects relative to kidney injury affecting proximal and distal tubules in rodent models. The fourth presentation will further explore the utility of miRNAs as biomarkers of tubular kidney injury in larger animals. Finally, the fifth presentation will provide recent results obtained on miRNAs as biomarkers of glomerular injury in both rats and non-human primates.

**Introduction.** Jean-Charles Gautier, Sanofi, Alfortville, France.

**Introduction to miRNAs with Emphasis on Kidney Development and Pathophysiology.** Christos Argyropoulos, University of New Mexico School of Medicine, Albuquerque, NM.

**Urinary miRNA Biomarkers for Kidney Diseases in Humans.** Vishal Vaidya, Harvard Medical School, Boston, MA.

**Investigation of Urinary miRNAs Associated with Tubular Segment Specific Injury to the Nephron in Rodents.** Jean-Charles Gautier, Sanofi, Alfortville, France.

**Translation of Tubular Injury Kidney miRNA Biomarkers to Large Mammalian Species.** Eric McDuffie, Janssen Research & Development, LLC, San Diego, CA.

**Urinary miRNAs as Biomarkers of Glomerular Injury in Rats and Nonhuman Primates.** Rounak Nassirpour, Momenta Pharmaceuticals Inc., Cambridge, MA.
Low-Dose Non-Monotonic Responses

Tuesday, March 14, 2:00 PM to 4:45 PM

Chairperson(s): Suzanne Fitzpatrick, US FDA, College Park, MD; and Michael Dourson, TERA Center, University of Cincinnati, Cincinnati, OH.

Endorser(s):
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

There is a growing gap and disagreements among scientists regarding the interpretation and relevance of some research findings on low-dose non-monotonic dose response relationships, and how best to use these data for determining human health risk in a regulatory setting. Greater understanding is needed regarding research and data related to low-dose effects and the use of risk-based approaches to evaluate risk using studies finding non-monotonic dose-response curves. This session will address several key issues, including what is meant by low-dose and non-monotonic, identification of critical effect, and the concept of hormesis. The challenge of current epigenetic findings is to determine where in the risk assessment spectrum these effects lie, and whether current risk assessment methods can be adequate to address them.

Introduction. Suzanne Fitzpatrick, US FDA, College Park, MD.

Harmonizing Terminology: Concepts of “Low-Dose” and Non-Monotonic Dose Response in Toxicological Research and Regulatory Science. Sue Yi, Syngenta, Greensboro, NC.

Examples of Discovery Science: Epigenetic Changes That May Impact the Judgment of Critical Effect. Michael Dourson, TERA Center, University of Cincinnati, Cincinnati, OH.

Hormesis: What It Means for Toxicology and Risk Assessment. Edward Calabrese, University of Massachusetts, Amherst, MA.

The Ability of Current Studies to Detect (or Not) Non-Traditional Effects. Alan Boobis, Imperial College, London, United Kingdom.

Strengths and Weaknesses of Low-Dose Observations and Their Relevance to Human Exposures and Risk Assessment. Rita Schoeny, US EPA (Retired), Washington, DC.

Safety or Prediction? What Is the Future of Regulatory Toxicity Testing?

Tuesday, March 14, 2:00 PM to 4:45 PM

Chairperson(s): Douglas Keller, Sanofi US LLC, Bridgewater, NJ; and Thomas Hartung, Johns Hopkins University, Baltimore, MD.

Endorser(s):
Clinical and Translational Toxicology Specialty Section
Drug Discovery Toxicology Specialty Section
Regulatory and Safety Evaluation Specialty Section

In 1944, the US FDA recommended a standard battery of safety pharmacology and toxicity tests for drugs in development, and the earlier passage of the Food, Drug and Cosmetic Act mandated testing of drugs for safety before they were introduced into commerce. This Act and its subsequent changes were largely the result of the Elixir Sulfanilamide and other drug safety tragedies, ushering in the era of standardized toxicity testing in animals that continues to this day. The battery of tests has been updated and expanded in response to emerging experience with novel chemical entities and endpoints of concern. The performance of nonclinical testing in pharmaceutical development has been quite good when considering that the objective is to minimize harm to human volunteers and patients (safety) by identifying potential target organs, and providing a monitoring and exposure framework. Overall, there is a 70–80% negative predictive value for whole animal tests in predicting whether a clinical adverse event will occur or not. However, prediction of specific target organ toxicities is not as robust. Within this framework, the impact of animal testing to inform human safety can be quantitated, and data will be presented for both the discovery and development phases of pharmaceutical research. While testing on animals remains the regulatory requirement for pharmaceuticals, the accumulated knowledge regarding toxicity mechanisms and pathways gathered over the past 40 years could provide the basis for additional information that could streamline the approach for predicting human toxicity with a reduction in animal use. The 2007 NAS report on Toxicity Testing in the 21st Century initiated a major push in the direction of predictive toxicity testing, but how it can be implemented is a subject of debate. Despite the level of enthusiasm for non-animal safety testing, there remains little evidence that this can approach can be confidently implemented to ensure human safety. Nevertheless, the integration of mechanistic and pathway information, along with exposure data (or prediction), into computational models may provide the systems toxicology basis for prediction of effects, in addition to the absence of effects, leading to broader use of these processes in nonclinical research. With successful development and validation of these high-content information processes, the need for extensive guidelines on animal testing may be reduced, instead relying on the biological information gained in vitro and in silico to design targeted in vivo safety testing. Presenters in this session will discuss several aspects of the current drug development paradigm and how animal testing is being used to inform patient safety, efforts to improve toxicity testing with mechanistic data and human cells, and regulatory approaches/implications of a change in paradigm towards more in vitro data and modeling.

Introduction. Douglas Keller, Sanofi, Bridgewater, NJ.

The History and Performance of Nonclinical Safety Testing in Pharmaceutical Research and Development. Thomas Jones, Eli Lilly, Indianapolis, IN.

Pre-Development Attrition of Pharmaceuticals: How to Identify the Bad Actors Early. Sherry Ralston, AbbVie, North Chicago, IL.


Systems Toxicology: The Final Goal of the Emerging New Approach Methods. Thomas Hartung, Johns Hopkins University, Baltimore, MD.

FDA Efforts to Enhance Safety Testing of Pharmaceuticals. Karen Davis-Bruno, US FDA (CDER), Silver Spring, MD.
EDUCATION-CAREER DEVELOPMENT SESSION

Careers for Toxicologists at Primarily Undergraduate Institutions: Everything You Need to Know about the Job, Hiring Process, and Strategies for Success in Teaching and Research

Tuesday, March 14, 5:00 PM to 6:20 PM

Chairperson(s): Karen Stine, Auburn University at Montgomery, Montgomery, AL; and Wade Powell, Kenyon College, Gambier, OH.

Endorser(s):
Career Resource and Development Committee
Education Committee
Postdoctoral Assembly

Primarily Undergraduate Institutions (PUIs) offer a substantial portion of the available tenure-track faculty positions in the life sciences. For toxicologists interested in careers that combine research and teaching, a PUI can provide an excellent setting for interdisciplinary research collaborations and the opportunity to introduce undergraduate students to toxicology, in both the classroom and the laboratory. But the process of preparing for, finding, interviewing for, and launching a PUI career differs in terms of strategy and approach from that for a faculty position at a research university, often leaving graduate students and postdoctoral trainees with few role models and limited information on where to start to pursue this career path. This session brings together PUI toxicologists at different career stages to discuss the roles available for toxicologists in traditional academic undergraduate-oriented departments, and to provide advice on how to strategically navigate the competitive job market for tenure track positions at PUIs. Strategies also will be offered for laying the groundwork for success in the critical first few years on the job. The topics discussed will include: (1) a broad overview of the job responsibilities and expectations for PUI tenure-track faculty members; 2) what to expect from the hiring and interview process, and how toxicologists can prepare and present themselves as qualified candidates for PUI positions; (3) strategies, tools, and resources for achieving early successes in both the research and teaching aspects of the job. The session will conclude with a panel discussion, giving postdocs and graduate students considering this career option the opportunity to further explore these topics and others that were not explicitly covered.

Introduction. Karen Stine, Auburn University at Montgomery, Montgomery, AL.

Is a Career at a PUI Right for You? An Overview of Expectations and Opportunities on the Career Path at Primarily Undergraduate Institutions. Karen Stine, Auburn University at Montgomery, Montgomery, AL.

Navigating the Hiring Process. Larissa Williams, Bates College, Lewiston, ME.

Launching and Maintaining a Successful Undergraduate Research Program. Wade Powell, Kenyon College, Gambier, OH.

Teaching Toxicology: Preparing Future Faculty for the Toughest Job You’ll Ever Love. Christine Curran, Northern Kentucky University, Highland Heights, KY.

Daily Plenary Session—Keynote Medical Research Council (MRC) Lecture

The Exposome: Challenges and Opportunities

Wednesday, March 15, 8:00 AM to 9:20 AM

Lecturer: Paul Elliott, Imperial College, London, United Kingdom.

See full descriptions on page 77.
The combination of the general population living longer, consuming a Western diet rich in saturated fats, and leading a sedentary lifestyle, among other risk factors, has led to the prevalence of metabolic diseases worldwide. For example, it is estimated that 20-25% of the US population have fatty liver disease, and approximately 35% of US adults have metabolic syndrome. Advances in next generation DNA sequencing, RNASeq methods, and novel mass spectrometry tools have provided access to large amounts of data that are able to be deciphered using computational approaches and new statistical methods to generate new hypotheses. Since the building blocks of a cell (DNA, RNA, proteins, metabolites) do not work in isolation and must orchestrate functions across global networks, it is important to utilize these molecular tools to understand biological functions in an entire system. The goal of this symposium is to demonstrate the use of different ‘omics technologies as a tool to decipher possible mechanisms in the development of toxicant exposure-induced metabolic diseases. The first two speakers will present data using toxicogenomics and proteomics tools, respectively, in liver disease. The remaining four speakers will take an integrative approach combining multiple technologies (i.e. redox-based proteomics, transcriptomics, metabolomics, ChIP sequencing, epigenomics, lipidomics) in the setting of metabolic dysfunctions. Using ‘omics applications in these settings will enhance understanding of known molecular mechanisms involved in metabolic diseases, aid in identifying undiscovered pathways underlying adverse health effects, and further develop integrated models to identify risk factors to improve human health.

**Introduction.** Samantha Snow, US EPA, Durham, NC.

**Using Publicly Available Toxicogenomics Data to Identify Absorption, Distribution, Metabolism, and Excretion (ADME) Genes Relevant to Steatosis.** Samuel Suarez, US EPA, Durham, NC.

**Chronic Alcohol Consumption Alters Mitochondrial Protein Hyperacetylation and Induces Hepatic Oxidative Stress.** Mohammed Assiri, University of Colorado Denver Skaggs School of Pharmacy, Denver, CO.

**Redox Proteomics for the Detection of Protein Cysteine- and Protein Network-Mediated Mechanisms of Toxicity.** Joshua Chandler, Emory University School of Medicine, Atlanta, GA.

**Elucidation of Hepatic Metabolic Reprogramming in AhR-Mediated NAFLD through the Integration of Complementary ‘Omic Datasets.** Rance Nault, Michigan State University, East Lansing, MI.

**Epigenomic and Lipidomic Techniques Used to Identify Non-Alcoholic Fatty Liver in Mice Perinatally Exposed to Bisphenol A and High Fat Diets.** Elizabeth Marchlewicz, University of Michigan, Ann Arbor, MI.

**Whole-Genome Bisulfite Sequencing Provides Insights into Metabolic Dysfunction in Male Mice Exposed In Utero to Bisphenol A.** Suzanne Martos, John Hopkins University, Baltimore, MD.

**The Skin As a Metabolic and Immune-Competent Organ: Implications for Pharmaceutical Development and Safety Assessment**

**Wednesday, March 15, 9:30 AM to 12:15 PM**

**Chairperson(s):** Yoshiro Saito, MHLW, Kaniyoga, Japan; and Jeanine Bussiere, Amgen, Inc., Thousand Oaks, CA.

**Endorser(s):**
- **Dermal Toxicology Specialty Section**
- **Immunotoxicology Specialty Section**
- **Regulatory and Safety Evaluation Specialty Section**

One of the most important recent advances in the study of cutaneous adverse drug reactions is the understanding that the skin is both a metabolically and immunologically competent organ. Recent mechanistic insights into the ability of the skin to serve as a protective barrier with limited drug biotransformation ability, yet highly active immune function, has provided insight into the biological capability of the skin. While the immune response of the skin to drugs is quite different from that of the liver due to evolutionary conditioning, it frequently occurs in response to various drug classes and manifests as a spectrum of hypersensitivity reactions. The skin is a common site of adverse and even idiosyncratic drug reactions; drug-specific T cells, as well as involvement of an adaptive immune response, appear to be key mechanistic drivers in the scenarios. Association of other factors such as HLA polymorphisms may play a significant role for particular drugs. The purpose of this symposium is to integrate emerging findings into proposed mechanisms of drug metabolism and immunity in the skin that are likely responsible for rashes and other local allergic responses. Although the focus will be on toxicology, current information about genetic associations and novel mechanisms with drugs such as immunotherapies and immune checkpoint inhibitors will be incorporated. The unique biological aspects of the skin, and current issues and implications on drug development, will be discussed. Lastly, current methodologies cannot predict cutaneous adverse drug reactions, and this symposium aims to highlight the recent data to support various mechanisms of drug-induced skin reactions, and the implications for predictive clinical safety.

**Scientific Sessions**

**Wednesday**

**Introduction to the Skin as a Target for Immune-Mediated Drug Hypersensitivity (What Are the Issues We’re Seeing in the Clinic/Patients).** Yoshiro Saito, MHLW, Kamiyoga, Japan.

**The Nevirapine Idiosyncratic Adverse Drug Reaction Model to Understand Cutaneous Immunology and Screening Methods.** Amy Sharma, Amgen, Inc., South San Francisco, CA.

**Drug Metabolism and Immune Responses in the Skin.** Jack Uetrecht, University of Toronto, Toronto, ON, Canada.

**Towards the Development of a Novel T Cell Priming Assay to Screen for Skin Sensitization Potential.** Dean Naisbitt, University of Liverpool, Liverpool, United Kingdom.

**Molecular Interaction between Drugs and HLA/TCR in Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis.** Shuen-lu Hung, National Yang-Ming University, Taipei, Taiwan.

**WORKSHOP SESSIONS**

**3D Cell Platforms to Advance Toxicological Sciences**

**Wednesday, March 15, 9:30 AM to 12:15 PM**

*Chairperson(s):* Peggy Guzzie-Peck, Janssen Pharmaceutical Company, Chalfont, PA; and Brian Berridge, GlaxoSmithKline, Research Triangle Park, NC.

*Endorser(s):*
- Drug Discovery Toxicology Specialty Section
- In Vitro and Alternative Methods Specialty Section
- Mechanisms Specialty Section

Microphysiological and 3 dimensional (3D) model systems represent a compelling and provocative technological advancement for improving current *in vitro* static, cell-based models with the potential to more accurately recapitulate organ function, and therefore better predict *in vivo* toxicological mechanisms, improve compound selection during lead optimization, and enable “personalized toxicology” assessments using patient-derived iPSCs in these systems. Development of these platforms is being funded by DARPA and NIH NCATS, and includes collaboration with pharmaceutical companies with the intent to improve the clinical relevance of translational research and become less reliant on traditional animal model-based studies of safety. However, significant challenges, including qualification/validation of these models and scalability, remain to fully integrate these models in drug development. This workshop will provide insights into the evolution of these platforms with “real world” experiences of the evaluation and use of “organ-on-a-chip” (microphysiological) and organoid (3D) platforms from the pharmaceutical industry perspective. This will include discussions on the need for validation/qualification for specific context of use, examples of applications for screening or investigating the underlying mechanisms of target organ toxicity, and the experiences gained regarding advantages, disadvantages, challenges, and limitations of these platforms.

- **Microphysiological Systems in Drug Development—Evolving a Paradigm.** Lorna Ewart, AstraZeneca, Saffron Walden, United Kingdom.
- **Organs-on-Chips: 3D Microphysiological Systems for Understanding Mechanism of Action in Drug Discovery and Development.** Geraldine Hamilton, Emulate, Inc., Boston, MA.
- **Human-on-a-Chip Systems for Mechanistic Toxicology Investigations.** James Hickman, University of Central Florida, Orlando, FL.
- **A Human “Kidney-on-a-Chip” Microphysiological System for Assessing Nephrotoxicity.** Jonathan Himmelfarb, University of Washington, Seattle, WA.
- **An Industry Perspective on New and Emerging In Vitro Models for Assessing Hepatotoxicity Risk in Drug Discovery.** Will Proctor, Genentech, Inc, South San Francisco, CA.
Challenges and Novel Approaches Evaluating Developmental and Reproductive Toxicity of Biotherapeutics

Wednesday, March 15, 9:30 AM to 12:15 PM

Chairperson(s): Christopher Bowman, Pfizer, Groton, CT; and Joy Cavagnaro, Access BIO, Boyce, VA.

Endorsers:
Biotechnology Specialty Section
Regulatory and Safety Evaluation Specialty Section
Reproductive and Developmental Toxicology Specialty Section

Biotherapeutics can present unique challenges and opportunities for developmental and reproductive safety testing compared to small molecules. The ICH S6 guideline that governs these molecules provides useful principles and detailed guidance when designing safety studies. It states that the specific study design and dosing schedule can be modified for many reasons including: our understanding of species specificity; the nature of the product; the mechanism of action; immunogenicity; pharmacokinetics; pharmacodynamics; and embryo-fetal exposure. Because these considerations can differ widely among different biotherapeutics, unique product-specific studies must be designed not only for the specific characteristics of the molecule, but also the suitability of relevant test systems. For instance, biotherapeutics are often more specific with fewer off-target effects and less ability to pass into the fetus; however, specificity can limit the species available for in vivo testing, as can issues with immunogenicity. In addition, the target patient population and the risk/benefit balance can impact the amount and extent of safety testing. These presentations will include how ICH S6 and other guidance documents, as well as best practices and recent experience, shape the development of biotherapeutics, including monoclonal antibodies and oligonucleotides. As experience with biotherapeutics is relatively limited compared to small molecules, our knowledge is evolving rapidly. In order to adhere to everchanging regulatory expectations, minimize the use of animals, and improve the performance of developmental and reproductive safety assessment/ toxicology, innovative strategies using a combination of animal models and study designs are currently being developed and applied by many companies. The talks in this workshop are designed to summarize the current regulatory landscape and to showcase recent examples addressing these regulatory needs, and answering relevant biological questions associated with safety.

Experience and Challenges Presented by Developmental and Reproductive Toxicology of Biotherapeutics. Christopher Bowman, Pfizer, Inc., Groton, CT.

Alternate Embryofetal Toxicity Assessments of Anti-Cancer Biopharmaceuticals. LaRonda Morford, Eli Lilly, Indianapolis, IN.

Mechanism-Based DART Risk Assessment for Biopharmaceuticals Blocking the PD-1/PD-L1 Pathway. Danuta Herzyk, Merck Research Laboratories, West Point, PA.


Thinking Beyond DART Studies for Risk Assessment of Biotherapeutics. Pedro Del Valle, US FDA-CDER, Silver Spring, MD.

Circulatory Mechanisms Underlying the Systemic Effects of Inhaled Nanoparticles and Complex Combustion Mixtures: Common Pathways for Diverse Toxicants

Wednesday, March 15, 9:30 AM to 12:15 PM

Chairperson(s): Matthew Campen, University of New Mexico, Albuquerque, NM; and Andrew Ottens, Virginia Commonwealth University, Richmond, VA.

Endorsers:
Cardiovascular Toxicology Specialty Section
Inhalation and Respiratory Specialty Section
Nanotoxicology Specialty Section

Numerous studies highlight that inhaled agents may cause systemic health effects, including cardiovascular, neural, and renal diseases, yet the mechanisms underlying this relationship remain uncertain and highly contentious. Most inhaled xenobiotics are confined to the lung. Inhaled gases are metabolized and particulates are largely removed to the gut by mucociliary action, with only trace concentrations attaining extrapulmonary compartments; however, systemic pathophysiological outcomes of inhaled pollutants are routinely reported. Recent findings show that pulmonary toxicity can cause production and release of novel biomolecules into the blood, with downstream implications for vascular cell activation and extrapulmonary inflammation. Progress in this area provides not only knowledge with which to protect public health from environmental and occupational hazards, but also informs the basis of comorbidities in complex inflammatory clinical conditions, such as metabolic syndrome and cardiorenal disease. This workshop will highlight the latest evidence for lipid, protein, and metabolite modification in response to a diverse array of inhaled agents and the transduced effect, such modifications on the vasculature, brain, and other major organ systems.

Introduction. Matthew Campen, University of New Mexico, Albuquerque, NM.

Evidence for Mechanistic Specificity Driving Pulmonary Particulate Exposure-Induced Cardiovascular Dysfunction. Aaron Erdely, NIOSH, Morgantown, WV.

Nanomaterial Inhalation-Induced Serum Biomarkers Associated with Extrapulmonary Microvascular Dysfunction. Timothy Nurkiewicz, West Virginia University, Morgantown, WV.

Discriminatory Circulating Peptides from Different Inhalation Exposures—Biomarker and Cerebrovascular Implications. Andrew Ottens, Virginia Commonwealth University, Richmond, VA.


Vascular Effects after Exposure to Particles: Systematic Literature Review and Plasma Bioactivity in Carbon Black Exposed ApoE Knockout Mice. Peter Moller, University of Copenhagen, Copenhagen, Denmark.
Increasing the Utility and Acceptance of Chemical Specific Adjustment Factors—International Experience

Wednesday, March 15, 9:30 AM to 12:15 PM

Chairperson(s): Bette Meek, University of Ottawa, Ottawa, ON, Canada; and Richard Brown, World Health Organization, Geneva, Switzerland.

Endorser(s):
- Biological Modeling Specialty Section
- Regulatory and Safety Evaluation Specialty Section
- Risk Assessment Specialty Section

The application of chemical-specific toxicokinetic (TK) or toxicodynamic (TD) data to address interspecies differences and human variability in the quantification of hazard has potential to reduce uncertainty and better characterize variability compared to the use of traditional default uncertainty factors. This workshop will summarize the state of the science since the introduction of the WHO/IPCS guidance on chemical-specific adjustment factors (CSAF) in 2005, including the impact of more recent guidance, such as the IPCS guidance on physiologically-based pharmacokinetic modeling (PBPK), and the US EPA guidance on data-derived extrapolation factors. The session also illustrates how CSAF principles complement ongoing research initiatives to develop more innovative testing and assessment strategies based on additionally evolving frameworks to consider Adverse Outcome Pathways/mode of action and combined exposures. A summary of lessons learned from an analysis of approximately 100 case studies identified in the literature and information provided by regulatory agencies globally illustrates the nature of evolution of CSAF in regulatory application. It also identifies associated challenges, including adequacy of supporting data and assessments in which CSAF were considered but not adopted. Based on this analysis, recommendations for relevant interdisciplinary research and engagement are included. The session ends with a panel discussion on enhancing uptake of CSAF in chemical risk assessment, including an opportunity for the audience to discuss principal aspects with representatives from key stakeholder groups. Researchers, biological modelers, and risk assessors interested in increasing their knowledge concerning the application of relevant toxicological data to reduce uncertainty associated with interspecies differences or human variability will find this session of interest. The content of the session also is relevant to regulators interested in expanding their knowledge of the scope of application and nature of supporting data considered most valuable in the development of CSAF over the last couple of decades.


Analysis of International Experience on CSAFs and Potential Path Forward. Bette Meek, University of Ottawa, Ottawa, ON, Canada.

Data-Derived Extrapolation Factors, Modes of Action, and Target Tissues. John Lipscomb, US EPA, Cincinnati, OH.

Harmonization of Chemical-Specific Adjustment Factors (CSAfs) with Other Recent Research Efforts—Adverse Outcome Pathways (AOP) and Mode of Action (MOA) Frameworks. Alan Boobis, Imperial College, London, United Kingdom.

Measurement and Prediction of Chemicals in Consumer Products

Wednesday, March 15, 9:30 AM to 12:15 PM

Chairperson(s): John Wambaugh, US EPA, Research Triangle Park, NC; and Kristin Isaacs, US EPA, Research Triangle Park, NC.

Endorser(s):
- Mixtures Specialty Section
- Regulatory and Safety Evaluation Specialty Section
- Risk Assessment Specialty Section

In many cases, no exposure data are available for placing possible chemical hazard within a relevant human exposure context. The aim of this workshop is to bring experts from industry, academia, and government together to discuss existing and emerging methods for characterizing chemicals in various categories of consumer products (e.g., cosmetics, cleaning products, building materials, and food contact materials). The presence of chemicals in such “near field” sources has been shown to be a key driver of high exposure levels in Centers for Disease Control (CDC) National Health and Nutrition Survey (NHANES) biomonitoring data. Information on chemical constituents of products, while only a prerequisite, provides heuristics for estimating human exposure. New high-throughput measurement strategies that combine high-resolution mass spectrometry with chemo-informatics data could enable rapid forensic analysis of chemicals present in these products. In addition, government requirements for product testing and new industry initiatives are providing additional inventories of chemicals present in products due to either intentional inclusion or contamination. These new data sources, in concert with data-driven or mechanistic modeling approaches, can elucidate potential human exposures to thousands of commercial chemicals and reduce uncertainty in modeling approaches. For example, new models have been developed to predict from chemical structure the probable functional roles in products where that information is unavailable. The new data can also provide methods to address specific case studies on chemicals in imported products or products manufactured from recycled materials. Although thousands of chemicals have undergone high-throughput screening for bioactivity as a surrogate for hazard, corollary approaches for estimating exposure are sorely needed to understand potential risks. The first talk in this session will briefly summarize the current state of the field, including the integration and linkage of exposure information with toxicological information in support of risk-based chemical evaluation, and the current need for new information on consumer products. This presenter will then describe new data sources for identifying markers of potential chemical exposure. The next three presentations will address interpreting these and other data in terms of real world human exposures, respectively, from the academic, industry, and regulatory points of view.
The final presenter, from the Consumer Product Safety Commission, will address the use of exposure information in consumer product risk assessment and the need to address emerging consumer technologies. Speakers will discuss objectives, approaches, technologies, knowledge gaps, and suggestions for future research; a panel discussion will follow the concluding presentation. This workshop will be of high interest to a broad audience interested in the assessment of the safety of both individual chemicals and mixtures that result from consumer product exposures. Presenters will consider: What is the potential for new rapid forensic measurement techniques for characterizing substances in consumer products (formulations, articles, building materials, food contact materials)? How can modeling approaches that consider chemical structure and/or chemical use information add value to rapid forensic measurement data? How should consumer product chemicals be categorized in terms of their use or properties for informing read-across in terms of exposure pathways and sources? What efforts exist or are being initiated to manage, inventory, or quantify chemicals used in products from manufacturing source through supply chain to finished product? How can consumer product chemical inventories be used to evaluate exposure information in consumer products be integrated with exposure-based risk assessments? Ultimately, how can improved exposure assessment and management approaches that consider multiple types of toxicological information to support frameworks for risk-based chemical evaluation and decision-making?

**Introduction.** John Wambaugh, US EPA, Research Triangle Park, NC.

**Consumer Product Data from the EPA’s Exposure Forecasting (ExpoCast) Project.** John Wambaugh, US EPA, Research Triangle Park, NC.

**Integrated Model Framework for Assessing Exposure to Consumer Products.** Deborah Bennett, University of California, Davis, Davis, CA.

**Aggregate Exposure Assessment for the Safety Evaluation of Fragrance Materials.** Cian O’Mahony, Creme Global, Dublin, Ireland.

**Prediction of Chemical Function: Model Development and Application.** Kristin Isaacs, US EPA, Research Triangle Park, NC.


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**ROUNDTABLE SESSIONS**

**Designing a Carcinogenic Mode-of-Action Research Program Useful for Regulatory Decision Making: Challenges and Lessons Learned**

**Wednesday, March 15, 12:30 PM to 1:50 PM**

**Chairperson(s):** James Klaunig, Indiana University, Bloomington, IN; and Angela Lynch, ToxPlus Consulting, Haymarket, VA.

**Endorser(s):**
- Carcinogenesis Specialty Section
- Regulatory and Safety Evaluation Specialty Section
- Risk Assessment Specialty Section

In 2001, the World Health Organization’s International Programme on Chemical Safety (IPCS) published the Conceptual Framework for evaluating an (animal) Mode of Action (MOA) for Chemical Carcinogenesis. The framework provided an approach to principles commonly used for evaluating mode of action, and outlined elements to be considered when deciding whether available experimental data support a particular mode of action. In 2006, the document was updated to include a Framework for Analyzing the Relevance of a Cancer MOA for Humans. In addition, the US EPA published a framework for determining a mutagenic mode of action for carcinogenicity using the 2005 Guidelines for Carcinogen Risk Assessment and supplemental guidance for assessing susceptibility from early-life exposures to carcinogens. The International Agency for the Research on Cancer (IARC) identified and published determination of human relevance criteria for a-2 urinary globulin (a2u) MOA for male-specific rat kidney tumors. The US EPA and NTP ostensibly follow IARC’s lead when evaluating chemicals for this particular MOA. However, criteria and guidance for collecting and interpreting MOA data from authorities for other genotoxic and epigenetic MOA are limited. Currently no validated guideline studies or guidance from regulatory authorities are available for MOA research design. The lack of such information creates scientific challenges in initiating MOA research programs that lead to data useful to make regulatory decisions, and can lead to the inefficient use of research funds and animals. This session explores the challenges of generating MOA data deemed acceptable by regulatory authorities to determine whether experimentally induced genotoxic or epigenetic carcinogenesis is relevant to humans. The speakers and invited panelists will participate in a discussion on utilization of MOA in regulatory assessment. Questions for the panel will include those generated from the audience, as well as the following: What additional guidance from regulatory agencies can be provided to help define the extent of MOA research necessary to address human relevance? How much MOA data is enough? Is there a point at which enough data exist to make a regulatory decision about human cancer risk? And, how should epidemiology data, and what types of epidemiology data, be considered in the MOA framework?

**The IPCS Framework and How It Is Used to Initiate a MOA Research Plan.** Angela Lynch, ToxPlus Consulting, Haymarket, VA.

**Current Status and Regulatory Challenges for Ongoing CYP 2F2 MOA Research.** George Cruzan, ToxWorks, Bridgeton, NJ.
Scientific Sessions
Wednesday

Evaluation of Modes of Action for Rodent Liver Tumor Formation by CAR and PPARα Activators. Brian Lake, CXR Biosciences, Dundee, United Kingdom.


Panel Discussion/Q&A. James Klaunig, Indiana University, Bloomington, IN.

Herbo-Metallic Mixtures in Traditional Medicines

Wednesday, March 15, 12:30 PM to 1:50 PM

Chairperson(s): J. Christopher States, University of Louisville, Louisville, KY; and Jie Liu, Zunyi Medical College, Zunyi, China.

Endorser(s):
American Association of Chinese in Toxicology Special Interest Group
Metals Specialty Section
Mixtures Specialty Section

Metals are ubiquitous in our lives; people are exposed to metals through the food we eat, the water we drink, the polluted air we breathe, and the medicines we take. Some metals are essential to human health such as zinc (Zn), copper (Cu), and iron (Fe), while other metals are of serious toxicological concern such as lead (Pb), cadmium (Cd), mercury (Hg), and the metalloid arsenic (As). Medicinal metals include platinum (Pt)-derived anticancer drugs, lithium carbonate as antimanics, aluminum hydroxide as antacids, and herbo-metallic mixtures with a long history of use in traditional medicines. In traditional medicines, metals often undergo specific processing procedures (e.g., heating, grinding). The addition of “processed” metals to herbal mixtures is thought to assist the efficacy, or reduce toxicity, in a given remedy. The goal of this session is to bring to light the history of use, toxicological consequences, and risk assessment considerations for metals in complex botanical mixtures common to traditional medicines around the world. The session will start with historical aspects of arsenic-containing mixtures as cancer chemotherapeutics, which are still used today. The session will progress in assessing complex botanical mixtures for toxicity, and incorporating comparisons of biological responses in addition to chemistry in evaluating mixture efficacy and toxicity. The final presentation will cover the current status of herbo-metal mixtures used in Ayurvedic medicines, Tibetan medicines, and Chinese medicines. Throughout this discussion, the presentation will consider how metals in traditional medicines differ from nominally related metals in the environment based on their interactions with the botanical matrix, effects of processing, and differences in disposition. The rationale for including metals in traditional remedies, and their interactions with drugs, remains a topic of great interest. The beneficial effects of herbo-metallic mixtures often go hand-in-hand with toxicity, and appropriate evaluation of herbo-metallic mixtures is needed. Presentations will highlight the latest science on traditional medicines and complex botanical mixtures and discuss areas that require further investigation. Expected outcomes: 1) herbo-metallic mixtures, rather than individual pure compounds, should be a research strategy for traditional medicines; 2) metals used in traditional medicines are different from environmental pollutants, for example, HgCl₂ and MeHg, and are never included in traditional remedies; thus, chemical form of metals matters; 3) the disposition, pharmacology, toxicology of herbo-metallic mixtures should be considered to balance the benefits and risks.

Introduction. J. Christopher States, University of Louisville, Louisville, KY.

Arsenic in Cancer Chemotherapy: A Historical Perspective. J. Christopher States, University of Louisville, Louisville, KY.

Understanding Chemical and Biological Similarity across Complex Mixtures in Hazard Characterization of Botanical Dietary Supplements. Cynthia Rider, NIEHS-NTP, Research Triangle Park, NC.

Clinical and Toxicological Aspects of Ayurvedic Medicinal Remedies with High Levels of Heavy Metals. Madhusudan Soni, Soni & Associates Inc, Vero Beach, FL.

Traditional Tibetan Medicine Zuotai: Mercury Chemical Speciation Transformation in Gastro-Intestinal Tract. Lixin Wei, Chinese Academy of Sciences-CAS, Xining, China.

Chemical Forms of Metals Are a Major Determinant of Metal Toxicity and Therapeutic Effects in Traditional Medicines. Jie Liu, Zunyi Medical College, Zunyi, China.
INFORMATIONAL SESSIONS

Communicating Toxicology to the Public

Wednesday, March 15, 12:30 PM to 1:50 PM

Chairperson(s): Philip Wexler, National Library of Medicine, Bethesda, MD; and Sidharta Ray, Manchester University College of Pharmacy, Fort Wayne, IN.

Endorser(s):
- Education Committee
- Ethical, Legal, and Social Issues Specialty Section
- Specialty Section Collaboration and Communication Group

The general public is expressing an increasing need and desire to learn about scientific issues affecting their daily lives. At the same time, scientists are recognizing the importance of making their work engaging and understandable to general audiences. Many educational efforts are aimed at training toxicologists and the K–12 community about toxicological principles. The non-homogenous general public, though, tends to be an overlooked audience. Much of what they learn these days about toxicology is “catch as catch can” via not always reliable, and sometimes misleading, sources. Print and broadcast media, the Internet, and social networking offer mixed results tools for finding credible news and information about chemical hazards and safety. Efforts to enhance the public’s understanding of science, toxicology included, may be considered among the last frontiers of science communication, which goes hand in hand with science education. Innovative approaches are beginning to appear to allow toxicologists to communicate more effectively about the nature and impact of their work to non-specialists with differing levels of existing technical knowledge, public officials, the media, potential funders, and colleagues in other disciplines. This informational session will explore a variety of recent approaches taken to inform the public about toxicology and chemical risk. The Toxicology Education Foundation (TEF) is an organization which recognized, early on, the importance of addressing public needs and concerns. To that end, a TEF presentation will address their new project of developing a series of YouTube videos to reach audiences with concise and practical information related to chemical safety and risk. A second talk will describe efforts by the chemical industry via the American Chemistry Council, to relate safety, hazard, and risk to the public. The Agency for Toxic Substances and Disease Registry has recently released a unique eBook, The Story of Health, which is the topic of another presentation, which takes a multi-factorial approach, including environmental and toxicological determinants, to explaining disease causation. Following this, a presentation will focus on Toxipedia, a Wiki-based online site, offering an encyclopedic approach to toxicological topics, including science, risk, hazards, and regulations, for general audiences. The final talk will describe a series of programs held in conjunction with previous SOT Annual Meetings to bring toxicology to the public in less conventional, non-academic settings, including public affairs institutes, public libraries, science cafes, department stores, and pubs. This session will enable attendees to gain a better grasp of how toxicological research and, more generally, information concerning potential chemical hazards, is perceived by various public audiences. The target audience for the session itself encompasses toxicologists of various persuasions seeking approaches that can be used to make their research clear and engaging to people with limited science and technical backgrounds. It cuts across and should be of value to a broad array of toxicological sub-disciplines. Finally, it will encourage more toxicologists to communicate their own work and related information on toxics in a scientifically accurate and understandable fashion, and describe existing efforts and tools which can serve as models for presenting similar information to the public.

Introduction. Philip Wexler, National Library of Medicine, Bethesda, MD.

The Toxicology Education Foundation: Enabling Public Interest with YouTube. Jeffrey Jenkins, Oregon State University, Corvallis, OR.

Communicating Information on Chemical Safety. Nancy Beck, American Chemistry Council, Washington, DC.

Presenting Environmental Health Content to a Variety of Audiences Using Case Stories. Brian Tencza, Agency for Toxic Substances and Disease Registry, Atlanta, GA.

Toxipedia: An Online Toxicology Encyclopedia for the Public. Steven Gilbert, Institute of Neurotoxicology & Neurological Disorders, Seattle, WA.

Opportunities for Unconventional Public Engagement about Toxicology. Philip Wexler, National Library of Medicine, Bethesda, MD.

Data Science to Generate Toxicity Signatures

Wednesday, March 15, 12:30 PM to 1:50 PM

Chairperson(s): Jane Bai, US FDA, Silver Spring, MD; and Ravi Iyengar, Icahn School of Medicine at Mount Sinai, New York, NY.

Endorser(s):
- Cardiovascular Toxicology Specialty Section

Adverse events associated with the use of therapeutically efficacious drugs remain a serious problem. Rare adverse events are generally identified in animal and clinical studies, both of which are expensive. It would be useful and cost-effective if there were cell-based signatures that could predict toxicity in animal models and humans. LINCS (Library of Integrated Network Cellular Signatures), a NIH Common fund program, has funded DTOxS (Drug Toxicity Signature Generation Center) center (www.dtoxs.org) to develop cellular signatures for drug toxicity. The center has been operational since September 2014. The DTOxS center is currently focused on experimentally-gathering transcriptomic and proteomic signatures of cancer drugs that can cause cardiac adverse events. Future studies include generation of signatures for hepatotoxicity and peripheral neuropathy. For cancer drugs, the DTOxS center uses primary cardiomyocytes differentiated from induced pluripotent stem cells from healthy human subjects. Data are gathered using mRNASeq and discovery-based proteomics. Both the raw and the processed data are posted on the website as they are generated and are freely available. All released data pass extensive quality control measures, and are accompanied by metadata as well as SOPs. Users can download both high-throughput molecular data and the results of initial computational analyses, such as ranked lists of differentially expressed genes/proteins, relevant cellular subnetworks, and enriched cellular processes. The molecular signatures are linked to clinical data on adverse event propensity using data from FAERS and academic medical center EMRs. The raw and processed data and the signature

Endorser(s):
- Pharmacy, Fort Wayne, IN.
- Bethesda, MD; and Sidharta Ray, Manchester University College of Pharmacy, Fort Wayne, IN.
- Philip Wexler, National Library of Medicine, Bethesda, MD.

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Scientific Sessions

lists are freely available for further analyses. The session will describe currently available datasets for cardiotoxicity associated with cancer drugs as a prototype, and how these can be accessed and downloaded. The session will also take the audience through the types of computational analyses that can be performed on these data sets with publicly available computational tools to identify differences between drugs and between drug responses in individuals. As these freely available datasets analyses can be downloaded and used for further analyses, this session will conclude with a discussion of how the resource can be best exploited for the development of mechanistic research projects.

Translational Data Science for Predictive Assessment of Cardiac Contractility-Related Toxicity. Jane Bai, US FDA, Silver Spring, MD.

Transcriptomics Data and Signatures for Protein Kinase Inhibitor Responses of Cardiomyocytes. Marc Birtwistle, Icahn School of Medicine at Mount Sinai, New York, NY.

Exploiting Cellular Data to Infer Toxicity Mechanisms. Shankar Subramaniam, University of California at San Diego, San Diego, CA.

Ensuring Rigor and Reproducibility of Drug Toxicity Signatures. Ka Yeung-Rhee, Institute of Technology at the University of Washington, Seattle WA.

HISTORICAL HIGHLIGHT
SESSION

NIEHS Superfund Research Program: A History of Cutting-Edge Science and Innovative Technologies

Wednesday, March 15, 12:30 PM to 1:50 PM

Chairperson(s): Danielle Carlin, NIEHS, Research Triangle Park, NC; and Rebecca Fry, University of North Carolina-Chapel Hill, Chapel Hill, NC.

Endorser(s):
- Metals Specialty Section
- Mixtures Specialty Section
- Molecular and Systems Biology Specialty Section

The National Institute of Environmental Health Sciences (NIEHS) Superfund Hazardous Substance Basic Research and Training Program (SRP) is a critical player in the national effort to protect human health and the environment from hazardous substances. The Program funds a wide range of university-based and small business research to address public health concerns related to hazardous substances in the environment. SRP takes a problem solving, solution-oriented approach that combines laboratory, field, and population-based studies to improve our understanding of and minimize the health effects associated with exposures to contaminants. Created by the same legislative framework that created the US Environmental Protections Agency’s (US EPA) Superfund hazardous waste remediation program and the Center for Disease Control and Prevention’s Agency for Toxic Substances and Disease Registry (ATSDR), the SRP’s role is to support science-based decision making by elucidating the basic principles underlying hazardous substance toxicity and risk. SRP-funded researchers are focusing on the health effects of individual contaminants, as well as complex chemical mixtures, determining relevant chemical exposures, identifying developmental windows of susceptibility, analyzing patterns in toxicologic data to assess risks to human health presented by hazardous substances, and development of tools to facilitate assessment of exposure and mitigation of toxicity. The Program’s central goal is to understand and break the link between chemical exposure and disease. This session will highlight the scientific findings from the SRP’s extramural community over the past 30 years, as well as ongoing state-of-the-art science, which includes a focus on various chemical classes (e.g. metals, PCBs, PAHs), mixtures, and emerging contaminants. We also will discuss future scientific areas of interest to the Program and how the Program will continue to support the understanding of hazardous substance toxicity and risk to exposure to hazardous substances and relevant mixtures.


Systems Toxicology Approaches to Understand the Harms of Toxic Metals in Vulnerable Populations. Rebecca Fry, University of North Carolina-Chapel Hill, Chapel Hill, NC.

Integrating New Research Models to Understand and Mitigate the Adverse Effects of PAH Mixtures. Robert Tanguay, Oregon State University, Corvallis, OR.
Scientific Sessions

**Wednesday**

**Novel Methods for Detection and Prevention of Emerging Superfund Contaminants.** Stephanie Cormier, University of Tennessee Health Sciences Center, Memphis, TN.

**Emerging Prevention Paradigms with Nutrition: The Impact of the NIEHS SRP.** Bernhard Hennig, University of Kentucky, Lexington, KY.

**SYMPOSIUM SESSIONS**

**Enhancing the Clinical Benefit of Cancer Drugs: Toxicity As a Therapeutic Target**

Wednesday, March 15, 2:00 PM to 4:45 PM

**Chairperson(s):** Syril Pettit, HESI, Washington, DC; and Brian Berridge, GlaxoSmithKline, King of Prussia, PA.

**Endorser(s):**
- Cardiovascular Toxicology Specialty Section
- Clinical and Translational Toxicology Specialty Section
- Immunotoxicology Specialty Section

Recent advances in cancer drug therapy have significantly contributed to survivability in cancer patients. Clinical protocols that are increasingly including more targeted therapies, or leveraging the patient’s own immune response, are benefiting patients that previously had very little hope. But, cancer treatment has been an area where we have tolerated toxic liabilities (both acute and delayed effects) more than any other class of pharmaceuticals. These liabilities include cardiovascular toxicity, peripheral nerve deficits, cognitive dysfunction, respiratory disease, and immune-inflammatory reactions. These liabilities come at incredible cost to the patients (with respect to quality of life as well as adherence to treatment) and the healthcare system overall. These effects are not limited to a single drug class, and are associated with both traditional oncologic therapies as well as novel targeted therapies. The translational toxicology research community has the opportunity to benefit patients and survivors with generation of translational data on biomarkers of toxicity, by defining mechanism of action, and investigating novel dosing and protective strategies. This session will provide preclinical, clinical, translational, and patient perspectives on the need to address those liabilities to not only increase survivability, but also improve post-cancer quality of life.

**Introduction.** Syril Pettit, HESI, Washington, DC.

**An Overview of Cancer Drug-Related Toxicity.** Charles Cleeland, MD Anderson Cancer Center, Houston, TX.

**Identifying and Mitigating the Toxic Effects of Novel Immunotherapies.** Laura Cappelli, Johns Hopkins School of Medicine, Baltimore, MD.

**Balancing Toxicity and Efficacy: Perspective from a Researcher Who Also Is a Patient.** Jamie Holloway, Independent Consultant, Arlington, VA.

**There Are Solutions: Efforts to Mitigate and Manage Cancer Drug-Related Cardiotoxicties.** Steven Lipshultz, Children’s Hospital of Michigan, Detroit, MI.

**Opportunities, Hurdles, and Networks to Spur Research on Toxicity As a Therapeutic Target for Cancer Drugs.** Syril Pettit, HESI, Washington, DC.
Incorporating Improved Physiological Relevance, Xenobiotic Metabolism, and Data-Rich Assay Approaches into Tox21 (Phase III). Stephen Ferguson, NTP, NIEHS, Research Triangle Park, NC.

In Silico Predictions and In Vitro Experimental Results of Toxicity as Part of an Integrated Testing Strategy. Bas Blaauwboer, Utrecht University, IRAS, Utrecht, Netherlands.

Consideration of Biokinetics and Metabolism in Repeated Dosing In Vitro Toxicity Assays. Emanuela Testai, Istituto Superiore di Sanita, Rome, Italy.

**III** Novel In Vitro and In Silico Platforms for Modeling Developmental and Reproductive Toxicity

**Wednesday, March 15, 2:00 PM to 4:45 PM**

**Chairperson(s):** Thomas Knudsen, US EPA, Research Triangle Park, NC; and Nicole Kleinstreuer, NIEHS, Research Triangle Park, NC.

**Endorser(s):**
- Biological Modeling Specialty Section
- In Vitro and Alternative Methods Specialty Section
- Reproductive and Developmental Toxicology Specialty Section

Recent progress in systems toxicology and synthetic biology have paved the way to new thinking about in vitro/in silico modeling of developmental processes and toxicities, both for embryological and reproductive impacts. Novel in vitro platforms, such as 3D organotypic culture models, engineered microscale tissues, and complex microphysiological systems (MPS), together with computational models and computer simulation of tissue dynamics, lend themselves to integrated testing strategies for predictive toxicology. As these methodologies continue to evolve, for the purposes of effects assessment, they must be integrally tied to maternal/fetal physiology and toxicity of the developing individual across early life stage transitions, from fertilization to birth, puberty, and beyond. This symposium will focus on how the novel technology platforms can help now and in the future, with in vitro/ in silico modeling of complex biological systems for developmental and reproductive toxicity issues, and translating systems models into integrative testing strategies. The symposium is based on three main organizing principles: (1) that novel in vitro platforms with human cells configured in nascent tissue architectures with native microenvironments yield mechanistic understanding of developmental and reproductive impacts of drug/chemical exposures; (2) that novel in silico platforms with high-throughput screening (HTS) data, biological models of complex adaptive systems, and chemical structure information, yields predictive understanding of developmental and reproductive impacts of drug/chemical exposures; and (3) that a combination of technologies is necessary for analytical (to understand) and theoretical (to predict) application for probing the relevant biological processes and toxicological mechanisms to inform safety assessments. After a brief introduction, the first two presentations will cover reproductive issues: a novel MPS to recreate the ovarian axis in vitro using iPSC technology in a linked microfluidics environment that provides a 3-dimensional support system mimicking the complexity of human in vivo physiology; and pathway-based computational models that integrate HTS data from...
ORTHOLOGICAL ASSAYS TO MEASURE NUCLEAR HORMONE RECEPTOR PATHWAYS AND PERFORMANCE-BASED APPROACHES TO APPROPRIATELY VALIDATE THEM FOR REGULATORY DECISION-MAKING. THE SECOND TWO PRESENTATIONS WILL COVER EMBRYOLOGICAL ISSUES: A NOVEL IN VITRO PLATFORM (BRAIN MAPS) DESIGNED AND SYNTHETICALLY ENGINEERED TO INSTRUCT MORPHOGENESIS FROM HUMAN NEURAL STEM CELLS (hNSCs) AND PRINT MICROSCALE ARRAYS OF ORGANOIDS FOR PHENOTYPE-SPECIFIC, QUANTITATIVE HIGH-THROUGHPUT DEVELOPMENTAL NEUROTOXICITY STUDIES; AND COMPUTER MODELS STRUCTURED TO SIMULATE COMPLEX CELL SIGNALING NETWORKS IN A HEURISTIC FRAMEWORK THAT TRANSLATES TOXCAST HTS DATA INTO PREDICTIONS OF DEVELOPMENTAL TOXICITY. THE FINAL PRESENTATION WILL ADDRESS THE INTEGRATION OF RESULTS FROM NOVEL IN VITRO/IN SILICO MODELS WITH CHEMICAL/EXPOSURE INFORMATION FOR DEVELOPMENTAL AND REPRODUCTIVE SAFETY ASSESSMENT. MODELS COMBINING IN VITRO DATA FROM SYNTHETIC HUMAN TISSUE ARCHITECTURES, COUPLED WITH IN SILICO MODELS INSPIRED BY BIOLOGICAL UNDERSTANDING FROM ANIMAL STUDIES, YIELD MECHANISTIC UNDERSTANDING OF DEVELOPMENTAL AND REPRODUCTIVE IMPACTS OF DRUG/CHEMICAL EXPOSURES. A COMBINATION OF IN VITRO/IN SILICO APPROACHES IS NECESSARY FOR PREDICTIVE UNDERSTANDING OF TOXICOLOGICAL PROCESSES AND INFORMING SAFETY ASSESSMENTS.

**Introduction.** Thomas Knudsen, US EPA, Research Triangle Park, NC.

**Microphysiological Modeling of the Female Reproductive Tract.** Shuo Xiao, University of South Carolina, Columbia, SC.

**Pathway Based Models to Predict Developmental and Reproductive Toxicities.** Nicole Kleinstreuer, NIEHS/NTP/NICEATM, Research Triangle Park, NC.

**Brain Model for Analysis of Developmental Pathways.** Randolph Ashton, University of Wisconsin, Madison, WI.

**Computer Simulation of Developmental Processes and Toxicities.** Thomas Knudsen, US EPA, Research Triangle Park, NC.

**Combining Cheminformatics and In Vitro/In Silico Models for Developmental and Reproductive Toxicity Assessment.** George Daston, Procter & Gamble Co., Cincinnati, OH.

**WORKSHOP SESSIONS**

**Anesthetics, Analgesics, and Ionizing Radiation: Balancing Utility and Safety in Pregnant Women, Infants, and Children**

**Wednesday, March 15, 2:00 PM to 4:45 PM**

**Chairperson(s):** Henrik Viberg, Uppsala University, Uppsala, Sweden; and William Slikker, US FDA-NCTR, Jefferson, AR.

**Endorser(s):**
- Clinical and Translational Toxicology Specialty Section
- Neurotoxicology Specialty Section
- Specialty Section Collaboration and Communication Group

Use of anesthesia, analgesia, and ionizing radiation (IR) in pregnant women, neonates, toddlers, and children is sometimes necessary therapeutically, surgically, or to relieve pain and/or painful procedures. Despite safety concerns, to refrain from use of these agents may be unethical, inhumane, and potentially harmful to normal development. Yet, accumulating data from animal models have recently shown that exposure to anesthetic and analgesic agents, such as ketamine, sevoflurane, and paracetamol, during critical periods of development causes neurotoxicity, manifested as neuronal cell death, synaptic remodeling, and altered morphology of the developing brain, and subsequently result in long-term deleterious effects, including cognitive deficits. Possible mechanisms of action for these functional effects include changes in several different systems, for example GABAergic neurons, NMDA-receptors, endocannabinoid system, and neurotranspheric factors, and in different parts of the brain, e.g. hippocampus and cerebral cortex. Despite these agents being physically and chemically different, developmental neurotoxic effects have similarities. Also, IR has been proposed to induce developmental neurotoxic effects, during early postnatal development, both in humans and in experimental animals. These behavioral effects are similar to those induced by anesthesia and analgesia, when exposure occurs during a critical period of perinatal life. Furthermore, IR can interact with ketamine in the induction of developmental neurotoxicity, making it important to find ways to prevent these effects, and some compounds, e.g. melanin and clonidine, have been put forward to have these effects. Because of the necessity of anesthetics and analgesics, millions of children are exposed to these agents on an annual basis worldwide, with 5 million episodes of anesthesia yearly in the United States alone. The results from animal models are corroborated by epidemiological studies indicating neurotoxic effects, including delayed motor development and increased risk for developing attention-deficit/hyperactivity disorder (ADHD)-like behavior problems or hyperkinetic disorders (HKDs) in children, after developmental exposure to the analgesic agent paracetamol (acetaminophen). This is a multidisciplinary session and attendees will gain knowledge about functional defects observed in humans and experimental animals, as well as possible mechanisms of action, common and specific, behind these developmentally induced disorders. Fundamental researchers, clinicians, and regulators will be informed of the full spectrum of anesthetic/analgesic-induced developmental neurotoxic effects in animal models, and early data gathered from epidemiological studies in children.
Introduction.
Henrik Viberg, Uppsala University, Uppsala, Sweden.

Epidemiological and Experimental Findings Concerning Developmental Exposure to Anesthetic Agents. Vesna Jevtovic-Todorovic, University of Colorado School of Medicine, Denver, CO.


Interaction between the Anesthetic Agent Ketamine and Gamma-Radiation Exacerbate Neurotoxicological Defects. Sonja Buratovic, Uppsala University, Uppsala, Sweden.


Panel Discussion. Thomas Jones, Eli Lilly and Company, Indianapolis, IN.

Data Standardization Across ‘Omic Platforms in Regulatory Toxicology

Wednesday, March 15, 2:00 PM to 4:45 PM

Chairperson(s): Weida Tong, US FDA-NCTR, Jefferson, AR; and Timothy Gant, Centre for Radiation, Chemical and Environmental Effects, Oxfordshire, United Kingdom.

Endorser(s):
Molecular and Systems Biology Specialty Section
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

Molecular events associated with the effects of chemical, biological, and physical agents on biological systems can be globally determined using ‘omic high-throughput technologies. These technologies are playing a major role in the generation of new knowledge and understanding in mechanisms of toxicity. However, use and application of these technologies has been slower in hazard identification and regulatory risk assessment. This slow uptake has been associated with technical issues of data quality and reproducibility. Although such challenges still exist, the main challenge now is achieving consistency in data processing and biological interpretation. Consistent methods and agreed frameworks and processes for collection/curating, processing, analyzing, and interpreting data are paramount to support regulatory assessments. Consensus amongst stakeholders including industry, academia, and regulatory agencies on this issue will provide guidance and confidence on how ‘omic technologies can be applied in regulatory decision-making. To that end, this workshop will propose transparent frameworks and suitable processes to provide a baseline and confidence on the application of ‘omics in regulatory decision making, with a specific emphasis on data analysis and interpretation in risk assessment. Challenges and issues in the regulatory application of ‘omic data will be addressed in the context of status and future direction for developing objective protocols for the analysis, interpretation, and reporting of ‘omic results. The presenters will give their views on a path forward with time for the audience to respond and discuss. The session will be of interest to bioinformaticians, research toxicologists, and regulators alike, and will welcome input from all of these sectors.

Introduction.
Weida Tong, US FDA-NCTR, Jefferson, AR.


Standardization in Metabolomics—The Current Effort and Future Directions. Hector Keun, Imperial College London, London, United Kingdom.

Is There a Concern for Neurotoxicity from Replacement Organophosphorus Flame-Retardants?: Insights Using Molecular Approaches, Systems Biology, and Human Exposure

Wednesday, March 15, 2:00 PM to 4:45 PM

Chairperson(s): Helena Hogberg, Johns Hopkins University, Baltimore, MD; and Mamta Behl, NTP, NIH, Research Triangle Park, NC.

Endorser(s):
Molecular and Systems Biology Specialty Section
Neurotoxicology Specialty Section
Regulatory and Safety Evaluation Specialty Section

The global flame retardants (FR) consumption has surpassed 2 million tons and yet is expected to increase in order to meet international flammability standards. FRs are widely used in products such as upholstered furniture, electrical devices, baby products, textiles, and plastic, where the potential exposure is high. Especially, the use of FR in baby products and the exposure to children are of concern, as the developing brain is much more vulnerable to environmental perturbation than the brain of an adult. Prior to 2005, polybrominated diphenyl ethers (PBDEs) were the primary FRs used in the US. PBDEs have been banned in Europe and phased out in the US due to several health issues, specifically concerns for developmental neurotoxicity (DNT) following exposure in infants and children, and have now been replaced by organophosphorus FRs (OPFRs). However, there is limited information on potential health effects of these novel replacements. This is of concern, as the OPFR resembles organophosphate pesticides that are well known to induce neurotoxicity. In fact, there are in vitro data demonstrating neurotoxicity and developmental toxicity of many OPFRs. At this time it is not clear if these effects are observed at concentrations relevant to human exposure. Epidemiology studies show that metabolites of OPFRs are detected in the urine in more than 93% of infants at much higher concentrations than in adults. This workshop will begin with
addressing current flammability standards and issues relating to the use of FRs in household products. Presenters will then address latest findings on in vitro and alternative species using a wide range of models (e.g. human and rodents cell lines, 3D cell cultures, and zebrafish) and methods (e.g. neurite outgrowth, electrical activity, transcriptomics, metabolomics, and behavioral studies). In addition, limited rat in vivo data will be presented. The relevance of these findings will be discussed based on the observation of human exposure to OPFRs. The main goal of the workshop is to shed light and discuss the current status of OPFRs, specifically related to DNT and neurotoxicity, and to link human exposures with findings in experimental models using point of departure methods and in vitro in vivo extrapolation. Attendees will gain national and international perspective from academia, government, and industry. The introduction will present the agenda of the workshop, including the overall goals, speaker line up, and the intended outcome. Dr. Behl will introduce the current status of the replacement OPFRs and their potential concern for DNT. The first presenter will describe current flammability standards and how FRs may be used in consumer products to meet these standards. The exposure, toxicity concerns, and data gaps for OPFRs will be discussed. The second presenter will report on the neurotoxicity observed in different in vitro cell lines using a variety of cellular and molecular endpoints. The data will be discussed in perspective to the in vivo study by the group showing that FRs were not detected in the brain and did not induce appreciable neurotoxicity in exposed neonate rat pups. Gaps in both the in vitro and in vivo studies will be discussed. The third presenter will then present DNT effects using organotypic cell cultures that better mimic the in vivo situation than traditional monolayer cultures. This study evaluates longer exposure time during development and goes more in mechanistic depth to describe pathways of toxicity of some OPFRs. The next presentation will discuss the actual human exposure of OPFRs, with focus on children and the presence of OPFRs in baby products. The research has showed that the urinary metabolites of these OPFRs are commonly detected in the US population, raising the concern of exposure. The final presenter will summarize by discussing how a battery of in vitro tests using different models and endpoints targeting different closely inter-related molecular pathways for developmental and DNT can be used in determining a point of departure for prioritizing compounds for further in vivo testing. It will then compare the in vitro findings with in vivo data in rodents (gene expression and functional end-points) to truth the data, and will highlight the need for a “systems biology” approach while determining a point of departure value. It will finally link in vitro and rodent data to human exposure using in vitro/in vivo extrapolations (IVIVE) to provide some insight on margins of safety.

**Introduction.** Helena Hogberg, Johns Hopkins University, Baltimore, MD.


**In Vitro and Ex Vivo Neurotoxicity Assessment for Prioritization and Risk Assessment of Alternative Flame Retardants.** Remco Westerink, Utrecht University, Utrecht, Netherlands.

**Pathway Evaluation of the Developmental Neurotoxicity of Organophosphorus Flame-Retardants.** Helena Hogberg, Johns Hopkins University, Baltimore, MD.

**Children’s Exposure to Organophosphate Flame Retardants: Are They a Better or Worse Replacement for PBDEs?** Heather Stapleton, Duke University, Durham, NC.

**Putting It into Perspective: Relating Experimental Data to Human Exposure—Is Neurotoxicity Really a Concern?** Mamta Behl, NTP, NIH, Research Triangle Park, NC.
ROUNDTABLE SESSION

Implementing Developmental Thyroid Toxicity Guidance into Practice: What’s Working, What’s Not, and How Can We Do Better?

Wednesday, March 15, 5:00 PM to 6:20 PM

Chairperson(s): Abby Li, Exponent Health Science, San Francisco, CA; and Steffen Schneider, BASF, Ludwigshafen, Germany.

Endorser(s):
- Neurotoxicology Specialty Section
- Regulatory and Safety Evaluation Specialty Section
- Reproductive and Developmental Toxicology Specialty Section

Thyroid hormone is essential for normal brain development both in the fetus and the neonate. In humans, thyroid function is not fully engaged until week 20 of gestation; in rodents, it is day 17. Chemicals that change circulating levels of thyroid hormone can be associated with neuro-behavioral disorders and alterations in neurological development. Because of the complexity of brain development and its behavioral manifestations, it is important to target testing strategies based on the putative mode of action to focus time and resources on the critical endpoint(s) of concern. In 2015, US EPA OPP and OECD included thyroid measurements as part of new toxicity testing data requirements. US EPA has included comparative thyroid measures as part of Tier 2 testing for some pesticides as part of the Endocrine Disrupter Screening Program. Guidance for this study includes thyroid histopathology and serum hormone measurements (T4, T3 and TSH) for Gestation Day (GD) 20 dams and fetuses, offspring at postnatal day (PND) 4, and dams and offspring on PND 21 (www.epa.gov/sites/production/files/2015-06/documents/thyroid_guidance_assay.pdf). OECD added thyroid measurements to reproductive and developmental screening tests (OECD 421, 422), including thyroid hormone measurements in pups at PND 13, adult males at the end of reproductive period, and, if available, PND 4 pups and dams at day 13 of lactation. As more new studies with developmental thyroid endpoints are being conducted in response to these 2015 requirements, technical and regulatory issues have arisen regarding the variability and sensitivity of the hormone measurements in rat fetus and pups at different ages. In addition, there are questions on how to interpret the thyroid hormone data within the context of thyroid physiology and brain development. While there might be greater agreement on the clinical features that may be considered adverse following severe impacts on the thyroid system, there is greater uncertainty and disagreement regarding the appropriate point of departure for more modest effects. This roundtable brings together academic, industry, and government scientists to share knowledge, experience, and perspective from these recently conducted studies to address technical issues, discuss data interpretation, and collectively develop a perspective that can inform future work. The session will begin with a brief introduction of the current guideline recommendations and regulatory need to address developmental thyroid toxicity (DTT). This first presenter also will discuss how DTT data can be used to determine a point of departure and/or the magnitude of uncertainty factors used in risk assessments. The next three presentations initially will be asked to take contrasting scientific positions with data to illustrate the issues raised. These presenters include scientists who are on the forefront of conducting or sponsoring studies according to US EPA guidance and OECD 421/422 requirements, and an academic expert on developmental thyroid toxicity. During the balance of the time, these same speakers will be asked to step back from their positions and consider solutions and approaches that will improve implementation and interpretation of developmental thyroid toxicity studies. To set the tone for the discussion, the last speaker will argue the stated position with data, and then discuss data that supports a contrasting position. This roundtable is timely and provides a forum for constructive cross-communication with the goal of improving laboratory capabilities and safety evaluations for developmental thyroid toxicity.


Implementing Developmental Thyroid Guidelines into Practice: A Survey of Current Capabilities and Challenges. Steffen Schneider, BASF SE, Ludwigshafen, Germany.

Minor Perturbations in Thyroid Assays Should Not Be Assumed to Be Adverse Due to Variability, Species Differences, and Compensatory Feedback. Sue Marty, The Dow Chemical Company, Midland, MI.

Any Measurable Change in Perinatal Thyroid Hormone Can Affect Brain Development, and There Are Sensitive Measures to Detect These Changes. Thomas Zoeller, University of Massachusetts, Amherst, MA.

Discussion: What’s Working, What’s Not, and How Can We Improve Implementation and Interpretation of Developmental Thyroid Toxicity Studies? Abby Li, Exponent Health Sciences, San Francisco, CA.
INFORMATIONAL SESSIONS

Addressing Rigor and Transparency in Research and Journal Publications

Wednesday, March 15, 5:00 PM to 6:20 PM

Chairperson(s): Sally Darney, NIEHS, Research Triangle Park, NC; and Nancy Beck, American Chemistry Council, Washington, DC.

Endorser(s):
- Graduate Student Leadership Committee
- Postdoctoral Assembly
- Specialty Section Collaboration and Communication Group

Driven by changes throughout the research and user community, increased efforts are being directed to ensuring scientific rigor and transparency in both the conduct and publication of toxicological and environmental health research. Up front, funding agencies are adding criteria for rigor and reproducibility as an integral part of a grant application. At the end of the pipeline, regulatory agencies are honing their requirements for using data in risk assessment and regulatory decision making. In between, journals are playing an increasingly important role in these efforts with the dual goals of publishing highly credible science, and making it more accessible and discoverable within the broad community of scientists and research users. This session will explore the many challenges inherent in achieving rigor and reproducibility from the perspective of researchers, information specialists, and journal editors, while highlighting the availability of new tools and approaches for addressing them. Of broad interest across all SOT specialty sections, special interest groups, and disciplines in toxicology, public health, and risk assessment, the session starts with an overview of established reporting guidelines (such as ARRIVE for animal studies), and introduces new initiatives to foster openness and transparency, the use of valid and appropriate statistics, and the acceptance of data quality standards. Next, the audience will hear about how the NIH is developing innovative programs and tools to enable all domains of biomedical research to become more data-centric and open, and to make all types of research products more "discoverable" and useable. In this new biomedical science, not only publications, but other objects, such as data, software, workflows, and identifies (of investigators, grant numbers, reagents, etc.) will be digital, as well as findable, accessible, interoperable, reusable, and citable. The editors-in-chief of Environmental Health Perspectives (EHP) and Toxicological Sciences (ToxSci) will add their insights on how this information revolution is impacting journal submission guidelines, peer review policies, and data access requirements. For example, ToxSci recently launched a partnership with the Dryad Digital Depository, which enables investigators to make their underlying data available to peer reviewers, and later to the broader community once the paper is accepted. In addition to toxicology studies, EHP publishes research findings derived from exposure and ecosystem modeling, as well as epidemiological approaches that integrate biological, social, and environmental determinants of health. These fields face their own unique challenges in making data accessible (while protecting human subjects) and suitable for meta-analyses when data cut across spatial scales and human populations. A discussion period at the end of the session will enable audience members to share their experiences using these new data access tools and responding to the challenge of ensuring reproducibility in their research and publishing endeavors.

Bioinformatics Tools for Accelerated Hypothesis Generation and Mechanistic Insights

Wednesday, March 15, 5:00 PM to 6:20 PM

Chairperson(s): Susan Bello, Mouse Genome Informatics (MGI), Bar Harbor, ME; and Marc Gillespie, St. John's University, New York, NY.

Endorser(s):
- Biological Modeling Specialty Section
- Molecular and Systems Biology Specialty Section

There are a wide range of freely available, web-based bioinformatics resources and tools for hypothesis generation and data analysis. Finding and picking the best tool for a specific research question can be challenging and time consuming. A tool or resource may be used to investigate gene function, identify genes sharing common features (pathway, expression pattern, phenotypes), narrow candidate gene lists, and find gene, protein, or compound interactions. Selecting a tool or resource requires at least some understanding of the design, function, and limits of the tool. To generate reliable results, researchers need to understand what types of data are integrated, how those types of data are integrated, how to access the data, and what sorts of outputs may be produced. This session features four resources representing different types of freely available, internet-based, bioinformatic resources, followed by a practical example of use of these types of tools in a research program. Mouse Genome Informatics (informatics.jax.org), the premier international database resource for the laboratory mouse, will demonstrate the use of the Human–Mouse: Disease Connection portal to leverage mouse and human phenotype data in candidate gene analysis. Reactome (reactome.org) is a free, open-source, manually curated, and peer reviewed human pathway database. Reactome's intuitive bioinformatics tools for data visualization and interpretation will be used to analyze gene expression, small molecule (metabolite data), and cancer gene sets. ToxCast provides a significant amount of chemical bioactivities (data for nearly 2,000 chemicals and over 450 gene targets), many not found in the literature, with findings implicating gaps in knowledge about chemical effects on biological systems. GeneWeaver (geneweaver.org) facilitates the integration of functional genomics resources, and will show how to combine user submitted data with data from public resources to gain novel insights into the biomolecular basis of toxicological effects. The session will conclude with case studies centered on the practical applications of toxicogenomics databases.
in nonclinical safety assessment, including species selection, cross species comparison around organ toxicity, and immunomodulation in nonhuman primates. At the end of this session, participants will have an understanding of how to make use of each resource, and which bioinformatic tools will accelerate their research.

**Introduction.** Marc Gillespie, St. John’s University, Jamaica, NY.

**Using Mouse Genome Informatics’ Human-Mouse: Disease Connection Tool in Candidate Gene Analysis.** Susan Bello, Mouse Genome Informatics (MGI), Bar Harbor, ME.

**Using Reactome as a Foundation for Adverse Outcome Pathway (AOP) Identification.** Marc Gillespie, St. John’s University, New York, NY.

**Integration of Heterogeneous Functional Genomics Data in GeneWeaver.org with Applications in Toxicology.** Elissa Chesler, The Jackson Laboratory, Bar Harbor, ME.

**ToxCast Data Expands Universe of Chemical-Gene Interactions.** Sean Watford, National Center for Computational Toxicology, US EPA, Chapel Hill, NC.

**Applications of Toxicogenomics Database in Nonclinical Safety Assessment.** Jing Yuan, Boehringer Ingelheim Pharmaceutical, Ridgefield, CT.

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**EDUCATION-CAREER DEVELOPMENT SESSION**

**Mastering Soft Skills to Advance Your Scientific Career**

**Wednesday, March 15, 5:00 PM to 6:20 PM**

**Chairperson(s):** Karilyn Sant, University of Massachusetts, Amherst, MA; and Samantha Snow, US EPA, Chapel Hill, NC.

**Endorser(s):**
- Career and Resource Development Committee
- Graduate Student Leadership Committee
- Postdoctoral Assembly

The overwhelming majority of the typical training experience focuses upon doing excellent science and identifying a career path. However, without a bit of personality, even trainees with the most exceptional resume may not stand out in a saturated applicant pool. Soft skills are often ignored in training, but can have a huge impact on the amount of success one obtains throughout their career. This session is designed to bring charismatic leaders in the field to discuss the non-scientific attributes that have contributed to their success and also the qualities they seek out when identifying candidates for their organizations. Presentations will focus on: (1) how to network effectively; (2) how to present oneself in a professional environment using proper body language and etiquette; and (3) effective communication, leadership, and management skills. These interactive presentations will utilize demonstrations when applicable, and will be followed by a panel of young toxicologists who have successfully mastered these soft skills to transition from trainee to professional across the sectors. These discussions will be highly relevant to all student and postdoctoral attendees, as well as senior toxicologists who want to improve the professional training of mentees. This session will stimulate a discussion about underserved aspects of professional development and enable trainees to learn and implement an essential skill set which will improve professional relationships throughout their careers.

**Introduction.** Karilyn Sant, University of Massachusetts Amherst, Amherst, MA.

**Networking Effectively to Gain Traction for Your Science.** Ruth Roberts, ApconiX, Alderley Edge, United Kingdom.

**First Impressions Matter: Etiquette for the Professional.** Martin Philbert, University of Michigan, Ann Arbor, MI.


**Early-Career Scientist Panel Discussion.** Shaun McCullough, US EPA, Chapel Hill, NC.

**Early-Career Scientist Panel Discussion.** Bethany Hannas, DOW Chemical Company, Midland, MI.

**Early-Career Scientist Panel Discussion.** Jonathan Shannahan, Purdue University, West Lafayette, IN.
SYMPOSIUM SESSIONS

Evaluating the Reproductive and Developmental Effects of Botanical Dietary Supplements

Thursday, March 16, 8:30 AM to 11:15 AM

Chairperson(s): Kembra Howdeshell, NIEHS/NTP, Research Triangle Park, NC; and Cynthia Rider, NIEHS/NTP, Research Triangle Park, NC.

Endorser(s):
  - Food Safety Specialty Section
  - Mixtures Specialty Section
  - Reproductive and Developmental Toxicology Specialty Section

Use of botanical dietary supplements is widespread, with approximately 18% of adults in the US reporting use of natural products, including botanical dietary supplements. Many diverse botanical products are marketed for their purported support of reproductive health, from black cohosh for gynecological and menopausal issues, to maca for male enhancement. There is a public perception that “natural” products (i.e., derived from plants or fungi) are safer than pharmaceuticals. However, there is often inadequate data to support the safety of these products. There are many factors that raise concerns about potential reproductive and developmental effects of botanical dietary supplements. Primarily, several plant or fungi constituents have well-characterized endocrine activity, such as genistein from soy and the mycotoxin zearalenone. In addition to these biologically-active constituents, numerous reports have documented adulteration of botanicals with pharmaceutical compounds or structurally-related analogs. Contributing to the difficulty in characterizing potential reproductive and developmental effects of botanical dietary supplements is the fact that they are complex mixtures that can vary significantly depending on source material and manufacturing processes. Therefore, inconsistent results in animal studies of toxicity or clinical trials for efficacy can be expected based on differences in product composition. Finally, botanical dietary supplements are regulated under the Dietary Supplement Health and Safety Act, which treats botanical ingredients that were on the market prior to its 1994 passage as food, which is assumed to be safe. Instead of requiring pre-market safety assessment, there is a reliance on adverse effect reporting, which is particularly problematic for identifying reproductive and developmental consequences that can manifest years after exposure. In this session, speakers will address different aspects of evaluating the reproductive and developmental effects of botanical dietary supplements. The session will begin with a presentation on applying rigorous evaluation methods to measure efficacy, toxicity, and chemopreventive potential of botanicals traditionally associated with treatment of menopausal symptoms. Next, speakers will present specific cases of identifying and characterizing reproductive and developmental effects of botanicals or their constituents. A discussion of adulterants with reproductive and developmental implications will follow. Finally, screening methods for rapid identification of reproductive and developmental toxicity of botanicals will be addressed. A multi-faceted discussion of botanicals and associated reproductive and developmental endpoints will help guide future research and inform public health decisions on this important topic.

Introduction. Kembra Howdeshell, NIEHS, Research Triangle Park, NC.

Botanicals as Natural Alternatives to Traditional Pharmaceuticals for Women’s Reproductive Health. Judy Bolton, University of Illinois Botanical Research Institute, Chicago, IL.

Evaluation of Reproductive Health Effects for the Caffeine in an Energy Shot. Mary Hixon, Gradient, Acton, MA.

Embryo-Fetal Toxicity in the Rat and Rabbit as a Result of Dietary Supplement Exposure: Vincovicina as a Case Study. Natasha Catlin, NIEHS/NTP, Research Triangle Park, NC.


An Industry’s Approach to Testing the Safety of Botanicals. Karen VanderMolen, New Chapter Inc./The Procter & Gamble Company, Brattleboro, VT.

In Vitro and Alternative Methods in Ocular Toxicology: The “Eyes” Have It

Thursday, March 16, 8:30 AM to 11:15 AM

Chairperson(s): Mercedes Salvador-Silva, Alcon, a Novartis Company, Fort Worth, TX; and Chris Somp, Pfizer, Inc., Groton, CT.

Endorser(s):
  - In Vitro and Alternative Methods Specialty Section
  - Ocular Toxicology Specialty Section
  - Regulatory and Safety Evaluation Specialty Section

Advanced tissue engineering and microfluidics technologies are providing new opportunities for more predictive in vitro ocular models, including three-dimensional (3D) tissue culture, self-forming organoids, and organ-on-a-chip models. These exciting technologies promise better, more physiologically and structurally relevant, models of the human eye, which will improve predictions of ocular toxicity. The goal of the session is to bring together experts from the pharmaceutical and biotechnology industries, academic institutions, as well as government agencies, to discuss current uses and future challenges of in vitro models for ocular toxicity, and safety assessment of drugs, chemicals, and cosmetics, as well as environmental toxins and medical device materials. The current state of these advanced techniques, the unique issues confronting their development and application, and challenges for validation and regulatory acceptance, will be discussed. This session will start with a broad overview of in vitro ocular safety assessment models, including internationally recognized and validated in vitro ocular irritant models, and their application for cosmetic, pharmacology, and medical device safety assessments. The second speaker will summarize regulatory efforts associated with the development, validation, and international acceptance of alternative in vitro methods for prediction of ocular toxicity, and will discuss the current hurdles and challenges regarding validation and acceptance of alternative methods for ocular toxicity prediction. The third and fourth speakers will describe examples of novel 3D and organ-on-a-chip models, and their application to the physiology and pathophysiology of glaucoma, tear production, and dry eye. The final speaker will discuss the current state and challenges of using stem cells to generate of 3D retinal organoids, and the potential use of organoids for retinal disease models, drug development, and
from ‘omics data, as well as the integration of such data in computational biology approaches to extract relevant biological information. The past years have seen major progress in both bioinformatics and content technologies, providing the large amounts of data necessary to understand biological responses, e.g., time, dose, etc. High throughput and high levels of systems biology are envisioned. Firstly, the integrated interpretation of large scale ‘omics datasets allows for the identification of common denominators that can explain and/or predict adverse biological events. These large datasets together with our rapidly improving understanding of cell biological processes in health and disease, has created the opportunities to re-create biology in silico through mathematical biological modeling. In the latter case these models can be populated in a quantitative way with cell biological experimental data. Both systems biology approaches conceptually fit with the Adverse Outcome Pathway (AOP) framework, with the firm advantage of making such AOP models now computable. In this symposium, we will discuss these different approaches and the opportunities for future safety testing strategies.

**Introduction.** Mercedes Salvador-Silva, Alcon, a Novartis Company, Fort Worth, TX.

**Alternative Methods for Ocular Toxicology Testing.** Frank Barile, St. John’s University, Queens, NY.

**Gaining Acceptance of Alternative Approaches for the Assessment of Serious Eye Damage/Eye Irritation.** João Barroso, EURL ECVM/ Systems Toxicology Unit—IHC, European Commission Joint Research Centre, Ispra (VA), Italy.


**Microengineered Physiological Biomimicry: Human Organ-on-Chips.** Dan Huh, University of Pennsylvania, Philadelphia, PA.

**Structure and Composition of Human Pluripotent Stem Cell-Derived 3D Retinal Structures: Potential Tools for Studying Outer Retinal Toxicity.** David Gamm, University of Wisconsin School of Medicine and Public Health, Madison, WI.

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**ITS** Quantitative Systems Toxicology for Chemical Safety Assessment

**Thursday, March 16, 8:30 AM to 11:15 AM**

**Chairperson(s):** Bob van de Water, Leiden University, Leiden, Netherlands; and Richard Paules, NIEHS, Research Triangle Park, NC.

**Endorser(s):**
- Mechanisms Specialty Section
- Molecular and Systems Biology Specialty Section

The past years have seen major progress in both bioinformatics and systems biology approaches to extract relevant biological information from ‘omics data, as well as the integration of such data in computational biology approaches for safety assessment. This work also has strongly influenced the toxicological community to translate these systems biology findings and methods into approaches that can find ultimate application in chemical safety testing strategies. Different levels of systems biology are envisioned. Firstly, the integrated interpretation of large scale ‘omics datasets allows for the identification of common denominators that can explain and/or predict adverse events, preferably human. Such systems approaches offer great value in risk assessment because they allow an individual observation to be placed in the context of an entire system. To be effective, models must encompass the multiple scales of complexity of biological systems, e.g., from cells to tissues and organs, as well as the multiple dimensions of biological responses, e.g., time, dose, etc. High throughput and high content technologies provide the large amounts of data necessary to create multi-scale and multi-dimensional systems models. Secondly, these large datasets together with our rapidly improving understanding of cell biological processes in health and disease, has created the opportunities to re-create biology in silico through mathematical biological modeling. In the latter case these models can be populated in a quantitative way with cell biological experimental data. Both systems biology approaches conceptually fit with the Adverse Outcome Pathway (AOP) framework, with the firm advantage of making such AOP models now computable. In this symposium, we will discuss these different approaches and the opportunities for future safety testing strategies.

**Introduction.** Bob van de Water, Leiden University, Leiden, Netherlands.

**Systems Biology Strategies for Translational Risk Assessment Using Gene Expression Networks.** James Stevens, Eli Lilly, Indianapolis, IN.

**Implementing Approaches for Moving Tox21 towards Quantitative Systems Toxicology.** Richard Paules, NIEHS, Research Triangle Park, NC.

**Quantitative and Functional Assessment of the Dynamics of Toxicological Key Events in Safety Testing.** Bob van de Water, Leiden University, Leiden, Netherlands.

**Computational Cellular Stress Systems Models to Define the Tipping Point between Adaptive Cellular Capacity and Adverse Outcomes: Implications for Safety Decision Making.** Andrew White, Unilever, Colworth, United Kingdom.

**In Silico Dynamics: Computer Simulation in a Virtual Embryo.** Thomas Knudsen, US EPA, Research Triangle Park, NC.

**Concluding Remarks and Wrap-Up.** Richard Paules, NIEHS, Research Triangle Park, NC.

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**ITS** The Next Technology Wave: Biosensors, Extreme Computing, and Organ Chips for Predicting Cardiovascular Toxicity

**Thursday, March 16, 8:30 AM to 11:15 AM**

**Chairperson(s):** Anthony Bahinski, GlaxoSmithKline, King of Prussia, PA; and Amy Kim, H3 Biomedicine, Cambridge, MA.

**Endorser(s):**
- Cardiovascular Toxicology Specialty Section
- Drug Discovery Toxicology Specialty Section
- In Vitro and Alternative Methods Specialty Section

Development of safe and effective drugs is currently hampered by the poor predictive power of existing preclinical animal models that often lead to failure of drug compounds late in their development after they enter human clinical trials. Given the tremendous cost of drug development and the long timelines involved, major pharmaceutical companies and government funding agencies are now beginning to recognize a crucial need for new technologies that can quickly and reliably predict drug cardiovascular safety and efficacy in humans in preclinical studies, and approaches to integrate these novel technologies within regulatory science and use. This symposium will highlight innovative approaches to developing much-needed new toxicological methods for evaluation of cardiotoxicity, and the role that regulatory agencies such as the US FDA have in developing criteria and potential guidance for quali-
fying these new testing methods. The symposium brings together key experts from the fields of high performance computing using a human heart electrophysiological model, optical electrophysiology to assess arrhythmogenicity, gene editing developing human-induced isogenic pluripotent stem cell models, fluorescent protein biosensors, and Organ Chips developing a 3-dimensional AngioChip. They will highlight and discuss the advantages and challenges inherent in new innovative tools being applied towards identification and characterization of cardiotoxicity. Lastly, the process of qualifying new testing methods into use as a drug development tool will be discussed by the US FDA.

**Introduction.** Anthony Bahinski, GlaxoSmithKline, King of Prussia, PA.

**Towards Predictive Biology with Extreme Computing.** Frederick Streitz, HPC Innovation Center, Lawrence Livermore National Laboratory, Livermore, CA.

**Optical Electrophysiology for Probing Arrhythmogenic Risk in Human iPSC-Derived Cardiomyocytes.** Kit Werley, Q-State Biosciences, Cambridge, MA.

**Human Genome and Tissue Engineering for Cardiac Disease Modeling.** Luke Judge, University of California, San Francisco, San Francisco, CA.

**Applying Fluorescent Protein Biosensors in Microphysiological Systems.** D. Lansing Taylor, University of Pittsburgh, Pittsburgh, PA.

**AngioChip: Vascularization Platform for Organ-on-a-Chip Engineering and Direct Surgical Anastomosis.** Milica Radisic, University of Toronto, Toronto, ON, Canada.

**Advancing FDA Regulatory Science through Innovation.** Suzanne Fitzpatrick, US FDA, College Park, MD.

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**WORKSHOP SESSIONS**

**Biological Advances to Help Navigate the Nonclinical Safety Assessment Strategy in Cancer Immunotherapy: Utility, Limitations, and Future Direction**

**Thursday, March 16, 8:30 AM to 11:15 AM**

**Chairperson(s):** Robert Li, Genentech, South San Francisco, CA; and Jacintha Shenton, Janssen, Philadelphia, PA.

**Endorser(s):**
- Biotechnology Specialty Section
- Immunotoxicology Specialty Section

Therapeutically harnessing the immune system to kill cancer cells is arguably the most significant advance in the treatment of cancer in the past several years. Novel immunotherapies recently approved by the US FDA include two checkpoint inhibitors targeting PD-1, a bispecific T cell redirector targeting CD19, and one oncolytic viral therapy. These drugs have led to long-term responses in a subset of patients that had failed prior therapies. As exciting as these achievements are, tremendous efforts are being invested in the field to increase the proportion of patients benefiting from these therapies. For example, identification of new molecules involved in immune tolerance to cancer cells and their application in immunotherapy as single agents, or in combination to enhance clinical efficacy, are actively being pursued. In addition, there is a multitude of other strategies under investigation, including novel T cell redirectors, genetically-modified T cell therapies, and cancer vaccines. In fact, more than half of the current cancer clinical trials include some form of immunotherapy, many of which are investigating possible combination strategies. In parallel with this paradigm shift in therapeutic options for cancer, safety-related questions are also raised in terms of how to design/tailor nonclinical safety assessment for clinically relevant hazard identification and risk management. The objective of this scientific session is to 1) provide a general overview of the field of cancer immunotherapy (CIT): the current status and the future direction driven by the advances in cancer immunology (e.g. new checkpoints) and bioengineering platforms (e.g. hexamer vs. monomer); 2) highlight the unique challenges in safety assessment for CIT drug development; and 3) promote discussion in regard to assessing the unique challenges of developing these new oncology therapeutics to ensure patient safety.

**Introduction.** Robert Li, Genentech, South San Francisco, CA.

**The Biology of Cancer Immunotherapy.** Brendan Curti, Earle A. Chiles Research Institute, Portland, OR.


**Nonclinical Safety Assessment of a P-Cadherin-Specific T Cell-Recruiting Bispecific Molecule for Cancer.** Cris Kampschroer, Pfizer, Groton, CT.

**Cytokines, T Cell Homeostasis, and Safety Risk: Lessons from CAR T Cell Therapeutics.** Rafael Ponce, Juno, Seattle, WA.

**The Use of Pharmacology in Nonclinical Safety Evaluation of Cancer Immunotherapeutics.** Whitney Helms, US FDA, Washington, DC.
**Microparticles and Exosomes in Cardiopulmonary System-Stem Cell and Microenvironment Regulation by Toxicants**

**Thursday, March 16, 8:30 AM to 11:15 AM**

**Chairperson(s):** Irfan Rahman, University of Rochester, Rochester, NY; and Daniel Conklin, University of Louisville, Louisville, KY.

**Endorser(s):**
- Carcinogenesis Specialty Section
- Cardiovascular Toxicology Specialty Section
- Inhalation and Respiratory Specialty Section

Exosomes are membrane bound extracellular microvesicles that are loaded with a variety of bioactive molecules capable of directly regulating target cells by delivering bioactive components to alter the distal cells. Microparticles (MPs) and exosomes are released from different cell types such as epithelial, fibroblasts, endothelial (MPs or exosomes), tumor cells, and stem cells, including immune inflammatory cells in pulmonary and cardiovascular system. Recent data suggested that environmental agents, PM2.5, inhaled oxidants/toxicants, including cigarette smoke, profibrotic agents, and carcinogens can affect the secretion of exosomes. Exosomes can function as endocrine signal mediators to target cell phenotype. Exosomes released from target cells may have toxicological impact on a paracrine via an intercellular communication in cardiovascular, lung, liver, and circulatory systems. Emerging studies of mesenchymal stem cells (MSC)-derived exosomes show promising therapeutic and beneficial effects. For example, mitochondrial-derived vesicles can encapsulate bioenergetics, which are transported from MSCs to damaged cells. This session will unravel the specific cell-type that is responsible for enriched circulating exosome markers/signatures in toxicology and the pathogenesis of systemic diseases. Intercellular communication, tissue repair vesicles, immunomodulatory effects, biomarkers, nomenclatures and technological advances, and toxicological impact on exosomes and MPs research also will be presented Overall, the workshop will present the novel findings on development of novel exosome signatures as biomarkers, toxicological endpoints by toxicants, and beneficial effects via stem cells in systemic toxicity and diseases. This includes toxicological perspectives of exosomes and microvesicles, e.g., agents and actions by toxicants creating microenvironment for systemic or organ toxicity in cardiopulmonary systems, microenvironment, and toxicants-induced injuries.

**Introduction.** Irfan Rahman, University of Rochester, Rochester, NY.

**The Biology and Function of Exosomes in Microenvironment.**
Raghu Kalluri, University of Texas MD Anderson Cancer Center, Houston, TX.

**Endothelial Microparticles are Associated with PM2.5 Exposure: Implications for Cardiovascular Events.** Tim O’Toole, University of Louisville, Louisville, KY.

**Cellular Microparticles and Exosomes in Stress Responses and Inhaled Toxicant-Induced Pulmonary Diseases.** Luis Ortiz, University of Pittsburgh, Pittsburgh, PA.

**Characterization of Microparticles and Exosomes in Toxicological and Lung Injurious Responses.** Irfan Rahman, University of Rochester, Rochester, NY.

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**Exosome Biogenesis: Models, Predictions and Results in Toxicity.**
Stephen Gould, Johns Hopkins University School of Medicine, Baltimore, MD.

**New Findings on Pyrethroid Developmental Neurotoxicity: An Alternate Approach to Charactering Age-Related Differences to Hazard Identification**

**Thursday, March 16, 8:30 AM to 11:15 AM**

**Chairperson(s):** Charles Vorhees, Cincinnati Children’s Research Foundation & University of Cincinnati, Cincinnati, OH; and Derek Gammon, FMC Corp., Ewing, NJ.

**Endorser(s):**
- Neurotoxicology Specialty Section
- Reproductive and Developmental Toxicology Specialty Section

The neurotoxicity of Type I and Type II pyrethroids in adult rats has been investigated for many years, and the principal mechanism of action on voltage-sensitive sodium channels (VSSC) is well established. By contrast, there is relatively little published data on the developmental effects of these compounds, on potential sex differences, on their long-term effects, or on neurotransmitter systems. This is important because household pyrethroid use has increased following restriction of organophosphorus insecticides. The prevailing view is that these compounds have no long-term effects, but new evidence suggests this may not be the case. Recent data also demonstrate that early exposure can affect neurotransmitter systems. There are also newer data showing differences as a function of age and sex and these differences depend
on the type of pyrethroid and dose. The purpose of this workshop is to bring forward new data on the above topics with deltamethrin (Type II) and permethrin (Type I) as examples for effects on voltage-gated ion channels, startle, locomotor activity, learning and memory, and their relationship to brain and plasma concentrations. The relative sensitivity of young vs. adult animals, the long-term effects of early exposure, pharmacokinetics, and sex effects, provide new insights into these compounds. This is timely because the US EPA has pyrethroids under review and has noted need for data to better characterize effects in children. The workshop will begin with a presentation that will lay the foundation for how Type I and Type II pyrethroids affect VSSC and other ion channels in different species. The presenter also will describe atypical (Type III) pyrethroids that have mixed effects. This will be followed with a presentation that will show new data on the pharmacokinetics of deltamethrin and permethrin in young rats. The next talk will present new data on the effects of deltamethrin exposure on sodium channel expression and glutamate release. This will be followed with a presentation on new data on early versus adult effects of deltamethrin and permethrin on acoustic startle, and of deltamethrin on learning and memory. As a conclusion, the panel will be joined by California EPA scientist Dr. Poorni Iyer who, along with Dr. Gammon, will lead a discussion of the implications of the new data for hazard characterization for protecting children and place the data in context.

**Effects of Pyrethroids on Voltage-Sensitive Ion Channels.**
Derek Gammon, FMC Corp., Ewing, NJ.

**Lack of Age-Dependent Differences in Pyrethroid Internal Dosimetry at Low Exposure Levels.** James Bruckner, University of Georgia, Athens, GA.

**Developmental Deltamethrin Exposure Causes Long-Term Downregulation of Nav Protein and Reduced Neurotransmitter Release.** Jason Richardson, Northeast Ohio Medical University, Rootstown, OH.

**Developmental Effects of Pyrethroids on Acoustic Startle and on Learning and Memory.** Charles Vorhees, Cincinnati Children’s Research Foundation & University of Cincinnati, Cincinnati, OH.

**Panel Discussion.** Poorni Iyer, California EPA, Sacramento, CA.

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**MONDAY**

**Drug Development and SEND: Evolving Current Practices Toward Future Opportunities**

**Monday, March 13, 9:00 AM to 10:00 AM**

**Presented by:**

MPI Research

SEND represents a unifying platform with the potential to revolutionize the approach to, and context of, drug safety evaluation efforts. The session explores this potential by comparing and contrasting methodologies in the period before SEND with those anticipated in the period after SEND implementation.

**Immunology—Worth All the Hype? You Bet It Is.**

**Monday, March 13, 9:00 AM to 10:00 AM**

**Presented by:**

Envigo

Non-clinical safety assessment studies with products designed to activate or suppress the immune system are increasingly complex. But with the availability of reagents to quantitatively and qualitatively measure immunopharmacology and immunotoxicology increasing, this means the acquisition of high quality data on safety studies has entered a golden age.

**An Overview of Preclinical Microsampling Techniques and Their Bioanalytical Challenges**

**Monday, March 13, 10:30 AM to 11:30 AM**

**Presented by:**

Altasciences Clinical Research

This session will outline the pros and cons of various microsampling techniques such as DBS, capillary microsampling (CMS) and volumetric absorptive microsampling (VAMS). The bioanalytical challenges of each technique for use in regulated bioanalysis will be highlighted. Case studies using VAMS will be presented.

**From Cells to Society and Beyond: Diversity and Scope of Neurotoxicology Testing at Battelle**

**Monday, March 13, 10:30 AM to 11:30 AM**

**Presented by:**

Battelle

Explore the diverse applicability of neuroscience-based endpoints in toxicology studies. Highlights include neurobehavioral testing for pharmaceutical and chemical safety, novel applications like simultaneous cardiovascular measurements during real time performance in behavioral tests, *in vitro* and *in vivo* chemical weapon and nerve agent countermeasures, and preclinical support for clinical applications.

**In Silico Strategies to Assess Potentially Mutagenic Impurities under ICH M7**

**Monday, March 13, 10:30 AM to 11:30 AM**

**Presented by:**

Lhasa Limited

Lhasa Limited, the world leader for knowledge and data sharing in chemistry and the life sciences will present on the different strategies that can be used to assess the risk of impurities under ICH M7, including the generation of purge based arguments and mutagenicity prediction methodologies.

**Mechanistic Insights into Contractility and Electrophysiology Complemented by Optical stimulation of iPS Cardiomyocytes**

**Monday, March 13, 10:30 AM to 11:30 AM**

**Presented by:**

Nanion Technologies and Axiogenesis

Here we present 1) a pioneering approach for simultaneous optogenetic stimulation and recording of electrophysiological and contractile parameters of iPS cardiomyocytes; 2) multiple high-throughput patch clamping platforms for assessment of acute/chronic drug effects; and 3) the application of these technologies for cardiac safety assessment in accordance with CiPA.
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Begin with the SEND in Mind: Learnings, Challenges and Opportunities
Monday, March 13, 12:00 Noon to 1:00 PM
Presented by: Covance, Inc.
Leading up to the December 2016 deadline, SEND has been a highly anticipated and widely discussed topic. Now that we’re “live,” what have we learned in implementing SEND 3.0 that can help the next evolution go more smoothly?

Developing an Implementation Strategy for Toxicity Testing in the 21st Century
Monday, March 13, 12:00 Noon to 1:00 PM
Presented by: National Institute of Environmental Health Sciences and the National Toxicology Program
A strategy for the safe, effective, and timely implementation of 21st century toxicity testing approaches in the US is under development. This session will provide an update on ongoing efforts towards developing this strategy, and foster engagement in this process from stakeholders from the industrial, academic, animal welfare, and regulatory sectors.

Novel Pulmonary Exposure Studies Examine the Effects of Airborne Toxins
Monday, March 13, 12:00 Noon to 1:00 PM
Presented by: Data Sciences International
3D printer emissions and Firefighters have what in common? Join us to learn how researchers maximized their study designs to evaluate the effects of airborne toxins. Discussion will highlight inhalation technology for post-exposure studies and the use of implantable telemetry for respiratory breathing rate/amplitude experiments.

The Minipig as a Disease Model in Translational Medicine
Monday, March 13, 12:00 Noon to 1:00 PM
Presented by: Sinclair Research Center, LLC
The minipigs are becoming routinely used both in experimental pharmacology and as a therapeutic model for human diseases. Translational preclinical minipig data presented here support the current understanding that minipigs are the animal model of choice for the assessment of drugs targeting endocrine, dermal, and ocular disorders.

Beyond REACH
Monday, March 13, 1:30 PM to 2:30 PM
Presented by: Charles River
Recent changes to REACH legislation and its guidance, the substance identity focus, etc., make it challenging to meet the 2018 deadline, and to register new substances. Companies should consider a global approach to testing of industrial chemicals, including regions such as China or USA with its updated TSCA requirements.

Generating Dry Powder Aerosols from Nanomaterials: A Precision Art
Monday, March 13, 1:30 PM to 2:30 PM
Presented by: Inhalation Sciences Sweden AB
How do you generate dry powder aerosols from nanoparticles to enhance your research results? Aerosol authority Per Gerde explain why PreciseInhale dry powder aerosol technology is the system of choice for nanoparticle researchers at Dow Chemicals, Karolinska Institutet and more.

Optimized Testing of Nanomaterials: A Case Report
Monday, March 13, 1:30 PM to 2:30 PM
Presented by: Fraunhofer ITEM
As an example of sophisticated nanomaterial testing, this session will present a tiered approach for different multi-walled carbon nanotubes. Information will include the generation of specific test atmospheres, results from different types of in vivo studies and innovative in vitro studies for elucidation of biological effects and their underlying mechanisms.

Replacement of Animal Testing for CLP/GHS Potency Classification of Skin Sensitizers Is Now Possible using a Modified Genomic GARDskin [OECD TGP 4.106] Assay
Monday, March 13, 1:30 PM to 2:30 PM
Presented by: SenzaGen AB
SenzaGen presents the latest development towards reliable potency classification of chemicals according to CLP 1A and 1B, taking both LLNA and Human potency data in consideration. The assay is based on GARDskin and utilizes a refined gene expression signature developed specifically for potency categorization with high predictability.
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**Global Initiatives for Replacement, Refinement and Reduction in Animal Use within Toxicology Programs**

**Monday, March 13, 3:00 PM to 4:00 PM**

**Presented by:**
NC3Rs

This session will highlight opportunities for reductions or refinements in animal use, within (bio)pharmaceutical toxicology programs. Organized by the UK’s national centre for the 3Rs (NC3Rs), it brings together scientists and regulators from NC3Rs-led, international consortia to discuss initiatives investigating future efficiencies in study designs and promoting best practice.

**Highly Relevant Proprietary Data and Predictive Models for Drug Development**

**Tuesday, March 14, 9:00 AM to 10:00 AM**

**Presented by:**
Lhasa Limited and Molecular Networks

Lhasa Limited and Molecular Networks will provide an overview of a new resource to improve early drug candidate safety assessment. Resulting from the eTOX project, eTOXsys provides high quality proprietary toxicity data and predictive models integrated into an overall decision-making tool.

**TUESDAY**

**Challenges in Addressing Testicular Toxicity: A Pathologist’s Perspective**

**Tuesday, March 14, 9:00 AM to 10:00 AM**

**Presented by:**
MPI Research

Testicular toxicity is a common finding in nonclinical toxicity testing. Histopathology of the tests is the most sensitive method for detection of effects on spermatogenesis, and the toxicologic pathologist plays a key role in hazard characterization and mitigation of risk when testicular toxicity is identified in nonclinical safety studies.

**EU REACH Submissions; Learn the Lessons—Avoid the Mistakes**

**Tuesday, March 14, 9:00 AM to 10:00 AM**

**Presented by:**
Envigo

REACH has changed the toxicological landscape—the demand for maximum information coupled with an obligation to minimize animal consumption, has meant the development of net new tests and the refinement of others. Using a case study approach, these developments will be described with all-aspect data generation examples.

**Detect Apoptosis in Real Time with a Plate Reader Using a Novel Homogeneous Luminescent Assay**

**Tuesday, March 14, 10:30 AM to 11:30 AM**

**Presented by:**
Promega Corporation

We will describe novel homogeneous, multimode plate reader assays to detect apoptosis and necrosis in real time. Addition of annexin v-luciferase fragment fusion proteins generate light only when bound to apoptotic cells. Multiplexing with a DNA dye enables detection of necrotic cells from the same wells over multiple days.

**Integrated Approaches for Inhalation Toxicity Assessment**

**Tuesday, March 14, 9:00 AM to 10:00 AM**

**Presented by:**
Fraunhofer ITEM

This session will focus on integrated approaches to testing and assessment (IATA) in inhalation toxicology combining the data from different alternative approaches such as human airway epithelial cells and fresh human lung material. A case study using these methods for a stepwise approach in risk assessment will be critically discussed.

**Hepatocyte Spheroids for Toxicity Evaluation**

**Tuesday, March 14, 10:30 AM to 11:30 AM**

**Presented by:**
In Vitro ADMET Laboratories Inc.

Hepatocyte spheroids maintain in vivo-like cell-cell contact with long-term maintenance of liver functions, including drug metabolic enzyme activities. Properties of spheroids cultured from human and animal hepatocytes as hepatocyte monocultures and as hepatocyte/Kupffer cell co-cultures, and their application in the evaluation of drug metabolism and hepatotoxicity will be reviewed.
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Neurotox and Cardiac Safety Assessment: Case Studies Employing iPS Cell Lines, MEA, and Optogenetic Techniques

Tuesday, March 14, 10:30 AM to 11:30 AM

Presented by:
Axiogenesis AG and Axion Biosystems

Discover the predictive power of Axiogenesis iPS cardiomyocytes and neurons with Axion BioSystems’ Maestro multiwell MEA platform. Experts in the field will present their case studies in neurotoxicology (HESI NeuTox) and cardiac safety (CiPA) in conjunction with innovative new products that control in vitro assays through optogenetic techniques.

Quantitation of Biotherapeutics by LC/MS: Finding Its Groove in Preclinical Toxicology

Tuesday, March 14, 10:30 AM to 11:30 AM

Presented by:
Charles River

LC/MS quantitation of biotherapeutics has evolved as a differentiated tool supporting investigative toxicology. Research demonstrates this methodology 1.) satisfies FDA criteria for TK assessments; 2.) addresses limitations of ligand binding assays techniques related to selectivity of endogenous analogs and metabolites; and 3.) mitigates reagent generation issues.

DILIsym: A Computational Tool for Assessing the Risk of Drug-Induced Liver Injury

Tuesday, March 14, 12:00 Noon to 1:00 PM

Presented by:
DILIsym Services Inc.

A quantitative systems toxicology (QST) model of drug-induced liver injury (DILI) has been developed through the DILI-sim Initiative over the past 7 years (DILIsym) to assist in the safety characterization of compounds in clinical development. Case studies will be presented demonstrating how drug metabolism and disposition intersect with hepatotoxicity. Lunch will be provided to attendees while supplies last.

Advantages with Genome Testing Opening up the Landscape for New Application Possibilities for Sensitization Testing using SenzaGen’s Genomic GARD Assay

Tuesday, March 14, 1:30 PM to 2:30 PM

Presented by:
SenzaGen AB

SenzaGen’s GARD assay is based on expression analysis of predictive genomic biomarker signatures. Prediction calls of test substances are generated by computational methods based on machine learning. SenzaGen presents their experience in skin and respiratory sensitization testing, working with challenging compounds and mixtures, active substances, potency classification and NOEL interpretation.

Novel in Vitro Models for the Study of Drug-Induced Hepatotoxicity

Tuesday, March 14, 12:00 Noon to 1:00 PM

Presented by:
Corning Incorporated

Corning Life Sciences offers several novel in vitro model systems for drug-induced hepatotoxicity. This workshop will provide an applications overview using Corning® HepatoCells, which are single-use, cryopreserved cells, derived from primary human hepatocytes, and cellular fractions from mammalian cells expressing recombinant ABC transporters, which are important hepatotoxicity targets.

A New Pathway and Related Assay Systems and Biomarkers for the Study and Prediction of Cholestasis Side Effects of Xenobiotics

Tuesday, March 14, 12:00 Noon to 1:00 PM

Presented by:
Biopredic International

Our lecture will rely on two papers published that year and that explain that the bile canalicular contraction and the RhoK and the MLCK enzymes regulating the level of phosphorylated light chain myosin are the targets of cholestatic compounds.
Get your fast pass into this year’s event on Monday, March 13, in booth 2243.
Exhibits

Exhibitor-Hosted Sessions

Comprehensive Solutions for Genotoxicity Evaluation of All Products (QSAR to Screening, to GLP Assays)

Tuesday, March 14, 1:30 PM to 2:30 PM

Presented by: MilliporeSigma

Genotoxicity Experts from MilliporeSigma will outline and discuss the myriad of assays and paradigms for the hazard, safety assessment or preclinical evaluation of all types of products. BioReliance’s complete line of services includes: QSAR, HTP and predictive screening, GLP regulatory, and assays to follow up a Genetox positive result.

Functional Assays for Assessing Mitochondrial Toxicity and Metabolism of Live Cells

Tuesday, March 14, 1:30 PM to 2:30 PM

Presented by: Agilent Technologies

As toxicology testing moves more toward in vitro methods, robust cell-based assays for the assessment of mitochondrial toxicity of drug candidates are required. The Seahorse XF Analyzer has been successfully used to screen for mitochondrial toxicity and can distinguish mitochondrial toxicity from overall loss of viability.

Neurotoxicology Investigations in the Minipig

Tuesday, March 14, 1:30 PM to 2:30 PM

Presented by: Marshall BioResources, Ellegaard Göttingen Minipigs, and CiToxLAB

Neurotoxicology is critical in various therapeutic indications such as anti-infectives, oncology, CNS and metabolic diseases. The limited translational value of rat FOB has raised interest for non-rodent neurotoxicology/neuropharmacology. A full battery of minipig neurological investigations to support drug development will be discussed in the context of this growing concern.

Evaluating the Developmental Toxicity Potential of the ToxCast Chemical Library with devTOX quickPredict

Tuesday, March 14, 3:00 PM to 4:00 PM

Presented by: Stemina Biomarker Discovery

devTOX quickPredict is a reliable, in vitro, human pluripotent stem cell-based assay used to assess chemicals for potential developmental toxicity affecting differing developmental lineages. We will discuss how the assay performs with the ToxCast chemical library and how the US EPA is using the data in support of Tox21.

New Life for Natural Killer Cell Assays Using Non-Radioactive Approaches

Tuesday, March 14, 3:00 PM to 4:00 PM

Presented by: Covance, Inc.

The Natural Killer cell is a key component of the innate immune system. Historically a chromium-release cytotoxicity assay has been used in preclinical drug development studies. We will present data using nonradioactive plate- and flow-based methods and discuss the use of the NKc assay to complement standard toxicology studies.
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Exhibits

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**Trends, Trials, and Triumphs in In Vitro Toxicology**
**Tuesday, March 14, 3:00 PM to 4:00 PM**

Presented by:  
Charles River and  
National Institutes of Environmental Health Sciences

*In vitro* alternatives for toxicology screening and animal testing are increasing in variety. While validation against animal tests is costly and may result in false rejection, human clinical, and/or mechanistic data is revolutionizing our acceptance and understanding of these tests. Such knowledge will serve to guide our future testing strategies.

**WEDNESDAY**

**IACUC 101: Balancing Requirements for Animal Welfare and Defining Test Article Safety**
**Wednesday, March 15, 9:00 AM to 10:00 AM**

Presented by:  
MPI Research

An attending veterinarian and a senior toxicologist, who are members of an IACUC, discuss common challenges institutions face for meeting the expectations of animal welfare regulations, while still ensuring the validity of data. Although approaches can differ based on perspective, strategies for win-win solutions will be discussed.

**Quantitative Measures Associated with DNA and RNA Therapeutics**
**Wednesday, March 15, 9:00 AM to 10:00 AM**

Presented by:  
Charles River

Increasing interest in the development of Oligonucleotide therapeutics among Biotech and Large Pharma companies has been recently fuelled by the approval of Mipomersen. Sensitive and selective bioanalytical methodologies are key to the development process. Chromatographic and hybridization ELISA approaches will be reviewed, compared and contrasted.

**Genetic Toxicology—Is It Still Relevant or Even More Critical?**
**Wednesday, March 15, 10:30 AM to 11:30 AM**

Presented by:  
Envigo

Genetic toxicity remains one of the few areas that can stop the development of a material. Since its birth in the 1970s it is still regarded as an arcane branch of toxicology with often unruly assays and immeasurable interpretation; but things are changing. Long standing traditions being called into question.

**Minipigs in Translational Immunosafety Sciences**
**Wednesday, March 15, 10:30 AM to 11:30 AM**

Presented by:  
Ellegaard Göttingen Minipigs, Marshall BioResources, and  
Novartis Pharma

The increasing number of new drug targets to modulate immunological pathways has triggered interest to explore the porcine immune system. More systematic comparisons regarding the innate and adaptive immune system in pigs and minipigs are needed to assess the significance of immunological findings in minipigs to support translational safety sciences.

**ICCVAM Tools for Validation and Regulatory Application of Alternative Methods**
**Wednesday, March 15, 1:30 PM to 2:30 PM**

Presented by:  
National Institutes of Environmental Health Sciences

New technologies have enabled the development of complex cell-based and computational models to assess toxicity. Creating bridges between these technologies and regulatory applications requires access to computational tools and data. This session will detail existing tools available from ICCVAM member agencies as resources for stakeholders.
Global **Toxicology** Issues SLR can help with

**Stewardship**
- Worker Safety
- Animal Studies
- *In vitro* Studies
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- Dose range finding (DRF)
- Sub-chronic & chronic toxicity, with recovery phases
- 14-day & 28-day repeat dose
- Systemic toxicology
- Specialty toxicology, including but not limited to: ocular, dermal & subcutaneous, bone, juvenile, & phototoxicity

**Miniature swine specialty studies**
- Repeat-dose dermal irritation & dermal toxicology
- Phototoxicity
- Reproductive toxicology (Segments I & II)

**Other studies**
- Target animal safety (TAS) studies
- FDA Redbook feeding trials
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Deadline: May 15, 2017

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1. To present new developments in toxicology
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Session Types

Continuing Education—Emphasis on quality presentations of generally accepted, established knowledge in toxicology
Note: CE Courses will be held on Sunday.

Symposia—Cutting-edge science, new areas, concepts, or data

Workshops—State-of-the-art knowledge in toxicology

Roundtables—Controversial subjects

Historical Highlights—Review of a historical body of science that has impacted toxicology

Informational Sessions—Scientific planning or membership development

Education-Career Development Sessions—Sessions that provide the tools and resources to toxicologists that will enhance their professional and scientific development

Regional Interest—Central topics of relevance that describe public health and/or ecological problems of a particular region

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