



Preliminary Program

55th Annual Meeting and ToxExpo™

March 13–17, 2016

*New Orleans,
Louisiana*



SOT | Society of
Toxicology
Creating a Safer and Healthier World by Advancing
the Science and Increasing the Impact of Toxicology
www.toxicology.org



Dear Colleagues:

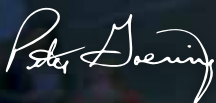
The Society of Toxicology 55th Annual Meeting and ToxExpo, March 13–17, 2016, in New Orleans, Louisiana, promises stimulating lectures and presentations on scientific breakthroughs, important education and professional training opportunities, and time to connect with friends and create new collaborations.

I am pleased to announce that this year's meeting contains an exciting twist to our familiar program, as we will be featuring five talented and cutting-edge scientists through two plenary sessions, one each on Monday and Tuesday, and the Medical Research Council keynote on Wednesday. This new format allows you more access to emerging scientific knowledge. Our goal is to provide a forum for novel discoveries and approaches related to toxicology and to facilitate the advancement of toxicology by fostering the integration of toxicology with other biomedical disciplines. Through these endeavors we are working towards fulfilling our mission of creating a safer and healthier world by advancing the science and increasing the impact of toxicology.

Beyond this change, the program for our meeting at the Ernest N. Morial Convention Center in New Orleans contains all of the activities for which this premier event is known: more than 150 scientific sessions; thousands of abstract presentations; continuing education courses; approximately 350 ToxExpo vendors offering you the latest information on services and technology; awards presentations; receptions; career guidance and support; student activities; and more.

Please join me in New Orleans for our 55th Annual Meeting and ToxExpo, where collaborations begin and learning never ends.

Sincerely,



Peter L. Goering, PhD
2015–2016 SOT President

Welcome



Preliminary Program Contents



55th Annual Meeting and ToxExpo

March 13–17, 2016

2	SOT 2016 Annual Meeting Mobile Event App
5	<i>Preliminary Program</i> Content Reference Guide
6	Scientific Program Overview
10	Thematic Approach Index
14	SOT Annual Meeting
18	Hotel and Travel
24	Registration
30	General Information
42	Career Advancement and Development Resources
46	Awards and Fellowships
52	Special Events
64	Continuing Education
74	Scientific Sessions
118	ToxExpo Exhibits
134	Support and Marketing Opportunities

SOT 2016 Annual Meeting Mobile Event App

Download the SOT 2016 Mobile Event App in February. The Mobile Event App synchronizes with your schedule built in the Online Planner. Use these tools to manage your time and maximize your experience during the Annual Meeting.

The Mobile Event App will allow you to:

- Connect with fellow attendees
- Build your own schedule and synchronize from the Online Planner to your iPad, tablet, and smartphone simply by logging in
 - ▶ Add individual presentations or entire sessions to your schedule
 - ▶ Add a specific session abstract to your schedule
 - ▶ Add your own items to your schedule
- View presentation details, abstracts, and ePosters
- Boolean search for items based on session title, abstract title, abstract keywords, thematic track, and author name or affiliation
- View and interact with speakers
- View the New Orleans Ernest N. Morial Convention Center map and New Orleans city maps
- Navigate the real-time ToxExpo floor plan and search for products, specials, and exhibitors
- Contact exhibitors
- Integrate with ToXchange, Twitter, and Facebook

Available via the SOT website in January—Use the Online Planner to build your custom Annual Meeting schedule from your computer.

Online Planner Features:

- Boolean search schedule
- Separate speaker and abstract tabs
- Collapse/expand by day, view abstracts
- Schedule export for iCal and PDF
- Synchronizes with Mobile Event App

Download the app early February from your favorite app marketplace and access the Online Planner beginning in January via the SOT website.

To purchase an advertisement on the mobile app, please go to **www.toxexpo.com**.





Dear Colleagues,

On behalf of the Scientific Program Committee and the Society of Toxicology, I would like to invite you to join us at our 55th Annual Meeting to be held from March 13–17, 2016, at the New Orleans Ernest N. Morial Convention Center.

As always, it is our goal to construct a program that reflects the best science as well as the breadth of interests across the SOT membership. We believe that the 2016 Symposia, Roundtables, Workshops, and other special sessions are timely and highly informative and span a broad spectrum of topics to meet the diversity of our membership.

We are excited to introduce a new format to this year's program: Two Plenary sessions (on Monday and Tuesday morning), highlighting two timely themes, and featuring two world-renowned lecturers for each Plenary session. The Monday Plenary session is built around the theme of Regenerative Medicine and Tissue Engineering, and will feature Dr. Doris Taylor, Director of Regenerative Medicine Research at the Texas Heart Institute in Houston, Texas, who will provide a presentation titled "Building a Heart: From Cells to Tissues to Organs," and Dr. Joan Nichols, Associate Director of the University of Texas Medical Branch in Texas, who will offer a presentation on lung bioengineering: "From 3D Microchip to Human Organ Culture Models: Trachea, Bronchi/Bronchiole and Lung Biomimetic Models for Disease Modeling, Drug Discovery and Toxicology Evaluation."

The Tuesday Plenary session is on the theme of Inflammation and Neurodegenerative Disease, and will feature Dr. Stephen Skaper, University of Padua, with the presentation "Mast Cells and Glia: Two Tracks on the Road to Neuroinflammation," and Dr. Alan I. Faden, Director, Center for Shock, Trauma and Anesthesiology Research at the University of Maryland School of Medicine, who will present "Inflammation and Neurodegeneration in CNS Injury: Evolving Concepts and New Therapeutic Targets."

This year's keynote Medical Research Council (MRC) lecture will be Regenerating CNS Myelin—From Mechanisms to Medicines, featuring Dr. Robin J. M. Franklin. Dr. Franklin is Head of Translational Science at the Wellcome Trust-Medical Research Council Cambridge Stem Cell Institute and Director of the UK MS Society Cambridge Centre for Myelin Repair at the University of Cambridge. His main research questions are *how stem cells in the adult brain respond to injury, how do they contribute to regeneration, and how are they affected by aging?*

The 2016 Meet the Directors session will feature a conversation with Dr. Linda Birnbaum, Director of the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH), and Dr. Christopher Austin, Director of the National Center for Advancing Translational Sciences (NCATS), National Institutes of Health, concerning scientific directions and priorities for NIEHS and NCATS, including funding priorities and outlooks, and training opportunities.

In addition to the diverse scientific sessions and featured Plenary, MRC, and Meet the Directors sessions, the meeting will feature lectures from the recipients of distinguished Society Awards. These include the Merit and Distinguished Toxicology Scholar Awards reflecting sustained contributions in toxicology, along with the Translational Impact and Leading Edge in Basic Science Awards, which will highlight significant contributions that impact toxicology and contribute to enhancing human health. Although a busy scientific program, this year's program has been organized to dedicate some time for networking with colleagues, an important adjunct to the outstanding scientific content of the meeting.

We are very excited about returning to New Orleans for the first time since 2005. The newly renovated convention center is located directly on the Mississippi River, adjacent to the Warehouse/Arts District, and a leisurely 15 minute walk to the French Quarter. Nearby attractions include the Aquarium of the Americas, Woldenberg Riverfront Park, Lafayette Square, and the riverboat docks. A \$2 Canal Street Ferry ride across the river will take you to the historic Algiers section of New Orleans.

In addition to the almost 2,500 abstracts currently scheduled to be presented during the Annual Meeting, interested participants are welcome to submit late-breaking abstracts from December 5, 2015, through January 12, 2016. The submission fee for late-breaking abstracts will be \$50. Abstracts accepted during this final submission phase will be programmed into poster sessions that will be presented on Thursday, March 17, and will not be included in the printed copy of *The Toxicologist*, but will be available through the Mobile Event App. Late-breaking abstracts should be submitted online at www.toxicology.org. We look forward to welcoming you to lively New Orleans!

Warmest regards,

John B. Morris, PhD, ATS

SOT Vice President and Scientific Program Committee Chairperson, 2015–2016



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55th Annual Meeting
Past Presidents' 5K Fun Run/Walk
New Orleans, Louisiana
March 15, 2016
Audubon Park

"People who get together to sweat together, stay together!"
—Jay Goodman, SOT Past President

Register by February 5 to receive a commemorative t-shirt!
www.toxicology.org/funrun

Supported by:



Additional Support Opportunities Are Available!
Visit www.ToxExpo.com for Details.

Please see page 54 for more details.

Key Deadlines

Late-Breaking Abstract Submission
January 12, 2016

Early-Bird Registration
January 15, 2016

Housing Reservation
February 12, 2016

Standard Registration
February 12, 2016

Registration Cancellation
February 12, 2016



Important Program Information

In an effort to conserve resources, the printed *Program* will be mailed **ONLY** by request—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 15, 2016, 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

Section	Description
Scientific Program Overview (pages 6–9)	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 <i>Program</i> or Annual Meeting website for detailed information.
Thematic Session Index (pages 10–11)	All of the Annual Meeting sessions highlighted within the six themes are indicated through the use of six unique symbols, one for each theme. The themes and symbols are listed in the following pages of the <i>Preliminary Program</i> . There are 53 Scientific Sessions and 13 CE courses aligned to one or more of the themes.
Special Events (pages 52–63)	The 55th Annual Meeting Recognition and Social Events details are provided in this section—including the Regional Chapter, Special Interest Group, and Specialty Section reception schedules; Student/Postdoctoral Scholar Events. This section includes the Educational Outreach initiatives, including the Undergraduate Education Program.
Continuing Education Courses (pages 64–72)	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.
Featured Sessions (pages 75–79)	This section lists the Daily Plenary Sessions and other special lectures and scientific sessions for the 2016 Annual Meeting. Detailed information for these sessions will be available in the final <i>Program</i> .
Scientific Sessions (pages 81–117)	The <i>Preliminary Program</i> layout is similar to that of the final <i>Program</i> . Specifically, this section lists the scientific sessions in date, time, and alphabetical order for Symposia, Workshops, Historical Highlights, Roundtables, Informational, Education-Career Development, and the Regional Interest sessions.
Exhibits (pages 118–130)	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.

Session Types

Education-Career Development Sessions (80 minutes)—

Sessions that provide tools and resources to toxicologists that will enhance their professional and scientific development (page 115).

Exhibitor-Hosted Sessions (60 minutes)—Informative sessions developed by an exhibiting company (page 122).

Featured Sessions (50–165 minutes)—Plenary, Keynote, and other special lectures (page 74).

Historical Highlight Sessions (165 minutes)—Sessions that provide a review of a historical body of science that has impacted toxicology (page 112).

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 (page 113).

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*).

Regional Interest Sessions (165 minutes)—Central topics of relevance that describe public health and/or ecological problems related to the region (page 117).

Roundtable Sessions (80 minutes)—These provide an overview of controversial subjects, followed by questions and discussion (page 110).

Symposium Sessions (165 minutes)—Cutting-edge science, emphasizing new areas, concepts, and data (page 81).

Workshop Sessions (165 minutes)—Generally accepted, state-of-the-art knowledge in toxicology in informal interactive presentations with ample time for discussion (page 92).



Use the Mobile Event App or the Online Planner to plan your schedule to make the most of your time during the Annual Meeting. See page 2 for details.

Scientific Program Overview



Scientific Themes

- Advances in Neurotoxicology
- Developmental Toxicity: Mechanisms and Evaluation
- Health and Environmental Impacts of Man-Made and Naturally Released Toxicants

- Molecular Toxicology: Mechanistic Insights and Hazard Assessment
- Recent Advances in Safety Assessment
- Toxicity of Metals

Sunday, March 13

7:00 AM to 7:45 AM

CONTINUING EDUCATION SUNRISE MINI-COURSE

- SR01 Basic Principles and Practices for Applying Epigenetics in Mechanistic Toxicology

8:15 AM to 12:00 Noon

CONTINUING EDUCATION MORNING COURSES

- AM02 Advancing the Detection, Imaging, and Pitfalls in Monitoring Oxidative Stress in Health and Disease
- AM03 Adverse Outcome Pathway (AOP) Development and Evaluation
- AM04 Contribution of Mitochondria to Drug-Induced Organ Toxicities
- AM05 Discovery and Validation of miRNA Biomarkers Bridging Preclinical and Clinical Toxicity: Lessons Learned from Hepatotoxicity
- AM06 Embryology and Developmental Toxicity Testing
- AM07 Next-Generation Sequencing in Toxicogenomics

1:15 PM to 5:00 PM

CONTINUING EDUCATION AFTERNOON COURSES

- PM08 Approaches to Investigate and Assess Risks Associated with Drug-Induced Liver Injury (DILI)
- PM09 Exploring Chemical Space in the New Toxicity Testing Paradigm: From Data Curation to Computational Simulations
- PM10 Genetics and Population Variability in Chemical Toxicity: The What, the How, and So What?
- PM11 Human Health Risk Assessment: A Case Study Application of Principles
- PM12 Unique Approaches to Safety Assessment of Gene, Cell, and Nucleic Acid-Based Therapies
- PM13 Zebrafish As a Tool in Toxicology and Drug Discovery Screening

Monday, March 14

8:00 AM to 9:20 AM

DAILY PLENARY SESSION

- Regenerative Medicine and Tissue Engineering
Lecturers: Doris Taylor, Texas Heart Institute; and Joan Nichols, University of Texas Medical Branch



9:30 AM to 12:15 PM

SYMPOSIUM SESSION

- Opening the Black Box: Understanding the Molecular Mechanisms of Developmental Toxicity

WORKSHOP SESSIONS

- Dietary Exposures to Heterocyclic Amines As a Potential Risk Factor for Neurological Disease
- Mitochondria As the Central Target of Environmental Contaminants, Pharmaceutical Agents, and Toxicants: Mechanisms of Toxicity and Disease
- Nanotoxicology and Ocular Drug Delivery: One Size Does Not Fit All
- Scientific Reproducibility: Does This Pose a Problem for 21st Century Toxicology?
- The Cancer Risk Assessment for Ingested Hexavalent Chromium: Challenges and Controversies
- Transient Receptor Potential A1 (TRPA1) Cation Channels: Fluttering Hearts, Headaches and Hot Flashes—Can One “Environmental Sensor” Be the Cause of All the Pain?

REGIONAL INTEREST SESSION

- The Toxicological Implications of the Gulf Oil Spill: Research Accomplishments and Research Needs

PLATFORM SESSIONS

- Investigating Mode of Action in Chemical Carcinogenesis
- Ozone Research

9:30 AM to 12:45 PM

POSTER SESSIONS

- Arsenic Toxicity
- Bioinformatics and Toxicology
- Biomonitoring
- Cell Death and Apoptosis
- Immunotoxicology
- Neurotoxicology of Therapeutic Agents and Abused Substances
- Neurotoxicology—Developmental Neurotoxicity
- Neurotoxicology—Emerging Technologies for Neurotoxicity Screening
- Neurotoxicology—General
- Neurotoxicology—Halogenated Hydrocarbons
- Respiratory Toxicology
- Systems Biology and Toxicology
- Toxicity of Metal Mixtures

9:30 AM to 4:30 PM

RESEARCH FUNDING DISCUSSIONS

- Network with Program Officers

12:00 Noon to 1:30 PM

RESEARCH FUNDING SESSION

- Research Funding Luncheon

12:30 PM to 1:20 PM

MERIT AWARD LECTURE



Lecturer: Melvin Andersen, The Hamner Institutes for Health Sciences

12:30 PM to 1:50 PM

ROUNDTABLE SESSIONS

- Is a “Thresholdable” Carcinogen Still a Delaney Carcinogen?
- Trichloroethylene Exposure and Development of Fetal Cardiac Malformations: What Do the Data Tell Us About Inhalation Exposures Resulting from Vapor Intrusion and Potential Health Risks to Pregnant Women?

1:15 PM to 4:30 PM

POSTER SESSIONS

- Exposure Assessment
- Genetic Toxicology I
- Genetic Toxicology II
- Mercury Toxicity ♣
- Metal Toxicity ♣
- Mixtures ♥
- Nanotoxicology: General
- Natural Products ♥
- Neurotoxicology—Mercury Neurotoxicity ♣
- Neurotoxicology—Metals: Lead, Cadmium, and Others ♣
- Ocular Toxicology
- Safety Assessment: Drug Development ♠
- Safety Assessment: Drug Discovery ♠
- Toxicology Education

1:30 PM to 2:30 PM

MEET THE DIRECTORS

- A Conversation with Linda Birnbaum and Christopher Austin
Lecturers: Linda Birnbaum, NIEHS; and Christopher Austin, NCATS



2:00 PM to 4:45 PM

SYMPOSIUM SESSIONS

- Health and Environmental Hazard Assessments of Nanomaterials Along Their Lifecycle ♥
- The Promise and Reality of Alternative Methods in Inhalation Toxicology and the Development of Inhaled Therapeutics

WORKSHOP SESSIONS

- Moving Beyond Prioritization towards True *In Vitro*-Based Safety Assessment ♠
- Quantitative Cumulative Risk Assessment: Is It Feasible Today? ♠
- The Role of the Epigenome in Exposure Effects, Susceptibility, and Public Health ♦
- Using 21st Century Approaches to Evaluate Endocrine-Active Compounds ♠

HISTORICAL HIGHLIGHTS

- Toxicologic Legacies of Major 21st Century Man-Made/Natural Disasters ♥

PLATFORM SESSIONS

- AhR and Disease Processes ♥
- Pluripotent Stem Cells in Cardiovascular Research

4:45 PM to 6:00 PM

SOT/EUROTOX DEBATE

- Preclinical (Safety) Toxicology Testing Predicts the Clinical Outcome
Lecturers: Thomas M. Monticello, Amgen; and Ruth Roberts, Apconix Ltd



Tuesday, March 15

8:00 AM to 9:20 AM

DAILY PLENARY SESSION

- Inflammation and Neurodegenerative Disease
Lecturers: Stephen Skaper, University of Padua; and Alan I. Faden, University of Maryland School of Medicine



9:30 AM to 12:15 PM

SYMPOSIUM SESSIONS

- Drug-Induced Taste Change in Clinical Practice and Preclinical Safety Evaluation
- Genotypic and Intrinsic Risk Factors That Increase Susceptibility to Inhaled Pollutants
- Systems Understanding of the Impact of the Nrf2 Pathway on Chemical Toxicity and Cell Fate ♦
- Unknown, Unknowns: Exploring the Unidentified Fraction of Complex Mixtures

WORKSHOP SESSIONS

- Bioactivity-Based Margin of Exposure Safety Assessment: The Next Stop along the Road to 21st Century Safety Assessments ♠
- Maternal Exposure to Nanoparticles—How Does It Affect the Fetus? Status, Mechanisms, and Future Directions ♠
- Multi-Omics in Predictive Toxicology: Development and Application in Environmental Monitoring Programs ♦
- Scientific and Regulatory Advances in Safety Evaluation of Heavy Metals in Food ♠ ♣

PLATFORM SESSIONS

- Zebrafish Models: Advances and Applications in DART

9:30 AM to 12:45 PM

POSTER SESSIONS

- Alternative Models: Fish, Worms, and More ♦ ♠
- Carcinogenesis I
- Carcinogenesis II
- Chemical and Biological Weapons ♥
- Developmental Basis of Adult Disease ♠
- Endocrine Toxicology
- Inflammation in Disease
- Inflammation: Methods and Mechanisms
- Liver—Mechanisms ♦
- Liver—Models
- Risk Assessment 1
- Stem Cell Biology and Toxicology
- Toxic Inhalants Research

9:30 AM to 4:30 PM

RESEARCH FUNDING DISCUSSIONS

- Network with Program Officers

12:30 PM to 1:20 PM

LEADING EDGE IN BASIC SCIENCE AWARD LECTURE



Lecturer: Cheryl Lyn Walker, Texas A&M Institute of Biosciences and Technology

Scientific Program Overview

1:15 PM to 4:30 PM

POSTER SESSIONS

- 3D Cell and Organ-on-a-Chip Models ♦ ♠
- Alternative Models for Ocular and Skin Toxicity
- Biological Modeling
- Clinical and Translational Toxicology
- Food Safety/Nutrition 1 ♥
- Gene Regulation and Signal Transduction ♦
- Medical Devices
- Neurotoxicology—Dopaminergic Systems and Toxicants 🏰
- Neurotoxicology—Manganese Neurotoxicity 🏰 ♣
- Neurotoxicology—Neurodegenerative Diseases 🏰
- Neurotoxicology—Pesticide Neurotoxicity 🏰
- Non-Pharmaceutical Safety Assessment ♠
- Oxidative Injury and Redox Biology ♦
- Particulate Matter Toxicology
- Receptors

2:00 PM to 4:45 PM

SYMPOSIUM SESSIONS

- New Mechanistic Insights into How the Immune System Drives Hepatic Adverse Drug Reactions
- Reciprocal Synergism: New Insights into Thyroid Hormone Action in Brain Development and Neurodevelopmental Toxicity 🏰 🌱
- The Role of Gene SLC30A10 on Manganese Homeostasis and Functional Outcomes: Implications for Homeostasis and Neurotoxicity 🏰 ♣
- Using Multi- and Transgenerational Effects of Environmental Exposures in Diverse Animal Models for Assessment of Human Health Risks 🌱

WORKSHOP SESSIONS

- Cannabis in the Courtroom 🏰
- Read-Across: Building Scientific Confidence in the Development and Evaluation of Read-Across for Regulatory Purposes Using Tox21 Approaches ♦ ♠
- Safety Assessment of Topically Exposed Cosmetic Ingredients: Lessons Learned ♠

PLATFORM SESSIONS

- Nanotoxicology: *In Vivo*
- Qualification of “New” DART Tools for Hazard Identification 🌱

4:45 PM to 6:15 PM

SOT ANNUAL BUSINESS MEETING

Wednesday, March 16

8:00 AM to 9:20 AM

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

- Regenerating CNS Myelin—From Mechanisms to Medicines



Lecturer: Robin J.M. Franklin,
Wellcome Trust-MRC
Cambridge Stem Cell Institute,
University of Cambridge

9:30 AM to 12:15 PM

SYMPOSIUM SESSIONS

- Patient-Specific Stem Cells As Models for Gene, Drug, and Environment Interactions in Disease
- Sulfur Mustard Poisoning: Mechanisms of Dermal and Pulmonary Toxicity and New Treatment Approaches ♥

WORKSHOP SESSIONS

- An Update on Juvenile Animal Testing 🌱
- Moving Beyond Cancer: Current State of the Science of Noncancer Health Effects of Arsenic ♣
- Paradigm Change in Toxicology: What Will It Take to Bring Advances in the Science of Toxicology into Regulatory Use? ♦ ♠
- Screening Chemicals for Neurotoxicity Outcomes—Using Large Datasets and Multiple Endpoints to Develop “Toxicity Profiles” 🏰 ♦

INFORMATIONAL SESSION

- Tox21 Challenge To Build Predictive Models of Nuclear Receptor and Stress Response Pathways As Mediated by Exposure to Environmental Toxicants and Drugs ♦

PLATFORM SESSIONS

- Effects of Food-Associated Agents on Inflammation, Metabolic Disease, and Cancer ♥
- Nrf2 in Redox Biology

9:30 AM to 4:30 PM

RESEARCH FUNDING DISCUSSIONS

- Network with Program Officers

9:30 AM to 12:45 PM

POSTER SESSIONS

- Autoimmunity/Hypersensitivity
- Biomarkers
- Cardiovascular Toxicology
- Computational and Systems Toxicology I ♠
- Computational and Systems Toxicology II ♠
- Ecotoxicology
- Nanotoxicology: *In Vitro*
- Nanotoxicology: *In Vivo*
- Pesticides
- Pharmacogenetics/Genetic Polymorphisms ♦
- Risk Assessment 2
- Risk Assessment 3

12:30 PM to 1:20 PM

DISTINGUISHED TOXICOLOGY SCHOLAR AWARD LECTURE



Lecturer: I. Glenn Sipes,
University of Arizona



View featured speaker biographies, connect with other attendees, and create your own schedule using the Mobile Event App or the Online Planner.
See page 2 for details.

12:30 PM to 1:50 PM

ROUNDTABLE SESSION

- Combination Toxicology: Are We Testing the Right Things?

INFORMATIONAL SESSIONS

- Updating FDA's Redbook: The Importance of Stakeholder Involvement ♠
- Why Did the Scientific Program Committee Reject My Proposal? Developing a Good Idea Into an Accepted SOT Session

EDUCATION-CAREER DEVELOPMENT SESSION

- The Evolution of the Postdoc: Transitioning from Trainee to Professional in the Modern Era

1:15 PM to 4:30 PM

POSTER SESSIONS

- Alternative *In Vitro* Toxicity Models ♠
- Animal Models of Disease
- Animal Models: Methods and Measurements
- Cytochrome P450
- Developmental and Juvenile Toxicology ♠
- Developmental Toxicology (Non-Rodent) ♠
- Epidemiology and Public Health
- Epigenetics ♦
- Food Safety/Nutrition 2
- Kidney—Models to Mechanisms and Molecular Biomarkers
- Liver—Translational
- Regulation and Policy
- Reproductive Toxicology ♠
- Tobacco Products

2:00 PM to 4:45 PM

SYMPOSIUM SESSIONS

- High-Content Imaging for Predictive Toxicology: Discriminating between Adverse and Adaptive Outcomes ♦
- Novel Roles of Reactive Oxygen Species (ROS) in Human Diseases: Why ROS Never Gets Stale
- Use of the Adverse Outcome Pathway (AOP) Concept to Link Epidemiological to Mechanistic Data on the Correlation of Pesticide Exposures and Parkinson's Disease ♠ ♦

WORKSHOP SESSIONS

- Advanced Techniques in PBPK Modeling to Improve Quantitative Risk Assessment for Infants and Children ♠ ♠
- "Breaking Bad": Cardiovascular Autophagy Gone Rogue: A Putative Mechanism of Toxicity and a Drug Target in Disease
- In Vitro* Dosimetry of Engineered Nanomaterials: Too Complicated to Consider, Too Important to Ignore
- Medical Device Biomaterials: Challenges in Assessing the Toxicity and Biocompatibility of Nanomaterials, Bioabsorbables, and Tissue Scaffolds

PLATFORM SESSIONS

- Heavy Metals: Mechanisms and Disease Pathogenesis ♠
- Innovations in Toxicology Education

5:00 PM to 6:20 PM

EDUCATION-CAREER DEVELOPMENT SESSION

- "Talksicology": Effective Oral Presentation Techniques

5:00 PM to 5:50 PM

TRANSLATIONAL IMPACT AWARD LECTURE

- Translational Non-Invasive Biomarkers of Acetaminophen-Induced Liver Injury



Lecturer: Richard Beger,
US FDA-NCTR

Thursday, March 17

9:30 AM to 12:15 PM

SYMPOSIUM SESSION

- Mitochondrial Dysfunction as a Pathogenic Mechanism and Therapeutic Target for Neurodegenerative Diseases ♠ ♠

WORKSHOP SESSIONS

- Beyond Benchmark Dose: Advancing Probabilistic and Bayesian Approaches in Hazard Characterization ♠
- Bringing More Science into the Process of Risk Assessment for Endogenous Chemicals with Exogenous Exposures ♠
- Developmental Immunotoxicology—Are We Adequately Evaluating Safety? ♠
- Potential Health and Environmental Effects of Unconventional Hydraulic Fracturing ♠
- Which Human Cell Lines Should I Use? Choosing the Appropriate Biological Systems for High-Throughput Toxicity Testing ♠

PLATFORM SESSIONS

- Advances in Mammary Gland Biology and Toxicology
- Electronic Cigarette Research
- Flame Retardants

9:30 AM to 12:45 PM

POSTER SESSIONS

- Biotransformation
- Disposition and Pharmacokinetics
- Emerging Technologies
- Late Breaking Posters
- MicroRNA Biomarkers ♦
- Nanotoxicology—Carbon Based
- Persistent Organic Pollutants ♠
- Skin Responses and Toxicology

LATE-BREAKING POSTER SESSION

See page 78 for submission information.



Do You Know about These Events?

A Contemporary Concepts in Toxicology (CCT) Meeting will be held prior to the start of the SOT Annual Meeting. See page 22 for details.

Following the completion of the SOT Annual Meeting, there will be two Satellite Meetings. See page 63 for details.

CONTINUING EDUCATION COURSES AND SCIENTIFIC SESSIONS: THEMATIC APPROACH

The Scientific Program Committee has developed a slate of timely and highly informative Symposium Sessions, Workshop Sessions, Roundtable Sessions, and other special sessions that span the spectrum of topics of interest to our diverse membership.

The 2016 scientific themes listed here illustrate the core contributions toxicology makes to these areas, and the sessions that will be highlighted within these themes are indicated.



Scientific Themes

- Advances in Neurotoxicology
- Developmental Toxicity: Mechanisms and Evaluation
- Health and Environmental Impacts of Man-Made and Naturally Released Toxicants
- Molecular Toxicology: Mechanistic Insights and Hazard Assessment
- Recent Advances in Safety Assessment
- Toxicity of Metals

Workshop Sessions

- Advanced Techniques in PBPK Modeling to Improve Quantitative Risk Assessment for Infants and Children
- An Update on Juvenile Animal Testing
- Beyond Benchmark Dose: Advancing Probabilistic and Bayesian Approaches in Hazard Characterization
- Bioactivity-Based Margin of Exposure Safety Assessment: The Next Step along the Road to 21st Century Safety Assessments
- Bringing More Science into the Process of Risk Assessment for Endogenous Chemicals with Exogenous Exposures
- Cannabis in the Courtroom
- Developmental Immunotoxicology—Are We Adequately Evaluating Safety?
- Dietary Exposures to Heterocyclic Amines As a Potential Risk Factor for Neurological Disease
- Maternal Exposure to Nanoparticles—How Does It Affect the Fetus? Status, Mechanisms, and Future Directions
- Moving Beyond Cancer: Current State of the Science of Noncancer Health Effects of Arsenic
- Moving Beyond Prioritization towards True *In Vitro* Based Safety Assessment
- Multi-Omics in Predictive Toxicology: Development and Application in Environmental Monitoring Programs
- One Toxicological Health: Environmental Chemicals and Their Impacts on Humans, Laboratory Animals, and Wildlife
- Paradigm Change in Toxicology: What Will It Take to Bring Advances in the Science of Toxicology into Regulatory Use?

Symposium Sessions

- Health and Environmental Hazard Assessments of Nanomaterials Along Their Lifecycle
- High-Content Imaging for Predictive Toxicology: Discriminating between Adverse and Adaptive Outcomes
- Mitochondrial Dysfunction As a Pathogenic Mechanism and Therapeutic Target for Neurodegenerative Diseases
- Opening the Black Box: Understanding the Molecular Mechanisms of Developmental Toxicity
- Reciprocal Synergism: New Insights into Thyroid Hormone Action in Brain Development and Neurodevelopmental Toxicity
- Sulfur Mustard Poisoning: Mechanisms of Dermal and Pulmonary Toxicity and New Treatment Approaches
- Systems Understanding of the Impact of the Nrf2 Pathway on Chemical Toxicity
- The Role of Gene SLC30A10 on Manganese Homeostasis and Functional Outcomes: Implications for Homeostasis and Neurotoxicity
- Use of the Adverse Outcome Pathway (AOP) Concept to Link Epidemiological to Mechanistic Data on the Correlation of Pesticide Exposures and Parkinson's Disease
- Using Multi- and Transgenerational Effects of Environmental Exposures in Diverse Animal Models for Assessment of Human Health Risks

- Potential Health and Environmental Effects of Unconventional Hydraulic Fracturing
- Quantitative Cumulative Risk Assessment: Is It Feasible Today?
- Read-Across: Building Scientific Confidence in the Development and Evaluation of Read-Across for Regulatory Purposes Using Tox21 Approaches
- Safety Assessment of Topically Exposed Cosmetic Ingredients: Lessons Learned
- Scientific and Regulatory Advances in Safety Evaluation of Heavy Metals in Food
- Scientific Reproducibility: Does This Pose a Problem for 21st Century Toxicology?
- Screening Chemicals for Neurotoxicity Outcomes—Using Large Datasets and Multiple Endpoints to Develop “Toxicity Profiles”
- The Cancer Risk Assessment for Ingested Hexavalent Chromium: Challenges and Controversies
- The Role of the Epigenome in the Exposure Effects, Susceptibility, and Public Health
- Transient Receptor Potential A1 (TRPA1) Cation Channels: Fluttering Hearts, Headaches and Hot Flashes—Can One “Environmental Sensor” Be the Cause of All the Pain?
- Using 21st Century Approaches to Evaluate Endocrine-Active Compounds
- Which Human Cell Lines Should I Use? Choosing the Appropriate Biological Systems for High-Throughput Toxicity Testing

Roundtable Sessions

- Is a “Thresholdable” Carcinogen Still a Delaney Carcinogen? ♠
- Trichloroethylene Exposures Resulting from Vapor Intrusion: What Do the Data Tell About Potential Health Risks to Pregnant Women 🌿

Informational Sessions

- Tox21 Challenge To Build Predictive Models of Nuclear Receptor and Stress-Response Pathways As Mediated by Exposure to Environmental Toxicants and Drugs 💎
- Updating the FDA's Redbook: The Importance of Stakeholder Involvement ♠

Historical Highlights

- Toxicologic Legacies of Major 21st Century Man-Made/Natural Disasters ♥

Regional Interest Session

- The Toxicological Implications of the Gulf Oil Spill: Research Accomplishments and Research Needs ♥

Continuing Education Courses

- SR01—Basic Principles and Practices for Applying Epigenetics in Mechanistic Toxicology 💎
- AM02—Advancing the Detection, Imaging, and Pitfalls in Monitoring Oxidative Stress in Health and Disease ♥💎
- AM03—Adverse Outcome Pathway (AOP) Development and Evaluation 💎♠
- AM04—Contribution of Mitochondria to Drug-Induced Organ Toxicities 💎
- AM05—Discovery and Validation of miRNA Biomarkers Bridging Preclinical and Clinical Toxicity: Lessons Learned from Hepatotoxicity 💎♠
- AM06—Embryology and Developmental Toxicity Testing 🌿
- AM07—Next-Generation Sequencing in Toxicogenomics 💎♠
- PM08—Approaches to Investigate and Assess Risks Associated with Drug-Induced Liver Injury (DILI) ♥♠
- PM09—Exploring Chemical Space in the New Toxicity Testing Paradigm: From Data Curation to Computational Simulations ♠
- PM10—Genetics and Population Variability in Chemical Toxicity: The What, the How, and So What? ♥💎
- PM11—Human Health Risk Assessment: A Case Study Application of Principles ♥
- PM12—Unique Approaches to Safety Assessment of Gene, Cell, and Nucleic Acid-Based Therapies ♠
- PM13—Zebrafish As a Tool in Toxicology and Drug Discovery Screening ♥♠

Platform Sessions

- AhR and Disease Processes ♥
- Effects of Food-Associated Agents on Inflammation, Metabolic Disease and Cancer ♥
- Heavy Metals: Mechanisms and Disease Pathogenesis 🌿
- Ozone Research ♥
- Qualification of “New” DART Tools for Hazard Identification 🌿

Poster Sessions

- 3D Cell and Organ-on-a-Chip Models 💎♠
- Alternative *In Vitro* Toxicity Models ♠
- Alternative Models: Fish, Worms, and More 💎♠
- Arsenic Toxicity 🌿
- Bioinformatics and Toxicology ♠
- Chemical and Biological Weapons ♥
- Computational and Systems Toxicology I ♠
- Computational and Systems Toxicology II ♠
- Developmental and Juvenile Toxicology 🌿
- Developmental Basis of Adult Disease 🌿
- Developmental Toxicology (Non Rodent) 🌿
- Epigenetics 💎
- Food Safety/Nutrition 1 ♥
- Gene Regulation and Signal Transduction 💎
- Liver—Mechanisms 💎
- Mercury Toxicity 🌿
- Metal Toxicity 🌿
- MicroRNA Biomarkers 💎
- Mixtures ♥
- Natural Products ♥
- Neurotoxicology of Therapeutic Agents and Abused Substances 🏰
- Neurotoxicology—Developmental Neurotoxicity 🏰
- Neurotoxicology—Dopaminergic Systems and Toxicants 🏰
- Neurotoxicology—Emerging Technologies for Neurotoxicity Screening 🏰
- Neurotoxicology—General 🏰
- Neurotoxicology—Halogenated Hydrocarbons 🏰
- Neurotoxicology—Manganese Neurotoxicity 🏰🌿
- Neurotoxicology—Mercury Neurotoxicity 🏰🌿
- Neurotoxicology—Metals: Lead, Cadmium, and Others 🏰🌿
- Neurotoxicology—Neurodegenerative Diseases 🏰
- Neurotoxicology—Pesticide Neurotoxicity 🏰
- Non-Pharmaceutical Safety Assessment ♠
- Oxidative Injury and Redox Biology 💎
- Persistent Organic Pollutants ♥
- Pharmacogenetics/Genetic Polymorphisms 💎
- Reproductive Toxicology 🌿
- Safety Assessment—Drug Development ♠
- Safety Assessment—Drug Discovery ♠
- Systems Biology and Toxicology ♠
- Toxicity of Metal Mixtures 🌿



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.

Mark Your Calendar KEY DEADLINES

Late-Breaking
Abstract
Submission
Deadline
January 12, 2016

Early-Bird
Registration
January 15, 2016

Housing
Reservation
February 12, 2016

Standard
Registration
February 12, 2016

Registration
Cancellation
February 12, 2016



New Orleans, Louisiana

New Orleans Ernest N. Morial Convention Center

**Contribute Your Science—
Late-Breaking Abstract
Submission Open**

See details on page 78.



SOT | Society of
Toxicology
Creating a Safer and Healthier World by Advancing
the Science and Increasing the Impact of Toxicology

www.toxexpo.com
www.toxicology.org/2016

SOT Global Partners

The Society of Toxicology has established a special category for private, public, and not-for-profit organizations that wish to contribute to the success of SOT toward "creating a safer and healthier world by advancing the science and increasing the impact of toxicology." These organizations provide support for activities aligned with the prediction and prevention of toxicity and disease.

AbbVie

Abbott Park, Illinois

American Petroleum Institute

Washington, DC

AstraZeneca

Mecclesfield, United Kingdom

Bristol-Myers Squibb Company

Princeton, New Jersey

Celgene Corporation

Summit, New Jersey

Charles River

Wilmington, Massachusetts

Chevron Corporation

San Ramon, California

The Coca-Cola Company

Atlanta, Georgia

Colgate-Palmolive Company

Piscataway, New Jersey

Covance

Madison, Wisconsin

CRC Press/Taylor & Francis Group

Boca Raton, Florida

Dow Chemical Company

Midland, Michigan

Dow Corning Corporation

Midland, Michigan

The DuPont Haskell Global Centers for Health and Environmental Sciences

Newark, Delaware

Eli Lilly and Company

Indianapolis, Indiana

Envigo

East Millstone, New Jersey

ExxonMobil Biomedical Sciences, Inc.

Annandale, New Jersey

Genentech, Inc.

South San Francisco, California

Gilead Sciences, Inc.

Foster City, California

The Hamner Institutes for Health Sciences

Research Triangle Park, North Carolina

Honeywell International, Inc.

Morristown, New Jersey

Janssen Pharmaceutical Companies of Johnson & Johnson

Raritan, New Jersey

MPI Research

Mattawan, Michigan

Organovo, Inc.

San Diego, California

Oxford University Press

Oxford, United Kingdom

Pfizer, Inc.

Groton, Connecticut

Procter & Gamble Company

Cincinnati, Ohio

Regeneron Pharmaceuticals, Inc.

Tarrytown, New York

Sanofi

Bridgewater, New Jersey

SNBL USA, Ltd.

Everett, Washington

Syngenta Crop Protection, Inc.

Greensboro, North Carolina

Takeda Pharmaceutical Company Limited

Cambridge, Massachusetts

TERA Center, University of Cincinnati

Cincinnati, Ohio

Western Slope Laboratory, LLC

Troy, Michigan

WIL Research Laboratories, LLC

Ashland, Ohio

WuXi AppTec

Saint Paul, Minnesota

XRpro Sciences, Inc.

Cambridge, Massachusetts

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



SOT Annual Meeting



Your Invitation to Attend

You are cordially invited to attend the Society of Toxicology (SOT) 55th Annual Meeting and ToxExpo, March 13–17, 2016, at the New Orleans Ernest N. Morial Convention Center in New Orleans, Louisiana. The SOT Annual Meeting is the largest meeting of its kind. This annual event features a broad range of scientific sessions and a thematic program that provides 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 and other featured sessions, Symposia, Workshops, Roundtable discussions, Informational Sessions, and a Regional Interest Session, as well as Platform and Poster Sessions. The Society anticipates that more than 6,500 toxicologists from more than 50 countries will attend. The SOT Annual Meeting also includes the ToxExpo, which is the largest exhibition dedicated to toxicology and the biomedical sciences. The 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.

You will want to attend because...

Innovative Perspectives: The SOT Annual Meeting provides the most complete and in-depth coverage of toxicology. The Scientific Program Committee mission is to devise a scientific program that covers the diverse areas of science that toxicology encompasses. The meeting is the venue for toxicologists to learn about the scientific advances that have taken place over 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.

In-Depth Analysis: The Scientific Program Committee has devised a thematic approach that encompasses six themes of topical interest:

-  Advances in Neurotoxicology
-  Developmental Toxicity: Mechanisms and Evaluation
-  Health and Environmental Impacts of Man-Made and Naturally Released Toxicants
-  Molecular Toxicology: Mechanistic Insights and Hazard Assessment
-  Recent Advances in Safety Assessment
-  Toxicity of Metals

Countless Networking Opportunities: Thousands of networking opportunities exist during the Annual Meeting. From exhibits to posters and scientific sessions to receptions you have the opportunity to network with colleagues and leading scientists from around the world.

A Global Audience: 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. Toxicologists can explore lessons learned, and share scientific findings and novel approaches with other toxicologists at this annual event, which is designed to showcase the year's latest in research.

Value: The SOT Annual Meeting is one of the most cost-effective meetings you can attend. For example, you pay \$310 for early-bird registration, compared to an average cost of \$461 for other toxicology society meetings. Also, SOT has arranged air carrier discounts and has reserved SOT meeting attendee discounted rooms at various hotels in the New Orleans area through the SOT hotel room block. If you need to provide your employer with additional justification for attending the SOT Annual Meeting, visit the SOT Annual Meeting website to find more information about the importance of this annual five-day event and why it should be the one meeting you attend.



An Invitation to International Attendees

Scientists from around the world are invited to register for the 55th Annual Meeting and ToxExpo in New Orleans, March 13–17, 2016. Please note that individual invitations are not required for attendance. Because the meetings are open scientific events, SOT extends an invitation to all interested individuals to attend.

Visa Information

If your travels require a visa, note that the United States is advising applicants to apply at least three to four months in advance of their travel date. We suggest that you contact the United States Consulate in your own country regarding documentation and necessary information for your visit to the United States.

If for visa purposes you need a formal invitation letter, you may request an invitation by sending your name, address, and email address to the SOT Registration Department. 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. If you need assistance, please contact the SOT Registration Department at tel: 703.438.3115, fax: 703.438.3113, or email: sothq@toxicology.org.

Here is information to help you obtain a visa:

US Department of State, Bureau of Consular Affairs—A website designed with you in mind about current visa policies and procedures.

www.nationalacademies.org/visas—For additional visa information, contact the International Visitors Office (IVO) of the National Academies of the Sciences at the above website. A survey is available that can be used to assist future travelers with the visa process.

Make an Appointment—Before visiting the United States 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 at **<http://travel.state.gov/content/visas/en/business.html>**.

Get Your Documents Ready—Organize your passport, applications, documents to support the application with employment details (reason for travel along with financial status), and proof of payment of fees.

Submit Your Application—Send your application and passport along with supporting documents to the United States Embassy or Consulate.

Start Early—Additional reviews may be required. This could add an additional four to six weeks to the processing time.

ToxExpo

ToxExpo is the toxicology profession's largest exposition, uniting attendees and exhibitors from around the world to exchange information on the latest products and services. More than 350 exhibitors demonstrate innovative technology and novel methods to more than 6,500 attendees. The benefits of ToxExpo extend beyond the three-day event—resulting in significant partnerships benefiting attendees and exhibitors.

Use the enhanced 2016 Mobile Event App to view the floorplan and note the exhibitors with whom you want to connect. You can search the exhibitor listing to view detailed exhibitor information and pinpoint their location on the interactive ToxExpo map.

The following are the 2016 ToxExpo hours:

Monday 9:15 AM–4:30 PM
 Tuesday 9:15 AM–4:30 PM
 Wednesday 9:15 AM–4:30 PM

ToxExpo also 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.



TOX EXPO™ The Toxicology Marketplace

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 | • Medical Devices |
| • Biomarkers | • Metals |
| • Biotechnology | • Mixtures |
| • Carcinogenesis | • Molecular Biology |
| • Cardiovascular Toxicology | • Nanotoxicology |
| • Clinical and Translational Toxicology | • Neurodegenerative Disease |
| • Comparative and Veterinary | • Neurotoxicology |
| • Dermal Toxicology | • Occupational and Public Health |
| • Drug Discovery Toxicology | • Ocular Toxicology |
| • Epigenetics | • Pharmacology |
| • Ethical, Legal, and Social Issues | • Regulatory and Safety Evaluation |
| • Food Safety | • Reproductive and Developmental Toxicology |
| • Immunotoxicology | • Risk Assessment |
| • <i>In Vitro</i> and Alternative Methods | • Stem Cells |
| • Inflammation and Disease | • Toxicologic and Exploratory Pathology |
| • Inhalation and Respiratory | |
| • Mechanisms | |

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.



Hotel and Travel

Housing Information

The Society of Toxicology has reserved and arranged for discounted room rates at various New Orleans 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 new housing reservations is February 12, 2016. Please choose only one option to make your reservation:

www.toxicology.org/events/am/am2016/housing.asp

Mail Housing Form to:

Connections Housing
950 Scales Road, Building 200, Suite 201
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:
9:00 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 (3) business days, please call Connections Housing.

Changes and Cancellations

The deadline date for new reservations is Friday, February 12, 2016. 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. 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.

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. Access this option from the Annual Meeting section of the SOT website.

Transportation

Ride-Share Program

SOT is offering a ride-share program in conjunction with the Annual Meeting. For those who live close enough to the New Orleans 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.

New Orleans International Airport (MSY)

New Orleans is serviced by Louis Armstrong New Orleans International Airport (MSY), which is a 20-minute drive from the New Orleans Ernest N. Morial Convention Center and the downtown hotel area. Fourteen carriers offer daily flights. For more information visit www.flymsy.com.

Air Transportation

SOT Travel Provider—ATC Travel Management

ATC Travel is the official travel management firm for SOT's 55th Annual Meeting. To take advantage of their services and savings, visit www.atcmeetings.com/sot, or call toll-free 800.458.9383 Monday through Friday, 8:30 am–7:00 pm (Eastern Standard Time) and ask to speak to anyone on our SOT-dedicated team, or email reservations@atcmeetings.com.

To obtain the maximum discounted fares, call at least 60 days prior to departure. Please note that depending on your reservation method, ATC Travel Management charges a \$10 online service fee or a live agent reservation fee. 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 New Orleans
- 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)

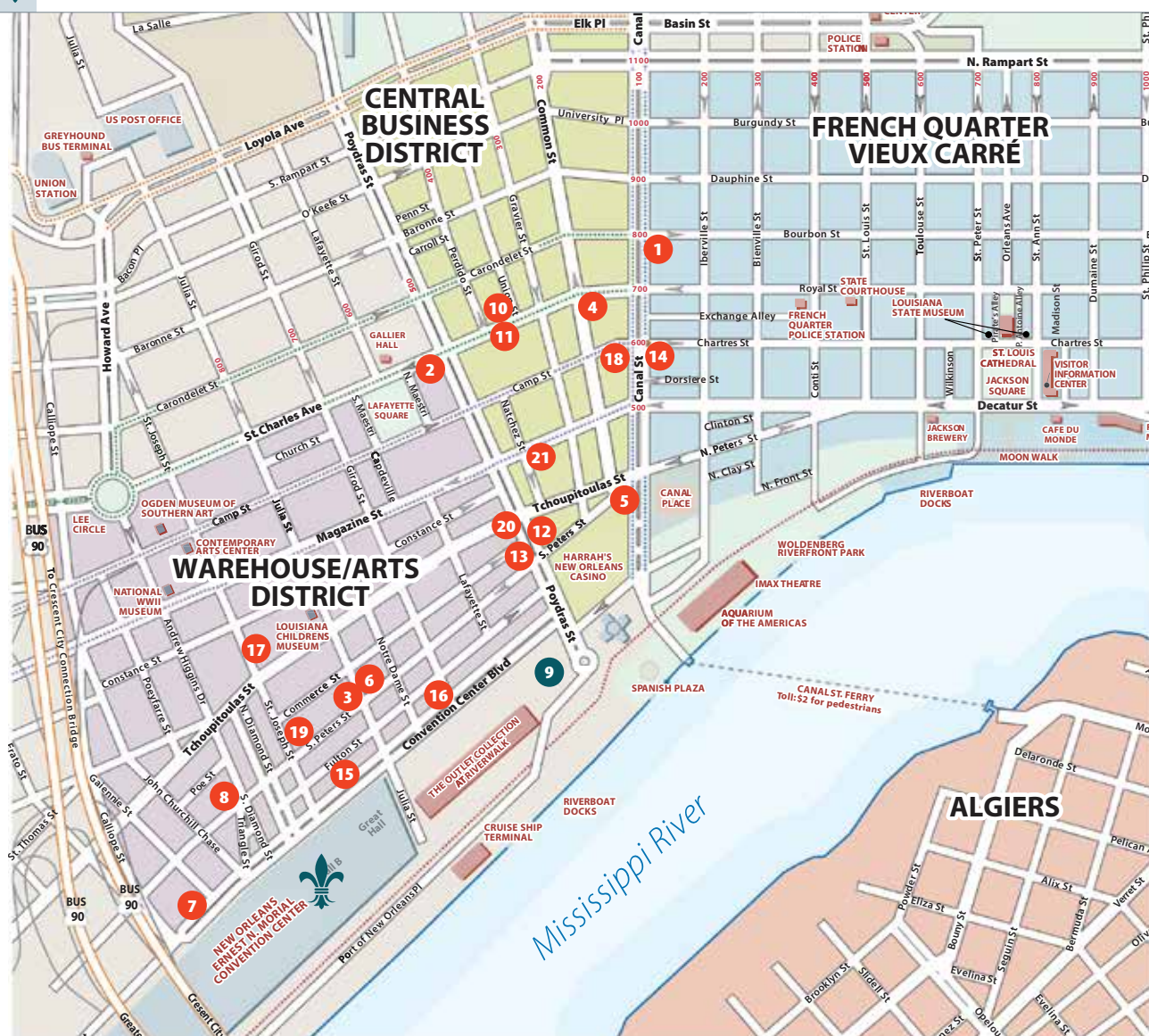
Identify yourself as a Society of Toxicology attendee. ATC Travel Management will find the best fare for you and email you an itinerary.

Hotel Map

1	Astor Crowne Plaza	8	Hilton Garden Inn New Orleans Convention Center	15	New Orleans Downtown Marriott at the Convention Center
2	Blake Hotel	9	Hilton New Orleans Riverside <i>SOT Headquarters Hotel</i>	16	Omni Riverfront New Orleans
3	Courtyard by Marriott Convention Center	10	Hilton New Orleans St. Charles Avenue	17	Residence Inn by Marriott New Orleans Downtown
4	Courtyard by Marriott Downtown near the French Quarter	11	InterContinental New Orleans	18	Sheraton New Orleans
5	Doubletree by Hilton New Orleans	12	Le Meridien New Orleans	19	SpringHill Suites by Marriott Convention Center
6	Embassy Suites New Orleans Convention Center	13	Loews New Orleans	20	Staybridge Suites French Quarter Downtown
7	Hampton Inn & Suites New Orleans Convention Center	14	New Orleans Marriott	21	St. James Hotel New Orleans



New Orleans Convention Center



Use the enhanced 2016 Mobile Event App to access a complete New Orleans city guide including hotels, restaurants, attractions, nightlife, and shopping.

Hotel Services

															
Hotel	Rewards Program	Blocks to Convention Center	Single/Double Rate†	Restaurant	Complimentary Breakfast	In-Room Safe	Fitness Center	Swimming Pool	Business Center	Complimentary In-Room Internet	Room Service	Gift Shop	Overnight Self-Parking	Valet Parking (per night)	Rating
1) Astor Crowne Plaza 739 Canal Street	IHG	10 blocks	\$239/\$239	✓		✓	✓	✓	✓	✓	✓			\$39	4 Stars
2) Blake Hotel 500 St. Charles Avenue	Choice Hotel	10 blocks	\$189/\$189	✓		✓	✓		✓	✓		✓		\$34	2 Stars
3) Courtyard by Marriott Convention Center 300 Julia Street	Marriott Rewards	2 blocks	\$225/\$225	✓			✓	✓	✓	✓		✓		\$28	3 Stars
4) Courtyard by Marriott Downtown near the French Quarter 124 St. Charles Avenue	Marriott Rewards	9 blocks	\$212/\$212	✓			✓		✓	✓		✓	✓	\$34	3 Stars
5) Doubletree by Hilton New Orleans 300 Canal Street	Hilton Honors	5 blocks	\$216/\$216	✓			✓	✓	✓	✓	✓	✓		\$36	3 Stars
6) Embassy Suites New Orleans Convention Center 315 Julia Street	Hilton Honors	2 blocks	\$236/\$236	✓	✓		✓	✓	✓	✓	✓	✓		\$35	3 Stars
7) Hampton Inn & Suites New Orleans Convention Center 1201 Convention Center Boulevard	Hilton Honors	Across street from Hall E	\$189/\$199 Suite \$239		✓		✓	✓	✓	✓				\$34	3 Stars
8) Hilton Garden Inn New Orleans Convention Center 1001 South Peters Street	Hilton Honors	1 block	\$205/\$205	✓		✓	✓	✓	✓	✓	✓			\$35	3 Stars
9) Hilton New Orleans Riverside SOT Headquarters Hotel 2 Poydras Street	Hilton Honors	1 block	Standard \$256 Deluxe \$276	✓			✓	✓	✓	✓	✓	✓	✓	\$43	4 Stars
10) Hilton New Orleans St. Charles Avenue 333 St. Charles Avenue	Hilton Honors	8 blocks	\$229/\$229	✓		✓	✓	✓	✓	✓	✓	✓		\$40	4 Stars
11) InterContinental New Orleans 444 St. Charles Avenue	IHG	7 blocks	\$245/\$245	✓		✓	✓	✓	✓	✓	✓	✓		\$36	4 Stars
12) Le Meridien New Orleans 333 Poydras Street	Starwood Preferred Guests	4 blocks	\$249/\$249	✓		✓	✓	✓	✓	✓	✓			\$45	4 Stars
13) Loews New Orleans 300 Poydras Street	You First	3 blocks	\$249/\$249	✓		✓	✓	✓	✓	✓	✓			\$42	4 Stars
14) New Orleans Marriott 555 Canal Street	Marriott Rewards	7 blocks	\$229/\$229	✓		✓	✓	✓	✓	✓	✓	✓		\$38	3 Stars
15) New Orleans Downtown Marriott at the Convention Center 859 Convention Center Boulevard	Marriott Rewards	Across street from Hall A	\$234/\$234	✓		✓	✓	✓	✓	✓	✓	✓		\$38	3 Stars
16) Omni Riverfront New Orleans 701 Convention Center Boulevard	Select Guest Program	1 block	\$236/\$246	✓		✓	✓	✓		✓	✓			\$34	4 Stars
17) Residence Inn by Marriott New Orleans Downtown 345 St. Joseph Street	Marriott Rewards	3 blocks	\$225/\$225	✓	✓		✓	✓	✓	✓		✓		\$34	3 Stars
18) Sheraton New Orleans 500 Canal Street	Starwood Preferred Guests	6 blocks	\$225/\$225	✓		✓	✓	✓	✓	✓	✓	✓		\$40	3 Stars
19) SpringHill Suites by Marriott Convention Center 301 St. Joseph Street	Marriott Rewards	3 blocks	\$225/\$225		✓		✓	✓	✓	✓		✓	✓	\$25	3 Stars
20) Staybridge Suites French Quarter Downtown 501 Tchoupitoulas Street	IHG	5 blocks	\$199/\$199		✓		✓	✓	✓	✓			✓	\$34	3 Stars
21) St. James Hotel New Orleans 330 Magazine Street	Choice Hotel	6 blocks	\$189/\$189		✓	✓		✓	✓	✓				\$38	3 Stars

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 we understand that 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, 2015.

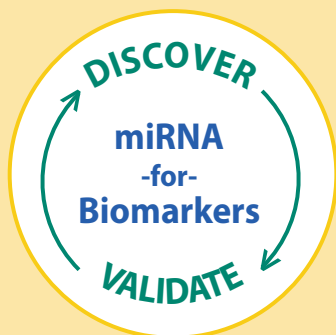


miRNA Biomarkers for Toxicology

MARCH 12, 2016

ERNEST N. MORIAL CONVENTION CENTER

NEW ORLEANS, LOUISIANA



Injury
Location

Mode of
Action

Gold
Standard
Detection

REGISTRATION | SCIENTIFIC PROGRAM | HOUSING
ON

WWW.TOXICOLGY.ORG/miRNA

(continued from page 19)

Preferred Carrier Airfare Discounts

SOT has established discounted rates through Southwest and United Airlines originating in the United States and Canada. Be sure to use the reference numbers when making your reservations. You may purchase your ticket online, call the airline directly using the toll-free numbers, or provide your travel agent with the reference/discount numbers listed below to receive the discount.

Southwest Airlines

Tel: 800.435.9792 | www.swabiz.com
SOT Discount Code: 99150833

SOT's conference attendees will receive a discount and bonus Rapid Reward points from Southwest Airlines through our SWABIZ® account. Southwest Airlines is offering a 10% discount off Anytime and Business Select® fares and a 3% discount off select Wanna Get Away® fares for travel to and from the conference. Book your travel between December 15, 2015 and March 21, 2016, to take advantage of the discounted rates. (Discounts are available for travel March 9–21, 2016.)

United Airlines

Tel: 800.426.1122 (a service fee will apply) | www.united.com
SOT Discount Code: ZVJ6151867

United Airlines is offering up to a 10% discount off fares for attendees traveling to New Orleans for the SOT Annual Meeting. The discount is valid March 7–24, 2016. You may book your ticket at www.united.com (to receive an additional 3% discount and have service fees waived); in the offer code box, type **ZVJ6151867** to receive the discount.

You may also book your reservation by calling United Meetings at 800.426.1122; however, a service fee will apply. International attendees should call their local United Airlines reservations office or email group-meetings@united.com with their preferred itinerary and discount codes. If you are booking through a travel professional, please give them the following information: **Agreement Code: 151867, Z Code: ZVJ6.**

Train Transportation

AMTRAK

Tel: 800.872.7245 | www.amtrak.com

Amtrak operates out of Union Station which is located in the Central Business District. There are always taxis ready and waiting at the station.

Ground Transportation—From the Airport

Ground transportation is located curbside outside the baggage claim area.

Taxi Cabs

The taxi cab stand is located on the lower level, outside the baggage claim area. A trip from the airport to the Central Business District is \$33 for up to two people, and \$14 per person for three or more passengers. There may be a charge for additional baggage. All cabs accept credit cards.

Shuttle Services

Airport Shuttle provides the easiest and most cost-effective ground transportation service between New Orleans International Airport and major hotels in the downtown area. Shuttles depart from 3:30 am to 2:00 am daily for downtown hotels every 30 minutes. Passengers may purchase tickets at the airport baggage claim area. Ticket fares are \$20 per person to downtown hotels or \$38 for a round-trip ticket. Book using the SOT discount link (<http://airportshuttleneworleans.hudsonltd.net/res?useridentry=sot0316&login=go>) at least 24 hours prior to your departure and receive an additional discount. Discounted online rates are \$20 one-way and \$35 for roundtrip per person. For more information, visit Airport Shuttle (www.airportshuttleneworleans.com). The SOT discount is only available online, only changes to existing reservations can be made over the phone. For more information about Airport Shuttle, call 866.596.2699.

Car Rental

On the lower level of the airport you will find the Consolidated Car Rental Facility accessible by covered walkway. The nine different car rental agencies that service the airport can be found (www.flymsy.com/pagedisplay.asp?p1=6017).

Public Transportation—Getting around Town

New Orleans Regional Transit Authority

A system of streetcars and buses run throughout many areas of New Orleans with fares starting at \$1.25. Visit NORTA website (www.norta.com) to plan your route.

Convention Center Location and Parking

New Orleans Ernest N. Morial Convention Center

900 Convention Center Boulevard

Ample parking is available in close proximity to the convention center for an hourly/daily fee.

Metered street parking is available in areas surrounding the convention center at a rate of \$1.50 per hour. Parking meters are enforced 8:00 am–6:00 pm, Monday through Saturday, unless otherwise noted.

Check the Visit New Orleans Ernest N. Morial Convention Center website (www.mccno.com/about-us/maps-directions) for more information about parking.

Overnight Parking

Fulton Place Parking Center

901 Convention Center Boulevard

This secure parking garage is located across from the convention center and offers the best rate for overnight parking near the convention center.

Please check the SOT Hotel Services chart on page 21 for valet and self-parking rates for your hotel.

Registration

Registration Information

Registration for the Annual Meeting is available now. Register by January 15 to obtain the Early-Bird rate and to ensure that you receive your registration materials before the meeting. Registration is available online, via fax, or by mail to SOT Headquarters.

Registration Deadlines

Early-Bird Registration: **January 15, 2016**

Standard Registration: **February 12, 2016**

Final Registration after: **February 12, 2016**

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 you have a nonscientist accompany you to the meeting, Guest Registration is available. If the person the guest is accompanying already is registered, he or she must use the Guest Registration Form and send it to SOT Headquarters along with a copy of the regular registrant's confirmation.

The SOT Guest/Spouse Hospitality Room provides guest registrants with a place to meeting and socialize; plus the opportunity to attend the Welcoming Reception. Located at the Hilton New Orleans Riverside, the room will be open Sunday through Thursday.

Reminder: Guest registrants and children under the age of 15 are not permitted in the Exhibit Hall at any time or in scientific session. Only the scientific session chair 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 12, 2016. These refunds will be processed, less a \$50 cancellation fee, following the Annual Meeting. Refund requests received after February 12, 2016, **will not be processed.**

Special Assistance

The New Orleans Ernest N. Morial Convention Center is accessible to persons with special needs. If you have special needs, please check the special accessibility requirement box or contact Heidi Prange at SOT Headquarters: 703.438.3115 ext. 1424 or email: heidi@toxicology.org.

Online Registration

SOT members and nonmembers are invited to register for the 2016 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 10, 2016, 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 15, 2016. If your registration is received after January 15, 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 26–27.

Please **type** or **print** clearly.

No phone registrations will be accepted.

Please send registration forms to:

SOT Headquarters
(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. All mailed and faxed registration forms will be processed online by SOT staff.

DO NOT mail your registration form to SOT if it will arrive after March 10, 2016. SOT will accept Annual Meeting registrations until March 10. After March 10, 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



Registration Form

SOT 55th Annual Meeting • March 13–17, 2016

R2016

FOR OFFICE USE ONLY

Date Received: _____

Input: ☐ Initials: _____

(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 Name: _____

(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: _____

If you are a Student or Postdoc registrant, please provide the following information:

☐ 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: _____

REGISTRATION FEES:

☐ I'm Already Registered

Early-Bird Registration

Standard Registration

Final Registration

(Received by Jan. 15)

(Jan. 16 to Feb. 12)

(After Feb. 12*)

SOT Member	\$310	\$370	\$430	\$ _____
Nonmember**	\$660	\$720	\$780	\$ _____
SOT Retired/Emeritus Member	\$ 70	\$120	\$170	\$ _____
Postdoctoral SOT Member	\$ 85	\$135	\$185	\$ _____
Postdoctoral Nonmember**	\$170	\$220	\$270	\$ _____
Graduate Student Member	\$ 65	\$115	\$165	\$ _____
Graduate Student Nonmember**	\$130	\$180	\$230	\$ _____
Undergraduate Student (Copy of Student ID Required)	\$ 0	\$ 0	\$ 0	\$ _____
High School Student (Copy of Student ID Required)	\$ 0	\$ 0	\$ 0	\$ _____
SOT Affiliate	\$ 0	\$ 0	\$ 0	\$ _____
Press	\$ 0	\$ 0	\$ 0	\$ _____
Guest/Spouse (Nonscientist/No access to the scientific sessions or ToxExpo)	\$ 70	\$ 85	\$100	\$ _____

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: _____

Registration Fee(s) (from part 1) \$ _____

Continuing Education Courses (from part 2) \$ _____

Student and Postdoc Functions (from part 2) \$ _____

Print Materials (from part 2) \$ _____

TOTAL DUE \$ _____

By registering for the SOT Annual Meeting you agree to the terms and conditions outlined in the registration policies on page 28.

* After February 12, Final Registration rates apply. SOT will accept faxed registration forms until March 10. Online registration will be open until March 17. On-Site registration forms will be available at the Annual Meeting Registration Desk.

** Special offer to nonmember 2016 Annual Meeting attendees: submit your completed application for the May review cycle (deadline May 1, 2016) and, upon acceptance, SOT will waive your 2016 membership dues.

RETURN THIS TWO-PAGE FORM WITH PAYMENT TO:

SOT Headquarters Registration Dept., 1821 Michael Faraday Drive, Suite 300, Reston, VA 20190-5332

Faxed forms are accepted only if using a credit card. Fax form to: 703.438.3113.

US GOVERNMENT PURCHASE ORDERS MUST BE FAXED OR MAILED WITH THE REGISTRATION FORM.

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



Registration Form

SOT 55th Annual Meeting • March 13–17, 2016

(Part 2 continued from previous page)

CONTINUING EDUCATION COURSES:

☐ Yes, I would like to attend the following CE courses. (Only meeting registrants may enroll in a CE course.) AM # _____ PM # _____ (Only 1 per time slot)

	Early-Bird Registration (Received by Jan. 15)	Standard Registration (Jan. 16 to Feb. 12)	Final Registration (After Feb. 12)	# of Courses	
SOT Member/Affiliate	\$150 each	\$185 each	\$220 each	x _____	\$ _____
SOT Retired/Emeritus Member	\$110 each	\$145 each	\$180 each	x _____	\$ _____
Nonmember	\$300 each	\$335 each	\$370 each	x _____	\$ _____
Postdoctoral (SOT Member/Nonmember)	\$ 90 each	\$125 each	\$160 each	x _____	\$ _____
Graduate or Undergraduate Student (SOT Member/Nonmember)	\$ 45 each	\$ 80 each	\$115 each	x _____	\$ _____
Press	\$ 0 each	\$ 0 each	\$ 0 each	x _____	\$ _____

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

SOT Member/Affiliate	\$ 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) \$ Complimentary

☐ 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) \$ Complimentary

☐ Yes, I would like to attend the Mentoring Breakfast on Monday, 6:15 am–7:45 am, as a mentee. (Limited seating and ticket required) \$ 10

Yes, I am a graduate student or postdoctoral member registrant and would like to attend the complimentary Trainee Discussion

Select one only: (Limited seating and ticket required)

☐ Monday, 10:00 am–11:00 am Daily Plenary Speakers Doris Taylor, Joan Nichols

\$ Complimentary

☐ Tuesday, 10:00 am–11:00 am Daily Plenary Speakers Stephen Skaper, Alan I. Faden

\$ Complimentary

☐ Wednesday, 10:00 am–11:00 am Daily Plenary/MRC Speaker Robin J. M. Franklin

\$ Complimentary

☐ Yes, I am a student or postdoctoral registrant and would like to attend the *In Vitro* Lecture and Luncheon on Monday, 11:30 am–1:00 pm. (Ticket required) \$ 10

☐ Yes, I am a postdoctoral registrant and would like to attend the Postdoctoral Luncheon on Tuesday, 12:00 noon–1:15 pm. (Limited seating and ticket required) \$ 10

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 before the meeting, please mark this checkbox and it will be mailed to you in early March (in the US and Canada only). The Program will also 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 12, 2016). \$ 20

2016 registrants will receive the abstracts, a PDF of *The Toxicologist* download via the SOT website, as part of the Annual Meeting registration fee. A printed version of *The Toxicologist* will be available for purchase at \$40 per copy (available while supplies last).

☐ Yes, I want to purchase the printed version of *The Toxicologist*. \$40 each x _____ \$ _____

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

- | | | | | |
|---|---|--|---|---|
| A. Type of Organization:
1. Academia
2. Consultant
3. Contract Research
4. Government
5. Military
6. Private Industry
7. Other _____
B. Job Function:
8. Analytical
9. Financial/Purch.
10. Computer/Statistics
11. Health and Safety
12. Mgmt. Corporate
13. Mgmt. Facilities
14. Mgmt. Personnel
15. Marketing/Sales
16. Quality Assurance
17. Regulatory | 18. R&D Admin.
19. R&D Operations
20. R&D Technical
21. Teaching
22. Other _____
C. Field of Work:
23. Biological Modeling
24. Biotechnology
25. Carcinogenesis
26. Cardiovascular
27. Clinical & Transl. Tox.
28. Comparative and Vet.
29. Dermal Tox.
30. Drug Discovery Tox.
31. Epidemiology
32. Ethical, Legal, and Social Issues
33. Food Safety
34. General Tox. | 35. Genetic Tox.
36. Immunotoxicology
37. Infusion Tox.
38. Inhalation Tox.
39. <i>In Vitro</i> and Alt. Methods
40. Mechanisms
41. Medical Devices
42. Metals
43. Methods
44. Mixtures
45. Molecular Biology
46. Mutagenicity
47. Nanotoxicology
48. Neurotoxicology
49. Occup. and Public Health
50. Ocular Tox.
51. Pathology
52. Pharmacokinetics
53. Pharmacology | 54. Risk Assessment
55. Reg. and Safety Eval.
56. Repro. and Develop. Tox.
57. Stem Cells
58. Other _____
D. Product Interest:
59. Publications
60. Contract Services:
a. Analytical
b. Aquatic Tox.
c. Clinical Tox.
d. Computer
e. <i>In Vitro</i> Tox.
f. Metabolic Profile
g. Pathology
h. Preclinical Tox.
i. Quality Assurance
j. Wildlife Tox. | 61. Supplies/Equipment
a. Analytical
b. Clinical Chem.
c. Hardware
d. Software
e. <i>In Vitro</i>
f. <i>In Vivo</i>
g. Lab Animal
h. Neurotoxicology
i. Pathology
j. Radioactive Isotope
62. Other _____
E. Purchasing Responsibilities:
63. 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 12, 2016.

SOT will accept faxed registration forms until March 10. Online registration will be open until March 17.

On-Site registration forms will be available at the Annual Meeting Registration Desk.

(continued from page 25)

Nonmember Attendee Offer

JOIN SOT AND SAVE!

Special offer to nonmember 2016 Annual Meeting attendees: submit your completed application for the May review cycle deadline is May 1, 2016, and, when accepted, SOT will waive your 2016 membership dues. See the following page for membership information.

Registration Materials

Badges

Badges and event tickets will be mailed in advance if you register by January 15, 2016. 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.

Tickets

Tickets are required for Continuing Education 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 or special events.

Program

In an effort to increase resources, 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 mark the checkbox on the registration form by February 12, and it 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 31 for more details about the *Program* and *The Toxicologist*.

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.

ToxExpo Directory

The *ToxExpo Directory* is a complimentary resource available on-site which identifies exhibitors who are demonstrating products and services in demand on the ToxExpo floor. The directory features a brief description of each exhibitor along with their booth number. The index feature assists attendees who are looking to identify a specific product or service. The *ToxExpo Directory* is a widely available resource for all attendees.



2016 SOT Annual Meeting Policies

By registering for the 2016 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 policies adopted above will be enforced by the Society. Those individuals who do not comply will be asked to leave the session or ToxExpo floor. If you have any questions regarding these policies, please contact the SOT Headquarters Office.

Join the Society of Toxicology or upgrade your membership to a level that's right for you.

Membership is affordable and adds value!



Communicate, connect, and collaborate with colleagues via ToXchange. If it is happening within SOT, it is in ToXchange.



Access *Toxicological Sciences*, the official journal of SOT.



Qualify for reduced SOT member rates for SOT meetings, courses, and events.



Join one or more of the 27 Specialty Sections, 18 Regional Chapters, and 6 Special Interest Groups.



Utilize career resources such as the SOT Job Bank and Mentor Match throughout the year.



Qualify for SOT member awards—more than 45 awards are available to members.

Full members demonstrate a continuing professional interest in toxicology and have conducted and published original research, and/or are generally recognized as expert in some area of toxicology.

Associate members are engaged in continuing professional scientific activities in toxicology.

Postdoctoral members hold a PhD or other doctoral degree (e.g., MD, DVM) with an interest in toxicology and are under the direction of a research mentor.

Student members are enrolled in a graduate degree program related to toxicology.

Dues assistance opportunities exist for approved members in developing countries. Undergraduate students can become involved as SOT Undergraduate Student Affiliates.

8,000 members from more than 70 countries worldwide

Use the online membership application to join or upgrade your membership. Visit www.toxicology.org and select Join SOT at the top of the page.

Special offer to nonmember 2016 Annual Meeting attendees: submit your completed application for the May review cycle (deadline May 1, 2016) and, upon acceptance, SOT will waive your 2016 membership dues.

General Information

Questions? Tel: 703.438.3115 SOT Headquarters Staff Contacts

Awards and Fellowships

Raul Suarez Extension 1461
raul@toxicology.org

Career Resource and Development

Kevin Merritt Extension 1601
kevin@toxicology.org

Continuing Education

Rachel Froberg Extension 1435
rachel@toxicology.org

Education and K-12 Activities

Betty Eidemiller Extension 1430
bettye@toxicology.org

Exhibits

Tonja Morrow Extension 1454
tmorrow@toxicology.org

Global Gallery of Toxicology

Kevin Merritt Extension 1601
kevin@toxicology.org

Marketing and Advertising Opportunities

Tonja Morrow Extension 1454
tmorrow@toxicology.org

Media

Michelle Werts Extension 1640
michelle@toxicology.org

Meetings and Housing

Heidi Prange Extension 1424
heidi@toxicology.org

Membership

Kimberly von Brook Extension 1600
kimberly@toxicology.org

Past Presidents' 5K Fun Run/Walk

Amy Willis Extension 1406
amy@toxicology.org

Regional Chapters

Ashley Pomper Extension 1402
ashley@toxicology.org

Registration

Jim Dailey Extension 1428
jimd@toxicology.org

Satellite and Ancillary Meetings

Amy Willis Extension 1406
amy@toxicology.org

Scientific Program

David Rossé Extension 1438
davidr@toxicology.org

SOT Global Partners

Marcia Lawson Extension 1446
marcia@toxicology.org

Special Interest Groups

Ashley Pomper Extension 1402
ashley@toxicology.org

Specialty Sections

Raul Suarez Extension 1461
raul@toxicology.org

Support Opportunities

Laura Helm Extension 1403
laura@toxicology.org

Volunteer Information

Rosibel Alvarenga Extension 1432
rosibel@toxicology.org

General Information

SOT Services

SOT Pavilion

Stop by the SOT Pavilion anytime during ToxExpo hours. Get answers to SOT questions and have impromptu (or scheduled) conversations with friends and colleagues. You can:

Chat with *Toxicological Sciences* Editor-in-Chief Gary Miller and Managing Editor Virginia Hawkins.

Meet representatives from SOT Regional Chapters, Special Interest Groups, and Specialty Sections.

Share your Annual Meeting, SOT, and toxicology experiences in our social media corner.

Receive guidance on how to communicate your science more effectively.

Learn about SOT activities, programs, and membership.

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



The Toxicologist: The Official Record of the 2016 Annual Meeting Abstracts

The Toxicologist is an important scientific resource, as it is the official compilation of all accepted abstracts for the 55th Annual Meeting of the Society of Toxicology. With over 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 \$40 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 available on the SOT website and app market places.



Viewing Abstracts

***The Toxicologist* will be available to download as a PDF via the SOT website in early March. The Late-Breaking Abstracts Supplement will be available for download in March and these abstracts will also be searchable in the Mobile Event App and Online Planner.**

(Please see complete details on page 78.)

(continued on page 33)

Tell the world why you love toxicology.



Tao Wang @SOToxicology Mar 13

I ♥ #TOXICOLOGY because...
toxicological testing helps to ensure
the safety of medicines to patients
#YouTox #IAMATOXICOLOGIST

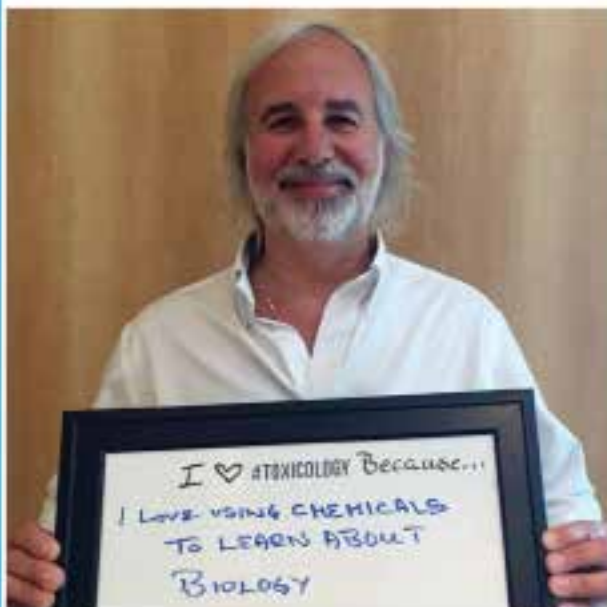


Stop by the SOT Pavilion to learn about the GSLC #YouTox campaign.



Norbert E. Kaminski
20 hours ago

I ♥ #TOXICOLOGY because...
i love using chemicals to learn about biology #YouTox
#IAMATOXICOLOGIST



Like • Comment • Share

2

100 people like this.



Write a comment...



Calling All Contestants!

TOX SHOWDOWN

Hosted by: Graduate Student Leadership Committee



Join us for 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 rachel@toxicology.org.

Tuesday, March 15 | 7:30 PM | Hilton New Orleans Riverside

The Program: The Official Guide to the SOT 2016 Annual Meeting and ToxExpo

The *Program* is the official guide to all the activities of the 2016 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.

The *Program* details the schedule of events by name and lists all the special events, including the 2016 award recipients, 2016 Honorary member, SOT Endowment Fund 2015 award recipients, recognition and special events; and Regional Chapter, Special Interest Group, and Specialty Section meetings and receptions. In addition, the *Program* includes a general section that highlights travel, hotel, registration, parking, and safety and security information. The complete listing of the ToxExpo exhibitors is provided, along with the floor plan for the ToxExpo and a complete listing of Exhibitor-Hosted Sessions.

The *Program* PDF is available for download via the SOT website (early February).

Copies of the *Program* can be picked up on-site. In an effort to better use resources, 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 12), 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).

ToxExpo Directory

The *ToxExpo Directory* is a complimentary resource available on-site which identifies exhibitors who are demonstrating products and services in demand on the ToxExpo floor. The directory features a brief description of each exhibitor along with their booth number. The index feature assists attendees who are looking to identify a specific product or service. The *ToxExpo Directory* is a widely available resource for all attendees.

Attire

The official attire for the Annual Meeting is business casual. No coat or tie is required! We encourage you to bring comfortable clothing and shoes. Because meeting rooms may seem cold, please bring a sweater or jacket and/or dress in layers.

Badge

Annual Meeting attendees who register by January 15, 2016, will receive badges and registration materials in the mail. Attendees who already have their 2016 Annual Meeting badges do not need to stand in the registration line. If you have registered by the meeting date and have NOT received your badge by mail, or need a replacement badge, go to the "BADGE PICK UP" registration counter to pick up your badge. You will be asked to show a photo ID.

If you have not registered for the meeting before you arrive in New Orleans, please complete the on-site registration form found at the kiosks in the registration area and proceed to the appropriate registration line. Registration information is available on page 25.

Guest/Spouse Hospitality Room

The SOT Guest/Spouse Hospitality Room will be located in the Hilton New Orleans Riverside. 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 25.

Internet Access at the Convention Center

SOT understands the importance of being connected to your daily activities while attending the Annual Meeting and provides several ways for you to access the Internet while at the New Orleans Ernest N. Morial 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 on the Lobby Level of the New Orleans Ernest N. Morial Convention Center.

Free Wireless Internet Access

As a service to Annual Meeting registrants, SOT will be providing free wireless Internet access throughout the New Orleans Ernest N. Morial Convention Center in all locations where SOT events are being held. Information on how to gain access to the wireless Internet will be made available in the final *Program*.

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
SOT Headquarters: 703.438.3115
Email: michelle@toxicology.org



Why wait until the rooms are gone?

Book your hotel reservation today!

Go to www.toxicology.org/events/am/am2016/housing.asp or call SOT's official housing company.

Connections Housing, 800.262.9974 or 404.842.0000.

The deadline is February 12, 2016.

See details on page 18.



51 Ways to Enhance Your Annual Meeting Experience

Regional Chapters

Participate in the reception of your hometown chapter while you are in New Orleans—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!



Participate—You'll be glad you did!

Be involved with a Regional Chapter, Special Interest Group, or Specialty Section. 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 58 for the schedule component group events.

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, 2016, will be listed in the *Program*.

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 are scheduled at the end of the Society's program. The 2016 satellite meetings will be held in and around the New Orleans area. Proposals for a satellite meeting should be sent by email to heidi@toxicology.org to the attention of John B. Morris, SOT Vice President and Scientific Program Committee Chair. Requests approved by January 4, 2016, will be published in the *Program*. All requests must be received by January 19, 2016. Two events have been scheduled, see details on page 63.

Poster Displays

Global Gallery of Toxicology

Toxicology societies from around the world are invited to participate in the Global Gallery of Toxicology. Now in its fifth year, posters of these sister societies will be prominently displayed during the meeting, showcasing their formation, key accomplishments, strategic initiatives, and activities. The 2016 Global Gallery poster session will be listed in the scientific program with a "Representative Attended" poster time from 11:45 am to 12:15 pm on Monday, March 14. 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, 2016.



High School Poster Exposition

On Tuesday, March 15, from 10:00 am–12:00 noon, high school students will present their research posters in a special area near the SOT Pavilion. Some students will be on-site and others will present through a virtual connection.

RC, SIG, and SS Posters

Dedicated poster space is available for the SOT Regional Chapters, Special Interest Groups, and Specialty Sections during the 2016 SOT Annual Meeting. The poster area will be located adjacent to the SOT Pavilion in the ToxExpo Exhibit Hall and will be attended on Monday, March 14, from 11:45 am–12:15 pm.



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 through the Mobile Event App anytime during the meeting. Scientific ePosters also will be available through the app until May 11, 2016.

Scientific Poster Printing Services

SOT is pleased to offer our poster presenters a convenient printing service through Shepard Exposition Services, the official general service contractor for the Annual Meeting. No need to worry about traveling with your poster or having your poster lost in shipping. Simply complete the online form, email or upload your poster using the link provided, review and approve the final layout of your poster, and then pick up your poster on-site. Shepard will produce the materials for a reasonable price, which will include production, transportation, and storage for the show. **The deadline to take advantage of this service is February 27, 2016.**

For more information you can contact Michael Graham with Shepard Exposition Services at 703.352.4900 or mgraham@shepardes.com. The order form is located online on the SOT Annual Meeting website at www.toxicology.org/events/am/am2016/forms.asp.

High School Student and Teacher Workshop Safety Matters: Toxicology and Product Safety

Tuesday, March 15, 8:30 AM to 2:15 PM

South Central Regional Chapter will host an interactive toxicology workshop that is coordinated with the High School Poster Exposition.

Toxicologists, please volunteer to help with this exciting activity.

Participants and volunteers can register at the link given in the Special Events section of the Annual Meeting website.

Contact: bettye@toxicology.org



High School Poster Exposition

Tuesday, March 15, 10:00 AM to 12:00 Noon

High school students with research projects related to toxicology apply by submitting information by January 30, 2016, at the link given in the Special Events section of the Annual Meeting website.

Students who are accepted will present on-site or by a virtual connection.

Toxicologists, please volunteer to mentor presenters.

Contact: bettye@toxicology.org



New Orleans Ernest N. Morial Convention Center

The SOT 55th Annual Meeting and ToxExpo will be held at the New Orleans Ernest N. Morial Convention Center located at 900 Convention Center Boulevard in downtown New Orleans. This recently renovated convention center sits on the banks of the Mississippi River and is a short walk to the French Quarter. It is considered one of the top ten convention venues in North America.

Accessibility for Persons with Disabilities

The New Orleans Ernest N. Morial Convention Center and most of the SOT hotels are accessible to persons with disabilities. If you require special services, please mark the appropriate box on the Annual Meeting Registration Form.

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

If you require more handicapped information about accessibility, please contact Heidi Prange at SOT Headquarters: 703.438.3115 ext. 1424.

Child Care Services

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

First Aid and Emergency Services at the Convention Center

If an emergency should occur while at the New Orleans Ernest N. Morial Convention Center, proceed directly to the nearest house phone, located throughout the facility, and dial 5911 for security. You will be connected directly to the 24-hour manned security department at the convention center.

A First Aid room will be located across from Hall B, near Registration.

An emergency medical technician will be on duty:

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.

Green in New Orleans

The city's compact downtown area is very walkable and minimizes the need for transportation. At the New Orleans Ernest N. Morial Convention Center, new green practices are helping save water, conserve energy, and reduce waste. Look for recycling bins around the center and put your paper products to better use. For more information, visit the MCCNO website (www.mccno.com). Outside of the convention center, the city of New Orleans also is doing its part to be green, with its New Orleans Area Green Business Project encouraging "green" practices among businesses in the region, by offering tools to implement more efficient and sustainable business operations.



Weather

New Orleans has a subtropical climate.

72°
TO
52°
F



For an up-to-date, detailed weather forecast, visit the National Weather Service Forecast Office at www.srh.noaa.gov/lix.

New Orleans General Information

New Orleans is the birthplace of jazz, home to Creole cuisine, and rich with history and culture. It is centrally located with an easy to walk downtown and world-class convention facilities. It's a place of chefs and delectable cuisine and a unique blend of French, Spanish, Caribbean, and African cultural influences in its architecture, food, people, and music. Most of the city's restaurants, attractions, tours, accommodations, and event venues are within walking distance of each other, it's easy to get around the "Big Easy" and is the perfect setting for networking. Within the 12-blocks of the historic French Quarter, come enjoy the charm of New Orleans, while attending the SOT Annual Meeting. New Orleans combines big city choices with the small town friendliness. *Laissez les bons temps rouler*—let the good times roll!

Science-Based Attractions in New Orleans

Audubon Aquarium of the Americas

1 Canal Street | Tel: 504.581.4629

One of the top five aquariums in the country is located just steps away from the New Orleans Ernest N. Morial Convention Center in the historic French Quarter! The aquarium is home to more than 10,000 animals representing 400 species, including rare and endangered species. See the only two Sea Otters in the South play, or view exotic frogs, animal presentations and feedings help you understand these underwater creatures.

SOT FDA Colloquia on Emerging Toxicological Science Challenges in Food and Ingredient Safety

Upcoming Events and Live Webcasts • FDA, College Park, Maryland

State of the Art in the Cramer Classification Scheme and Threshold of Toxicological Concern

Ivan Rusyn, Chair, *Texas A&M, College Station, TX*

March 29, 2016

Safety Assessment Approaches to Sensitive Subpopulations

Allen Rudman, Chair, *FDA CFSAN, College Park, MD*

April/May 2016

Role of Mode of Action in Dose-Response Assessment for Carcinogens

Date to be determined in 2016



Access Event Materials

Recordings, Presentation Slides, Captioning Record

Find materials on the event webpage

www.toxicology.org/fda.

Complexities in Evaluating Human Clinical and Observational Data for Ingredient Safety Assessment: Partially Hydrogenated Oils (PHOs) as a Case Study

November 7, 2014

Application of ADME/PK Studies to Improve Safety Assessments for Foods and Cosmetics

February 23, 2015

Immunotoxicology in Food and Ingredient Safety Assessment: Approaches and Case Studies

April 14, 2015

Contemporary Issues in Risk Assessment

June 17, 2015

Contemporary Issues in Computational and In Silico Methods for Food Ingredient Assessment

October 13, 2015

Audubon Butterfly and Insectarium

423 Canal Street | Tel: 504.581.4629

The Audubon Butterfly Garden and Insectarium is dedicated to the largest group of animals on the planet: insects. This family friendly attraction allows you to experience insect encounters, bug animation and surprises in an immersion theater, a serene Japanese butterfly garden and much more.

Audubon Zoo

6500 Magazine Street | Tel: 504.581.4629

Visit the Audubon Zoo and see animals from all over the world in natural habitat settings, including the natives at the Louisiana Swamp Exhibit. The zoo grounds include more than 50 acres, and are located on the former site of an 18th-century sugar plantation and the 1884 World Exposition. Take a ride on the swamp train to easily view all their major exhibits, and bring your bathing suit for the Cool Zoo water park stop!

New Orleans Area Activities

For things to do in New Orleans, go to www.neworleanscvb.com.

Blain Kern's Mardi Gras World

1380 Port of New Orleans Place | Tel: 504.361.7821

Take a tour of Blaine Kern Studios, where they have been building Mardi Gras floats for over 60 years. See what it takes to create these magnificent centerpieces of the parade, at the place where Mardi Gras lives all year long.



French Quarter

Between Canal Street and Esplanade Avenue

New Orleans's French Quarter, also known as Vieux Carré, comprises 78-square blocks which are situated between Canal Street and Esplanade Avenue. Founded in 1718 by Jean-Baptiste Le Moyne de Bienville, the whole city developed around this area, which has now been designated a National Historic Landmark. From Bourbon Street and beyond you can view the Quarter's architecture, which is a mix of Spanish, French, Creole, and American styles, or find some of the best restaurants in the city and explore eclectic shops. The Quarter is a vibrant place where you can always discover something new, whether it is a local artist or a jazz band playing on the street corner.

Garden District

St. Charles Avenue to Magazine Street,
and Jackson Avenue to Louisiana Avenue

After a pleasant ride on the St. Charles Avenue Streetcar, take some time to explore one of New Orleans prettiest neighborhoods, which happens to be home to one of the best-preserved collections of historic Southern mansions, many of which are owned by local celebrities. Walk down Magazine Street to enjoy its numerous boutique shops and wonderful restaurants, or explore Lafayette Cemetery No.1 to see why New Orleans is considered one of the most haunted cities in America.



St. Charles Avenue Streetcar Line

St. Charles Avenue

Made famous by Tennessee Williams' "A Streetcar Named Desire" you can hop on the oldest continually operating street railway system in the world to explore areas of New Orleans such as the Garden District, Uptown, and Riverbend for only a \$1.25 fare each way.

St. Louis Cathedral

615 Père Antoine Alley | Tel: 504.525.9585

The jewel of Jackson Square, originally built in 1718, the current cathedral dates back to the mid 1800's, making it one of the oldest cathedrals in the United States. St. Louis Cathedral's beautiful architecture is a blend of Renaissance and Spanish Colonial styles that is uniquely New Orleans. Each year hundreds of pilgrims flock to the cathedral's cemetery to see the tomb of Marie Laveau, a renowned Voodoo priestess in New Orleans.

The Cabildo

701 Chartres Street | Tel: 504.568.6968

Now the flagship building of the Louisiana State Museum, this building was once the site of the Louisiana Purchase and the home of the Louisiana State Supreme Court until 1908. This historic building where monumental decisions such as Plessy v. Ferguson originated, now houses exhibitions on Louisiana's history.

Meet the Editor-in-Chief of *Toxicological Sciences*

Gary W. Miller

**SOT Pavilion
Monday–Wednesday
March 14–16**



Attend.

Discover.

Share.



Volunteer to serve as an SOT Reporter to help capture the science and events in New Orleans.

Contact marcia@toxicology.org to sign up and for more information.

The Ogden Museum of Southern Art

925 Camp Street | Tel: 504.539.9650

The Ogden Museum of Southern Art is the home of wonderful collections of paintings, photography, and ceramics all from below the Mason-Dixon Line. Every Thursday night the museum stays open late for Ogden After Hours, featuring live music and soul food while you peruse the galleries.



The National World War II Museum

945 Magazine Street | Tel: 504.528.1944

While you're in New Orleans visit one of the top museums in the country on World War II, for a special, immersive, and enlightening experience. Walk through three grand pavilions to view larger than life exhibits with retellings of stories of survival. Be sure to see "Beyond All Boundaries," a 4D film narrated by Tom Hanks in the museum's Solomon Victory Theater.

New Orleans Golf Courses

Audubon Park Golf Course

6500 Magazine Street | Tel: 504.212.5290

(19 minutes from the convention center)

Re-designed in 2001 by Dennis Griffiths, this course sits in the middle of the city and boasts a competitive executive-18-hole course that is a par 62, while its 4,220-yard layout is set among hundred year-old oak trees.

Lakewood Golf Club

4801 General DeGaulle Drive | Tel: 504.373.5926

(12 minutes from the convention center)

This recently renovated course has hosted 26 New Orleans Opens, and celebrated its 50th Anniversary in 2011. You can expect thrilling courses to play with challenging fairways, tees and greens, all tucked among gorgeous cypress and oak trees.

English Turn Golf and Country Club

1 Clubhouse Drive | Tel: 504.391.8018

(18 minutes from the convention center)

This 18-hole championship course was designed by world famous golfer Jack Nicklaus in 1988. This former PGA Tour stop boasts expansive green lawns surrounded by flower gardens.

New Orleans Fun Facts

- The first Mardi Gras parade took place on Shrove Tuesday in 1838 in New Orleans.
- Riders on Mardi Gras floats are required, by law, to be masked.
- New Orleans is the birthplace of Jazz, the only true American musical art form. Jazz gave birth to the Blues and Rock and Roll music. Jazz was originally called jass, in reference to the fragrant jasmine that women in New Orleans Storyland red light district wore. Jazz musicians originally played in the district bordellos.
- The total mileage of canals both above and below ground in New Orleans exceeds that of Venice in Italy.
- Originally built in 1718, the St. Louis Cathedral in New Orleans is the oldest cathedral in the US. The present structure, the third one on the site, dates from 1789.
- Living up to its reputation as Hollywood South, 25 feature-length films and 12 TV series or pilots were shot in New Orleans in 2014, and 130 feature-length films have been shot here in the last five years.
- Poker and craps were invented in New Orleans during the 1700s.
- The formal transfer of the Louisiana Purchase was made at the Cabildo building in New Orleans on December 20, 1803.
- New Orleans has more than 140 registered festivals, providing year-round entertainment for locals and visitors alike.
- The famous beignet is the Louisiana State donut.





Career Advancement and Development Resources

Education-Career Development Opportunities

Chat with an Expert

Monday, March 14 to Thursday, March 17

Time Varies by Group

(Meet at the Chat with an Expert Poster Board in Lobby A near the ToxExpo Entrance)

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 2016. Details for each group meeting will be sent to participants in advance of the meeting.

Poster Tours for Trainees

Monday, March 14 to Wednesday, March 16

Time Varies by Group

(Meet at the Poster Tour Board in Lobby A near the ToxExpo Entrance)

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 2016. Details for each group will be distributed to the participants in advance of the meeting.

Research Funding Information Room

Monday, March 14 to Wednesday, March 16, 9:30 AM to 4:30 PM

Hosted by:

Career Resource and Development Committee

Representatives from federal agencies funding research, including NIH program and review staff of the Center for Scientific Review and NIEHS, 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 the staff member who can discuss with you aspects of scientific review or specific grant opportunities. New investigators are especially encouraged to meet with program staff.

SOT Mentoring Breakfast

Monday, March 14, 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, the Career Resource and Development Committee, in conjunction with the Postdoctoral Assembly and Graduate Student Leadership Committee, is pleased to announce the fifth annual Mentoring Breakfast.

The Mentoring Breakfast is for SOT members at any career stage—from graduate students and postdoctoral scholars to senior scientists—who are seeking a mentor. Brief presentations will be followed by small group discussions led by trained facilitators. Facilitators will work to match participants with compatible mentors. Note that mentor information will be provided after the Annual Meeting, and only mentees should attend the breakfast.

A limit of 50 mentees will be accepted on a first-come, first-served basis for this event at a cost of \$10/person, which includes a continental breakfast.

Trainee Discussion with Plenary Session Presenters: Drs. Taylor and Nichols

Monday, March 14, 10:00 AM to 11:00 AM

(Ticket Required; Limited Seating) ➡



Lecturers: Doris Taylor, Director, Regenerative Medicine Research at the Texas Heart Institute, Houston, TX; and Joan Nichols, University of Texas Medical Branch, Galveston, TX.



Drs. Taylor and Nichols will both 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.

Research Funding Luncheon

Monday, March 14, 12:00 Noon to 1:30 PM

Investigators from various federal agencies will be on hand for this luncheon meeting to talk about the art of preparing successful grant packages. Panelists will discuss the grant submission process and offer advice about how to submit a potentially successful grant and offer tips about how to make a submission stand out.

Free Job Search Service for Members

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Recruit
Highly Qualified
Candidates



Supplement
Your Hiring Process

WWW.TOXICOLOGY.ORG/JOBANK



Education-Career Development Sessions

The Evolution of the Postdoc: Transitioning from Trainee to Professional in the Modern Era

Wednesday, March 16, 12:30 PM to 1:50 PM

"Talksichology": Effective Oral Presentation Techniques

Wednesday, March 16, 5:00 PM to 6:20 PM

See full descriptions on page 115.

Trainee Discussion with Plenary Session Presenters: Drs. Skaper and Faden



Tuesday, March 15, 10:00 AM to 11:00 AM

(Ticket Required; Limited Seating) ➡

Lecturers: Stephen Skaper, University of Padua, Padua, Italy; and Alan I. Faden, University of Maryland School of Medicine, Baltimore, MD.



Drs. Skaper and Faden will both 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. Franklin

Wednesday, March 16, 10:00 AM to 11:00 AM

(Ticket Required; Limited Seating) ➡



Lecturer: Robin J.M. Franklin, Wellcome Trust-MRC Cambridge Stem Cell Institute, University of Cambridge, Cambridge, United Kingdom.

Dr. Franklin 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.

Annual Meeting Job Bank Center

Located in the New Orleans Ernest N. Morial Convention Center, the on-site Job Bank Center provides access to the SOT Job Bank as well as assistance in facilitating interviews during the SOT Annual Meeting. We offer personalized assistance if you are new to the Job Bank or have questions. For your convenience, printers will be available for producing hard copies of candidate resumes and interview information. All candidates and positions must be sought online.

The center is available during the following hours of operation:

Sunday	1:00 PM–5:00 PM
Monday	9:00 AM–5:00 PM
Tuesday	8:30 AM–5:00 PM
Wednesday	8:30 AM–5:00 PM

Employers recognize and appreciate that the Annual Meeting Job Bank Center provides a cost-effective and efficient way to interview a distinguished pool of candidates. For your convenience, we provide five interview rooms on-site during the hours listed above. Employers may reserve interview rooms ahead of time or at the meeting on a first-come, first-served basis.

Job Bank access will be available, as always, through your computer or mobile device, and at the Annual Meeting @SOT Center. Access to the online Job Bank in the Job Bank Center is encouraged, and interested Job Seekers and Employers are welcome to come to the Job Bank Office to ask questions and learn more about the system. For additional information, contact Kevin Merritt at SOT Headquarters: 703.438.3115 ext. 1601 or email: careerresources@toxicology.org.

Mentor Match

Online Mentoring Program

The Society of Toxicology recognizes the importance of mentoring in the scientific and professional development of its members throughout the year. The objective of the Mentor Match online mentoring program is to provide a service that matches mentees with potential mentors from the SOT membership to provide advice on career path selection, professional development, and life/work 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 accessible to all active SOT members by visiting www.toxicology.org/mentormatch.





Awards and Fellowships

AWARDS CEREMONY

**Sunday, March 13, 2016 • 5:15 PM to 6:30 PM • Music Starting at 4:45 PM
New Orleans Ernest N. Morial Convention Center**

Awards Ceremony Music

Sunday, March 13, 4:45 PM to 5:15 PM



Performed by Clarence Johnson III

Known for his fierce and often sultry saxophone sound and astounding virtuosity, New Orleanean Clarence Johnson III enjoys a successful career as a recording and performing artist, an educator, and also appears in films and television. Currently, Clarence is celebrating the national release of his latest recording, "Watch Him Work," his first release in nearly 15 years. The new original material, which features himself and his latest creation, Cornerstone, can best be described as a fresh take on jazz fusion, which is reminiscent of the compositional styles of Stanley Clarke, George Duke, the Brecker Bros., and the Yellow Jackets. Clarence Johnson III will perform for SOT Annual Meeting attendees prior to the SOT Awards Ceremony.

Awards Ceremony

Sunday, March 13, 5:15 PM to 6:30 PM

Please join the Awards Committee, in conjunction with Council, the Board of Publications, and the Education Committee, as we honor distinguished scientists with presentation of Awards at our prestigious SOT Awards Ceremony (pages 48–51). Also conferred at this ceremony are a number of grants, fellowships, and awards 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.

Endowment Fund 2015 Awards

The Endowment Fund awards are conferred during the Annual Meeting. SOT will display the 2015 recipients of the SOT Endowment 2015 Awards during the musical performance. 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.

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 the meeting of their in New Orleans. Visit the website for full details at www.toxicology.org/awards.

SOT Developing Country Travel Awards

The SOT/SOT Endowment Fund/IUTOX Travel Awards for several individuals from developing countries selected in December 2015 will be honored during the Awards Ceremony.

Outstanding Graduate Student Leadership Committee Award

The Outstanding Graduate Student Leadership Committee (GSLC) 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 Graduate Student/Postdoc Mixer on Sunday, March 13.



SOT Honors and Awards



Honorary Membership

Raymond B. Nagle, MD, PhD
University of Arizona Health Sciences Center, Tucson, AZ



Achievement Award

Lauren Aleksunes, PharmD, PhD
Rutgers University, Piscataway, NJ



Arnold J. Lehman Award

Alan Boobis, OBE, BSc, PhD, FSB, FBTS
Imperial College London, London, United Kingdom



Distinguished Toxicology Scholar Award

I. Glenn Sipes, PhD, ATS
University of Arizona, Tucson, AZ

Distinguished Toxicology Scholar Award Lecture—
Wednesday, March 16, 12:30 PM to 1:20 PM



Education Award

Kenneth Reuhl, PhD, DABT
Rutgers University, Piscataway, NJ



Education Award

John Wise Sr., PhD
University of Louisville, Louisville, KY



Enhancement of Animal Welfare Award

Warren Casey, PhD, DABT
NIH, Durham, NC



Founders Award

Richard Adamson, PhD
TPN Associates LLC, Walpole, MA



Leading Edge in Basic Science Award

Cheryl Lyn Walker, PhD, ATS
Texas A&M Institute of Biosciences and Technology, Houston, TX

Leading Edge in Basic Science Award Lecture—
Tuesday, March 15, 12:30 PM to 1:20 PM



Merit Award

Melvin Andersen, PhD, DABT, CIH, ATS
The Hamner Institutes for Health Sciences, Research Triangle Park, NC

Merit Award Lecture—
Monday, March 14, 12:30 PM to 1:20 PM



Public Communications Award

Steven Gilbert, PhD, DABT
Institute of Neurotoxicology & Neurological Disorders, Seattle, WA



Public Communications Award

Gary Ginsberg, PhD
Connecticut Dept of Public Health, Hartford, CT



Translational Impact Award

Richard Beger, MS, PhD
US FDA-NCTR, Jefferson, AR

Translational Impact Award Lecture—
Wednesday, March 16, 5:00 PM to 5:50 PM



Translational/Bridging Travel Award

Mohamed Salama, MD, PhD
Mansoura University, Mansoura, Egypt



Undergraduate Educator Award

Antonio Baines, BS, PhD
North Carolina Central University, Durham, NC



SOT Honors and Awards

Board of Publications for the Best Paper in *Toxicological Sciences* Award

A Systems Biology Approach Utilizing a Mouse Diversity Panel Identifies Genetic Differences Influencing Isoniazid-Induced Microvesicular Steatosis

Toxicological Sciences, 2014, 140(2) 481–492

Rachel J. Church, Hong Wu, Merrie Mosedale, Susan J. Sumner, Wimal Pathmasiri, Catherine L. Kurtz, Matthew T. Pletcher, John S. Eaddy, Karamjeet Pandher, Monica Singer, Ameesha Batheja, Paul B. Watkins, Karissa Adkins, and Alison H. Harrill

Global Senior Scholar Exchange Program



Scholar: **Oladipo Ademuyiwa**, PhD
Federal University of Agriculture, Abeokuta, Nigeria



Host:
Weimin Gao,
MD, MS, MPH, PhD
Texas Tech University, Lubbock, TX



Scholar: **Wafa Hassen**, PhD
High Institute of Biotechnology, Monastir, Tunisia



Host:
Mohamed B. Abou-Donia,
PhD, ATS, DABT
Duke University Medical Center, Durham, NC

Best Postdoctoral Publication Awards

Presented at the Postdoctoral Assembly Luncheon on Tuesday.



Alicia Bolt, PhD
Lady Davis Institute for Medical Research, Montreal, QC, Canada

Bolt AM, Sabourin V, Flores Molina M, Police AM, Negro Silva LF, Plourde D, Lemaire M, Ursini-Siegel J, and Mann KK. **Tungsten Targets the Tumor Microenvironment to Enhance Breast Cancer Metastasis**
Toxicological Sciences, 2015 Jan, 143(1):165–177



Pamela Noyes, PhD
Chevron Energy Technology Company, Houston, TX

Noyes PD, Haggard DE, Gonnerman GD, and Tanguay RL. **Advanced Morphological-Behavioral Test Platform Reveals Neurodevelopmental Defects in Embryonic Zebrafish Exposed to Comprehensive Suite of Halogenated and Organophosphate Flame Retardants**
Toxicological Sciences, 2015 May, 145(1): 177–195.



Pei-Li Yao, PhD
Pennsylvania State University, State College, PA

Yao PL, Chen L, Dobrzański TP, Phillips DA, Zhu B, Kang BH, Gonzalez FJ, and Peters JM. **Inhibition of Testicular Embryonal Carcinoma Cell Tumorigenicity by Peroxisome Proliferator-Activated Receptor- β/δ - and Retinoic Acid Receptor-Dependent Mechanisms**
Oncotarget, 2015 Jul, DOI: 10.18632/Oncotarget.5415.

Perry J. Gehring Diversity Student Travel Award



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

Lizbeth Perez-Castro,
University of Puerto Rico at Cayey, Gurabo, PR



SOT Undergraduate Intern Travel Award



Jessica Ray,
Michigan State University, East Lansing, MI

Institution where research was conducted:
University of Montana, Missoula, MT



Pfizer SOT Undergraduate Student Travel Awards



Sarah Burnett
University of Arkansas, Fayetteville, AR



James M. Ding
University of Texas at Austin, Austin, TX



Benjamin Alan Elser
Indiana University, Bloomington, IN



Emily B. Fabyanic
West Virginia University, Morgantown, WV



Laura Fisch
Montana State University, Bozeman, MN



Eduardo Aztlan Gonzalez
University of California Davis, Davis, CA



Mina Huerta
Oberlin College, Oberlin, OH



Haydee M. Jacobs
University of Massachusetts Amherst, Amherst, MA



Rachael A. McMinimy
Oberlin College, Oberlin, OH



Chimwemwe Mwase
Paine College, Augusta, GA



Danyelle B. Osowski
University of North Dakota, Grand Forks, NC



Lizbeth Perez-Castro
University of Puerto Rico at Cayey, Gurabo, PR

Institution where research was conducted:
Michigan State University, East Lansing, MI



Jiwon Seo
John Jay College of Criminal Justice, New York, NY



Carolyn Anne Smith
United States Coast Guard Academy, New London, CT



Stephanie N. Thiede
Purdue University, West Lafayette, IN



Nancy Ly Tran
Bates College, Lewiston, ME



Jamie Weimer
Northern Kentucky University, Highland Heights, KY

Supported Grants, Fellowships, and Awards

Colgate-Palmolive Grant
for Alternative Research

David Pamies, MD
Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Colgate-Palmolive Postdoctoral Fellowship
Award in *In Vitro* Toxicology

Katherine Dunnick, PhD
The Hamner Institutes for Health Sciences, Durham, NC



Lei Yin, PhD
University of Georgia, Athens, GA

Colgate-Palmolive Award for Student Research
Training in Alternative Methods

Shih-Yu Chang, MS
University of Washington, Seattle, WA

Syngenta Fellowship Award in Human Health
Applications of New Technologies

Thomas Luechtefeld, BS
Johns Hopkins Bloomberg School of Public Health, Baltimore, MD



Tshepo Moto, BS, MPH
University of Pretoria, Pretoria, South Africa

SOT | Society of
Toxicology
Creating a Safer and Healthier World by Advancing
the Science and Increasing the Impact of Toxicology



Call for 2017 Award Nominations

SOT recognizes many distinguished toxicologists, postdoctoral researchers, and students with prestigious awards each year. While SOT Awards Season formally opens on July 1, it is never too early to begin collaborations with your colleagues to start the nomination process. Many of SOT's prominent awards require two full members of the Society to provide a primary and secondary letter of nomination.

Nominations and applications for most SOT Awards and Supported Awards are made online via the Awards and Funding section of the SOT website.

Nominations due October 9, 2016

For award descriptions, requirements, and additional information, please visit www.toxicology.org/awards.

Questions? Contact SOT Headquarters at sothq@toxicology.org.

Special Events



SPECIAL EVENTS

All activities will be held at the New Orleans Ernest N. Morial Convention Center in New Orleans, Louisiana, unless otherwise noted.

Full details on the Special Events will be available in the *Program*, on the website, and via the Mobile Event App and Online Planner.

Committee on Diversity Initiatives Reunion

Saturday, March 12, 7:30 PM to 8:30 PM

Hosted by:

Committee for Diversity Initiatives

Join the Committee on Diversity Initiatives (CDI) 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 27 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 2016 Perry J. Gehring Diversity Student Travel Award. Dessert, coffee, and tea will be served, so please mark your calendars and start the 55th Annual Meeting with a fun and interactive evening at the CDI Reunion.

Welcome Reception

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

Continue the celebration by attending the Welcome Reception following the Awards Ceremony. 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.



25-Year (Or More) Member Reception

Sunday, March 13, 7:00 PM to 8:00 PM

If you have been a member of the Society of Toxicology for 25 years or more, please join your colleagues in recognition and celebration of your contributions to the Society. Be sure to wear your membership anniversary pin.



Global Collaboration Coffee

Monday, March 14, 9:30 AM to 11:30 AM

The SOT Council invites all Global Gallery participants and representatives of societies from around the world to the Global Collaboration Coffee. 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 14. 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 15, 7:00 AM
Audubon Park

Supported by:
IDEXX Laboratories, Inc.

When you pack for the meeting, don't forget your running shoes so you can join us for the sixth 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 5 to receive a complimentary souvenir t-shirt; visit the Special Events 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 15, 4:45 PM to 6:15 PM

SOT Members are invited and encouraged to attend the 55th SOT Annual Business Meeting. The agenda includes discussion of plans for next year, a financial summary, and a review of the 2015–2016 accomplishments.



Attention: Students and Postdoctoral Scholars

- Chat with an Expert
- Poster Tours for Trainees
- Research Funding Luncheon
- SOT Mentoring Breakfast
- Trainee Discussion with MRC Lecturer
- Trainee Discussions with Plenary Session Lecturers

See full descriptions on page 42.

Tox ShowDown

Tuesday, March 15, 7:30 PM to 9:00 PM
Hilton New Orleans Riverside

Chairperson(s): Joanna Kreitinger, GSLC Secretary, University of Montana, Missoula, MT.

Produced by:
Graduate Student Leadership Committee



Join hosts Phil Wexler and Sue Ford along with the Graduate Student Leadership Committee (GSLC) and your peers Tuesday night for the *Tox ShowDown*, an engaging quiz game patterned off the popular long-running show *It's Academic*. Three teams—The Endocrine Disruptors, The Free Radicals, and the Toxic Metabolites—will compete while answering questions concerning toxicology in its scientific context, as it relates to society, the arts, and culture.

Supported by GSLC, this event is sure to be both informative and entertaining and a perfect way to celebrate the halfway point of the SOT Annual Meeting. The game will provide attendees with a break, albeit still toxicologically oriented, from the more technical business of the meeting.

Undergraduate Educator Network Meeting

Wednesday, March 16, 2:15 PM to 4:00 PM

Chairperson(s): Joshua Gray, US Coast Guard Academy, New London, CT.

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 for 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.

STUDENT AND POSTDOCTORAL SCHOLAR EVENTS



Undergraduate Diversity Program

Saturday, March 12 to Monday, March 14

Chairperson(s): Jorge Naciff, Procter & Gamble Company, Mason, OH.

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/events/am/am2016/edout.asp.

Sunday Undergraduate Education Program

Sunday, March 13, 8:00 AM to 5:00 PM

Chairperson(s): Jorge Naciff, Procter & Gamble Company, Mason, OH.

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/events/am/am2016/edout.asp.

cologists in various employment sectors to become more familiar with different career paths in toxicology. For schedule details go to www.toxicology.org/events/am/am2016/edout.asp.

Student/Postdoctoral Scholar Mixer

Sunday, March 13, 7:30 PM to 9:00 PM

(Ticket Required) ➡

Hosted by:

Graduate Student Leadership Committee

The Graduate Student Leadership Committee hosts 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.





Symposium

Genotypic and Intrinsic Risk Factors That Increase Susceptibility to Inhaled Pollutants

Organized by the Graduate Student Leadership Committee and Postdoctoral Assembly

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

See full description on page 83.

Education-Career Development Sessions

The Evolution of the Postdoc: Transitioning from Trainee to Professional in the Modern Era

Wednesday, March 16, 12:30 PM to 1:50 PM

"Talksicology": Effective Oral Presentation Techniques

Wednesday, March 16, 5:00 PM to 6:20 PM

See full descriptions on page 115.



In Vitro Toxicology Lecture and Luncheon

Multicellular Model Systems for *In Vitro* Toxicity Testing—Strengths and Challenges

Monday, March 14, 11:30 AM to 1:00 PM

(Ticket Required) ➡

Chairperson(s): Vicente Santa Cruz, Chevron Phillips Chemical Company LP, Conroe, TX; Co-Chairs: Barbara Kaplan, Mississippi State University, Mississippi State, MS; Emily G. Notch, Western New England University, Springfield, MA; and Daniel J. Spade, Brown University, Providence, RI.



Lecturer: Norbert E. Kaminski, Michigan State University, East Lansing, MI.

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. Dr. Kaminski will highlight how toxicologists determine appropriate models of how xenobiotics alter physiological systems and elaborate the strengths and challenges of multicellular model systems. Using a case study, participants will interpret data related to multicellular models and then report conclusions through an audience response system.

High School Student and Teacher Workshop—Safety Matters: Toxicology and Product Safety

Tuesday, March 15, 8:30 AM to 2:15 PM

Chairperson(s): Wesley Gray, Southern University and A&M College, Baton Rouge, LA.

Supported by:
South Central SOT Regional Chapter

Hosted by:
Education Committee
K-12 Subcommittee

High School teachers and students from the New Orleans area, plus high schoolers attending the SOT meeting, will learn that "Safety Matters" at an all-day workshop on Tuesday, March 15. The workshop will include presentations introducing toxicology, activities to learn ways toxicologists can assess product safety, tour of the Annual Meeting, and a scavenger hunt. Some students will have posters displayed in the High School Poster Exposition. Toxicologists are encouraged to volunteer to serve as mentors.

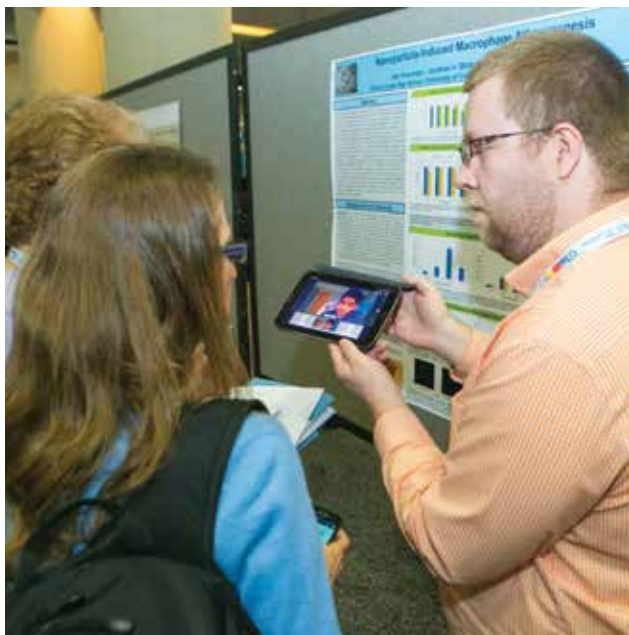
High School Poster Exposition

Tuesday, March 15, 10:00 AM to 12:00 Noon

Chairperson(s): Marie Meagher Bourgeois, University of South Florida, Tampa, FL.

Hosted by:
Education Committee
K-12 Subcommittee

High school students are invited to submit research posters for consideration for presentation in a special area near the SOT Pavilion. Students can present on-site or by a virtual connection. Many of the students displaying posters will also participate in the South Central Regional Chapter *Safety Matters* High School Student and Teacher Workshop that also is on Tuesday. Deadline for poster submissions is January 30, 2016. This display recognizes student effort and provides the high school students who have engaged in research with scientific meeting experience. Meeting attendees are invited to drop by to visit with these outstanding potential future toxicologists. More information is available on the SOT Annual Meeting website.



Postdoctoral Assembly Luncheon

Tuesday, March 15, 12:00 Noon to 1:15 PM

(Ticket Required) ➡

Chairperson(s): Caitlin J. Murphy, Smithers Avanza, Gaithersburg, MD.

Hosted by:
Postdoctoral Assembly

The Postdoctoral Assembly (PDA) 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 2016-2017 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.



Undergraduate Student Meeting

Tuesday, March 15, 4:00 PM to 5:15 PM

Chairperson(s): Joshua Gray, US Coast Guard Academy, New London, CT.

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, clubs, and majors on their campuses, and to provide feedback to the Undergraduate Education Subcommittee.

Regional Chapter, Special Interest Group, and Specialty Section Meeting/Receptions

Regional Chapter Meetings/Luncheons or Receptions

Monday, March 14, through Wednesday, March 16, Various Times and Locations

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

Many of the SOT Regional Chapters meet during the SOT Annual Meeting.

Event	Date	Time
Central States Regional Chapter Meeting/Breakfast	Monday, March 14	7:00 AM to 8:00 AM
Lone Star and South Central Regional Chapters Mixer	Tuesday, March 15	5:30 PM to 7:30 PM
Michigan and Allegheny-Erie Regional Chapters Joint Reception	Monday, March 14	4:30 PM to 6:00 PM
Mid-Atlantic Regional Chapter Luncheon	Monday, March 14	12:15 PM to 2:00 PM
Midwest Regional Chapter Mixer	Monday, March 14	5:00 PM to 6:30 PM
Northeast Regional Chapter Student Luncheon	Monday, March 14	12:30 PM to 2:00 PM
Northern California Regional Chapter Reception	Tuesday, March 15	7:30 PM to 10:00 PM
Ohio Valley Regional Chapter Reception	Monday, March 14	4:45 PM to 6:30 PM
Pacific Northwest Regional Chapter Reception	Monday, March 14	5:30 PM to 7:30 PM
Southern California and Mountain West Regional Chapters Mixer	Tuesday, March 15	6:30 PM to 9:30 PM

Special Interest Group Meetings/Luncheons or Receptions

Monday, March 14, through Wednesday, March 16, Various Times and Locations

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

Each of the six Special Interest Groups will hold a meeting/reception during the 2016 SOT Annual Meeting at various local locations. All current and prospective SOT Special Interest Group members are encouraged to attend.

Event	Date	Time
American Association of Chinese in Toxicology Distinguished Special Interest Group Chinese Toxicologist Lectureship Award and Reception	Monday, March 14	5:00 PM to 9:00 PM
American Association of Chinese in Toxicology Special Interest Group Career Development Workshop	Tuesday, March 15	12:15 PM to 1:45 PM
Association of Scientists of Indian Origin Special Interest Group Reception	Monday, March 14	7:00 PM to 9:30 PM
Association of Scientists of Indian Origin Special Interest Group Lunch and Learn	Tuesday, March 15	12:00 Noon to 1:30 PM
Hispanic Organization of Toxicologists Special Interest Group Reception and Awards Ceremony	Tuesday, March 15	6:30 PM to 9:30 PM
Korean Toxicologists Association in America Special Interest Group Meeting/Reception	Monday, March 14	6:00 PM to 9:00 PM
Special Interest Group Collaboration Group Global Hot Topics Event	Wednesday, March 16	6:45 AM to 8:00 AM
Women in Toxicology Special Interest Group Reception	Wednesday, March 16	5:00 PM to 7:00 PM

Specialty Section Meetings/Luncheons or Receptions

Monday, March 14, through Wednesday, March 16, Various Times and Locations

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

Each of the 27 SOT Specialty Sections will hold either a luncheon or early evening meeting/reception during the 2016 SOT Annual Meeting. All current and prospective SOT Specialty Section members are encouraged to attend.

Event	Date	TIME
Biological Modeling Specialty Section Meeting/Reception	Monday, March 14	6:00 PM to 7:30 PM
Biotechnology Specialty Section Meeting/Reception	Monday, March 14	6:00 PM to 7:30 PM
Carcinogenesis Specialty Section Meeting/Reception	Tuesday, March 15	6:00 PM to 7:30 PM
Cardiovascular Toxicology Specialty Section Meeting/Reception	Tuesday, March 15	6:00 PM to 7:30 PM
Clinical and Translational Toxicology Specialty Section Meeting/Reception	Tuesday, March 15	6:00 PM to 7:30 PM
Comparative and Veterinary Specialty Section Meeting/Luncheon	Tuesday, March 15	12:00 Noon to 1:30 PM
Dermal Toxicology Specialty Section Meeting/Reception	Monday, March 14	6:00 PM to 7:30 PM
Drug Discovery Toxicology Specialty Section Meeting/Reception	Wednesday, March 16	6:00 PM to 7:30 PM
Ethical, Legal, and Social Issues Specialty Section Meeting/Luncheon	Monday, March 14	12:00 Noon to 1:30 PM
Food Safety Specialty Section Meeting/Reception	Wednesday, March 16	6:00 PM to 7:30 PM
Immunotoxicology Specialty Section Meeting/Reception	Wednesday, March 16	6:00 PM to 7:30 PM
In Vitro and Alternative Methods Specialty Section Meeting/Luncheon	Monday, March 14	12:00 Noon to 1:30 PM
Inhalation and Respiratory Specialty Section Meeting/Reception	Tuesday, March 15	6:00 PM to 7:30 PM
Mechanisms Specialty Section Meeting/Reception	Monday, March 14	6:00 PM to 7:30 PM
Medical Device and Combination Product Specialty Section Meeting/Reception	Wednesday, March 16	6:00 PM to 7:30 PM
Metals Specialty Section Meeting/Reception	Wednesday, March 16	6:00 PM to 7:30 PM
Mixtures Specialty Section Meeting/Reception	Tuesday, March 15	6:00 PM to 7:30 PM
Molecular and Systems Biology Specialty Section Meeting/Reception	Tuesday, March 15	6:00 PM to 7:30 PM
Nanotoxicology Specialty Section Meeting/Reception	Wednesday, March 16	6:00 PM to 7:30 PM
Neurotoxicology Specialty Section Meeting/Reception	Wednesday, March 16	6:00 PM to 7:30 PM
Occupational and Public Health Specialty Section Meeting/Luncheon	Tuesday, March 15	12:00 Noon to 1:30 PM
Ocular Toxicology Specialty Section Meeting/Reception	Tuesday, March 15	6:00 PM to 7:30 PM
Regulatory and Safety Evaluation Specialty Section Meeting/Reception	Monday, March 14	6:00 PM to 7:30 PM

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

Event	Date	Time
Reproductive and Developmental Toxicology Specialty Section Meeting/Reception	Monday, March 14	6:00 PM to 7:30 PM
Risk Assessment Specialty Section Meeting/Reception	Wednesday, March 16	6:00 PM to 7:30 PM
Stem Cells Specialty Section Meeting/Reception	Monday, March 14	6:00 PM to 7:30 PM
Toxicologic and Exploratory Pathology Specialty Section Meeting/Luncheon	Monday, March 14	12:00 Noon to 1:30 PM



Thank You

Council

Peter L. Goering	President	Aaron Barchowsky	Councilor
John B. Morris.....	Vice President	Rosonald R. Bell	Councilor
Patricia E. Ganey	Vice President-Elect	Myrtle A. Davis	Councilor
Leigh Ann Burns Naas.....	Secretary	Ofelia A. Olivero.....	Councilor
Ruth A. Roberts	Secretary-Elect	Tao Wang.....	Councilor
George P. Daston	Treasurer	John A. Wisler	Councilor
Norbert E. Kaminski	Past President		

Continuing Education Committee

Gary O. Rankin	Chair	Monicah A. Otieno	Member
Kimberly A. Henderson	Co-Chair	Cynthia V. Rider	Member
Niranjan S. Goud.....	Member	James G. Wagner	Member
Michael F. Hughes	Member	Senthilkumar Perumal Kuppusamy	Postdoctoral Representative
Saber M. Hussain	Member	Kevin Trout.....	Student Representative
Bette Meek.....	Member		

Scientific Program Committee

John B. Morris.....	Chair	Paul C. Howard.....	Member
Patricia E. Ganey	Co-Chair	Matthew J. LeBaron.....	Member
William D. Atchison	Member	Donald R. Mattison.....	Member
Jeanine L. Bussiere	Member	Barry S. McIntyre	Member
Brian J. Day	Member	Sean E. Ottinger	Member
Jennifer L. Freeman.....	Member	Lisa M. Sweeney.....	Member
Mary Beth Genter	Member		



Ocular Toxicology

Pharmacology and Drug Delivery: *An Eye on the Future*

JUNE 27–28, 2016

SOUTH SAN FRANCISCO, CALIFORNIA

Improve Understanding of:

1 Ocular Toxicology, Pharmacology,
and Safety Assessment

Challenges Associated with the
Development of the Next Generation
of Ocular Drugs and Devices **2**

REGISTRATION | SCIENTIFIC PROGRAM | HOUSING
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WWW.TOXICOLGY.ORG/OCULAR

Satellite Meetings

3D or Not 3D: That Is the [Predictive Toxicology] Question...

Thursday, March 17, 1:00 PM to 5:00 PM

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

Purpose of the Meeting: How complex must cell cultures be to replicate the dynamics of tissue interactions and functions in order to be predictive of *in vivo* responses? We will discuss the latest successes and challenges in differing organotypic and three-dimensional cell culture systems. The US EPA's Chemical Safety for Sustainability program provided Science to Achieve Results (STAR) research grants to develop and evaluate medium to high throughput toxicity screening systems in order to assess chemicals. Their work, on tissue systems including the brain, liver, kidney, testis, breast tissue, heart and neurovascular systems, is intended to complement ongoing US EPA research and lead to refined models of how organs and tissues respond to environmental chemicals. Researchers from the four US EPA STAR grant Centers and from US EPA's Office of Research and Development will present their work.

Registration: Open registration. No fee to register and attend.

Lectures followed by Q&A and a hands-on tutorial of the tools.

For more information on this Satellite Meeting, contact Barbara Klieforth: klieforth.barbara@epa.gov.

A Toxicology User's Guide to the Roadmap Epigenomics and ENCODE Data Resources

Thursday, March 17, 1:00 PM to 6:00 PM

Hosted by: Ivan Rusyn, Texas A&M University, College Station, TX; and Lisa Chadwick, NIEHS, Research Triangle Park, NC.

Purpose of the Meeting: Improvements in DNA sequencing technologies have resulted in an exponential increase in the amount of genomic and epigenomic data available. Some of these data have been generated as part of large-scale, focused mapping efforts aimed at understanding how genes are regulated, such as the NIH Roadmap Epigenomics Program, and ENCODE (Encyclopedia of DNA Elements). Efforts such as these can be extremely valuable for hypothesis generation and data mining, but can only be useful if one knows what is available and how to use it. This SOT satellite meeting will provide toxicology researchers with an overview of these two NIH-funded programs, introduce attendees to the informatics tools that have been developed to help navigate these large datasets, and walk through several use cases. The meeting will be of broad interest to researchers interested in learning more about how environmental exposure might impact gene regulation.

Registration: Open registration. No fee to register and attend.

Lectures followed by Q&A and a hands-on tutorial of the tools.

For more information on this Satellite Meeting, contact Lisa Chadwick: chadwickl@niehs.nih.gov.

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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



Scientific Themes

- Advances in Neurotoxicology
- Developmental Toxicity: Mechanisms and Evaluation
- Health and Environmental Impacts of Man-Made and Naturally Released Toxicants
- Molecular Toxicology: Mechanistic Insights and Hazard Assessment
- Recent Advances in Safety Assessment
- Toxicity of Metals

The Continuing Education Program offers a wide range of courses that cover established knowledge in toxicology, as well as new developments in toxicology and related disciplines. Courses can be applied toward certifying and licensing board requirements and also may be used for recertification with the American Board of Toxicology (ABT). Both basic and advanced course topics are offered. The basic course is intended to provide a broad overview of an area or to assist individuals in learning new techniques or approaches. The advanced course is 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 13, 2016, at the New Orleans Ernest N. Morial 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 area 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.



Research Funding Insight

Visit with representatives from granting agencies to gain insight on submitting successful grant applications.

Monday, March 14 to Wednesday, March 16, 9:30 AM to 4:30 PM, Research Funding Room

See full descriptions on page 43.

SUNDAY

Basic Principles and Practices for Applying Epigenetics in Mechanistic Toxicology

Sunday, March 13, 7:00 AM to 7:45 AM

SR01 | CE BASIC | SUNRISE MINI-COURSE

- ◆ **Molecular Toxicology: Mechanistic Insights and Hazard Assessment**

Chairperson(s): Shaun D. McCullough, US EPA, Chapel Hill, NC; and Ronald N. Hines, US EPA, Research Triangle Park, NC.

Endorser(s):

***In Vitro* and Alternative Methods Specialty Section
Mechanisms Specialty Section
Molecular and Systems Biology Specialty Section**

The genetic material of every organism exists within the context of regulatory networks that govern gene expression collectively called the epigenome. These epigenetic regulators, chromatin modifications, DNA methylation, and noncoding RNAs, act in concert to shape the way that cells, tissues, and organisms respond to their environment and toxicant exposure. Incorporating epigenetics into both *in vitro* and *in vivo* toxicological studies allows for a better understanding of the molecular events underlying the adverse health effects of toxicant exposure, improves our ability to identify vulnerable populations, and facilitates the identification of modifiable risk factors. The goal of this course is to provide toxicologists from a broad range of backgrounds with an overview of the epigenome and general considerations for designing experiments to examine the role of the epigenetics in their toxicological studies. This course will mention noncoding RNAs but focus primarily on participants gaining a fundamental understanding of the role of chromatin and DNA methylation in the regulation of gene expression. The principles and applications of basic experimental techniques, such as chromatin immunoprecipitation (ChIP) and DNA methylation analysis for evaluating epigenetic changes in toxicological studies, will also be discussed. This course will be of broad interest to investigators that are interested in integrating epigenetic approaches into their current or future toxicological studies.

Part 1: Principles of Epigenetics: An Introduction to the Mechanisms of Gene Regulation. Ronald N. Hines, US EPA, Research Triangle Park, NC.

Part 2: Experimental Techniques for Incorporating Chromatin and DNA Methylation Analysis into Mechanistic Toxicology. Shaun D. McCullough, US EPA, Chapel Hill, NC.

Advancing the Detection, Imaging, and Pitfalls in Monitoring Oxidative Stress in Health and Disease

Sunday, March 13, 8:15 AM–12:00 Noon
AM02 | CE ADVANCED | MORNING COURSE

- ♥ Health and Environmental Impacts of Manmade and Naturally Released Toxicants
- ♦ Molecular Toxicology: Mechanistic Insights and Hazard Assessment

Chairperson(s): Maria B. Kadiiska, NIEHS/NIH, Research Triangle Park, NC; and Ronald P. Mason, NIEHS/NIH, Research Triangle Park, NC.

Endorser(s):

Immunotoxicology Specialty Section
Mechanisms Specialty Section
Molecular and Systems Biology Specialty Section

Oxidative stress is recognized to play a role in the etiology of numerous diseases as well as in environmental exposures. Exploration of oxidative stress mechanisms is a field of ever-increasing attention, both in science and in commerce. The field is maturing and there is a great effort to study and understand biomarkers at both a chemical and enzymatic molecular-mechanism level. Since increases in oxidative stress are measured using biomarkers, the goal of this course is to convey the most up-to-date knowledge on biomarkers; present novel approaches and advanced methods that can be employed *in vivo* to measure, predict, and even prevent oxidative stress; and to discuss the methods and pitfalls for distinguishing oxidative stress from systemic toxicities, immunotoxicities and inflammation. Technologically advanced methods, including molecular magnetic resonance imaging, HPLC-MS, spectro(-fluoro)metric assays, and immunoassays are potentially rich areas for innovation in systemic oxidative stress research. Consequently, the course outlines the most up-to-date developments in newly emerging methodologies that will enhance the understanding of oxidative stress mechanisms by measuring, detecting, and even imaging it *in vivo*. The panel of experts evaluates the advantages, applicability, and pitfalls of each method, discusses the most recent data on *in vivo* and *in situ* imaging of molecular free radical metabolites with emphasis on both the current state of technology, different areas of toxicology including immunotoxicology, crosstalks with the innate immune mediators, and likely future developments. Because the detection and understanding of oxidative stress could lead to better intervention strategies, output from the course will help identify the most useful applications for a given technique to detect oxidative stress *in vivo*. Attendees will leave the course with enhanced understanding that measurement of oxidative stress *in vivo* requires innovative, unconventional methodologies in combination with advanced technologies and often a multidisciplinary approach.

We Detect Free Radicals Not Because It Is Easy but Because It Is Hard. Ronald P. Mason, NIH/NIEHS, Research Triangle Park, NC.

In Vivo, In Situ Imaging of Free Radical Adducts in Animal Disease Models. Rheel A. Towner, Oklahoma Medical Research Foundation, Oklahoma City, OK.

Oxidative Damage Detection in Macromolecules: Free Radical-Innate Immune Crosstalk in Liver Disease. Saurabh Chatterjee, University of South Carolina, Columbia, SC.

Xenobiotic Free Radical Detection in Biological Systems Using HPLC: A Technique for All. Arno G. Siraki, University of Alberta, Edmonton, AB, Canada.

Oxidative Modification of Proteins: Detection and Role in Autoimmunity. M. F. Khan, University of Texas Medical Branch, Galveston, TX.

Validation of Best Detection Methods for Oxidative Stress Biomarkers in Biological Fluids. Maria B. Kadiiska, NIEHS/NIH, Research Triangle Park, NC.

Reinterpreting the Best Biomarker of Oxidative Stress: The 8-iso-PGF2a/PGF2a Ratio Distinguishes Chemical from Enzymatic Lipid Peroxidation. Thomas J. van't Erve, NIEHS/NIH, Research Triangle Park, NC.

Adverse Outcome Pathway (AOP) Development and Evaluation

Sunday, March 13, 8:15 AM–12:00 Noon
AM03 | CE BASIC | MORNING COURSE

- ♦ Molecular Toxicology: Mechanistic Insights and Hazard Assessment
- 🔥 Recent Advances in Safety Assessment

Chairperson(s): Stephen Edwards, US EPA, Research Triangle Park, NC; and Andrea Terron, EFSA (European Food Safety Agency), Parma, Italy.

Endorser(s):

In Vitro and Alternative Methods Specialty Section
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

The Adverse Outcome Pathway provides a construct for assembling mechanistic information at different levels of biological organization in a form designed to support regulatory decision making. In particular, it frames the link between molecular and cellular events that can be measured in high-throughput toxicity testing and the organism or population-level events that are commonly relevant in defining risk. Recognizing the importance of this emerging framework, the Organisation for Economic Co-operation and Development (OECD) launched a program to support the development, documentation, and consideration of AOPs by the international community in 2012. In 2014, a handbook was developed to guide users in the documentation and evaluation of AOPs and their entry into an official knowledgebase. The handbook draws on longstanding experience in consideration of mechanistic data (e.g., mode-of-action analysis) to inform risk assessment. To further assist users, a training program was developed by members of the OECD Extended Advisory Group to teach users the basic principles of AOP development and the best practices as outlined in the OECD AOP handbook. Training sessions began in early 2015, and this course will provide training for interested SOT scientists. Following this course, all participants will be familiar with the core principles of AOP development and assessment and the OECD efforts to support this effort. They will also know how the OECD guidance for AOP development has been implemented in the Wiki module of the AOP Knowledgebase. They will learn how to assemble and evaluate the evidence supporting the AOPs using established best practices from Mode of Action analysis.

To reinforce the concepts, they will participate in a live demo where an AOP is developed from a training case study with their assistance and entered into the AOP-Wiki. The value of AOP development will be

demonstrated via examples from the European Food Safety Agency and by considering integrated approaches to testing and assessment using the skin sensitization AOP, which was endorsed by the OECD in 2012.

Introduction. Stephen Edwards, US EPA, Research Triangle Park, NC.

Introduction to Adverse Outcome Pathways and International Activities Guiding AOP Development. Kristie Sullivan, Physicians Committee for Responsible Medicine, Washington, DC.

Principles and Best Practices for AOP Development. Dan Villeneuve, US EPA, Duluth, MN.

Weight of Evidence/Confidence Analysis in the Development and Documentation of AOPs. Bette Meek, University of Ottawa, Ottawa, ON, Canada.

Assembling AOP Information in the International AOP Knowledgebase. Carole Yauk, Health Canada, Ottawa, ON, Canada.

Applying AOPs to the Development of Integrated Approaches on Testing and Assessment (IATA). Gavin Maxwell, Unilever, Sharnbrook, United Kingdom.

Implementing the AOP Framework at EFSA. Andrea Terron, EFSA (European Food Safety Agency), Parma, Italy.

Contribution of Mitochondria to Drug-Induced Organ Toxicities

Sunday, March 13, 8:15 AM–12:00 Noon
AM04 | CE BASIC | MORNING COURSE

◆ Molecular Toxicology: Mechanistic Insights and Hazard Assessment

Chairperson(s): Varsha G. Desai, National Center for Toxicological Research, US FDA, Jefferson, AR; and Yvonne Will, Pfizer R&D, Groton, CT.

Endorser(s):

Drug Discovery Toxicology Specialty Section
Mechanisms Specialty Section
Regulatory and Safety Evaluation Specialty Section

Mitochondria generate more than 90% of energy essential for the cell. Impaired mitochondrial function, therefore, can affect virtually every tissue and organ in the living organism. Tissues with the highest energy needs, such as the heart, brain, liver, kidney, and skeletal muscle are particularly vulnerable to the defects in mitochondrial bioenergetics that can manifest into tissue-specific pathologies. A distinctive feature of mitochondria is that, besides the nucleus, these organelles contain their own genome (mitochondrial DNA). However, coordination between nuclear and mitochondrial genomes is crucial in regulating mitochondrial function. It is also becoming increasingly evident that mitochondria are a prime target of many therapeutic drugs and environmental toxins that can alter their function through different mechanisms, leading to cellular injury, resulting in organ toxicity, and, in the worst case, death. Additionally, mitochondria serve as an important player in the execution of apoptosis (programmed cell death), a process that serves as a major defense mechanism to remove unwanted and potentially dangerous cells. Collectively, these functions highlight a critical role of mitochondria in the life and death of the cell.

This course will provide an in-depth overview of mitochondrial biology and different mechanisms in which drugs can affect mitochondrial function. Particular emphasis is given to mitochondrial toxicity causing heart, liver, and kidney injury. In addition, we will describe novel high-

throughput *in vitro* screening technologies in isolated mitochondria and cell models to elucidate potential mitochondrial toxicity. Several other methodologies will also be discussed that can reveal the mitochondrial target(s) of drug toxicity in different organs. The utility and limitations of these approaches will also be described. This course concludes by providing the participants with in-depth knowledge of basic mitochondrial function and important insights into how subtle changes in mitochondrial activity can progress to overt pathology in tissues and help identify potential biomarkers of early stages of mitochondrial toxicity. Moreover, this course will present how preclinical data on mitochondrial toxicity can help in understanding toxicities in humans.

Contribution of Mitochondria to Drug-Induced Organ Toxicities: An Overview. Varsha G. Desai, National Center for Toxicological Research, US FDA, Jefferson, AR.

Mitochondrial Function and Dysfunction in Disease and Drug-Induced Toxicity. James A. Dykens, EyeCyte Therapeutics, San Diego, CA.

Mitochondrial Toxicity: A Decade of Technology Development, a Decade of Learnings. Yvonne Will, Pfizer R&D, Groton, CT.

Mitochondrial Dysfunction in Acute Kidney Injury. Rick G. Schnellmann, Medical University of South Carolina, Charleston, SC.

Doxorubicin-Induced Mitochondrial Cardiomyopathy. Kendall B. Wallace, University of Minnesota Medical School Duluth, Duluth, MN.

Discovery and Validation of miRNA Biomarkers Bridging Preclinical and Clinical Toxicity: Lessons Learned from Hepatotoxicity

Sunday, March 13, 8:15 AM–12:00 Noon
AM05 | CE ADVANCED | MORNING COURSE

◆ Molecular Toxicology: Mechanistic Insights and Hazard Assessment
♠ Recent Advances in Safety Assessment

Chairperson(s): Alison Harrill, University of Arkansas for Medical Sciences, Little Rock, AR; and Brian Chorley, US EPA, Research Triangle Park, NC.

Endorser(s):

Clinical and Translational Toxicology Specialty Section
Molecular and Systems Biology Specialty Section
Regulatory and Safety Evaluation Specialty Section

Micro(mi)RNAs are small, noncoding RNAs that play an important role in the regulation of biological processes in cells. Owing to recent findings that: (1) miRNA sequences are highly conserved across species, (2) certain miRNAs exhibit tissue-specific expression, and (3) miRNA are highly stable in biological fluids, significant effort has been spent to identify miRNA biomarkers for a variety of toxicological pathologies. However, in addition to basic research and discovery efforts, significant effort must be spent on qualification of biomarkers with regards to specificity for the organ of interest and for the ability of a biomarker to detect comparable injury across species. A major effort is to use miRNA profiles as a “liquid biopsy” that can inform underlying tissue pathology. Thus, the goal of this course is to provide investigators with an overview of the techniques and strategies necessary to progress a biomarker from the discovery stage to practical use in animal and human xenobiotic

safety assessment. Well studied biomarkers, such as miR-122, will be used as case studies to demonstrate the path from nonclinical discovery to a validated clinical biomarker.

Introduction. Brian Chorley, US EPA, Research Triangle Park, NC.

Utilizing miRNAs to Assess Organ Specificity: Using miR-122 to Distinguish between Liver and Muscle Injury. Warren Glaab, Merck Research Laboratories, West Point, PA.

Emerging Biomarkers of Liver Injury: From miR-122 to Liquid Biopsies in the Clinic. Jiri Aubrecht, Pfizer Inc., Groton, CT.

Clinical Qualification of a miRNA Biomarker in a Hospital Setting: miR-122 in Acute Liver Failure Patients. Daniel Antoine, University of Liverpool, Liverpool, United Kingdom.

Exosomes and Their miRNA Cargos: Potential Biomarkers for Liver Diseases. Banishree Saha, University of Massachusetts Medical School, Worcester, MA.

Embryology and Developmental Toxicity Testing

Sunday, March 13, 8:15 AM–12:00 Noon

AM06 | CE BASIC | MORNING COURSE

 **Developmental Toxicity: Mechanisms and Evaluation**

Chairperson(s): John M. DeSesso, Exponent, Alexandria, VA; and Anthony R. Scialli, Scialli Consulting LLC, Arlington, VA.

Endorser(s):

**Drug Discovery Toxicology Specialty Section
Regulatory and Safety Evaluation Specialty Section
Reproductive and Developmental Toxicology Specialty Section**

Mammalian embryo-fetal development comprises a complex and carefully orchestrated set of activities that can be perturbed by maternal and environmental factors. Perturbations of developing offspring can result in no discernible effect, reduced fetal weights at term, increased prevalence of anatomical variations, congenital defects, and/or the demise of the offspring. This course will focus on preclinical species and will begin by providing an overview of mammalian development, including important gestational milestones, comparative interspecies timelines, and definitions of critical periods in development. Next we will discuss how this information has factored into the design of traditional preclinical studies. The presentation will conclude with a brief introduction to normal variability in some organ systems. This variability is the source of considerable controversy when interpreting traditional developmental toxicity safety tests. Succeeding presentations will discuss two organ systems that are the center of debate among scientists charged with extrapolating results found in safety assessments to potential human risk. The normal embryological development of the first organ system to function, the cardiovascular system, will be described with consideration of normal anatomical variations and nonadverse structural changes. The second organ system to be described is the skeletal system. Particular attention will be paid to its state of maturity at term in various species, the potential influence of maternal toxicity on skeletal maturation, and postnatal development of the skeleton throughout the lactation period. The final presentation will address the development of new testing methods that might be used to prioritize substances for testing or even to replace whole animal testing for developmental toxicity. The presentation will describe basic methods for whole embryo culture, embryonic stem cell test, and a Zebrafish assay, along with various proposed improvements in each. It will finish with some thoughts about integrating the results from multiple assays, and a survey of the regulatory landscape for these

emerging methods. Information from the preceding presentations will provide the audience with an understanding of how the biological basis of prenatal developmental toxicity testing and the results of such tests should impact risk assessment and ultimately, the rationale for the design and use of drugs and chemicals that minimizes environmental impact and ensures human health.

Introduction. Anthony R. Scialli, Scialli Consulting LLC, Arlington, VA.

Comparative Embryological Development, Gestational Landmarks, and Their Influence on Test Designs. John M. DeSesso, Exponent, Alexandria, VA.

Details of Skeletal Development and How this Matters When Interpreting Results. John M. Rogers, US EPA, Research Triangle Park, NC.

Normal and Abnormal Development of Heart and Great Vessels: Understanding the Problem and Interpreting the Findings. H. Scott Baldwin, Vanderbilt University School of Medicine, Nashville, TN.

Principles of Validation. Anthony R. Scialli, Scialli Consulting LLC, Arlington, VA.

Developmental Toxicity Testing without Animals: The Big Slippery Mountain. Robert E. Chapin, Pfizer Inc., Groton, CT.

Next-Generation Sequencing in Toxicogenomics

Sunday, March 13, 8:15 AM–12:00 Noon

AM07 | CE ADVANCED | MORNING COURSE

♦ **Molecular Toxicology: Mechanistic Insights and Hazard Assessment**
♠ **Recent Advances in Safety Assessment**

Chairperson(s): Weida Tong, National Center for Toxicological Research, US FDA, Jefferson, AR; and Jos Kleinjans, Maastricht University, Maastricht, The Netherlands.

Endorser(s):

**Biotechnology Specialty Section
Molecular and Systems Biology Specialty Section
Regulatory and Safety Evaluation Specialty Section**

The purpose of toxicogenomics is to study the effects of chemical, biological and physical agents in biological systems at the molecular level and thereby elucidating the molecular mechanisms underlying the expression of toxicity. Recent technology developments in next-generation sequencing (NGS) have opened completely new possibilities for the deep characterization of molecular mechanisms of toxicity at various levels of cellular regulation providing information on substance-induced genomic variations, and on transcriptomic and epigenomic changes. We argue that these developments will strengthen our understanding of toxic mechanisms-of-action and ultimately lead to a systems-wide toxicity analysis thus enabling the development of safer drugs, industrial chemicals, consumer products and improved regulation. This course will discuss various NGS application for an enhanced understanding of underlying mechanisms of toxicity and potential utility in regulatory setting. The discussed topics include but are not limited to applicability of respective NGS platforms for analyzing mutational spectra, gene expression modifications, and epigenomic alterations induced by toxicants in a range of biological systems, compare their performance with standardized qPCR/microarray techniques, present use cases and highlight future challenges.

Next-Generation Sequencing: Next Wave of Opportunities, Challenges, and Anxiety. Jos Kleinjans, Maastricht University, Maastricht, The Netherlands.

Next-Generation Sequencing: Technology and Bioinformatics. Wenming Xiao, NCTR/US FDA, Jefferson, AR.

DNA-Seq: Toxicant-Induced Mutation Analysis. Florian Caiment, Maastricht University, Maastricht, The Netherlands.

Epigenomics: A New Opportunity in Toxicogenomics. Ralf Herwig, Max-Planck-Institute for Molecular Genetics, Berlin, Germany.

RNA-Seq: Mechanistic and Predictive Toxicology. Weida Tong, NCTR/US FDA, Jefferson, AR.

RNA-Seq As a Way to Access Transcriptomic Information in Archival Tissues. Susan Hester, National Health and Environmental Effects Research Laboratory, US EPA, Research Triangle Park, NC.

Approaches to Investigate and Assess Risks Associated with Drug-Induced Liver Injury (DILI)

Sunday, March 13, 1:15 PM–5:00 PM

PM08 | CE ADVANCED | AFTERNOON COURSE

- ♥ Health and Environmental Impacts of Manmade and Naturally Released Toxicants
- ♠ Recent Advances in Safety Assessment

Chairperson(s): *Monicah Otieno, Janssen Pharmaceuticals, Spring House, PA; and Paul Watkins, The Hamner-UNC Institute for Drug Safety Sciences, Research Triangle Park, NC.*

Endorser(s):

**Drug Discovery Toxicology Specialty Section
Mechanisms Specialty Section**

Drug-induced liver injury (DILI) in the clinic is a major cause for drug attrition during development. DILI can be characterized as intrinsic or idiosyncratic. Properties of intrinsic DILI include a dose-response in presentation of injury that may be predicted by animal studies enabling application of safety thresholds and inclusion of liver injury biomarkers for clinical risk assessment. Idiosyncratic DILI (iDILI) is unpredictable and usually occurs following drug exposure in large populations e.g., during Phase III clinical trials or postmarketing. Given that this is a major cause for costly drug withdrawals, there has been significant effort in identifying properties that predispose some compounds to a high risk for iDILI. Both immune and nonimmune mechanisms are hypothesized to contribute to iDILI. This course will discuss DILI hazards that can be used to identify a compound's potential to cause DILI. A general overview and introduction of DILI will be provided, followed by a clinician's perspective on DILI focusing on presentation of DILI using examples of key withdrawals. Subsequent presentations will focus on established and emerging science on DILI hazard risks; this will include a presentation on the role of reactive metabolites (RM) and covalent binding in increasing risk for immune or nonimmune mediated DILI. A basic overview on mechanisms of RM formation, methods for detection, and mechanistic studies correlating covalent binding with DILI will be discussed. The relationship between dose, covalent binding thresholds, and DILI also will be addressed. This will be followed by a presentation on hepatic transporters and the role they play in DILI, either through delayed hepatotoxicity resulting from liver accumulation of parent/metabolites and/or inhibition of efflux of toxic bile acids. Mitochondrial toxicity also has been identified as a key hazard for DILI compounds; an overview of mitochondrial toxicity, its role in iDILI, and how interplay with hepatic transport inhibition may increase risk for DILI will be presented. The

final presentation will introduce the concept of computational, systems pharmacology approaches integrating all of the mechanisms discussed by the previous speakers along with drug exposure, to put data from various sources into context.

Overview of DILI and Associated Risk Hazards. Monicah Otieno, Janssen Pharmaceuticals, Spring House, PA.

Clinical Perspective Including Risk Identification and Management. Paul Watkins, The Hamner-UNC Institute for Drug Safety Sciences, Research Triangle Park, NC.

Role of Reactive Metabolites in Immune DILI. Jack Uetrecht, University of Toronto, Toronto, ON, Canada.

Role of Hepatic Transporters in DILI. Kim Brouwer, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Role of Mitochondrial Toxicity in DILI. Yvonne Will, Pfizer Inc., Groton, CT.

Computational Approaches to Integrate DILI Hazards and Predict DILI Potential. Brett Howell, The Hamner-UNC Institute for Drug Safety Sciences, Research Triangle Park, NC.

Exploring Chemical Space in the New Toxicity Testing Paradigm: From Data Curation to Computational Simulations

Sunday, March 13, 1:15 PM–5:00 PM

PM09 | CE BASIC | AFTERNOON COURSE

- ♠ Recent Advances in Safety Assessment

Chairperson(s): *Cecilia Tan, US EPA, Research Triangle Park, NC; and Daniel Chang, Chemical Computing Group, Inc., Montreal, QC, Canada*

Endorser(s):

**Biological Modeling Specialty Section
In Vitro and Alternative Methods Specialty Section
Molecular and Systems Biology Specialty Section**

In an effort to determine mechanisms-of-action of toxicants known to induce adverse human health outcomes, traditional toxicity testing focuses on lengthy and costly *in vivo* animal studies on a chemical-by-chemical basis. In such a paradigm, there is no need to consider chemical space. The accelerated rate of production and distribution of new chemicals in the commercial market precludes such approaches today, and rather, high-throughput *in vitro* and *in silico* analyses are encouraged in order to rapidly screen hundreds to thousands of chemicals. The recent advancements in these high-throughput screening approaches, along with computational chemistry and cheminformatics, have provided toxicologists the foundation and opportunity to identify molecular fingerprints that impact each aspect of the source-to-outcome continuum for large amounts of chemicals. Inherent chemical structures and properties are key determinants of exposure potential (based on e.g., function and use), environmental persistence and transformation in environmental and biological systems, and toxicity potential. Computational approaches expand the chemical space through identification of chemicals with similar molecular descriptors capable of influencing these behaviors, thus allowing investigators to predict their toxicity or exposure potential, while foregoing actual testing. Attendees enrolled in this course will learn about the availability of different tools and vast numbers of resources to help them triage *in vitro* efforts, rationalize mode-of-action information, screen chemicals in a virtual world, and understand the issues of domain of applicability

in toxicological studies. Investigators specializing in computational, molecular, and environmental toxicology, as well as those conducting high-throughput analysis for drug discovery or chemical screening, will experience the opportunity to address critical issues regarding evaluation of chemical space along the source-to-outcome continuum through comprehensive lectures and case studies.

Computational Chemistry in Toxicity Testing, Hazard and Risk Assessments.

Daniel Chang, Chemical Computing Group, Inc., Montreal, QC, Canada.

Applications of Cheminformatics in the Regulatory Assessment of Chemicals.

Andrew Worth, European Commission—Joint Research Centre, Ispra, Italy.

Progress towards Predicting Potential Hazards and Assessing Risk in the Early Stage of Drug Discovery.

BinQing Wei, Genentech Inc., South San Francisco, CA.

Advancements in Applying Predictive Computational Tools to Prioritize Environmental Chemicals Investigated in High-Throughput Screening Assays.

Jeremy Leonard, North Carolina State University, Raleigh, NC.

The Contributions of Chemistry Standards and Database Tools at the Chemical-Biology Interface.

Antony Williams, US EPA, Durham, NC.

Conquering Chemical Space with Cheminformatics Workflow and *In Silico* Profiling to Complement High-Throughput Screening.

Rocky Goldsmith, Chemical Computing Group, Inc., Montreal, QC, Canada.

Genetics and Population Variability in Chemical Toxicity: The What, the How, and So What?

Sunday, March 13, 1:15 PM–5:00 PM

PM10 | CE BASIC | AFTERNOON COURSE

♥ Health and Environmental Impacts of Manmade and Naturally Released Toxicants

♦ Molecular Toxicology: Mechanistic Insights and Hazard Assessment

Chairperson(s): Ivan Rusyn, Texas A&M University, College Station, TX; and Barbara A. Wetmore, The Hamner Institutes for Health Sciences, Research Triangle Park, NC.

Endorser(s):

**Drug Discovery Toxicology Specialty Section
Molecular and Systems Biology Specialty Section
Risk Assessment Specialty Section**

The US EPA defines “variability” as “the range of toxic response or exposure—for example, the dose that might cause a toxic response can vary from one person to the next depending on factors such as genetic differences, preexisting medical conditions, etc.” What are “genetic differences”? How do toxicologists and regulators estimate “population variability”? What new computational and experimental tools are available to substitute default “uncertainty factor” to account for variation in susceptibility among the members of the human population (i.e., inter-individual variability)? This continuing education course is designed to review basics of genetics and demonstrate how appreciation for the role of genetic variability and novel experimental and *in silico* models can become key elements in human health assessments of chemicals. By superimposing the opportunities that are now afforded by sequencing technologies and novel experimental models and data onto the

risk assessment paradigm, this course will be informative to the risk assessment practitioners and the toxicology research community, and increase the scientific impact of the fundamental toxicology studies. In addition, this course is directly responsive to the new SOT Strategic Plan (2015–2018) and the Central Challenge of shaping the future of toxicology in a changing scientific landscape. By using case studies of how the scientific disciplines of genetics and toxicology intertwine, this course will strengthen the impact and relevance of toxicology.

Genetics for Toxicologists: Why Should We Care? Ivan Rusyn, Texas A&M University, College Station, TX.

Basic Concepts in Genetics, Heritability, Genome-Wide Association, and Related Toxicology Study Designs.

Fred A. Wright, North Carolina State University, Raleigh, NC.

Pharmacogenomics Tools to Unravel the Genetic Basis of Toxicodynamic Variability.

Nancy J. Cox, Vanderbilt University, Nashville, TN.

Strategies to Quantitate Chemical-Specific Toxicokinetic Variability Due to Genetics and Other Factors.

Barbara A. Wetmore, The Hamner Institutes for Health Sciences, Research Triangle Park, NC.

Advancing Risk Assessment with Genetic and Population

Variability Data. Weihsueh A. Chiu, Texas A&M University, College Station, TX.

Human Health Risk Assessment: A Case Study Application of Principles

Sunday, March 13, 1:15 PM–5:00 PM

PM11 | CE ADVANCED | AFTERNOON COURSE

♥ Health and Environmental Impacts of Manmade and Naturally Released Toxicants

Chairperson(s): John C. Lipscomb, US EPA, Cincinnati, OH; and Bette Meek, University of Ottawa, Ottawa, ON, Canada.

Endorser(s):

**Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section**

This advanced, case study application course will build on course content previously presented and archived by the Society of Toxicology through CE courses presented in 2013 (Basic Principles of Human Risk Assessment) and 2014 (Methodologies in Human Health Risk Assessment). In this course, real world examples from publicly available, peer reviewed, completed risk assessments will be used as teaching aids. Course modules will be organized according to the four components of the Risk Assessment Paradigm: Hazard Characterization, Dose-Response Assessment, Exposure Assessment, and Risk Characterization. The Hazard Characterization component will consist of a guided case study based evaluation of the strength and consistency of available hazard data culminating in a weight of evidence synthesis of hazard information; Dose-response information including default (allometric scaling), pharmacokinetic approaches including a live benchmark dose application from completed assessments will be presented and discussed; Information documenting actual (measured) exposure and/or data useful in determining a default measure of exposure will be presented and discussed; Risk Characterization will demonstrate the development of drinking water maximum contaminant levels, maximum contaminant level-goals, reference values, and cancer slope factors; as well as methods to estimate risk at a given contaminant level. The course

booklet will contain a worksheet on the risk assessment examples, to be completed during the class. Unique to this course, students will be provided a risk assessment problem consisting of fundamental environmental contamination levels and original publications describing toxicity studies and will be asked to characterize the hazard, estimate exposures via soil and water, develop measures of toxic potency, and develop risk values for a hypothetical environmental contaminant. The results will be provided through an open access “drop box” type application.

Introduction. Bette Meek, University of Ottawa, Ottawa, ON, Canada.

Hazard Characterization. Zhongyu (June) Yan, Dow AgroSciences, Indianapolis, IN.

Dose-Response Assessment. Q. Jay Zhao, US EPA, Cincinnati, OH.

Exposure Assessment. Robinan Gentry, Ramboll ENVIRON, Monroe, LA.

Risk Characterization. John C. Lipscomb, US EPA, Cincinnati, OH

Unique Approaches to Safety Assessment of Gene, Cell, and Nucleic Acid-Based Therapies

Sunday, March 13, 1:15 PM–5:00 PM
PM12 | CE BASIC | AFTERNOON COURSE

🔥 Recent Advances in Safety Assessment

Chairperson(s): Timothy MacLachlan, Novartis, Cambridge, MA; and Joy Cavagnaro, AccessBio, Boyce, VA.

Endorser(s):

Biotechnology Specialty Section
Regulatory and Safety Evaluation Specialty Section

The platforms used for therapeutic treatment of disease have been greatly expanding over the last decade beyond the standard small molecule approaches and the now widespread use of proteins and monoclonal antibodies. The prospect of gene therapy began several decades ago with the promise that malfunctioning genes could be simply replaced, but was stunted in its growth with several notable safety events in the clinic. Now gene therapy is making a furious comeback, with several industry and academic groups employing various technologies and racing to catch up. Cell therapy has experienced similar peaks and valleys in interest, with stem cells touted as a platform able to replace entire damaged organ systems. Multiple variants of what one would call a cell therapy now are in development ranging for treatment with fully differentiated somatic cells to naïve cells able to grow and differentiate *in vivo*. A combination of gene and cell therapy approaches is used in the widely popular T cell immunotherapy approaches for cancer treatment where cells are modified *ex vivo* to target tumors after reintroduction to the patient. Considering the potency of T cells it is not surprising that safety concerns have limited their target profile. Finally, the concept of knocking down expression of gene expression has gained significant momentum with the introduction of therapeutic RNA interference and most recently with gene editing via a variety of methods. All of these “advanced therapy” platforms require very unique approaches outside of the standards defined by internationally accepted guidance for preclinical safety assessment. Not only does the biopharmaceutical mantra of “case by case” apply, but standard issues such as immunogenicity, tumorigenicity and appropriate animal models take on new meaning when applied to these therapies. With start-up companies

being formed and larger pharmaceutical companies investing heavily in these therapeutic areas, there is a growing need for toxicologists to be familiar with these platforms. This course will aim to introduce the audience to each of these four general categories of advanced therapies as well as provide a regulatory perspective on these modalities and highlight where the standard approaches for safety assessment either do not apply or require unique application.

Toxicological Approaches to Gene Therapy. Joy Cavagnaro, AccessBio, Boyce, VA.

Toxicological Approaches to T-Cell Immunotherapies. Timothy MacLachlan, Novartis, Cambridge, MA.

Toxicological Approaches to Cell Therapies. Cliff Sachs, MedImmune, Gaithersburg, MD.

Toxicological Approaches to Genome Editing. Kathleen Meyer, Sangamo Biosciences Inc., Richmond, CA.

Think Like a Regulator: US FDA Considerations for Preclinical Studies for Cell and Gene Therapy Products. Becky Robinson, Center for Biologics Evaluation and Research, US FDA, Silver Spring, MD.

Zebrafish As a Tool in Toxicology and Drug Discovery Screening

Sunday, March 13, 1:15 PM–5:00 PM
PM13 | CE BASIC | AFTERNOON COURSE

♥ Health and Environmental Impacts of Manmade and Naturally Released Toxicants
🔥 Recent Advances in Safety Assessment

Chairperson(s): Mamta Behl, National Toxicology Program/ NIEHS, Research Triangle Park, NC; and Arantza Muriana, BBD Biophoesnix S.L.-Biobide, San Sebastián, Donostia, Spain.

Endorser(s):

In Vitro and Alternative Methods Specialty Section
Molecular and Systems Biology Specialty Section
Reproductive and Developmental Toxicology Specialty Section

The zebrafish is a powerful tool to screen compounds, especially for early development since it is a vertebrate, has a high genetic homology with humans, and the assays can be automated to provide relatively high-throughput along with high-content analysis. Adult and developing zebrafish are increasingly being used to assess development, gene expression, and behavior to screen and prioritize compounds for toxicity testing and safety evaluation. Specifically, the zebrafish has proven extremely relevant in the evaluation of acute toxicity and developmental toxicity, as well as organ-specific toxicities, including cardiotoxicity, hepatotoxicity, and neurotoxicity.

The purpose of this course is to bring together experts from the pharmaceutical industry, CROs, academia, and the Government to provide insight on the current developments in the use of zebrafish in the field of toxicology and drug safety and efficacy assessment, and to highlight some ongoing challenges in the field. The course will begin with important basics of zebrafish biology such as selection of strains, husbandry, dose-response and time course, and will highlight its application in toxicology. The second talk will focus on the recent advancements of zebrafish as a tool to assess developmental toxicity. The third talk will focus on the systematic optimization of variables for efficient screening, and tools for data management, visualization

and analysis. Speaker four will highlight the use of zebrafish in drug discovery as a rapid and cost effective method to screen for a number of new molecular entities entering clinical phases. Finally, speaker five will build upon the information presented by the previous speakers to shed light on the utility in screening of drugs for efficacy and safety, and ultimately for acceptance of data for regulatory purposes.

The course will address critical questions on the status of this model in hazard identification and risk assessment for environmental toxicants including progress in the field, loopholes, and data-gaps, novel upcoming developments, and the impact of this model on toxicology research in the 21st century, as well as the impact on safety assessment of drugs.

Introduction and Course Goals. Mamta Behl, National Toxicology Program/NIEHS, Research Triangle Park, NC.

The Ins and Outs of Using Zebrafish for Mechanistic Toxicology Studies. Antonio Planchart, Department of Biological Sciences, North Carolina State University, Raleigh, NC.

Developmental Toxicology Research in Zebrafish. Kimberly Brannen, Charles River Laboratories, Philadelphia, PA.

Optimizing Multi-Dimensional Bioactivity Screening in Zebrafish. Robert Tanguay, Oregon State University, Sinnhuber Aquatic Research Laboratory, Corvallis, OR.

Innovative Zebrafish Hepatotoxicity, Cardiotoxicity, and Neurobehavioral Toxicity Assays for Drug Selection. Arantza Muriana, BBD BioPhenix S.L.-Biobide, San Sebastián, Donostia, Spain

Recent Developments and Recognition of Zebrafish for Use in Safety Evaluation by the Regulatory Agencies. Gopala Krishna, Supernus Pharmaceuticals, Inc., Rockville, MD.

Zebrafish—Whatever You Ever Wondered About! Additional Discussion with All Panel Speakers



Daily Plenary Session

Regenerative Medicine and Tissue Engineering

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

Lecturers: Doris Taylor, Texas Heart Institute, Houston, TX; and Joan Nichols, University of Texas Medical Branch, Galveston, TX.

See full descriptions on page 75.



Continuing Education Courses Online

Expand your professional development or stay current in the field of toxicology, all year long!
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Immunotoxicology	Ocular Toxicology
In Vitro and Alternative Methods	Regulatory and Safety Evaluation
Inhalation and Respiratory	Reproductive and Developmental Toxicology
Mechanisms	Risk Assessment
Medical Device and Combination Product	Stem Cells
Metals	Toxicologic and Exploratory Pathology

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- Advances in Safety Assessment of Medical Devices
 - An Introduction to the Exposome
- Future of Developmental and Reproductive Toxicology—
Building a Bridge to the Animal Free Zone
- Interpretation of Cardiovascular Safety Data in Toxicology Studies
- New World of Cancer Immunotherapy: Challenges in Bench to Bedside Translation
 - Strategies in Investigative Toxicology in a Pharmaceutical Setting
 - Toxicogenomics Meets Regulatory Decision-Making
- Toxicology and Regulatory Considerations for Combination Products

For a complete list of online courses, or to register, visit **www.toxicology.org/cedtox.asp**.

Join us for the 55th Annual Meeting in New Orleans!

For more information on upcoming live CE courses, visit **www.toxicology.org/2016am**.



Scientific Sessions

Featured Sessions

Plenary Sessions

Daily Plenary Session

Regenerative Medicine and Tissue Engineering

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

**Building a Heart: From Cells to Tissues to Organs****Lecturer:** Doris Taylor, Texas Heart Institute, Houston, TX.

Cardiovascular disease (CVD) is the number one cause of death in the United States. However, few treatments for CVD provide a means to regain full cardiac function with no long-term side effects. Novel tissue-engineered products may provide a way to overcome the limitations of current CVD therapies by replacing injured myocardium with functioning tissue or by inducing more constructive forms of endogenous repair. Dr. Taylor will discuss some of the factors that must be considered in the development of tissue-engineered products and review the methods currently being investigated to generate more.

**From 3D Microchip to Human Organ Culture Models: Trachea, Bronchi/ Bronchiole and Lung Biomimetic Models for Disease Modeling, Drug Discovery, and Toxicology Evaluation****Lecturer:** Joan Nichols, University of Texas Medical Branch, Galveston, TX.

We have learned a great deal about respiratory tract and lung physiology or pathophysiology of disease from the study of animal disease models, tissues from patients isolated at autopsy or growth of monoclonal human cell populations in two dimensional (2D) cultures. Animal models, mainly mice, have been widely used in research and although animal models can simulate human disease they never fully mirror all aspects of human immune response or pathophysiology of disease. Because of this many drug treatments and vaccines developed solely using animal models have been ineffective when used in patient care. Recent advances in microfabrication technology, microfluidics, and tissue engineering have provided a new approach to the development of human 3D tissue culture models which enable production of robust long-lived human tissue analogs. Use of these models along with more complex 3D human organ culture models, containing multiple cell phenotypes, provides a more reasonable approximation of what occurs in the dynamic *in vivo* microenvironment of human tissues. Microfluidic supported 3D respiratory tract and lung models are currently being used as advanced human testing platforms for evaluating drug response or drug toxicity, hopefully reducing the cost of drug development. Human tissue models may also provide a mechanism for development of personalized medical care based on testing of drugs on a patient's own cells or engineered tissues in the future.

Daily Plenary Session

Inflammation and Neurodegenerative Disease

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

**Mast Cells and Glia: Two Tracks on the Road to Neuroinflammation****Lecturer:** Stephen Skaper, University of Padua, Padua, Italy.

One of the more important recent advances in neuroscience research is the understanding that there is extensive communication between the immune system and the central nervous system (CNS). Proinflammatory cytokines play a key role in this communication. The emerging realization is that glia and microglia, in particular, (which are the brain's resident macrophages), constitute an important source of inflammatory mediators and may have fundamental roles in CNS disorders from neuropathic pain and epilepsy to neurodegenerative diseases. Microglia respond also to proinflammatory signals released from other non-neuronal cells, principally those of immune origin. Mast cells are of particular relevance in this context. These immune-related cells, while resident in the CNS, are capable of migrating across the blood-spinal cord and blood-brain barriers in situations where the barrier is compromised as a result of CNS pathology. Emerging evidence suggests the possibility of mast cell-glia communication and opens exciting new perspectives for designing therapies to target neuroinflammation by differentially modulating the activation of non-neuronal cells normally controlling neuronal sensitization, both peripherally and centrally. This presentation will provide an overview of recent progress relating to the pathobiology of neuroinflammation, the role of microglia, neuroimmune interactions involving mast cells, in particular, and the possibility that mast cell-microglia crosstalk may contribute to the exacerbation of acute symptoms of chronic neurodegenerative disease and accelerate disease progression, as well as promote pain transmission pathways.

**Inflammation and Neurodegeneration in CNS Injury: Evolving Concepts and New Therapeutic Targets****Lecturer:** Alan I. Faden, University of Maryland School of Medicine, Baltimore, MD.

It has long been claimed that prior traumatic brain injury (TBI) increases the subsequent incidence of Alzheimer's disease (AD). However, recent larger epidemiological studies indicate a relationship to subsequent dementia but not to AD. There is also a well-recognized association between repeated mild TBI and progressive cognitive decline or other neuropsychiatric abnormalities. The latter was first described in boxers as dementia pugilistica, and has received widespread attention in relationship to high contact sports. The term chronic traumatic encephalopathy (CTE) has been used to define a "specific" entity marked by neurobehavioral changes and deposition of phosphorylated tau protein. Less well appreciated with regard to post-traumatic neurodegeneration is the role of sustained neuroinflammation, even though this association has been recognized pathologically for decades. More recent experimental work, as well as clinical neuroimaging studies, has underscored the relationship between chronic neuroinflammation and progressive brain neurodegeneration in a number of disorders including TBI, while providing

(continued on page 77)



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Featured Sessions

mechanistic support. Manifested by extensive microglial and astroglial activation, chronic traumatic brain inflammation (CTBI), or perhaps better termed chronic traumatic inflammatory encephalopathy (CTIE), appears likely to be the most important cause of post-traumatic neurodegeneration and related cognitive decline in terms of prevalence. Perhaps even more critically, emerging preclinical studies indicate that persistent neuroinflammation and associated neurodegeneration may be treatable weeks to months after the initiating insult(s).

Daily Plenary Session

Keynote Medical Research Council (MRC) Lecture

Wednesday, March 16, 8:00 AM to 9:20 AM

Regenerating CNS Myelin—
From Mechanisms to Medicines

Lecturer: Robin J.M. Franklin, Wellcome Trust-MRC Cambridge Stem Cell Institute, University of Cambridge, Cambridge, United Kingdom.

Remyelination, the process by which new myelin sheaths are restored to demyelinated axons, represents one of the most compelling examples of adult multipotent stem cells contributing to regeneration of the injured CNS. This process can occur with remarkable efficiency in multiple sclerosis (MS), and in experimental models, revealing an impressive ability of the adult CNS to repair itself. However, the inconsistency of remyelination in MS, and the loss of axonal integrity that results from its failure, makes enhancement of remyelination an important therapeutic objective. There is now compelling evidence that aging is the major contributor to the declining efficiency of remyelination and that this is largely due to a failure of stem cell differentiation. This talk will review recent studies we have undertaken aimed at obtaining a detailed understanding of the mechanisms of regulating differentiation during remyelination and hence identifying novel therapeutic targets.



SOT/EUROTOX Debate

Preclinical (Safety) Toxicology Testing Predicts the Clinical Outcome

Monday, March 14, 4:45 PM to 6:00 PM



Chairperson(s): Patricia E. Ganey, Michigan State University, East Lansing, MI; and Mumtaz Iscan, Ankara University, Ankara, Turkey.

SOT Debater: Thomas M. Monticello, Amgen, Inc., Thousand Oaks, CA.

EUROTOX Debater: Ruth Roberts, Apconix Ltd, Alderley Edge, United Kingdom.



Endorser(s):

Society of Toxicology (SOT)

European Societies of Toxicology (EUROTOX)

Each year the SOT Annual Meeting includes a debate that continues a tradition that originated in the early 1990s in which leading toxicologists advocate opposing sides of an issue of significant toxicological importance. This year, our debaters will address the proposition: Preclinical (Safety) Toxicology Testing Predicts the Clinical Outcome.

Preclinical safety testing of new drug candidates is a crucial step in pharmaceutical drug development and is a highly controlled process based on specific regional and global regulatory agency criteria. Preclinical toxicology testing includes a sequential series of *in silico*, *in vitro*, and *in vivo* toxicology studies prior to first in human (FIH) clinical trials. Specifically, data on genotoxicity, general toxicology and safety/secondary pharmacology are generated, and then used to characterize potential safety risks for humans by identifying tolerated doses and target organs of toxicity. These studies are also used to identify potential safety biomarkers to be used in the context of dose and exposure, informing clinicians of appropriate monitoring and also the potential for reversibility after a dose free period. Although preclinical toxicology studies are a regulatory requirement, there has been debate recently that has questioned their utility in evaluating human safety risks. On the one hand, toxicities noted in patients may differ from those noted in animals, questioning the relevance of the animal studies, advocating instead for alternative models such as the "organ/tissue on a chip." This is consistent with the concept introduced by Russell and Burch for the 3Rs; reduction, refinement, and replacement in animal experimentation. On the other hand, preclinical animal toxicology studies may play an important role in predicting toxic dose and exposure, even if the dose limiting toxicities in animals and humans differ. The debaters will discuss the state of the science on preclinical safety testing and whether it can predict clinical outcome.

Regardless of framework differences and personal convictions, each scientific debate delegate will present relevant evidence and compelling scientific arguments to persuade and appeal to the response of the audience in order to obtain the approval or refusal of the motion. In addition to being a featured session at the SOT Annual Meeting in New Orleans, Louisiana, this debate will again take place (with the debaters taking the reverse positions) in Istanbul, Turkey during the 52nd Congress of the European Societies of Toxicology (2016 EUROTOX Annual Congress), September 4–7, 2016.

(continued on page 79)



Submit Your Recent Scientific Research during a Late-Breaking Abstract Submission Phase

The Society is poised to have another successful Annual Meeting with currently more than 2,500 abstracts scheduled to be presented in New Orleans, March 13–17, 2016.

We invite you to submit an abstract during a late-breaking abstract submission phase which will occur from December 5, 2015, through January 12, 2016. All abstracts will be submitted online. The cost to submit an abstract is \$50.

All accepted abstracts will be programmed on Thursday, March 17, along with several dynamic symposia and workshop sessions.

An important criteria for abstract submission during this time is that the research must be new and of sufficient scientific importance to merit special consideration after the standard abstract deadline. Abstracts should describe high-impact original research that could not be completed prior to the original deadline.

Additional qualifications for submitting an abstract during this final submission phase include:

Scientists who had to wait until after the original October deadline to submit due to funding issues are encouraged to submit an abstract for consideration.

All abstracts will be reviewed by the Scientific Program Committee and held to the same standards used to evaluate abstracts submitted for the original deadline.

Not more than one abstract will be accepted by the same presenting author.

Your abstract should not be a revision of a previously submitted one that was not accepted unless you received specific communication from the Scientific Program Committee suggesting that resubmission during the late-breaking abstract period may be appropriate.

Given the Society's current publishing deadline, the abstracts accepted will be provided as a PDF addendum and are searchable through the Mobile Event App and Online Planner.

We look forward to welcoming you to the Society's Annual Meeting in New Orleans, Louisiana.

Featured Sessions

Meet the Directors

A Conversation with Linda Birnbaum and Christopher Austin

Monday, March 14, 1:30 PM to 2:30 PM



Chairperson(s): John B. Morris, Society of Toxicology Vice President; University of Connecticut, Storrs, CT.

Lecturers: Linda Birnbaum, NIEHS, Research Triangle Park, NC; and Christopher Austin, NCATS, Bethesda, MD.



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: Linda Birnbaum, PhD, Director, National Institute of Environmental Health Sciences (NIEHS), NIH, and Christopher Austin, MD, Director, National Center for Advancing Translational Sciences (NCATS), NIH. The entire session will be devoted to a question-and-answer format concerning scientific directions and priorities for NIEHS and NCATS including funding priorities and outlooks, and training opportunities. As NIEHS and NCATS are partners in the Tox21 initiative a focus will be upon the utility and future of high throughput testing. Dr. Birnbaum has served as the Director of the National Institute of Environmental Health Sciences and the National Toxicology Program since 2009. Christopher Austin was the inaugural director the NCATS Division of Pre-Clinical Innovation and was appointed director of NCATS in 2012.

Award Lectures

Merit Award Lecture

Monday, March 14, 12:30 PM to 1:20 PM



Lecturer: Melvin Andersen, The Hamner Institutes for Health Sciences, Research Triangle Park, NC.

Leading Edge in Basic Science Award Lecture

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



Lecturer: Cheryl Lyn Walker, Texas A&M Institute of Biosciences and Technology, Houston, TX.

Distinguished Toxicology Scholar Award Lecture

Wednesday, March 16, 12:30 PM to 1:20 PM



Lecturer: I. Glenn Sipes, University of Arizona, Tucson, AZ.

Translational Impact Award Lecture

Wednesday, March 16, 5:00 PM to 5:50 PM



Translational Non-Invasive Biomarkers of Acetaminophen-Induced Liver Injury

Lecturer: Richard Beger, US FDA-NCTR, Jefferson, AR.

Acetaminophen (APAP) overdose is both clinically relevant and a good model for the development of new translational biomarkers. APAP is primarily metabolized by CYP2E1 to form the reactive metabolite N-acetyl-p-benzoquinone imine (NAPQI) which can bind to cysteine residues of proteins and form APAP-protein adducts. APAP adducts in humans and rodents have been shown to correlate with ALT levels. 'Omics technologies (microRNA profiling, proteomics and metabolomics) have been employed to discover translational phenotype response biomarkers of APAP-induced liver injury in biofluids from nonclinical studies. These potential translational 'omics biomarkers of liver injury have been evaluated using clinical samples from healthy and APAP overdose patients. Data supporting the use of microRNAs as biomarkers for DILI using APAP will be presented. Metabolomics approaches have been used to discover that long-chain acylcarnitines and bile acids were significantly altered in blood from APAP-treated rodents. Increases in long-chain acylcarnitines may represent mitochondria injury and associated reduced β -oxidation capacity. Data show that glycine and taurine conjugated bile acids appear to be sensitive determinants of APAP-induced liver injury. Overall, exciting progress in the development of novel translational omics and protein adducts biomarkers of hepatotoxicity has been made using biofluid samples from humans and rodents with APAP-induced liver injury.



Advance the Science of Toxicology

Consider Organizing a Contemporary Concepts in Toxicology Meeting

Contemporary Concepts in Toxicology (CCT) Meetings expand the opportunities and forums for members to engage in the exchange of ideas and information relevant to toxicology. CCT Meetings are one- to two-day focused, open registration, scientific meetings in contemporary and rapidly progressing areas of toxicological sciences. CCT Meetings also can be held as webinars.

If you think that your research area could be enhanced by thought leader collaboration or that public health and safety could be improved by disseminating your research findings more broadly, please consider organizing an SOT CCT Meeting. The CCT Conferences Committee and the SOT Headquarters staff are prepared to help move your meeting forward.

The Society will underwrite all the liabilities of the CCT Meeting (up to the \$25,000 in seed money) with the expectation that the meeting at least break even financially. Profit sharing for SOT component groups is available. For more information about CCT Meetings, please visit the SOT website at www.toxicology.org/cct.

CCT Meetings focus on a wide range of topics and future CCT conferences address the following:

- **MiRNA Biomarkers for Toxicology**
March 12, 2016 | New Orleans, Louisiana
- **Ocular Toxicology—Pharmacology and Drug Delivery:
An Eye on the Future**
June 27–28, 2016 | South San Francisco, California

In order to sustain the quality standards of the Society, only meetings in which SOT maintains scientific and administrative control will be considered. Meetings developed and administered by other organizations may be eligible for sponsorship and/or endorsement by the Society of Toxicology.



MONDAY

Opening the Black Box: Understanding the Molecular Mechanisms of Developmental Toxicity

Monday, March 14, 9:30 AM to 12:15 PM

-  Developmental Toxicity: Mechanisms and Evaluation
-  Molecular Toxicology: Mechanistic Insights and Hazard Assessment

Chairperson(s): Barry McIntyre, NIEHS, Research Triangle Park, NC; and Joshua Gamse, Bristol-Myers Squibb, New Brunswick, NJ.

Endorser(s):
Mechanisms Specialty Section
Reproductive and Developmental Toxicology Specialty Section

The development of an organism from egg to adult is a complex series of interlocked events, which depends on precise coordination in time and space. When xenobiotic agents interfere with development, they can alter cellular growth and differentiation, leading to permanent changes in tissue/organ structure and function, i.e. developmental malformations. Over the past 40+ years, developmental toxicologists have strived to understand the mechanisms of action resulting in these lesions. With the advent of novel molecular tools, an enhanced understanding of developmental biology, and new model systems, great progress has recently been made in deciphering some of the fundamental drivers of altered development. In this session, we will explore recent findings in developmental toxicology that have begun to link teratogens with their potential mechanisms of action. The first speaker uses a zebrafish cardiovascular model to explore the role of the G-protein-coupled estrogen receptor on heart rate. In the second presentation, the speaker describes a novel mechanism for arsenic disruption in TGFβ-Smad signal transduction during formation of heart valves and coronary vessels. The third speaker demonstrates how altered TGF-β and FGF signaling impact the development of the forebrain. Using an *in vitro* murine limb bud culture system and classic histone deacetylase inhibitors, the fourth speaker reveals the role of protein acetylation in the action of some developmental toxicants. Finally, using thalidomide and its analogs, the fifth speaker presents compelling data on the mechanism of thalidomide action in phocomelia. These speakers, who come from a mix of academic and industry backgrounds, will demonstrate how understanding the mechanisms underlying developmental toxicology allows for the prediction of class effects, the discovery of subtle but important developmental changes, and the design of more informative *in vitro* and *in vivo* methods for detecting teratogenicity.

Acute Estrogen Exposure Increases Heart Rate via a G-Protein-Coupled Estrogen Receptor Mechanism in Zebrafish. Daniel Gorelick, University of Alabama, Birmingham, AL.

Fetal Arsenic Exposure Disrupts TGFβ2-SMAD Signaling and Developmental EMT. Todd Camenisch, University of Arizona, Tucson, AZ.

TGFβ and FGF Inhibition Elucidates Mechanisms Controlling the Formation of the Diencephalon. Joshua Gamse, Bristol-Myers Squibb, New Brunswick, NJ.

The Role of Histone Deacetylase Inhibition in Mediating the Effects of Developmental Toxicants on Limb Development.

Barbara Hales, McGill University, Montreal, QC, Canada.

Elucidation of the Mechanism of Action of Thalidomide and IMiD Compounds Gives Novel Insights into Their Pleiotropic Effects.

Rajesh Chopra, Celgene, Summit, NJ.

Health and Environmental Hazard Assessments of Nanomaterials Along Their Lifecycle

Monday, March 14, 2:00 PM to 4:45 PM

-  Health and Environmental Impacts of Man-Made and Naturally Released Toxicants

Chairperson(s): Aaron Erdely, NIOSH, Morgantown, WV; and James Bonner, North Carolina State University, Raleigh, NC.

Endorser(s):
Inhalation and Respiratory Specialty Section
Nanotoxicology Specialty Section
Occupational and Public Health Specialty Section

Unprecedented global investment in innovative nanoscale science and engineering has led to the production and utilization of novel materials in expanding fields of electronics, medicine, and composites. Incorporation of advanced materials into existing products through functionalization reactions improves performance, durability and efficiency in various consumer markets. However, health and environmental hazards of these critical nanomaterials during production, distribution, formulation, use, and disposal have raised concerns. To date, most toxicology research has focused on the as-produced nanomaterial while neglecting the potential health and environmental risks of downstream formulations and applications. This session will highlight 1) exposure potential during production, use, and disposal; 2) hazard identification along the lifecycle of a wide range of nanomaterials; 3) release-testing scenarios with efficacy testing for various nano-enabled products; and 4) the environmental fate of nanomaterials. The outcome of this session will be practical understanding of the most recent research of nanomaterials from a lifecycle perspective. Linking real-world exposures across the lifecycle of nano-enabled products to potential adverse health effects will provide regulators and researchers with essential data needed for effective risk assessment.

Rules and Rates of Release From Nano-Enabled Products: Correlating Aging Conditions, the Properties of Product Matrices, and Nanomaterials. Wendel Wohlleben, BASF, Ludwigshafen, Germany.

Linking Exposures of Particles Released Across Lifecycle of Nano-Enabled Products to Toxicology: An Integrated Methodology for Particle Sampling, Extraction, Dispersion, and Dosing. Philip Demokritou, Harvard School of Public Health, Boston, MA.

Toxicological Evaluation of Carbon Nanotubes from a Lifecycle Perspective. Aaron Erdely, NIOSH, Morgantown, WV.

Symposia

Quantifying Exposures from Nanotized Products While Assessing Product Efficacy Across Their Value Chain. Paul Westerhoff, Arizona State University, Tempe, AZ.

Environmental Interactions of Nanomaterials in Aquatic Ecosystems. Mark Wiesner, Duke University, Durham, NC.

The Promise and Reality of Alternative Methods in Inhalation Toxicology and the Development of Inhaled Therapeutics

Monday, March 14, 2:00 PM to 4:45 PM

Chairperson(s): Jon A. Hotchkiss, The Dow Chemical Company, Midland, MI; and Amy J. Clippinger, PETA International Science Consortium, Ltd., Norfolk, VA.

Endorser(s):

***In Vitro* and Alternative Methods Specialty Section
Inhalation and Respiratory Specialty Section
Regulatory and Safety Evaluation Specialty Section**

The respiratory tract is the portal of entry for inhaled gases, vapors, and aerosols into the body. The risk and impact of occupational and environmental exposures to inhaled xenobiotics on human health is often based on guideline-driven inhalation toxicity testing in animals. Similarly, testing the efficacy, pharmacokinetics, and toxicological profile of inhaled therapeutics and excipients is still often conducted in animals. The unique characteristics of the respiratory tract that make it both a potential target organ and a route of systemic exposure present a unique opportunity to develop alternatives to animal tests that are cheaper, faster, based on human mechanisms of action, and that adhere to the 3Rs of reducing, replacing, and refining animal use. Unfortunately, the development, validation, and regulatory acceptance of alternative testing methods for inhaled materials lags behind other exposure routes and organ systems. Much of this may be attributed to the complex interplay of the physical-chemical characteristics of test substances and the regional variation in cell types present along the upper and lower respiratory tract which together determine the dosimetry, absorption, and metabolism of inhaled materials. This symposium will highlight *in silico* and *in vitro* approaches, including the development and dosimetrically relevant exposure of organotypic air liquid interface (ALI) cultures of human airway epithelial, stromal, and effector cells and application of “organ on a chip” microdevices to rapidly and efficiently examine exposure-response relationships without the need for traditional *in vivo* inhalation exposure of laboratory animals. The goal of this symposium is to provide participants with a working knowledge of state-of-the-art computational tools and *in vitro* methods currently available and under development to predict acute inhalation toxicity, identify chemical respiratory sensitizers, enhance the testing of inhaled therapeutics and excipients, replace subchronic inhalation toxicity testing, and examine systemic effects and pharmacokinetic properties of inhaled materials.

Introduction. Jon A. Hotchkiss, The Dow Chemical Company, Midland, MI.

Integrating Alternative Methods within a Regulatory Framework and the Impact of AOPs in Designing an Integrated Testing Strategy to Replace Repeat Exposure Inhalation Toxicity Testing. David G. Allen, Integrated Laboratory Systems, Inc., Research Triangle Park, NC.

***In Silico* Models to Predict Acute Inhalation Toxicity and Identify Potential Chemical Respiratory Sensitizers.**

Daniel M. Wilson, The Dow Chemical Company, Midland, MI.

Air-Liquid Interface (ALI) Culture Systems and Exposure Modalities As Replacements for Inhalation Toxicity Testing. Samuel Constant, Epithelix, Geneva, Switzerland.

Co-Culture Systems Mimicking the Human Lung Barrier to Assess the Risk of Inhaled Nanomaterials. Barbara Rothen-Rutishauser, Adolphe Merkle Institute, University of Fribourg, Fribourg, Switzerland.

Microengineered Physiological Biomimicry: Human Organ-On-Chips. Dan Huh, Department of Bioengineering, University of Pennsylvania, Philadelphia, PA.

Concluding Remarks. Amy J. Clippinger, PETA International Science Consortium, Ltd., Norfolk, VA.

TUESDAY

Drug-Induced Taste Change in Clinical Practice and Preclinical Safety Evaluation

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

Chairperson(s): Tao Wang, Novartis Pharmaceuticals, Emeryville, CA; and Keith Mansfield, Novartis, Cambridge, MA.

Endorser(s):

**Clinical and Translational Toxicology Specialty Section
Regulatory and Safety Evaluation Specialty Section**

Drug-induced taste disorder is one of the most distressing adverse side effects reported by chemotherapy patients. Taste change (dysgeusia) not only reduces the quality of life for affected patients, but can lead to malnutrition, weight loss and, in severe cases, difficulty in maintaining a therapeutic regimen. The goal of this session is to review current understanding of taste changes in clinical practice, and how the identification of taste change in preclinical investigations in animal models can provide mechanistic insights and help develop mitigation strategies to guide clinical practice. The symposium will review taste change in patients, including clinical symptoms, type of dysgeusia, diagnostic methods, and current approaches to the treatment of taste disorders. Since smell and taste are closely related, a follow-up presentation will focus on the biochemical and physiological mechanisms of drug-induced changes, and describe enrichment procedures help patients overcome aberrant taste and smell. After presentation of the clinical perspective, the preclinical safety evaluation of taste changes with an emphasis on morphological evaluation and biomarker in rats and dogs will be presented. The description of morphological and molecular tests for taste change will be followed by a comprehensive presentation of physiological methods for functional evaluation of taste change in preclinical animal models. The presentations will also outline how these functional tests can facilitate the development of approaches to overcome dysgeusia.

Overview of Taste Change. Tao Wang, Novartis, Emeryville, CA.

Taste Disorders in Patients: Symptom, Diagnosis and Treatment. Miriam Grushka, William Osler Health System, Toronto, ON, Canada.

Drug-Induced Taste and Smell Disturbance. Thomas Hummel, Smell and Taste Clinic, TU Dresden, Fetscherstrasse, Dresden, Germany.

Preclinical Safety Investigations of Drug-Induced Taste Change in Animal Models—Histology and Biomarkers. Keith Mansfield, Novartis Pharmaceuticals, Cambridge, MA.

Chem sensory Assessment in Animal Models Undergoing Chemotherapy Treatment. John Glendinning, Barnard College, Columbia University, New York, NY.

Genotypic and Intrinsic Risk Factors That Increase Susceptibility to Inhaled Pollutants

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

Chairperson(s): Desinia B. Miller, University of North Carolina at Chapel Hill, Chapel Hill, NC; and Gabriel Knudsen, National Cancer Institute at NIEHS, Research Triangle Park, NC.

Endorser(s):

**Graduate Student Leadership Committee
Occupational and Public Health Specialty Section
Postdoctoral Assembly**

The mandated Clean Air Act (CAA) requires the Environmental Protection Agency to set National Ambient Air Quality Standards (NAAQS) to mitigate high-level harmful emissions from natural and man-made sources. These standards strive to protect the health of the most vulnerable human population from potential pollutant-induced adverse health outcomes. However, because of limited research on susceptible subpopulations, the determinations of NAAQS for at-risk groups have proven to be difficult. As a result, an uncertainty factor of 10 is employed in the absence of actual data on susceptibility. A few epidemiological and experimental studies have implicated risk factors such as genotype, sex, ethnicity, life stage, and underlying diseases in human inter-variation that increase susceptibility to adverse health effects of inhaled pollutants. However, the mechanisms of how these factors increase sensitivity to inhaled pollutants in at risk groups have not been well understood. The aims of this symposium are to 1) address the underlying health conditions that can influence risk of adverse health effects associated with inhaled pollutants and 2) identify biologically plausible mechanisms and/or interactions between these risk factors and inhaled pollutant injury. The six trainee presenters will focus on different risk factors and examine how underlying conditions alter the adverse health effects of inhaled pollutants, with the emphasis on potential mechanisms. The first two presenters will focus on gene-environment interactions that affect susceptibility to inhaled pollutants, while one of the speakers will also address the differential risk due to sex. The third speaker will use *in utero* data to discuss how air pollution exposure during different life stages can modify health risk. The last three presenters will focus on pre-existing respiratory and metabolic conditions that have been implicated in increased susceptibility to inhaled pollutants. Altogether, attendees will learn about different characteristics that influence susceptibility and gain insight into likely mechanisms by which air pollution effects are altered in at-risk groups.

Additionally, it will provide identification and further characterization of potential sensitive populations to consider in future epidemiological and inhalation risk assessment studies.

Interaction of Alpha-Synuclein with Divalent Metal Manganese Alters Disease Progression in Transgenic Models of Parkinson's Disease. Dilshan S. Harischandra, Iowa State University, Ames, IA.

Human Airway Epithelium: Ethinyl Estradiol-Mediated Sex Differences in Smokers and Non-Smokers. Megan Rubelli, University of North Carolina at Chapel Hill, Chapel Hill, NC.

In Utero Secondhand Smoke Exposures Increase the Lungs' Susceptibility to Developing Emphysema-Related Responses in Adults. Alexandra Noel, Department of Comparative Biomedical Sciences, School of Veterinary Medicine, Baton Rouge, LA.

The Effect of Diesel Exhaust Exposure on Patients with Allergic Rhinitis—Implications for NK Cell Physiology. Erica Pawlak, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Inhaled Ozone Causes More Severe Lung Lesions in Hyperglycemic, Insulin-Resistant KKAy Mice As Compared to Normoglycemic, Insulin-Sensitive C57BL/6 Mice. Daven N. Jackson-Humbles, Michigan State University, Ann Arbor, MI.

Obesity As Risk Factors for Ozone-Induced Cardiopulmonary Effects and Metabolic Impairment. Samantha J. Snow, US EPA, Durham, NC.

Systems Understanding of the Impact of the Nrf2 Pathway on Chemical Toxicity and Cell Fate

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

◆ **Molecular Toxicology: Mechanistic Insights and Hazard Assessment**

Chairperson(s): Chris Corton, US EPA, Durham, NC; and Thomas Kensler, University of Pittsburgh, Pittsburgh, PA.

Endorser(s):

**Mechanisms Specialty Section
Molecular and Systems Biology Specialty Section**

The transcription factor Nrf2 plays a significant role in protecting cells from endogenous and exogenous stresses. Initial studies of the Nrf2 pathway focused on altered metabolism of toxins, leading to their enhanced detoxication and elimination. Continuing studies expanded this view of Nrf2 action to include pathways affecting recognition, repair and removal of damaged macromolecules. Most recent studies have focused on the links between cellular metabolism and cell fate. Some of these actions are mediated through cross-talk with other signaling networks. This symposium will highlight recent exciting findings in the field that greatly extend our systems understanding of the function and regulation of Nrf2 using a broad range of omic tools. The first speaker will describe the first screen for genetic effectors of Nrf2 activity. The second speaker will discuss a novel screening strategy in a large gene expression compendium to identify signaling pathways that affect Nrf2. The third speaker will describe a unique role for Nrf2 in circadian rhythm. The fourth and fifth speakers will describe exciting work that

Symposia

links Nrf2, metabolic reprogramming and cell fate. The session will be of interest to scientists interested in stress pathways and how omics tools can be applied to study mechanisms of toxicity.

Imaging-Based RNA Interference Screening Identifies Novel Regulators of Nrf2 Signaling: Consequences for Drug-Induced Liver Injury. Bob van de Water, Leiden University, Leiden, Netherlands.

A Biomarker-Based Screen of a Large Gene Expression Compendium Reveals Regulation of Nrf2 by CAR and STAT5b. Chris Corton, US EPA, Durham, NC.

Closing the Loop: Defining the Role of Nrf2 in Clock Repression. Thomas Sutter, University of Memphis, Memphis, TN.

The Nrf2-Notch Axis: Expanding the Cell Fate Network. Thomas Kensler, University of Pittsburgh, Pittsburgh, PA.

Crosstalk Between Regulation of Redox Balance and Cell Proliferation by NRF2. Hozumi Motohashi, Tohoku University, Miyagi, Japan.

Unknown, Unknowns: Exploring the Unidentified Fraction of Complex Mixtures

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

Chairperson(s): Cynthia Rider, NTP/NIEHS, Research Triangle Park, NC; and Bethany Hannas, The Dow Chemical Company, Midland, MI.

Endorser(s):

**Mixtures Specialty Section
Occupational and Public Health Specialty Section
Risk Assessment Specialty Section**

Assessing risk from exposure to complex mixtures, ranging from botanical dietary supplements to traffic pollution, is exceptionally challenging. A hallmark of complex chemical mixtures is the presence of unidentified mixture mass. The contribution of these unknown chemicals is difficult to characterize. In terms of exposure, there is a prevailing tendency to measure only a select subset of target constituents (i.e., those with reason for toxicological concern or those that are present at the highest concentrations) within a complex mixture, resulting in a significant unidentified fraction. Paradoxically, toxicological assessments are typically limited to chemicals for which exposure data are available. These targeted strategies were developed to focus attention on the chemicals of greatest concern, but they implicitly overlook the unidentified fraction, which can represent the largest mass of the mixture. In risk assessment of chemical mixtures, component-based approaches, which deal exclusively with mixture constituents for which exposure and toxicological data are available, are far more common than those that consider whole mixtures. This is based on both a lack of available whole mixtures data and uncertainties in extrapolating from a reference mixture to a mixture of concern. In contrast to component-based approaches, whole mixture approaches account for the unknown mixture mass but do not identify the impact attributable to the unknown fraction. In this workshop, the unidentified fraction of complex mixtures will be brought to the forefront. Advances in chemical analysis, toxicology, and whole mixtures risk assessment

will be discussed in the context of exploring the unknown portion of complex mixtures. Speakers from academia, government and industry with diverse expertise will discuss the latest techniques for exploring complex mixtures, including the unidentified fraction. Throughout the discussion, areas that require further development or refinement will be identified. Finally, comparison of the current standard (i.e., targeted approaches) with more global whole mixtures methods will be made in terms of data needs, feasibility, and added value.

Bridging Chemical Exposures Technology with Bioactivity through Combining Passive Wristband Samplers and Bioassays to Better Understand Mixtures. Kim Anderson, Oregon State University, Corvallis, OR.

Predicting Network Activity from High-Throughput Metabolomics. Dean Jones, Emory University, Atlanta, GA.

Combining Toxicological and Chemical Characterization of Complex Mixtures to Understand the Impact of the Unknown Fraction. Jane Ellen Simmons, US EPA, Research Triangle Park, NC.

The Use of Statistical Models to Predict Systemic and Developmental Toxicity of Crude Oil As an Example of Complex Petroleum Substances. Richard H. McKee, American Petroleum Institute, Annandale, NJ.

Whole Mixtures Risk Assessment: Considering Sufficient Similarity. Glenn Rice, US EPA, Cincinnati, OH.

New Mechanistic Insights into How the Immune System Drives Hepatic Adverse Drug Reactions

Tuesday, March 15, 2:00 PM to 4:45 PM

Chairperson(s): Robert Roth, Michigan State University, East Lansing, MI; and Bob van de Water, University of Leiden, Leiden, Netherlands.

Endorser(s):

**Drug Discovery Toxicology Specialty Section
Immunotoxicology Specialty Section
Mechanisms Specialty Section**

Idiosyncratic drug-induced liver injury (IDILI) remains a public health problem and a major reason for curtailing the use of otherwise efficacious drugs. Why some patients are uniquely sensitive to IDILI and the mechanisms by which the death of hepatocytes occurs during these reactions remain incompletely understood. Studies in humans as well as in animal and *in vitro* models have begun to provide answers to these questions. A major working hypothesis for IDILI is the involvement of the immune system in its onset. Over the past years, groundbreaking progress has been made to decipher drug-immune interactions in IDILI. *In vivo* models and immunological approaches have yielded insight into mechanisms by which both the innate and adaptive immune system contribute to IDILI liabilities. In addition, integration of transcriptomics and systematic RNA-interference approaches allowed the deciphering of underlying molecular mechanisms by which liver cells are susceptible to injurious cytokines. For several drugs that cause IDILI in human patients, the reactions appear to involve activation of an adaptive immune response, and specific HLA polymorphisms are risk factors. The first presentation will summarize results of a novel,

murine model in which an HLA polymorphism resulted in sensitivity to flucloxacillin-induced liver injury that was associated with proliferation of CD8⁺ T-cells, hepatic leukocyte infiltration and secretion of interferon-gamma (IFN γ), and other factors. Liabilities for IDILI likely involve specific cellular perturbation due to patient-specific disease states. Given the high incidence of viral hepatitis infection, specific viral infections are likely contributors to IDILI. The second presentation will focus on a murine model of ximelagatran-induced liver injury, in which livers are sensitized to damage by combined viral infection and tumor necrosis factor alpha (TNF). Interestingly, many IDILI-associated drugs can sensitize hepatocytes to cytokine-mediated cell killing. This is exemplified by the synergistic liver cell killing mediated by exposure to nonsteroidal, anti-inflammatory drugs (NSAIDs) and TNF and/or IFN γ . Recent studies have begun to unravel mechanisms by which this synergistic drug-cytokine interaction causes cell death. For example, exposure to diclofenac causes endoplasmic reticular stress that renders hepatocytes susceptible to killing by TNF. Moreover, diclofenac modulates TNF-dependent activation of NF κ B signaling. State-of-the-art RNA-interference approaches in combination with live cell imaging have contributed to the deciphering of molecular determinants that drive the drug-mediated sensitization to TNF. Since liver cell injury also causes the activation of stress kinases, there is a contribution of specific, drug-induced kinase signaling perturbations to the onset of liver cell death caused by TNF coexposure. The role of MAPKs such as JNK and ERK in the cytotoxic, synergistic interaction of drugs with TNF and IFN γ will be discussed. Together, the presentations will convey a spectrum of factors that contribute to the mechanistic understanding of drug-immune interactions that contribute to IDILI. Integration of these novel insights into safety assessment strategies will likely reduce the late-stage attrition of drug candidates and bring safer drugs to the patient population.

Introduction. Robert Roth, Michigan State University, East Lansing, MI.

Immune Mechanisms of Idiosyncratic Liver Injury: Can We Predict the Unpredictable? Lois Lehman-McKeeman, Bristol-Myers Squibb Corp., Princeton, NJ.

Activation of Drug-Specific Cytotoxic T-Cells in Patients with IDILI and Modeling the Reaction in Experimental Animals. Dean Naisbitt, University of Liverpool, Liverpool, United Kingdom.

Viral Preconditioning Sensitizes Livers of Mice to Injury from Exposure to Ximelagatran and TNF. Percy Knolle, Technical University of Munich, Munich, Germany.

Mechanisms of Cytotoxic Interaction of Diclofenac and Tumor Necrosis Factor-Alpha (TNF). Bob van de Water, University of Leiden, Leiden, Netherlands.

Drugs Associated with Idiosyncratic Liver Injury Synergize with TNF and IFN γ to Cause Death of Hepatocytes: Role of MAPK Activation. Robert Roth, Michigan State University, East Lansing, MI.

Reciprocal Synergism: New Insights into Thyroid Hormone Action in Brain Development and Neurodevelopmental Toxicity

Tuesday, March 15, 2:00 PM to 4:45 PM



Advances in Neurotoxicology
Developmental Toxicity: Mechanisms and Evaluation

Chairperson(s): Ellen Fritsche, IUF - Leibniz Research Institute for Environmental Medicine, Duesseldorf, Germany; and Pamela Lein, University of California, Davis, CA.

Endorser(s):
Mechanisms Specialty Section
Neurotoxicology Specialty Section
Risk Assessment Specialty Section

Clinical studies have linked inadequate thyroid hormone (TH) levels during gestation to compromised neurodevelopment that manifests as moderate to severe mental retardation, ataxia, and sensory deficits. Even mild reductions (subclinical) in maternal TH levels during early pregnancy are associated with decreased IQ in offspring. Experimental studies in rodents confirm that TH is essential for normal neurodevelopment and can influence numerous neurodevelopmental processes including neural precursor cell (NPC) and glia proliferation, neural migration, axonal and dendritic morphogenesis, synaptogenesis, and myelination. Based on this background, the concept of “environmental goitrogenesis” postulates that agents in the environment can produce developmental neurotoxicity if they cause a reduction in serum TH. However, recent insight into thyroid hormone action demonstrates that some tissues can autonomously regulate TH action. This recognition means that a chemical may interfere with TH action in the absence of changes in serum TH by interfering with the proper delivery of TH to target cells and/or downstream signaling mechanisms. This session will discuss ongoing research aimed at elucidating the molecular mechanisms by which TH signaling influences specific neurodevelopmental processes, understanding their conservation across *in vitro* and *in vivo* models and different species ranging from *Xenopus* to human and applying this information to identify adverse outcome pathways of developmental neurotoxicity based on thyroid hormone disruption independent of changes in serum TH.

Setting the Stage: Overview of Evidence That TH Regulates Brain Development and Postulated Mechanisms of TH Disruption in DNT. Thomas R. Zoeller, University of Massachusetts, Amherst, MA.

Low-Level Thyroid Hormone Disruption and Neurodevelopmental Outcomes in Rodent Models. Mary Gilbert, US EPA, Research Triangle Park, NC.

Species-Specific Actions of TH on Fetal Neurodevelopmental Processes: An *In Vitro* Approach Using Neurospheres. Ellen Fritsche, IUF – Leibniz Research Institute for Environmental Medicine, Düsseldorf, Germany.

Species-Specific Actions of TH on Neuronal Maturation *In Vitro* and *In Vivo*. Pamela Lein, University of California, Davis, CA.

The Canary in the Coal Mine: *Xenopus* Tadpole Optic Tectum Development as a Biosensor for Disruption of Thyroid Hormone Signaling. Christopher K. Thompson, The Scripps Research Institute, La Jolla, CA.

Symposia

The Role of Gene SLC30A10 on Manganese Homeostasis and Functional Outcomes: Implications for Homeostasis and Neurotoxicity

Tuesday, March 15, 2:00 PM to 4:45 PM

 Advances in Neurotoxicology
 Toxicity of Metals

Chairperson(s): Roberto G. Lucchini, Icahn School of Medicine at Mount Sinai, New York, NY; and Donald R. Smith, University of California Santa Cruz, Santa Cruz, Santa Cruz, CA.

Endorser(s):

Clinical and Translational Toxicology Specialty Section
 Metals Specialty Section
 Neurotoxicology Specialty Section

A primary disorder of manganese homeostasis in humans was suggested by the observation of patients presenting with severe hyper-manganesemia, polycythemia, liver cirrhosis, and neurological disturbances including dystonia in absence of occupational or environmental sources of manganese intoxication. Autosomal-recessive homozygous mutations in the SLC30A10 were identified as the disease cause of this phenotype. The protein encoded by this gene has been shown to be an important manganese efflux transporter, and mutations of SLC30A10 block its intracellular trafficking and efflux activity. Early recognition of this disease is essential given that treatment with manganese chelation or oral iron supplementation, or their combination, might ameliorate symptoms and prevent progression of an otherwise potentially fatal illness. The knowledge of this new clinical disease caused by homozygous mutations of SLC30A10 gene has important implications in understanding mechanism of manganese neurotoxicity. This symposium will highlight the new evidence from human and experimental studies focusing on the influence of non-homozygous mutations in SLC30A10 on functional outcomes, parkinsonism, manganese homeostasis, and biomarkers. The impact of SLC30A10 expression will be presented on neurological performance of adolescents and elderly with environmental exposure to manganese, whereas the role of this Mn transporter will be considered as a potential determinant in a cohort of Parkinsonian cases and controls. Data on the variation of blood manganese in different human populations will be shown in relation to genetic variations of SLC30A10. The importance of new knowledge of possible mechanisms by which this manganese transporter contributes to neurotoxicity is essential to identifying early signs or pre-clinical damage in relation to manganese exposure. Cell and animal models will provide evidence of tissue- and cell-specific expression, and manganese-dependent regulation of SLC30A10. A focus on pregnancy and early-postnatal life will assess the hypothesis that altered SLC30A10 expression in maternal and infant liver function may influence manganese levels in maternal and infant blood—both demonstrated manganese toxicity in children. The *C. elegans* model will be presented, showing how SLC30A10 overexpression protects from manganese-induced toxicity and dopaminergic neurotoxicity. Overall, this symposium will integrate innovative basic science studies with cutting-edge clinical and translational work on SLC30A10, a central player in the regulation of manganese homeostasis and the pathobiology of manganese neurotoxicity.

Influence of SLC30A10 on Neurophenotypes Across the Life Span. Roberto G. Lucchini, Icahn School of Medicine at Mount Sinai, New York, NY.

SLC30A10 Determines the Mn Concentrations in Blood of Healthy Humans. Karin Broberg, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden.

Manganese-Dependent Regulation of the Efflux Transporter SLC30A10. Somshuvra Mukhopadhyay, The University of Texas at Austin, Austin, TX.

The Role of SLC30A10 in Body Mn Homeostasis Over Pregnancy and Early Postnatal Life: Implications for Mn Toxicity.

Donald R. Smith, University of California Santa Cruz, Santa Cruz, CA.

Gene SLC30A10 and Its Role in *C. Elegans*. Michael Aschner, Albert Einstein College of Medicine, New York, NY.

Using Multi- and Transgenerational Effects of Environmental Exposures in Diverse Animal Models for Assessment of Human Health Risks

Tuesday, March 15, 2:00 PM to 4:45 PM

 Developmental Toxicity: Mechanisms and Evaluation

Chairperson(s): Kristine L. Willett, University of Mississippi, University, MS; and Jennifer L. Freeman, Purdue University, Lafayette, IN.

Endorser(s):

Molecular and Systems Biology Specialty Section
 Reproductive and Developmental Toxicology Specialty Section

There is a new appreciation that environmental factors acting during key developmental stages can cause irreversible changes in gene expression, and tissue structure or function, and increase the risk of developing disease. Furthermore, certain epigenetic consequences can be passed between generations, impacting offspring that were never exposed to the stressor. The way in which exposures cause multi- (into a F2 generation) and transgenerational (into a F3 generation) effects is unclear. This symposium will bring together a group of investigators who are actively engaged in determining if and by what mechanisms exposures in one generation are passed onto future subsequent generations. Speakers will highlight their work with different stressors causing multi- and/or transgenerational effects using evidence from human populations and diverse laboratory animal models with considerations for human health risk assessment. The origins of this field, as mediated by an adverse nutritional environment during prenatal and early postnatal life, resulting in transcriptional, epigenetic, and metabolic regulation and manifested in increased diabetes risk to subsequent generations in human and rodent populations, will lead off the session. The second talk will highlight the state of this research area in the field of toxicology, reviewing the various exposures reporting health effects in transgenerational studies. Current studies applying the unique aspect of the zebrafish model for multi- and transgenerational mechanistic studies will be highlighted in the next two talks relating to dioxin and atrazine, with the final talk discussing the considerations of this paradigm in a regulatory perspective for human health risk assessment and product safety. This symposium will be of interest to toxicological

researchers engaged in developmental and reproductive toxicology and neurotoxicology; to those identifying epigenetic, genetic, and molecular mechanisms of adverse health outcomes in multi- and trans-generational exposure paradigms; and to those interested in health effects of exposure to endocrine disruptors, pesticides, and dioxins.

Introduction. Kristine L. Willett, University of Mississippi, University, MS.

Intergenerational Programming of Metabolic Disease: Evidence from Human Populations and Experimental Animal Models.

Mary Elizabeth Patti, Harvard Medical School, Boston, MA.

Transgenerational Effects of Environmental Exposures in Animals: A Literature Review. Vickie Walker, NIEHS, Research Triangle Park, NC.

Zebrafish As a Model for Adult-Onset and Transgenerational Male Infertility Due to TCDD Exposure. Tracie Baker, University of Wisconsin-Madison, Madison, WI.

Multigenerational Effects of the Endocrine-Disrupting Herbicide Atrazine in Zebrafish. Jennifer L. Freeman, Purdue University, Lafayette, IN.

Transgenerational Effects and Implications to Product Safety Assessment. Reza Rasoulpour, Dow AgroSciences, Indianapolis, IN.

WEDNESDAY

Patient-Specific Stem Cells As Models for Gene, Drug, and Environment Interactions in Disease

Wednesday, March 16, 9:30 AM to 12:15 PM

Chairperson(s): Aaron B. Bowman, Vanderbilt University Medical Center, Nashville, TN; and Jason R. Richardson, Northeast Ohio Medical University, Rootstown, OH.

Endorser(s):

**Mechanisms Specialty Section
Neurotoxicology Specialty Section
Stem Cells Specialty Section**

With the advent of adult stem cell technology there is an increasing interest in the potential for using stem cells for screening for drug and chemical toxicity and drug efficacy. More important, researchers are now using this technology in an attempt to understand mechanisms behind individual and population differences in these outcomes based on genetics. Indeed, by using a patient's own stem cells and converting them to disease-specific cells, better understanding of disease pathophysiology and ultimately, a personalized approach for therapeutic intervention may be attainable. Using the powerful tools of genetics and induced pluripotent stem cell (iPSC) technology, the speakers in this symposium will discuss new and cutting-edge research that provides examples of the power of this approach for mechanistic and clinical/translational studies. Speakers representing academia, government, and industry will provide diverse viewpoints on the utilization of iPSC-modeling in both broad and specific contexts. The session will begin with a brief 5-minute overview of iPSC and stem cell technology by one of the co-chairs. The first full speaker of the session will utilize several specific examples of how iPSC based models of genetic disease (diabetes, heart disease, and neurological disorders) have been used to predict drug efficacy and disease-specific vulnerabilities to toxicants.

The second speaker will provide a specific example of how iPSC technology can be used to translate pathophysiological mechanisms described in non-human models to this patient-specific human model system (e.g., gene-environment interactions between Huntington's disease and manganese) and utilization of the iPSC model for preclinical testing of small molecules developed in a non-human model system. The third speaker will present how iPSC technology led to discovery of gene-environment interactions in the context of a single common genetic risk factor for Alzheimer's disease. The fourth speaker will discuss how iPSC technology can be leveraged to screen for disease-modifying agents with neuroprotective and/or neurotoxic effects. The final speaker will detail genetic susceptibility to agents that induce carcinogenicity using this technology. By including examples of disease affecting distinct organ systems, this session provides diverse viewpoints of the utility of iPSC technology across disciplines. The format for the presentation will be 25-minute talks, with 4 minutes for audience questions. Following the programmed talks, a 20-minute panel discussion will address broad applications of the iPSC model system to explore gene x environment x drug interactions in human disease. The panel will address key determinants in successful of iPSC-based model applications, including (a) developmental lineage specificity, (b) cellular/tissue/organ modeling, (c) appropriate controls and sampling size, (d) multigenic versus monogenic effects, (e) statistical concerns, and sample size. Further, the panel will be open to discussions and topics of interest to members of the audience.

Use of Human iPSC-Derived Cells As a Means to Investigate the Relationship Between Genes and Disease. Blake Anson, Cellular Dynamics, Inc., Madison, WI.

Patient-Derived iPSC Models As a Translational Tool Between Human and Nonhuman Model Systems for Environmental Health Research. Aaron B. Bowman, Vanderbilt University Medical Center, Nashville, TN.

Modeling Gene-Environment Interactions in Alzheimer's Disease. Jason R. Richardson, Northeast Ohio Medical University, Rootstown, OH.

Leveraging Novel Technologies for Human iPSC-Based Screening. Xianmin Zeng, XCell Science Inc., Novato, CA.

Differential Susceptibility of Stem Cells in Inorganic Carcinogenesis. Erik Tokar, NIEHS, Research Triangle Park, NC.



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

Regenerating CNS Myelin—From Mechanisms to Medicines

Wednesday, March 16, 8:00 AM to 9:20 AM

Lecturer: Robin J.M. Franklin, Wellcome Trust-MRC Cambridge Stem Cell Institute, University of Cambridge, Cambridge, United Kingdom..

See full descriptions on page 75.

Symposia

Sulfur Mustard Poisoning: Mechanisms of Dermal and Pulmonary Toxicity and New Treatment Approaches

Wednesday, March 16, 9:30 AM to 12:15 PM

♥ Health and Environmental Impacts of Man-Made and Naturally Released Toxicants

Chairperson(s): Allister Vale, University of Birmingham, Birmingham, United Kingdom; and Horst Thiermann, Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany.

Endorser(s):
Clinical and Translational Toxicology Specialty Section

Sulfur mustard (Bis[2-chloroethyl] sulphide, SM), a chemical sometimes referred to as mustard gas, is a liquid that boils at 217°C and freezes at 13°C to 15°C, which explains its persistence in the environment. Droplets of SM released in an explosion can pose a risk to health from inhalation, ingestion of contaminated food and water, as well as contact with the skin and eyes. SM was first used as a chemical warfare agent almost 100 years ago (July 12, 1917) in Belgium in WWI. Since then it has been deployed in Ethiopia, China, Yemen, and Iran with several hundred thousand casualties resulting. The potential further use of SM in military conflicts and by terrorists remains a threat that if realized would result in a large number of casualties with severely incapacitating eye, skin, respiratory tract, and possibly systemic damage. SM produces acute damage to the skin (blisters, skin necrosis), to the eyes (corneal damage with temporary blindness), and to the respiratory tract (nose bleeds, tracheobronchitis and acute respiratory distress syndrome), and it can be lethal at high concentrations. SM depresses bone marrow function which may lead to secondary infection. Long-term disability due to respiratory complications is common. SM is also a recognized human carcinogen. Following SM inhalation, DNA damage, apoptosis, and autophagy are observed in the lung, along with increased expression of activated caspases and DNA repair enzymes, biochemical markers of these activities. This is associated with inflammatory cell accumulation in the respiratory tract and increased expression of tumor necrosis factor- α and other pro-inflammatory cytokines, as well as reactive oxygen and nitrogen species. Matrix metalloproteinases are also upregulated in the lung and skin after SM exposure, which are thought to contribute to the detachment of epithelial cells from basement membranes and disruption of the pulmonary epithelial barrier. Findings that production of inflammatory mediators correlates directly with altered lung function suggests that they play a key role in toxicity. Following skin contact with SM, keratinocytes of the stratum basale in the skin appear to be the most sensitive to its cytotoxic actions, and blistering involves the detachment of these cells from the supporting basal lamina of the basement membrane of the epidermal-derma junction. Studies on SM and its analogs in animals suggest that individual or combination therapies using anti-inflammatory agents (e.g., steroids), antioxidants (e.g., tocopherols, melatonin, acetylcysteine, nitric oxide synthase inhibitors), and protease inhibitors (e.g., doxycycline, aprotinin, ilomastat), may be effective in ameliorating the toxicity of SM-induced lung damage in humans. Experimentally, single and multiple infusions of mesenchymal stem cells have reduced SM-induced edema, necrosis, inflammation, and death at 5 weeks post-exposure. In addition to symptomatic and supportive treatment for SM-induced blisters, mechanical dermabrasion and laser debridement ("lasablation") have both produced an

increased rate of wound healing in animal models and may be of benefit in a clinical context. A rapid test using an antibody for the reliable detection of pure SM on the skin, which gives a result within 10 minutes, has been developed.

Sulfur Mustard: History of Use and Features of Exposure. Allister Vale, School of Biosciences, University of Birmingham, Birmingham, United Kingdom.

Pathophysiology of Sulfur Mustard-Induced Skin Lesions and Current Therapeutic Options. Paul Rice, Dstl Porton Down, Salisbury, United Kingdom.

Sulfur Mustard-Induced Toxic Lung Injury: Mechanisms of Toxicity. Alfred Sciuto, Research Division, US Army Medical Research Institute of Chemical Defense, Aberdeen, MD.

Sulfur Mustard-Induced Pulmonary Injury: Current Therapeutic Approaches to Mitigating Toxicity. Debra Laskin, Rutgers University, Piscataway, NJ.

Novel Developments and Advanced Molecular Targets for Diagnosis and Treatment of Sulfur Mustard-Induced Cell Damage. Horst Thiermann, Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany.

High-Content Imaging for Predictive Toxicology: Discriminating between Adverse and Adaptive Outcomes

Wednesday, March 16, 2:00 PM to 4:45 PM

♦ Molecular Toxicology: Mechanistic Insights and Hazard Assessment

Chairperson(s): Imran Shah, US EPA, Research Triangle Park, NC; and Bob van de Water, Leiden University, Leiden, Netherlands.

Endorser(s):
In Vitro and Alternative Methods Specialty Section
Risk Assessment Specialty Section
Toxicologic and Exploratory Pathology Specialty Section

High-content imaging (HCI) is a cellular systems approach to cataloging the biological effects of chemicals. Using multi-parametric analysis, HCI can measure integrated cellular responses following the activation or deactivation of multiple molecular functions at the single cell level. Because HCI measures multiple cytological features of fluorescently labeled cells, it provides unique quantitative insight into their phenotypic state in terms of stress, injury, recovery, and death. With technological advancements in creating fluorescently labeled markers, multiresolution imaging, and intelligent image analysis tools, it is feasible to generate HCI data for thousands of chemical perturbations. These complex and large-scale HCI data streams can be interpreted using new informatics and systems biology-based mathematical modeling tools. This makes HCI a powerful *in vitro* tool for predicting the adverse effects of chemicals, a key need in realizing the vision of toxicity testing in the 21st century. This symposium will bring together cutting-edge concepts on HCI as an alternative testing paradigm for predictive toxicology and will focus on 1) innovative tools for interrogating the molecular and cellular state of cells; 2) evaluating sentinel stress response pathways that can profile the chemical-induced perturbations in cells; 3) using

Symposia

HCI responses to analyze the balance between cellular injury and recovery through homeostatic mechanisms; 4) applying HCI data to predict drug-induced liver injury (DILI); and 5) computational systems-level analysis of HCI data to identify toxicological “tipping points.” This symposium will address these issues in a series of highly focused presentations on 21st century toxicology using HCI as an innovative tool for risk assessment, and for estimating points of departure for risk assessment. This symposium will be of wide interest to SOT members, including scientists working in the regulatory arena as well as those interested in the application of molecular and systems biology to risk assessment. A key challenge to using *in vitro* data in risk assessment is differentiating between adaptive and adverse cellular responses. To further investigate the balance between adaptation and adversity, we studied the effects of hundreds of chemicals in HepG2 cells using HCI. HCI assays were used to measure dose and time-dependent perturbations in p53, JNK, oxidative stress, cytoskeleton, mitochondria, and cell cycle progression. We analyzed this multidimensional HCI datastream using a novel computational model, which interpreted the dynamic response of the HepG2 system to chemicals as cell-state trajectories. The cell-state trajectories produced by different concentrations chemicals describe a range of rich responses of the HepG2 system in many cases. Further analysis of trajectories identified dose-dependent transitions in system recovery, which we call “tipping points.” The critical concentration of chemicals that produce tipping points was generally much lower than the concentration that produced cell loss. We believe that HCI can be used to reconstruct cell state trajectories, and provide insight into adaptation and resilience for *in vitro* systems.

A HCI Cellular Stress Response GFP-Reporter Platform for Chemical Safety Assessment. Bob van de Water, Leiden University, Leiden, Netherlands.

Imaging 3D Human Microtissues to Modernize Toxicity Testing. Kim Boekelheide, Brown University, Providence, RI.

Integration of High-Content Imaging for Predicting Drug-Induced Liver Injury. Weida Tong, US FDA/NCTR, Jefferson, AR.

Using High-Content Imaging to Analyze Cellular Tipping Points. Imran Shah, US EPA, Research Triangle Park, NC.

Utilizing High-Content Imaging Tools Toward Pathways-Based Safety Assessments: A Consumer Product Industry Perspective. Paul Carmichael, Unilever, Bedfordshire, United Kingdom.

Novel Roles of Reactive Oxygen Species (ROS) in Human Diseases: Why ROS Never Gets Stale

Wednesday, March 16, 2:00 PM to 4:45 PM

Chairperson(s): Bhagavatula Moorthy, Baylor College of Medicine, Houston, TX; and Donna Zhang, University of Arizona, Tucson, AZ.

Endorser(s):
Clinical and Translational Toxicology Specialty Section
Mechanisms Specialty Section
Molecular and Systems Biology Specialty Section

Oxidative stress mediated by reactive oxygen species (ROS) can have a profound effect on many cellular functions. The major goal of this symposium is to discuss the molecular and cellular mechanisms by which ROS, including free radicals, contribute to oxidative stress and alter various signaling pathways, which could in turn lead to inflammation and cell death in target organs, and ultimately lead to human diseases including chemically induced acute hepatitis, neurodegenerative diseases, and pulmonary diseases such as bronchopulmonary dysplasia (BPD), acute respiratory distress syndrome (ARDS), and cancer. The innovative aspect of the proposed symposium is to discuss the molecular mechanisms of oxidative stress and signaling that leads to inflammation and cell death in a cell- and organ-specific manner, and the mechanisms by which they contribute to target organ toxicities. The recent findings of the novel roles of oxidative stress in multiple human diseases warrant the need for a symposium to discuss the latest mechanistic research in this area and its impact on human health. Specifically, the symposium will discuss (i) molecular signaling pathways that selectively affect SNpc neurons, and how these studies could help unravel the mechanisms underlying selective vulnerability of these neurons in neurodegenerative diseases like Parkinson's disease (PD); (ii) the role of nuclear receptors, ER stress, and oxidative stress in fatty liver disease, and how modulation of FXR activity and the related bile acid metabolism in hepatocytes might be a promising strategy to treat chemically induced acute hepatitis; (iii) the mechanistic role of omega-3 epoxides, which are anti-inflammatory; inhibit angiogenesis, tumor growth, and tumor metastasis induced by TCDD; and recent studies have suggested, that omega-3 epoxides may act as antioxidants; (iv) the molecular role of Nrf2 as master regulator against oxidative stress, its implications for multiple human diseases including cancer, and the discovery of novel small molecule nrf2 modulators to improve human health; and (v) the novel roles of cytochrome P450 (CYP)1A and 1B1 enzymes in hyperoxic lung injury, in relation to BPD and ARDS. In conclusion, this symposium will discuss the latest developments in oxidative stress, molecular signaling, inflammation, and cell death, and offer new opportunities for clinical and translational research.

Introduction. Bhagavatula Moorthy, Baylor College of Medicine, Houston, TX.

Cell-Specific Activation of Redox-Driven Death Signaling Pathways in Neurodegeneration. Vijayalakshmi Ravindranath, Indian Institute of Science, Bangalore, India.

Role of Nuclear Receptors, ER Stress, and Oxidative Stress in Fatty Liver Disease. Frank Gonzalez, National Cancer Institute, Bethesda, MD.

Symposia

2,3,7,8-Tetrachlorodibenzo-p-dioxin Markedly Increases the Levels of Highly Bioactive Epoxide Metabolites of Omega-6 and Omega-3 Polyunsaturated Fatty Acids in Many Organs of Mice.

Oliver Hankinson, University of California Los Angeles, Los Angeles, CA.

Nrf2: Tumor Suppressor or Oncogene? Donna Zhang, University of Arizona, Tucson, AZ.

Mechanistic Roles of Cytochrome P4501A and 1B Enzymes in Oxidative Stress-Mediated Mechanisms Leading to Hyperoxic Lung Injury: Implications for BPD in Infants and ARDS in Adults. Bhagavatula Moorthy, Baylor College of Medicine, Houston, TX.

Use of the Adverse Outcome Pathway (AOP) Concept to Link Epidemiological to Mechanistic Data on the Correlation of Pesticide Exposures and Parkinson's Disease

Wednesday, March 16, 2:00 PM to 4:45 PM

-  Advances in Neurotoxicology
-  Molecular Toxicology: Mechanistic Insights and Hazard Assessment

Chairperson(s): Marcel Leist, University of Konstanz, Konstanz, Germany; and Susanne Hougaard Bennekou, Danish EPA, Copenhagen, Denmark.

Endorser(s):

Mechanisms Specialty Section
Neurotoxicology Specialty Section
Risk Assessment Specialty Section

A recent systematic review of epidemiological studies (EFSA External Scientific report, 2013) concluded that the weight of evidence supports an association between exposure to pesticides and increased risk of Parkinson's disease (PD). Analyses of epidemiological and experimental studies by ANSES (the French Agency for Food, Environmental and Occupational Health and Safety) reached a similar conclusion. Such data have attracted significant public attention, but it is unclear whether and how they can be used for risk assessment. It is possible that mixture effects, long-term low-dose exposure, and species differences contribute to effects observed in the human population that have not been predicted from animal experiments. This also has to be balanced against underlying understanding of this type of disease, which has a multifactorial etiology. Therefore, new approaches of data integration from heterogeneous sources (ranging from epidemiology to molecular and animal studies) are required. The goal of the proposed symposium is to use the Adverse Outcome Pathway (AOP) concept as a novel, mechanistically driven approach to assess the biological plausibility of the epidemiological data. This concept represents a shift toward a knowledge-driven approach to toxicological hazard and risk assessment. It relies on a mechanistic understanding of toxicity pathway, and attempts to align different types of information to these pathways. An AOP links information on molecular initiating events (MIE) to a final adverse outcome (AO). It provides a basis for multi-level data integration by defining the intermediate key events (KEs) that link the MIE to the AOP, and providing a scientifically firm rationale for the KE relationships, i.e., processes and their thresholds that lead to the activa-

tion of the next KE (considering relevant exposure and internal doses). Thus, AOP provides an ideal basis for a strategy that aims to evaluate the evidence of cause-effect relationships. The potential to combine various AOPs to larger networks allows judgments on mixture effects and complex scenarios, such as the one of pesticide exposure possibly leading to Parkinsonism. During this session, speakers with expertise in epidemiology, regulatory toxicology, and basic science will contribute different perspectives to a large and representative case study in which the AOP format is applied to integrate the epidemiological data with mechanistic research. The ultimate goal is to explore the link between exposure to specific pesticides and the risk of developing PD. Individual pesticides, such as rotenone, paraquat, and organochlorine compounds will be used to demonstrate the basic outline of the strategy. The defined examples will be used to highlight its strengths and challenges. The latter include exposure and toxicokinetics considerations, and, e.g., nonlinear network dynamics resulting from feedback and feedforward loops and pathway intersections. Eventually, the integration of individual AOPs to an AOP network underlying a complex human disease will be illustrated. The session will also include recommendations on how to improve the quality of this information and how to integrate these data into regulatory decision-making.

The Risk Assessment of Pesticide-Induced Neurotoxicity (Including Parkinson's Disease) in the Standard Regulatory Framework. Susanne Hougaard Bennekou, Danish EPA, Copenhagen, Denmark.

An Overall Mechanistic Map of Parkinson's Disease and Interaction Points for Various Pesticides. Marcel Leist, University of Konstanz, Konstanz, Germany.

AOP Construction Rules and Key Event Relationships: The Cascade of Key Events Initiated by Inhibition of Complex I and Leading to Parkinson's. Anna Price, European Commission Joint Research Center, Ispra, Italy.

Experimental Validation of an AOP: Probing Inhibition of Aldehyde Dehydrogenase (ALDH) as the Molecular Initiating Event Linking Exposure to Organochlorine Pesticides and Dithiocarbamate Fungicides to Parkinson's Disease. Pamela Lein, University of California, Davis, Davis, CA.

Multiple AOP Alignment Case Study: Pathways of Toxicity Induced by Exposure to Paraquat That Cause Symptoms of Parkinson Disease. Ellen Fritsche, Leibniz Research Institute for Environmental Medicine, Duesseldorf, Germany.

Mitochondrial Dysfunction As a Pathogenic Mechanism and Therapeutic Target for Neurodegenerative Diseases

Thursday, March 17, 9:30 AM to 12:15 PM

 Advances in Neurotoxicology

 Toxicity of Metals

Chairperson(s): Kim Tieu, Plymouth University, Plymouth, United Kingdom; and Aaron Bowman, Vanderbilt University, Nashville, TN, United Kingdom.

Endorser(s):

Clinical and Translational Toxicology Specialty Section

Metals Specialty Section

Neurotoxicology Specialty Section

Neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, Huntington's disease, and amyotrophic lateral sclerosis are characterized by a relatively selective loss of one or a few populations of neurons in specific brain regions. Major advances have been made over the past decades toward understanding mechanisms of neurodegeneration. These insights into how neurons die in disease can now be leveraged to develop effective therapeutic strategies. Mitochondrial dysfunction has emerged as a common feature in neurodegenerative disorders. This observation is consistent with the high vulnerability of mitochondria to environmental toxicants (such as herbicides, pesticides, and heavy metals) as well as disease-linked mutation in genes that are functionally associated to mitochondrial biology. This symposium has brought together six leading scientists from industry and academia to discuss the latest information about how various toxicants impair mitochondrial function contributing to neurodegenerative processes and how these experimental models are used for development of novel therapeutic strategies. Although the focus will be on toxicology, latest information about genetic mutations and gene-environment interactions that impact mitochondrial function will also be incorporated in this session. To emphasize how the diverse biology of mitochondria can contribute to disease, several of the talks are focused on a specific disease, Parkinson's disease (PD), to highlight the emerging understanding that mitochondria dysfunction is multifaceted. However, the mechanisms and therapeutic strategies highlighted in this symposium are relevant to other diseases with mitochondrial etiology. Further, speakers will present on the utility of diverse but complementary experimental models. To kick off the session, Ian Reynolds from Teva Pharmaceuticals will provide an overview of mitochondrial biology in neurological diseases, with focus on mitochondria as a therapeutic

target. This high-content introduction will establish a common frame of reference for the remaining five talks. Julie Andersen will discuss a novel mechanism by which a strong genetic risk factor for PD, PARK2 (parkin), influences mitochondrial quality control. To highlight potential links of this genetic risk factor with environmental risk, Aaron Bowman will discuss new data suggesting PARK2 mutations increase sensitivity of human neurons to Cu-induced mitochondrial dysfunction and mitochondrial fragmentation. These data support an involvement of mitochondrial fission and fusion imbalances in disease. The therapeutic potential of targeting mitochondrial fission/fusion machinery in PD will be detailed by Kim Tieu in primarily toxicant-induced mammalian cell culture and mouse models. Manganese (Mn) is an established environmental risk factor for PD. Michael Aschner will report on the protective effects of a novel protein, TMEM-135, against Mn-induced oxidative stress and toxicity in the genetic model organism, *C. elegans*. The final speaker, Dean Jones, will conclude the session with a cutting-edge omics approach to gain a broad and comprehensive picture of mitochondrial regulation and signaling in response to toxic insults. In summary, this session is designed to comprehensively cover the complex nature of mitochondria as a pathogenic pathway and therapeutic target for neurodegenerative disease(s) with environmental etiologies.

Mitochondrial Neurotherapeutics: Past, Present, and Future.

Ian Reynolds, Teva Pharmaceuticals, West Chester, PA.

Parkin-Mediated Mitochondrial Quality Control via the Master Lysosomal Regulatory Factor TFEB Is Disrupted in a Mutant Mouse Model of Parkinson's Disease.

Julie K. Andersen, Buck Institute for Research in Aging, Novato, CA.

PARK2 Mutations Alter Vulnerability of Human Neurons to Copper Neurotoxicity.

Aaron Bowman, Vanderbilt University, Nashville, TN.

Targeting Mitochondrial Dynamics As a Potential Therapeutic Strategy for Parkinson's Disease?

Kim Tieu, Plymouth University, Plymouth, United Kingdom.

Mitochondrial TMEM-135 Decreases Manganese-Induced Dopaminergic Neurodegeneration.

Michael Aschner, Albert Einstein College of Medicine, Bronx, NY.

Integrated Redox Proteomics, Metabolomics and Transcriptomics: A Holistic View of Mitochondrial Function.

Dean Jones, Emory University, Atlanta, GA.



Workshops

MONDAY

Dietary Exposures to Heterocyclic Amines As a Potential Risk Factor for Neurological Disease

Monday, March 14, 9:30 AM to 12:15 PM

 Advances in Neurotoxicology

Chairperson(s): Jason Cannon, Purdue University, West Lafayette, IN; and Kenneth Turteltaub, Lawrence Livermore National Laboratory, Livermore, CA.

Endorser(s):

Clinical and Translational Toxicology Specialty Section
Neurotoxicology Specialty Section

Neurodegenerative diseases, such as Parkinson's disease (PD), have been repeatedly linked to diverse risk factors, including genetics and environmental exposures such as pesticides, solvents and a variety of heavy metals. Further, epidemiological and genetic data suggest that no single toxicant class or genetic mutation is a major cause of the idiopathic forms of this disease. Aside from coffee (caffeine), dietary factors have not been examined to the same extent as environmental toxicants as potential etiological factors in PD. Heterocyclic aromatic amines (HAAs) may be encountered in a variety of foods, notably cooked meats and drinks. High-temperature cooking and resultant charring can produce several toxic compounds including, HAAs. There is limited knowledge on the neurological effects of HAAs. However, multiple HAAs affect dopamine metabolism, and specific HAAs have been linked to essential tremor and, more recently, PD. This workshop will focus on newly emerging data suggesting a potential role of HAAs in neurological diseases, including PD. A diverse group of experts have been assembled to address this especially timely topic. In fact, recent publications from the speakers' laboratories have shown that HAA blood levels are associated with essential tremor and PD and that *in vitro* and *in vivo* treatments are selectively toxic to dopaminergic neurons. Speaker expertise includes clinical studies (neurology, Elan Louis), *in vitro* and *in vivo* modeling (neurotoxicology, Jason Cannon), analytical/transport (PhIP quantification/pharmacokinetic analysis in biological fluids and tissue, Kenneth Turteltaub), and biomarkers (exposure and adduct formation, Robert Turesky). The session will begin with a brief introduction of the key findings to date and gaps in the literature. In each of the talks, the speaker will relate how doses in their cellular and animal studies relate to typical human exposures. The first speaker will discuss the association of HAA blood levels in humans with the essential tremor and PD. The second speaker will discuss the utilization of novel blood-brain-barrier models to predict HAA entry into the brain. This speaker will also discuss how this model system, in conjunction with significant pharmacokinetic data collected in both human studies and animal models, might be used in translational studies. The third speaker will discuss data on selective dopaminergic toxicity of specific HAAs. While the relationship between HAAs and essential tremor is much more established, published and preliminary data now suggests that more detailed studies in PD and PD models are needed. Multiple brain systems are affected in PD; however, loss of dopaminergic neurons in the substantia nigra or changes in their function are a major contributor to the characteristic motor phenotypes. Thus, initial studies in primary culture focus on determining if dopamine neurons exhibit heightened sensitivity to specific HAAs, compared to gamma-aminobutyric acid (GABA)-ergic neurons (spared

in PD). Emerging data on ET pathophysiology suggests that cerebellar abnormalities may be important. Thus, ET-relevant pathologies that should also be investigated will be discussed. The fourth speaker will broadly discuss mechanisms of toxicity and innovative biomarker studies being conducted in humans and animal models. Here, how actual human exposures and systemic biomarkers relate to laboratory animal studies will be discussed. Significant time will be allotted for a critical evaluation of the presentations to identify key gaps in the literature. Given that the literature on HAAs is focused on genotoxicity, the discussion will emphasize the following key gaps: 1) What is the potential overlap with key neurotoxic mechanisms of action? and 2) How should such mechanisms be explored? The limited identification of causative factors of neurological diseases provides an impetus for this timely workshop.

Introduction. Jason Cannon, Purdue University, West Lafayette, IN.

Relationship between Blood Harmane Levels and

Neurodegenerative Disease. Elan Louis, Yale School of Medicine, New Haven, CT.

Novel Blood-Brain Barrier Models to Assess PhIP Transport into

Brain. Kenneth Turteltaub, Lawrence Livermore National Laboratory, Livermore, CA.

PhIP Exposure and Dopaminergic Neuron Toxicity. Jason Cannon, Purdue University, West Lafayette, IN.

Heterocyclic Aromatic Amine Exposure: Biomarker Studies

from Rodents to Humans. Robert Turesky, University of Minnesota, Minneapolis, MN.

Panel Discussion/Q&A. Kenneth Turteltaub, Lawrence Livermore National Laboratory, Livermore, CA.

Mitochondria As the Central Target of Environmental Contaminants, Pharmaceutical Agents, and Toxicants: Mechanisms of Toxicity and Disease

Monday, March 14, 9:30 AM to 12:15 PM

Chairperson(s): Rodrigo Franco, University of Nebraska-Lincoln, Lincoln, NE; and Joel N. Meyer, Duke University, Durham, NC.

Endorser(s):

Drug Discovery Toxicology Specialty Section
Molecular and Systems Biology Specialty Section
Neurotoxicology Specialty Section

Mitochondrial dysfunction is widely recognized as a central component in the etiology of human diseases such as cancer and neurodegeneration, as well as in numerous other rare disorders. Furthermore, many pharmaceuticals, drugs, and contaminants have been identified as previously unrecognized mitochondrial toxicants. However, the exact molecular mechanisms by which mitochondrial dysfunction regulates disease progression are poorly understood. In this workshop we will review novel research findings regarding the causative role of mitochondria dysfunction and the resultant alterations in cellular bioenergetics, redox signaling, and DNA-damage response to disease progression induced by environmental contaminants, pharmaceutical agents, and toxicants (substance abuse). We will also discuss advances made by the pharmaceutical industry in investigating mitochondrial toxicities of

Workshops

drugs, and present novel toxicological approaches for metabolomics, high-throughput analysis of bioenergetics, and mitochondrial toxicity, as well as the importance of these approaches for the identification of novel mechanisms of disease progression and environmental and pharmacological/drug abuse risk factors. This topic will be of great importance to basic researchers, graduate students, postdoctoral trainees, and academics across disciplines as well as risk assessors, regulators, and individuals within distinct Specialty Sections.

Introduction. Rodrigo Franco, University of Nebraska-Lincoln, Lincoln, NE.

Mitochondrial Redox Signaling Regulates Cellular Metabolism and Drives Cancer Progression. Marcelo Bonini, University of Illinois at Chicago, Chicago, IL.

Energy Metabolism, Redox Homeostasis, and Dopaminergic Cell Death Induced by Gene-Environment Interactions. Rodrigo Franco, University of Nebraska-Lincoln, Lincoln, NE.

Gene-Environment Interactions in Mitochondrial Diseases. Sherine Chan, Medical University of South Carolina, Charleston, SC.

Genetic and Developmental Stage Sensitivity to Mitochondrial Toxicity. Joel N. Meyer, Duke University, Durham, NC.

Drug-Induced Mitochondrial Toxicity—A Decade of Assay Development, a Decade of Learning. Yvonne Will, Pfizer Inc., Groton, CT.

Nanotoxicology and Ocular Drug Delivery: One Size Does Not Fit All

Monday, March 14, 9:30 AM to 12:15 PM

Chairperson(s): Chris J. Somps, Pfizer, Inc., Groton, CT; and Donald A. Fox, University of Houston, Houston, TX.

Endorser(s):

**Nanotoxicology Specialty Section
Neurotoxicology Specialty Section
Ocular Toxicology Specialty Section**

Ocular drug delivery is impeded by numerous barriers the eye evolved to isolate and protect ocular tissues and preserve optimal visual function. For example, the blood-ocular barriers make delivery of therapeutic concentrations of systemically administered drugs more difficult. Local drug delivery (topical or peri-ocular) to ocular structures, at the front and back of the eye, are challenged by the various clearance and diffusional barriers such as lacrimation, mucosal barriers, cornea/sclera, choroidal, vitreous body, etc. Bypassing some of these barriers using direct injection or implants into the vitreous body carries safety, cost, and patient compliance concerns. Nanomaterials, because of their small size and potential to control surface properties and targeting, hold significant promise for improving transport of therapeutic agents across many of these ocular barriers. Hydrogels, polymeric micelles, liposomes, dendrimers, and cyclodextrins are just a few of the nanomaterials currently being developed for improved ocular drug and gene delivery. However, the potential ocular toxicity of these nanomaterials remains to be determined. Moreover, the efficacy and safety associated with their long term use is unknown. The goal of the proposed session is to bring together academic and industry researchers, as well as government

regulators, to further define and understand the unique safety issues confronting those that are developing and/or using nanoparticles for improved ocular drug delivery. The session will start with a broad overview of nanotoxicology and strategies for assessing the safety of nanoscale materials. The second speaker will focus on the current use of nanomaterials for enhanced delivery of ocular therapeutics to the eye. The third speaker will describe nanoparticles for the treatment of different diseases, particularly those associated with the retina and retinal pigment epithelium. The fourth speaker will discuss the retinotoxicity of current and proposed nanomaterials. The final speaker will address the current US FDA framework and strategies for regulating drug products using nanomaterials for ocular drug delivery. Special emphasis will be placed on the following emerging and evolving concepts as they relate to nano-sized drug delivery platforms for the eye: 1) current and future use of therapeutic nanomaterials for drug and gene therapies, 2) examples of nanomaterial-enabled ocular drug delivery platforms and associated toxicity evaluations, 3) mechanisms of retinotoxicity of nanomaterials, and 4) current US FDA thinking on efficacy and safety of nano-sized ocular drug delivery platforms.

Overview of Nanomaterial Toxicology and Strategies for Assessing the Safety of Nanoscale Materials. Nigel J. Walker, NIEHS, Durham, NC.

Nanomaterials and Drug Delivery to the Eye. Gerard A. Lutty, Johns Hopkins University, Baltimore, MD.

Lack of Toxicity Associated with Nanoparticle-Mediated Gene Therapy for Ocular Diseases. Muna I. Naash, University of Houston, Houston, TX.

Nanomaterials and Retinal Toxicity. William K. Boyes, US EPA, Research Triangle Park, NC.

FDA Perspective on Safety Assessment Needs for Nanoparticles Used for Drug Delivery to the Eye. Wiley A. Chambers, US FDA, Silver Spring, MD.

Scientific Reproducibility: Does This Pose a Problem for 21st Century Toxicology?

Monday, March 14, 9:30 AM to 12:15 PM

- ◆ **Molecular Toxicology: Mechanistic Insights and Hazard Assessment**
- ♠ **Recent Advances in Safety Assessment**

Chairperson(s): J. Craig Rowlands, The Dow Chemical Company, Midland, MI; and Alan Boobis, Imperial College, London, United Kingdom.

Endorser(s):

**Occupational and Public Health Specialty Section
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section**

The safe use of chemicals relies upon the identification of exposure levels below which there is reasonable certainty of no harm. Traditionally, this has been achieved using studies in experimental animals prospectively and/or epidemiological surveillance prospectively or retrospectively. However, rapid advances in the development of mechanism-based biomarkers of disease, predictive *in vitro* assays

Workshops

and *in silico*-based computational modeling offer the prospect of more efficient, accurate, and relevant assessments. The application of these advances to human clinical and observational studies has the potential to provide investigators with a fuller understanding of human effects from exposure to environmental chemicals and responses to therapeutic agents. However, an increasing number of biomedical journals and funding agencies are raising significant concerns that much of what is published in the biomedical literature cannot be reproduced. Given that the published literature provides much of the basis for the fundamental understanding of a toxicant's mechanism(s) of action, this lack of reproducibility raises important challenges for moving toxicology from an animal-based system to a system of mechanism of action-based toxicity predictions. Further, the impact on outcomes and confidence can be significant for human clinical and observational studies that rely upon biomarkers of human diseases. The workshop will comprise a series of highly focused presentations representing differing points of views of the extent, potential impacts, and solutions for the lack of reproducibility of published biomedical, epidemiological, and toxicological research. Each speaker will provide their views regarding the extent of the problem and, more importantly, approaches that are available to mitigate the problems.

Reproducibility and Reliability of Biomedical Research:

The Extent of the Problem. C. Glenn Begley, TetraLogic Pharmaceuticals, Malvern, PA.

Providing Advice to Risk Managers Based on Imperfect and

Potentially Incorrect Information. Alan Boobis, Imperial College, London, United Kingdom.

Evidence-Based Approaches for Enhancing the Reproducibility of Toxicological Studies.

Martin Stephens, CAAT, John Hopkins University, Baltimore, MD.

Interpreting Epidemiologic Studies: Quality Matters.

Judy LaKind, LaKind Associates, Catonsville, MD.

Addressing Data Reproducibility at the US Environmental Protection Agency Office of Research and Development.

Ronald N. Hines, US EPA, Research Triangle Park, NC.

The Cancer Risk Assessment for Ingested Hexavalent Chromium: Challenges and Controversies

Monday, March 14, 9:30 AM to 12:15 PM

Toxicity of Metals

Chairperson(s): Deborah Proctor, *ToxStrategies, Inc., Mission Viejo, CA*; and Annie Jarabek, *US EPA, Research Triangle Park, NC*.

Endorser(s):

Metals Specialty Section

Risk Assessment Specialty Section

In 2008, the National Toxicology Program (NTP) released the findings of its two-year drinking water bioassay of hexavalent chromium (Cr(VI)). NTP concluded that there was clear evidence of carcinogenicity based on increased incidence of small intestinal tumors in mice (at 20–180 mg/L), and oral cavity tumors in rats (at 60–180 mg/L). The tumor data

for the mouse small intestine have been used in several regulatory risk assessments from 2008 to 2011, and a linear low-dose extrapolation has been consistently applied based on the conclusion that Cr(VI) acts by an unknown or mutagenic mode of action (MOA). However, recent research challenges that characterization, supporting the hypotheses that intestinal tumors in mice arose by a non-mutagenic MOA involving cytotoxicity with regenerative hyperplasia and genomic instability associated with epigenetic mechanisms. Such data may have implications for low-dose extrapolation approaches for cancer risk assessment, and inform whether linear or nonlinear assumptions are appropriate. Furthermore, Cr(VI) is reduced to Cr(III) (and thus detoxified) in gastric fluid, a kinetic process which may greatly impact Cr(VI) absorption in the small intestine. The relevance of the dose levels administered to rodents by NTP to human exposure levels has also been debated. The lowest administered drinking water concentration was 5,000 ppb Cr(VI). Nationwide data collected by US EPA under the third Unregulated Contaminant Monitoring Rule (UCMR 3) shows that while approximately 80% of samples are below 0.5 ppb (10,000 fold lower than the lowest NTP concentration), 3% of samples were =5 ppb and <0.1% were between 50–100 ppb. Recognizing the importance of both low-dose extrapolation and inter-species differences in gastrointestinal toxicokinetics, physiologically based pharmacokinetic (PBPK) models have been developed to estimate target tissue dose and inform these issues. This symposium will present diverse perspectives, with supporting data, regarding approaches for PBPK modeling and analyses of mechanistic data supporting hypothesized MOAs for Cr(VI)-induced gastrointestinal tract tumors. Resulting implications for dose-response extrapolation will be presented for discussion. (Views expressed in this abstract are those of the authors and do not necessarily represent the views or policies of the US EPA).

Introduction to Cr(VI) Oral Cancer Risk Assessment. Deborah Proctor, *ToxStrategies, Inc., Mission Viejo, CA*.

Toxicokinetic Modeling of Cr(VI) in the Gastrointestinal Tract for Rodent-to-Human Extrapolation. Alan Sasso, *US EPA, Washington, DC*.

Mechanisms for Cr(VI)-Induced Carcinogenicity: Perspectives from Past and Current Research. John P. Wise, *University of Louisville, Louisville, KY*.

Non-Mutagenic MOA for Cr(VI) Involving Intestinal Cytotoxicity and Regenerative Hyperplasia. Chadwick Thompson, *ToxStrategies, Inc., Katy, TX*.

Systematic Analysis of Mechanistic Information for Cr(VI). Catherine Gibbons, *US EPA, Washington, DC*.

Dose-Response Analysis Options for Hexavalent Chromium-Induced Cancers. Michelle Deveau, *University of Ottawa, Ottawa, ON, Canada*.

Workshops

Transient Receptor Potential A1 (TRPA1) Cation Channels: Fluttering Hearts, Headaches, and Hot Flashes—Can One “Environmental Sensor” Be the Cause of All the Pain?

Monday, March 14, 9:30 AM to 12:15 PM

 Advances in Neurotoxicology

Chairperson(s): Mehdi Saeed Hazari, US EPA, Research Triangle Park, NC; and Daniel J. Conklin, University of Louisville, Louisville, KY.

Endorser(s):

Cardiovascular Toxicology Specialty Section
Inhalation and Respiratory Specialty Section
Neurotoxicology Specialty Section

The role of transient receptor potential (TRP) cation channels, particularly TRPA1, in numerous toxicological pathways has garnered great interest over the last decade. These investigations have focused on the ability of TRPA1 to act as an “environmental sensor” for chemical irritants such as acrolein, formaldehyde, and chloramines, which are found in disinfectants, but also as a mediator of pain, inflammation, and acute physiological changes given it is a target of reactive oxygen species such as hydrogen peroxide and even endogenous agonists such as 4-hydroxy-nonenol. These features, as well as its presence on sensory neurons throughout the body, make TRPA1 an important component in the mode of toxicity of not only gaseous irritants, but also chemicals transmitted in water or by direct contact with the skin. Although it has become clear that TRPA1 contributes to the acute adverse health effects of exposure, new studies have now revealed that it is also involved in the development and progression of chronic diseases. This latter phenomenon is likely related to variations in the TRPA1 gene, which manifest at a young age, but also due to a lifetime of accrued epigenetic changes that essentially alter the responsiveness of an individual to a given exposure. Therefore, this session will highlight the newly understood multifaceted roles of TRPA1 in environmental sensing. The presentations will focus on a broad array of topics including how TRPA1 mediates acute cardiovascular effects after inhalation of air pollutants. Findings will show that inhalation of not only typical TRPA1-activating gaseous irritants, but also particulate matter, causes cardiac arrhythmogenesis as well as vascular responses through TRPA1-mediated mechanisms. Attendees will also hear about the role of TRPA1 in the “masking” effects of flavorants such as menthol and cinnamon in e-cigarettes, which has important implications in both studying the health effects of these alternative tobacco products and their potential regulation. In addition, chemical sensitivity to environmental irritants will be explored in relation to TRPA1 and trigeminal-vascular mechanisms, which are nasal sensory pathways that alter blood flow to the brain and are linked to episodic headaches. Finally, the broader implications of TRPA1 variability, lifestyle, and environment will be addressed from an epigenetic perspective in a study of identical twins to demonstrate links to susceptibility and chronic pain.

TRP Ion Channels as Key Targets of Tobacco and Electronic Cigarette Irritants and Flavor Additives. Sven E. Jordt, Duke University, Durham, NC.

Examining the Role of TRPA1 in Air Pollution-Induced Cardiac Arrhythmias and Autonomic Imbalance. Mehdi Saeed Hazari, US EPA, Research Triangle Park, NC.

From Tobacco Smoke to Gas Attacks—How TRPA1 Modulates Cardiopulmonary Toxicity of Acrolein. Daniel J. Conklin, University of Louisville, Louisville, KY.

TRPA1 and Meningeal Vasodilation Due to Environmental Irritants—Mechanisms of Migraine. Joyce Hurley, Indiana University, Indianapolis, IN.

Epigenetic Changes in the TRPA1 Promoter Show Pain Sensitivity Is Affected by Lifestyle and Environment. Stephen B. McMahon, King's College, London, London, United Kingdom.

Moving Beyond Prioritization towards True In Vitro-Based Safety Assessment

Monday, March 14, 2:00 PM to 4:45 PM

 Recent Advances in Safety Assessment

Chairperson(s): Miyoung Yoon, The Hamner Institutes for Health Sciences, Research Triangle Park, NC; and Rebecca Clewell, The Hamner Institutes for Health Sciences, Research Triangle Park, NC.

Endorser(s):

Biological Modeling Specialty Section
In Vitro and Alternative Methods Specialty Section
Risk Assessment Specialty Section

The field of toxicity testing is undergoing a global paradigm shift toward the use of *in vitro* approaches for assessing chemical risk. There are already several global initiatives demonstrating the utility of high-throughput screening to prioritize compounds for further testing. The next step for *in vitro*-based toxicity testing is to move from prioritization to prediction—i.e., replacing animal-based risk assessment strategies with safety assessments based on human biology queried with *in vitro* assays. This session highlights research aimed at supporting this transition, including development of appropriate cellular assays, selection of predictive *in vitro* biomarkers, definition of points of departure (PoD) *in vitro*, and development and improvement of *in vitro*-*in vivo* extrapolation (IVIVE) tools. We also emphasize the current challenges associated with development and acceptance of these new methods. The first talk describes the need for an integrated testing approach when using *in vitro*-based point of departure with a focus on the development of *in vitro* metabolism systems and biokinetic models that allow dose extrapolation between *in vitro* and *in vivo* scenarios. We will also discuss the use of advanced *in vitro* metabolism systems for *in vitro*-based safety assessment, focusing on challenges for prediction of metabolite-mediated toxicity and tools for *in vitro*-based prediction of repeat exposure toxicity. The topic then transitions to the research efforts to identify biochemical and molecular markers predictive of mode of actions for adverse responses *in vivo*. This talk emphasizes the use of high-content -omic technologies for *in vitro* testing and determining *in vitro* PoDs. The next talk presents a case study of *in vitro*-only safety assessment for use of quercetin in skin lotions. This presentation describes the process of conducting a pathway-based safety assessment in the context of making product safety decisions. The case study demonstrates the process of developing fit-for-purpose *in vitro* assays, setting *in vitro* PoDs, and using IVIVE to translate that PoD to a safe human exposure. The final talk discusses challenges in applying *in vitro* assays for human safety prediction, focusing on approaches in the European Union to

Workshops

increase confidence and reliability of *in vitro* assays for *in vitro*-based safety assessments. Overall, the session provides an opportunity to learn more about the current efforts to merge multiple data streams in order to move *in vitro* testing tools beyond prioritization and create new *in vitro*-only safety assessment approaches.

Overview. Rebecca Clewell, The Hamner Institutes for Health Sciences, Research Triangle Park, NC.

Addressing Metabolism and Kinetics *In Vitro*—Not Just for Dose Extrapolation. Miyoung Yoon, The Hamner Institutes for Health Sciences, Research Triangle Park, NC.

Linking Adaptation to Adversity in Human *In Vitro* Experiments to Move Beyond Hazard Identification. Paul Jennings, Medical University of Innsbruck, Innsbruck, Austria.

Integrating Biokinetics and Biodynamics for Consumer Safety Assessment Using Quercetin As a Case Study. Yeyejide Adeleye, Unilever, Bedfordshire, United Kingdom.

Increasing Confidence and Reliability of *In Vitro* Assays for *In Vitro*-Based Safety Assessments. Sandra Coecke, JRC Institute for Health and Consumer Protection, European Commission, Ispra, Italy.

Quantitative Cumulative Risk Assessment: Is It Feasible Today?

Monday, March 14, 2:00 PM to 4:45 PM

🔥 Recent Advances in Safety Assessment

Chairperson(s): Gregory Brorby, ToxStrategies, Inc., Richmond, CA; and Moiz Mumtaz, Agency for Toxic Substances Disease Registry, Atlanta, GA.

Endorser(s):

**Mixtures Specialty Section
Risk Assessment Specialty Section**

Environmental exposures are complex and include a variety of stressors. Toxicologists and risk assessors continue to be greatly interested in assessing the cumulative risk associated with multiple chemical exposures (such as metals, solvents, pesticides, and persistent organic pollutants) and non-chemical stressors (e.g., stress, noise, biological agents, and socioeconomic status), particularly in underserved, environmental justice communities. Limited studies have been published that document joint exposures to some chemical and non-chemical stressors. Moreover, much of the work conducted to date is qualitative in nature, and methods for quantitatively accounting for the interaction between chemical and non-chemical stressors remain elusive. The workshop will focus on recent efforts to move beyond purely qualitative approaches to cumulative risk assessment, including leveraging existing chemical mixtures risk assessment methodologies, semi-quantitative screening tools, and case studies of unique modeling strategies for quantitatively combining risks from chemical and non-chemical stressors. Limitations of these approaches, and areas for future research, will also be discussed.

Can Chemical Mixtures Risk Assessment Methods Guide Development of Quantitative Cumulative Risk Assessment Methods? Glenn Rice, US EPA, Cincinnati, OH.

CalEnviroScreen: Current Applications and Future Directions in Cumulative Risk Assessment. Lauren Zeise, CAL EPA, Sacramento, CA.

Cumulative Risk and Adverse Birth Outcomes: The Gulf Resilience on Women's Health Study. Jeffrey Wickliffe, Tulane University, New Orleans, LA.

Cumulative Risk Assessment of Urban Air Toxics: A Pilot Study in San Antonio, Texas. Mina Suh, ToxStrategies, Inc., Mission Viejo, CA.

A Blood Pressure Effects-Based Cumulative Risk Assessment in a Low-Income Community. Junenette Peters, Boston University School of Public Health, Boston, MA.

The Role of the Epigenome in Exposure Effects, Susceptibility, and Public Health

Monday, March 14, 2:00 PM to 4:45 PM

◆ Molecular Toxicology: Mechanistic Insights and Hazard Assessment

Chairperson(s): Shaun D. McCullough, US EPA, Chapel Hill, NC; and Dana C. Dolinoy, University of Michigan, Ann Arbor, MI.

Endorser(s):

**Mechanisms Specialty Section
Molecular and Systems Biology Specialty Section
Women in Toxicology Special Interest Group**

The genome contains the blueprint for the structure and function of cells, tissues, and organs; however, the use of this information is controlled by three different regulatory mechanisms: (1) chromatin modifications, (2) DNA methylation, and (3) noncoding RNAs, collectively referred to as the epigenome. The epigenome is a dynamic framework that is responsive to acute environmental exposures, yet changes to the epigenome can also be stable enough to have chronic and even multi-generational implications. Investigations into the role of the epigenome in toxicology are rapidly evolving as a result of novel applications of epigenomics to toxicological studies that are constantly emerging. Thus it is critical to understand the role of the epigenome in cause and effect relationships among exposures, susceptibility, and health outcomes and how those relationships can be examined in the context of public health. The epigenome may hold the key to understanding mechanisms involved in many toxicological phenomena, including the effects of developmental exposures, trans-generational exposure effects, and interactions between chemical and non-chemical stressors in exposure outcomes. Further, recent publicly available tools for epigenomics analysis provide practical opportunities for a broad range of toxicologists to incorporate the epigenome into their translational research program. One such resource, the NIH Roadmap Epigenomics Project, is an integrative analysis of 111 reference human epigenomes from stem cells and primary tissues that represent organ systems that are frequently involved in disease. Through the integration of innovative tools and techniques, such as the Epigenomics Roadmap and longitudinal cohorts, current translational studies are providing novel approaches to understanding

Workshops

the epigenetic mechanisms underlying exposure effects, susceptibility, and risk modification. The goal of this workshop is to explore the recent applications of epigenomics to cutting-edge translational toxicology research. To achieve this we will bring experts together to discuss the involvement of the epigenome in the origins of exposure-related susceptibility and disease from development through adulthood and across generations. The session will open with an overview of the epigenome as a potential mediator of susceptibility and exposure effects following exposure to chemical and non-chemical stressors. The workshop will then focus on two examples of how environmental exposures induce changes in chromatin dynamics and DNA methylation that are associated with adverse health effects and susceptibility to the development of future disease. To complement these presentations the session will then discuss publicly available resources that toxicologists can use to integrate the epigenome into their research programs, as well as principles and examples of the integration of epigenomics into multi-omics (transcriptomics, metabolomics, genomics, etc.) datasets to identify biomarkers and characterize mechanisms of toxicity. Further, this workshop will include a panel discussion on the current and future prospects for epigenomics in toxicology. Following this workshop, attendees will have a better understanding of the role of the epigenome in health and disease, and learn how epigenomics can be integrated into translational toxicological studies.

Epigenome: Tool for Assessment of Health Impact of Cumulative Exposure to Chemical and Non-Chemical Stressors.

Kenneth Olden, US EPA, Washington, DC.

Environmental Epigenomics As a Mechanism in Developmental Reprogramming.

Cheryl L. Walker, Texas A&M University, Houston, TX.

Environmental Epigenomics—Translation to Large-Scale Human Studies.

Andrea Baccarelli, Harvard University, Boston, MA.

The NIH Roadmap Epigenomics Program, and How It Can Help You!

Lisa H. Chadwick, NIEHS, Research Triangle Park, NC.

Integration of Epigenomics Data with Other “-Omics” Datasets in Translational Toxicology Studies.

Ruchir Shah, Sciome LLC, Research Triangle Park, NC.

Using 21st Century Approaches to Evaluate Endocrine-Active Compounds

Monday, March 14, 2:00 PM to 4:45 PM

 Recent Advances in Safety Assessment

Chairperson(s): Sue Marty, *The Dow Chemical Company, Midland, MI*; and Katie Paul Friedman, *Bayer CropScience, Durham, NC*.

Endorser(s):

***In Vitro* and Alternative Methods Specialty Section**
Reproductive and Developmental Toxicology Specialty Section

New 21st century tools are providing valuable information that can contribute to chemical prioritization for endocrine screening and aid in the identification of early events in the mode of action of these chemicals. This session will examine 21st century approaches to evaluating potential endocrine bioactivity and how these data can be integrated

for endocrine screening prioritization, endocrine activity determination, and safety assessments. The first presentation will describe an estrogen receptor (ER) model based on the results of ToxCast high-throughput screening (HTS) *in vitro* assays, its performance with reference chemicals, and its application as an alternative assessment of estrogen bioactivity in the US EPA's Endocrine Disruptor Screening Program (EDSP). The second presentation will examine ToxCast HTS results for three triazole fungicides, and how these data can be integrated with other toxicity and exposure data to enable human health-protective EDSP prioritization. The third presentation will focus on the potential targets for chemical-induced epigenetic changes in endocrine signaling pathways during sensitive windows of development, including the role of micro RNAs in multigenerational toxicity, and relevant regulatory assays with potential for adaptation. The fourth presentation will describe the use of an HTS zebrafish embryo model to identify phenotypic and transcriptomic signatures of selected endocrine-active compounds to develop a predictive endocrine disruptor framework. The final presentation will describe the requirements for “fit for purpose” assays using ER models in a “top-down adverse outcome pathway” approach (defining key events leading to an apical outcome) or a “bottom-up toxicity pathway” approach (defining key events leading to a loss in cellular homeostasis), along with advantages and disadvantages of each in assessing potential endocrine activity. This session critically bridges development of 21st century tools to discussion of their current applications to pathway-based science and regulatory decisions.

Screening Chemicals for Estrogen Bioactivity Using Computational Approaches.

Patience Browne, US EPA, Washington, DC.

Predictive Data-Driven Framework for Endocrine Prioritization: Triazole Fungicide Case Study.

Katie Paul Friedman, Bayer CropScience, Durham, NC.

The Role of Epigenetics in Toxicity Responses to Endocrine-Active Compounds.

Miriam Jacobs, Public Health England, Chilton, United Kingdom.

Using Zebrafish Phenotypic and Transcriptomic Screening to Define Potential Endocrine Activity.

Robert Tanguay, Oregon State University, Corvallis, OR.

Development of Fit-for-Purpose Assays: Adverse Outcome Pathway and Toxicity Pathway Approaches to Defining *In Vitro* Assays Sufficient for Safety Assessment.

Rebecca Clewell, The Hamner Institutes for Health Sciences, Research Triangle Park, NC.



Daily Plenary Session

Inflammation and Neurodegenerative Disease

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

Lecturers: Stephen Skaper, *University of Padua, Padua, Italy*; and Alan I. Faden, *University of Maryland School of Medicine, Baltimore, MD*.

See full descriptions on page 75.

Workshops

TUESDAY

Bioactivity-Based Margin of Exposure Safety Assessment: The Next Stop along the Road to 21st Century Safety Assessments

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

 Recent Advances in Safety Assessment**Chairperson(s):** J. Craig Rowlands, *The Dow Chemical Company, Midland, MI*; and Nigel Walker, *NIEHS, Research Triangle Park, NC*.**Endorser(s):*****In Vitro* and Alternative Methods Specialty Section
Molecular and Systems Biology Specialty Section
Risk Assessment Specialty Section**

The ultimate goal of toxicity testing in the 21st century is the reduction and eventual replacement of animal-based toxicity testing with *in vitro* assays primarily using cultured human cells coupled with human exposure information. While significant progress has been made toward this end, there are numerous challenges that must be overcome before the final goal can be realized. Nevertheless, there are important regulatory decisions that these alternative approaches can be applied to that can serve as interim approaches to safety assessment. By using margin of exposure (MOE) as the primary metric for safety assessment, bioactivities measured in alternative approaches combined with human exposure determined through *in vitro* to *in vivo* extrapolations (IVIVE) or human biomonitoring studies can be used for regulatory decisions such as testing prioritization, emergency response assessments, and safety assessments. Bioactivity-based MOE provides a risk-based and animal-sparing approach to evaluate chemical safety, drawing broadly from previous experience but incorporating alternative 21st century alternative approaches to increase efficiency and reduce animal usage. The workshop will comprise a series of highly focused presentations that evaluate using bioassay-based points of departure for regulatory decision-making in chemical risk assessment. Each speaker will demonstrate how their recommended approach provides a practical solution to specific regulatory decision.

Biological Canaries in the Coal Mine: Strategic Implications for Utilizing Bioactivity-Based Margins of Exposures in Human Health Risk Assessments. Nigel Walker, *NIEHS, Research Triangle Park, NC*.**An Exposure: Activity Profiling Method for Interpreting High-Throughput Screening Data for Estrogenic Activity.** Richard A. Becker, *American Chemistry Council, Washington, DC*.**Moving Forward with Canada's Chemicals Management Plan: Opportunities for the Integration of High-Throughput Technologies in a Margin of Exposure Approach to Support Risk Assessment Activities.** Tara Barton-Maclaren, *Hazard Methodology Division, Health Canada, Ottawa, ON, Canada*.**Predicting the Benchmark Dose for Dioxin-Induced Liver Tumors from the Gene Expression Changes at 28-Days.** J. Craig Rowlands, *The Dow Chemical Company, Midland, MI*.**Application of Genomic Benchmark Dose Analysis in the NTP Response to the Elk River Chemical Spill.** Scott Auerbach, *NIEHS, Research Triangle Park, NC*.**Maternal Exposure to Nanoparticles—How Does It Affect the Fetus? Status, Mechanisms, and Future Directions**

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

 Developmental Toxicity: Mechanisms and Evaluation**Chairperson(s):** Flemming R. Cassee, *National Institute of Public Health and the Environment (RIVM), Bilthoven, Netherlands*; and Susan L. Makris, *US EPA, Washington, DC*.**Endorser(s):****Inhalation and Respiratory Specialty Section
Reproductive and Developmental Toxicology Specialty Section**

Information on the effects of maternal exposure and possible effects on the fetus to small particles (nanometer range) is scarce and fragmented. Yet both epidemiological and toxicological studies suggest that maternal exposure to NP can cause adverse health effects on embryonic development such as increased number of terminated pregnancies (Hougaard et al., 2015). In this workshop, we aim to present the latest scientific information on reproductive and developmental effects of nano-sized particles, either from environmental relevant exposure (i.e., diesel engine exhaust) or engineered nanoparticles (single-walled carbon nanotubes, silver, cadmium oxide). This workshop will include a panel discussion at the end on relevance of dose determination, animal model appropriateness for humans, and what the next steps are to understanding human risk.

Introduction: Reasons for Concern? Flemming R. Cassee, *National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands*.**The Reprotoxic Effect of Engineered Nanoparticles, *In Vivo* and *In Vitro*.** Luisa Campagnolo, *University of Rome Tor Vergata, Rome, Italy*.**Maternal Airway Exposure to Nanoparticles in Pregnancy—Effects and Lessons Learned from Rodent Models.** Karin Sørig Hougaard, *National Center for the Working Environment, Copenhagen, Denmark*.**Exposure to Nanoparticles During Pregnancy Can Impact Obstetric Outcomes and Early-Life Development in a Mouse Model: A Tale of Two Metals.** Judith T. Zelikoff, *New York University School of Medicine, Tuxedo, NY*.**Maternal Exposure to Nanoparticles—How Does It Affect the Fetus? Status, Mechanisms, and Future Directions.** Peter L. Goering, *US FDA, Silver Spring, MD*.**Potential Developmental and Early-Life Health Effects of Nanomaterials: Data Gaps and Research Needs for Risk Assessment.** Maureen R. Gwin, *US EPA, Washington, DC*.**Panel Discussion/Q&A.** Susan L. Makris, *US EPA, Washington, DC*.

Multi-Omics in Predictive Toxicology: Development and Application in Environmental Monitoring Programs

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

◆ Molecular Toxicology: Mechanistic Insights and Hazard Assessment

Chairperson(s): Susie Huang, AXYS Analytical Services Ltd., Sidney, BC, Canada; and Alvine Mehinto, Southern California Coastal Water Research Project, Costa Mesa, CA.

Endorser(s):
Molecular and Systems Biology Specialty Section

The development of diverse omics technologies holds promise for understanding adverse outcomes induced by exposure to environmental chemicals. Omics technologies offer an efficient and high-throughput alternative to conventional toxicity testing, which is often not sensitive enough to detect effects of low-level chemical exposures and environmental mixtures. By evaluating changes in RNAs, proteins, and/or metabolite levels, omics technologies can inform on molecular initiating events as well as key pathways on the trajectory to adverse outcomes for exposed animals. This approach, known as “adverse outcome pathway (AOP)” analysis, has gained considerable interest recently through OECD and US EPA initiatives. Molecular biomarkers and fingerprints identified using this approach will be useful to identify the types of toxicants present in the environment and predict adverse health outcomes in humans and animals. The integration of the various omics technologies in environmental monitoring programs is powerful for toxicity assessments that can be used by government, industry and academia to better define risk characterization. This workshop will focus on the development and application of omics techniques to investigate environmental issues. The speakers will present research studies that utilized omics technologies to identify chemical effects at different biological levels to develop AOPs. Their results will be used to discuss how omics data can be incorporated in monitoring programs and risk assessment.

Adverse Outcome Pathways and Enhancing the Role of Genomics in Chemical Risk Assessment. Gerald Ankley, US EPA, Duluth, MN.

Using Changes in the Transcriptome and Promoter Methylation to Explain Benzo[a]pyrene-Mediated Developmental Adverse Outcomes. Kristine Willett, University of Mississippi, University, MS.

Targeted Metabolomics Tools to Inform Systems Biology and Effects-Directed Analysis: Applications in Zebrafish Larvae and Sentinel Species. Bharat Chandramouli, AXYS Analytical Services Ltd., Sidney, BC, Canada.

Use of Genomic Tools to Determine Novel Adverse Outcome Pathways for the Assessment of Climate Change on Pesticide Toxicity in Salmonid Species of Fish. Daniel Schlenk, University of California Riverside, Riverside, CA.

No Genome? No Problem! Development of a High-Quality Computationally Frugal De Novo RNA-Seq Method to Enable Predictive Toxicology in Sentinel Species. Caren Helbing, University of Victoria, Victoria, BC, Canada.

Scientific and Regulatory Advances in Safety Evaluation of Heavy Metals in Food

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

♠ Recent Advances in Safety Assessment
♣ Toxicity of Metals

Chairperson(s): Brinda Mahadevan, Abbott Laboratories, Columbus, OH; and Mansi Krishan, ILSI North America, Washington, DC.

Endorser(s):
Association of Scientists of Indian Origin Special Interest Group
Food Safety Specialty Section
Metals Specialty Section

Recent reviews on the risk assessment of contaminants in food, the use of these data in the safety evaluation process, and the safety of the US food supply, in part through its monitoring programs, have led to significant advancements in regulatory and scientific recommendations in the area of food safety. It has also focused on the potential exposure posed by chemicals such as heavy metals, including metals that are essential and may be toxic. In order to prevent potentially unsafe food from reaching the marketplace, regulatory agencies such as the US Food and Drug Administration regulate four major heavy metals (arsenic, lead, cadmium, and mercury) in food. Globally, the Codex Committee on Contaminants in Foods (CCCF) plays a big role in setting safety limits for many of these heavy metals. For example, at the recent CCCF meeting, the maximum levels of lead in the General Standard on Contaminants in food and feed were established. Very few foods are totally free from heavy metals, although they may not be detectable. Therefore, while evaluating food safety from the point of view of heavy metal content, one has to bear in mind that the analysis and detection of heavy metals at the concentration levels commonly found in foods is fairly difficult. However, better analytical and diagnostic procedures have led to the detection of lower levels of heavy metals and how it links to human target organ damage. Most often zero risk/tolerance is expected in risk assessment when confronted with the detection of selected heavy metals in foods/ingredients. In an effort to broaden the understanding of the aforementioned issues pertaining to regulatory toxicology and safety of food, the following key aspects will be addressed in this workshop: 1) Approaches for an efficient method for large-scale surveying of potential toxicities for heavy metal contaminants; 2) global regulatory programs that help with enforcement and setting of safe exposure limits; 3) availability of heavy metal dietary exposure screening tool for rapid evaluation of potential public health risk; and 4) applicability of such a tool to support efficient food safety risk management practices.

Heavy Metals in ToxCast: Relevance to Food Safety. Keith Houck, US EPA, Research Triangle Park, NC.

FDA and Codex Activity on Heavy Metals in Food. Lauren P. Robin, US FDA, College Park, MD.

Introduction to the Metal Dietary Exposure Screening Tool. Nga Tran, Exponent Inc., Washington, DC.

Case Studies Demonstrating the Utility of the Metal Dietary Exposure Screening Tool. Craig Llewellyn, The Coca-Cola Company, Atlanta, GA.

Risk Assessment of Metals in Food Utilizing Mode of Action Analysis. Samuel M. Cohen, University of Nebraska Medical Center, Omaha, NE.

Workshops

Cannabis in the Courtroom

Tuesday, March 15, 2:00 PM to 4:45 PM



Advances in Neurotoxicology

Chairperson(s): George Corcoran, Wayne State University, Detroit, MI; and Sol Bobst, Nexeo Solutions LLC, The Woodlands, TX.**Endorser(s):**

Ethical, Legal, and Social Issues Specialty Section
Occupational and Public Health Specialty Section
Regulatory and Safety Evaluation Specialty Section

Presentations in this workshop build upon 2013 and 2014 roundtable and workshop sessions that laid a broad foundation for examining the legal applications and boundaries of toxicology and the law. They highlighted the fundamental time frame dichotomy and innate tension that exists between science and the law while critically exploring the validity and limitations of toxicology evidence. The current workshop focuses specifically on the scientific and legal issues surrounding cannabis and its various forms and congeners. For suspects charged with being under the influence of cannabis, challenges for forensic laboratories include drug pharmacokinetics and pharmacodynamics as well as supporting field evidence of impairment. Epidemiology has addressed degree and time of impairment and has advanced court claims of causation, negligence, and contributory negligence in motor vehicle accidents and psychotic episodes. Many forms of synthetic cannabinoids exist, including illegal agents and those new drugs being developed as therapies. Engineered cannabinoids can greatly exceed the potency of THC and endocannabinoid yet few are scheduled as controlled substances. This poses unique difficulties for legal intervention and the protection of public health. Federal and state cannabis laws differ substantially. States with legalized marijuana must deal with toxicological uncertainty, particularly as it relates to exposure-response relationships. The expanding availability of THC edibles and their consequences are considered from a poison center perspective, including dosing, delayed onset, adult deaths, and childhood near deaths. Finally, cannabis poses dilemmas for the forensic sciences as well as for toxicology and the SOT. One example is illustrated by growing efforts to establish per se blood or urine levels that would define impairment by statute, as currently exists for blood alcohol, with the potential passage of zero tolerance laws in some jurisdictions. The workshop closes with a panel discussion.

THC from the Forensics Lab. Kevin Schneider, State of Virginia Department of Forensics, Fairfax, VA.

Epidemiological Evidence Considerations with THC in Court. Martin Barrie, Oak Ridge Associated University, Oak Ridge, TN.

THC Cases in State versus Federal, Different Case Issues. Laura Plunkett, Integrative Biostrategies, Houston, TX.

General Population Experiences with THC Edibles—A New Kind of High. Christopher Hoyte, Rocky Mountain Poison Control Center, Denver, CO.

The Legal Dragnet for Elusive “THC.” Roderick T. Kennedy, New Mexico Court of Appeals, Albuquerque, NM.

Read-Across: Building Scientific Confidence in the Development and Evaluation of Read-Across for Regulatory Purposes Using Tox21 Approaches

Tuesday, March 15, 2:00 PM to 4:45 PM

- ◆ Molecular Toxicology: Mechanistic Insights and Hazard Assessment
- ♠ Recent Advances in Safety Assessment

Chairperson(s): Richard A. Becker, American Chemical 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, whereby chemical hazard data from data-rich chemicals are used to predict the hazards of another chemical lacking such data, is a well-established approach in chemical management. Even as read-across continues to generate considerable interest as a practical data gap-filling technique in category and analogue approaches for regulatory purposes, its acceptance by regulatory agencies remains a challenge. In an effort to enhance regulatory acceptance of read-across, several organizations have begun to develop systematic frameworks to characterize read-across justifications and make explicit the uncertainties and assumptions relied upon. Such efforts are intended to build scientific confidence associated with read-across for regulatory purposes. A growing strategy for reducing uncertainty in read-across is to incorporate Tox21 approaches in substantiating category rationales or their associated read-across justifications. For example, mechanistic information captured within Adverse Outcome Pathways (AOPs) could be used in category development as part of Integrated Approaches to Testing and Assessment (IATA). Additionally, data generated under the ToxCast program can be used in supporting read-across justifications for new and existing regulatory categories. This workshop will foster a cross-stakeholder discussion on what the key issues thwarting regulatory acceptance are and what progress has been made in investigating the utility of mechanistic information to meet different regulatory decision-making needs. The workshop will comprise a series of highly focused presentations that evaluate the development of chemical categories and associated read-across and their interpretation in regulatory decision-making in chemical risk assessment. Each speaker that is presenting a case study will be asked to consider how they are evaluating the confidence level of the read-across in terms of the supporting mechanistic data and whether, if appropriate, this anchors to a specific pathway(s) (e.g., AOPs). The session will be of broad interest to investigators and regulators across environmental, industrial, consumer products, and pharmaceutical toxicology that perform human and environmental risk assessment.

Introduction. Grace Patlewicz, US EPA, Research Triangle Park, NC.

Making the Key Issues Driving Uncertainty in Read-Across Explicit Using the RAAF—Opportunities for Enhancement with Modern Approaches. Derek Knight, European Chemicals Agency, Helsinki, Finland.

Workshops

Actualizing the OECD Revised Guidance on Grouping of Chemicals with Practical Examples. Joop deKnecht, OECD, Paris, France.

Propylene Glycol Ethers: A Read-Across Example for Low-Toxicity Chemicals. Nicholas Ball, The Dow Chemical Company, Midland, MI.

Do Tox21 Approaches Such as Data from ToxCast Enhance Existing OECD Chemical Categories? Grace Patlewicz, US EPA, Research Triangle Park, NC.

CAAT and the Work of the Read-Across Steering Group. Thomas Hartung, John Hopkins CAAT, Baltimore, MD.

Focused Discussion and Wrap-Up. Richard A. Becker, American Chemical Council, Washington, DC.

Safety Assessment of Topically Exposed Cosmetic Ingredients: Lessons Learned

Tuesday, March 15, 2:00 PM to 4:45 PM

🔥 Recent Advances in Safety Assessment

Chairperson(s): Andreas Schepky, Beiersdorf AG, Hamburg, Germany; and Bas Blaauboer, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, Netherlands.

Endorser(s):

Biological Modeling Specialty Section

Dermal Toxicology Specialty Section

In Vitro and Alternative Methods Specialty Section

The Cosmetics Europe Program aims to enable *in vitro*-only safety assessments of cosmetic ingredients performed on the basis of both hazard characterization and exposure assessment. The focus is on the development of models linking external exposure dose to local skin and internal exposure, and potential target organ toxicity after topical application. As a result of the 7th Amendment to the Cosmetic Directive, the use of animals for such studies is banned in the EU, and therefore information regarding systemic exposure of dermally applied chemicals must be derived from *in vitro* and/or *in silico* methods. This session provides an overview of three Task Force Projects, and how results will help in the animal-free safety assessment for skin sensitization and genotoxicity of topically applied chemicals. The session is rounded off with a regulator's perspective on how we may gain acceptance of predictive approaches to the safety assessment of cosmetic ingredients by regulators themselves, as well as end-users and the consumer. The Skin Bioavailability and Metabolism (Skin BM) Task Force was set up to improve the measurement and prediction of the bioavailability of topically exposed compounds, with a specific focus on endpoints such as skin sensitization and genotoxicity. The Skin BM project has generated data from standardized dermal-based assays for a set of physicochemically diverse chemicals, which are relevant to cosmetics and dermal toxicities. An example of how these data can improve the predictive capacity of an *in silico* dermal penetration model will be presented. In addition, we will demonstrate how bioavailability information (including dermal absorption and metabolism) can be utilized when assessing outcomes from skin sensitization assays and dermal genotoxicity assays (using 3D skin). The Skin Tolerance Task Force has studied the complex biology of skin sensitization and conducted a screen and evaluation of different

in vitro test methods, which provide insight into sensitizing characteristics of chemicals. Case studies demonstrating how the safety of topically applied cosmetic ingredients, e.g., resorcinol, cinnamic acid, or hair dyes, can be supported with this concept will be introduced. An evaluation of multiple integrated approaches to testing and assessment of skin sensitization will be presented, and a potential path toward regulatory acceptance of an optimized strategy will be discussed. The Genotoxicity Task Force has led three projects to help improve the predictive capacity of current *in vitro* genotoxicity assays and develop new *in vitro* models as follow-up alternatives to positive outcomes in the initial test battery. Work from these Task Forces will ultimately lead to a testing strategy to enable cosmetic industries to conduct safety assessments of chemicals without the use of animals.

Introduction. Bas Blaauboer, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, Netherlands.

Generation of Dermal Bioavailability Data Using *In Vitro* Studies for Local Dermal Concentrations and *In Silico* Models. Andreas Schepky, Beiersdorf AG, Hamburg, Germany.

Skin Penetration *In Silico* Modeling—Use of *In Vitro* Data to Improve Kasting Model. Gerry Kasting, University of Cincinnati, Cincinnati, OH.

Skin Sensitization Testing Strategy Evaluation. Nicole Kleinstreuer, Integrated Laboratory Systems, Inc. Contractor supporting the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), Research Triangle Park, NC.

Method Evaluation Process and Outcome for Skin Sensitization. Nathalie Alépée, L'Oréal Research & Innovation, Aulnay Sous Bois, France.

Use of Bioavailability Data to Interpret 3D Skin Genotoxicity Assay Outcomes. Stefan Pfuhler, The Procter & Gamble Co., Cincinnati, OH.

Gaining Acceptance of Predictive Approaches to the Safety Assessment of Cosmetic Ingredients. Maurice P. Whelan, EURL/ECVAM European Commission Joint Research Centre, Ispra, Italy.



Workshops

WEDNESDAY

An Update on Juvenile Animal Testing

Wednesday, March 16, 9:30 AM to 12:15 PM

 Developmental Toxicity: Mechanisms and Evaluation

Chairperson(s): Gerhard F. Weinbauer, Covance, Muenster, Germany; and Timothy P. Coogan, Janssen Research & Development, LLC, Spring House, PA.

Endorser(s):
Reproductive and Developmental Toxicology Specialty Section

In recent years, consideration of whether and when—relative to clinical plans—juvenile animal (JA) testing is needed to support the clinical development of a pharmaceutical has become an important part of the drug development portfolio. An increasing number of these studies are being performed or are planned. The purpose of this scientific session is to present the current scientific and regulatory environment focusing on the “hows” and “whats” of JA testing today, specifically, the perspectives of the pharmaceutical industry, including strategies both internal and through regulatory interaction. In terms of animal models used, these range from rodents to nonhuman primates, with a variety of different study design approaches to evaluate toxicity in JA. Real and hypothetical case study examples are being used to highlight when testing was considered necessary and to illustrate strategies and experiences. Five recognized topical experts will present their perspectives on JA testing; the first presentation provides a state-of-the-art overview and update on the ICH S11 (Nonclinical Safety Testing in Support of Development of Pediatric Medicines) status, the second presentation focuses on surprises encountered during JA study conduct, the third presentation highlights the importance of using an integrated approach and involving the toxicologist early in the drug development program, the fourth presentation addresses the impact of different strategies and JA study designs and the fifth presentation provides a US regulatory perspective and a review of the US FDA study database.

Juvenile Animal Testing Today. Paul Baldrick, Covance Laboratories Ltd, Harrogate, United Kingdom.

Expect the Unexpected—Learning from the Past. Graham P. Bailey, Janssen Pharmaceutica N.V., Beerse, Belgium.

Beyond Juvenile Animal Toxicity Studies: The Toxicologist's Broader Role in Pediatric Drug Development Plans. LaRonda L. Morford, Eli Lilly and Company, Indianapolis, IN.

Choose Your Own Adventure: Designing Juvenile Animal Toxicity Studies. Christopher J. Bowman, Pfizer Inc., Groton, CT.

Regulatory Perspectives on the Role of Juvenile Animal Studies in Global Pediatric Product Development. Timothy McGovern, US FDA, Silver Spring, MD.

Moving Beyond Cancer: Current State of the Science of Noncancer Health Effects of Arsenic

Wednesday, March 16, 9:30 AM to 12:15 PM

 Toxicity of Metals

Chairperson(s): Danielle J. Carlin, NIEHS, Research Triangle Park, NC; and Janice S. Lee, US EPA, Research Triangle Park, NC.

Endorser(s):
Metals Specialty Section
Occupational and Public Health Specialty Section

Inorganic arsenic (iAs) contamination from geologic, anthropogenic, and food origins is an increasing concern for the US and globally. This metalloid is associated with cancers of the bladder, kidney, liver, prostate, skin, lungs, and nasal cavity, as well as noncancer health effects. Moreover, other considerations in studying cancer and noncancer effects include prenatal exposure to iAs, individual variation in arsenic metabolism efficiency, bioavailability, transport, and speciation. This workshop will highlight the current state of research of iAs and its role in noncancer health effects. Discussions will focus on the impact of iAs exposure on cardiovascular disease, increased susceptibility to infectious diseases, alterations on lung development, and interference with reproduction. This workshop will also begin to address the substantial research gaps regarding the mode of action (MOA) by which iAs could induce or exacerbate these health effects. The United States Environmental Protection Agency (US EPA) Integrated Risk Information System (IRIS) Program is currently developing a new iAs assessment that considers both cancer and noncancer effects from oral, inhalation, and dermal routes of exposure. Discussion will include current research efforts from epidemiological, animal, and *in vitro* studies and will focus on noncancer health effects that are under consideration by the IRIS Program.

Introduction. Danielle J. Carlin, NIEHS, Research Triangle Park, NC.

Cardiovascular Outcomes Associated with Low-to-Moderate-Dose Arsenic Exposure in Bangladesh. Maria Argos, University of Illinois at Chicago, Chicago, IL.

Arsenic and Pulmonary Infections. Bruce Stanton, Dartmouth College, Hanover, NH.

Health Effects of Early-Life Inhalation Exposure to Arsenic-Containing Dusts. R. Clark Lantz, University of Arizona, Tucson, AZ.

The Impacts of Low-Moderate-Level Drinking Water Arsenic Exposure on Reproduction. Michael S. Bloom, University at Albany, State University of New York, Rensselaer, NY.

Current Status of the IRIS Arsenic Health Assessment. Janice S. Lee, US EPA, Research Triangle Park, NC.

Panel Discussion/Q&A. Janice S. Lee, US EPA, Research Triangle Park, NC.

Paradigm Change in Toxicology: What Will It Take to Bring Advances in the Science of Toxicology into Regulatory Use?

Wednesday, March 16, 9:30 AM to 12:15 PM

- ◆ Molecular Toxicology: Mechanistic Insights and Hazard Assessment
- ♠ Recent Advances in Safety Assessment

Chairperson(s): Katherine Tsaoun, Safer Medicines Trust, Cambridge, MA; and John-Michael Sauer, Critical Path Institute, Tuscon, AZ.

Endorser(s):

In Vitro and Alternative Methods Specialty Section
Regulatory and Safety Evaluation Specialty Section
Scientific Liaison Coalition

Most experts agree that current test methods for prediction of hazardous effects are not always adequate to ensure the safety of human subjects/consumers exposed to medicines and other chemicals. Major advancements in the science of mechanistic toxicology have produced a number of technologies that can predict various mechanisms of human toxicity. Although academic groups, large industry users and spun-out companies have made major headway in generating data in promising *in vitro* models, resulting in significant use of the technologies in discovery stages, less progress has been made toward qualification/validation of these models for regulatory use. Until consensus is achieved between all stakeholders on the needed level of qualification/validation, global regulatory authorities will be slow to accept the new methods. Old methods will continue to be required by global regulatory authorities if these technologies are not universally accepted. Hence, there is a missing step between the discovery/lead optimization stage and regulatory and commercial use of these technologies. To address this problem, we have assembled a group of academic and industry experts, and brought them together with nonprofit organizations and regulatory authorities to assess the current state of the field and discuss acceptable paths forward in the adoption of new methods. Validation and case studies of practical use in pharmaceutical, industrial chemicals, and cosmetic industries will be presented, and a panel of experts will offer their opinion on which bodies may be best suited to perform the task of standardization of the adoption process, how this process should be implemented, how these new types of data are incorporated into the assessment process, and how regulators assess these data in replacement of traditional *in vivo* studies to give product approvals. A discussion on key drivers for this process will follow stressing similarities and distinctions between pharmaceuticals, cosmetic, agrochemicals, and biocide safety assessments. A working group of the key stakeholders will be formed with the objective of defining agreed-upon criteria for inclusion of alternative tests into regulatory batteries for different industries.

REACH and Predictive Non-Animal Approaches. Derek Knight, European Chemicals Agency, Helsinki, Finland.

CDER Acceptance of Alternative Assays. Abigail Jacobs, US FDA, Washington, DC.

Learnings from Early-Safety Assessment in Pharmaceutical Industry: Pfizer. Yvonne Will, Pfizer, Groton, CT.

Chemicals and Agrochemicals Perspective on Moving Toward 21st Century Safety Assessment. Marco Covaro, Dow Agrosiences, Abingdon, United Kingdom.

Next Challenge for Cosmetic Industry in Europe: Systemic Toxicity Case Study. Gladys Ouedraogo, L'Oreal, Paris, France.

A Paradigm Shift to Advance the Relevance of Toxicology for Regulatory Policy. Daniele Mandrioli, Cesare Maltoni Cancer Research Center Ramazzini Institute, Bentivoglio (Bologna), Italy; and Ellen Silbergeld, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

Screening Chemicals for Neurotoxicity Outcomes—Using Large Datasets and Multiple Endpoints to Develop “Toxicity Profiles”

Wednesday, March 16, 9:30 AM to 12:15 PM

- ♠ Advances in Neurotoxicology
- ◆ Molecular Toxicology: Mechanistic Insights and Hazard Assessment

Chairperson(s): Timothy J. Shafer, US EPA, Research Triangle Park, NC; and Mamta Behl, NIEHS, Research Triangle Park, NC.

Endorser(s):

In Vitro and Alternative Methods Specialty Section
Molecular and Systems Biology Specialty Section
Neurotoxicology Specialty Section

The potential for neurotoxicity in adults and children following exposure to environmental chemicals remains a high public priority because of concerns that recent increases in the prevalence of neurological disorders (e.g., Parkinson's, ADHD, autism) may in part be due to chemical effects. In addition, neurotoxicity is one of the leading reasons for the failure of new drug candidates. Thus, the need for reliable and efficient screening tools to identify, prioritize, and evaluate chemicals for their potential to induce acute neurotoxicity in adults or developmental neurotoxicity (DNT) is well recognized. The past decade has thus seen increased efforts to develop high-throughput, high-content assays that are useful to screen compounds for neurotoxicity or DNT. To date, assay development has focused on relatively small sets (5–20) of compounds. Recently, however several studies have evaluated the comparative neurotoxicity/DNT of larger (30–100) sets of compounds, in some cases using a battery of assays or endpoints. This provides the opportunity to begin examining how such datasets can be used to develop toxicity profiles that better inform decisions regarding the potential neurotoxicity/DNT of chemicals. This workshop will present data from several studies examining larger numbers of compounds, discuss the strengths and limitations of the assays used to generate the data, and provide novel strategies to score relative biological activity across different assays. Attendees will gain a national and international perspective from academia, government, and industry using well-characterized high-throughput, high-content cell-based assays, and alternate animal models, spanning across multiple aspects of development, neurodevelopment, and neural activity to evaluate, compare, and contrast the biological activity in large sets of chemicals. The use of this information to build “toxicity profiles” can help inform decision-making related to neurotoxicity and DNT. The introduction will

Workshops

lay out the agenda of the workshop, including the overall goals, speaker lineup, and the intended outcome. The workshop will commence with an introduction by Timothy Shafer, who will introduce the concept of using data from multiple chemicals and endpoints to inform decisions about chemical neurotoxicity, and briefly provide an overview of each presentation. A major liability in drug development and evaluation of chemical toxicity is the development of seizures. Our first speaker, Chris Strock will discuss how multiple endpoints extracted from high-content recordings of neural network activity using microelectrode arrays can be used to identify and classify seizurogenic compounds early in the drug development process. The second speaker, Hennie Kamp will discuss how combination of neural network recordings, and plasma and brain metabolome data can be used for early identification of several classes of neurotoxic compounds. The next speaker, Marcel Leist has used a combination of transcriptomics and toxicity in peripheral sensory (dorsal root ganglion) nerve cells to determine patterns of toxicity responses that can identify different classes of chemicals. The last two speakers will focus on methods to identify and prioritize environmental chemicals with potential for DNT/NT. William Mundy will present the approach that the US EPA has used to evaluate a battery of assays to collectively predict DNT and NT associated with unknown compounds. One of the major challenges in comparing results across different assay platforms is the choice of a common metric to assess chemical effect since different assays use disparate approaches to define potency. Using an 80-compound library that was tested for different DNT and NT endpoints by several researchers, the last speaker, Mamta Behl, will present an approach that provides a uniform and robust metric for comparison of the biological activities across different assays to rank compounds by their toxicity for further hazard characterization *in vivo*. The workshop is designed to provide an overview of the current status and challenges in the DNT field, including the current national and international regulatory guidelines, and novel strategies that are currently being implemented in the field.

Introduction. Timothy J. Shafer, US EPA, Research Triangle Park, NC.

A Novel High-Throughput *In Vitro* and Multivariate Spike Train Analysis Platform for Drug Neurotoxicity and Method of Action Identification. Chris Strock, Cyprotex, Watertown, MA.

Identification of Neurotoxicity Using *In Vitro* and *In Vivo* Metabolomics Data. Hennie Kamp, BASF, Ludwigshafen, Germany.

Incorporation of Transcriptome Data in Functional Screening Assays of Peripheral Nervous System Toxicity for Improved Compound Grouping and Mechanistic Understanding. Marcel Leist, University of Konstanz, Konstanz, Germany.

Evaluating the Ability of *In Vitro* Assays Based on Key Events in Neurodevelopment to Predict Developmental Neurotoxicity (DNT). William Mundy, US EPA, Research Triangle Park, NC.

Using HTS Data for Decision-Making for Further *In Vivo* Testing. Mamta Behl, NIEHS, Research Triangle Park, NC.

Advanced Techniques in PBPK Modeling to Improve Quantitative Risk Assessment for Infants and Children

Wednesday, March 16, 2:00 PM to 4:45 PM



Developmental Toxicity: Mechanisms and Evaluation
Recent Advances in Safety Assessment

Chairperson(s): Susan Felter, Procter & Gamble, Cincinnati, OH; and Jeffrey Fisher, US FDA, Jefferson, AR.

Endorser(s):
Biological Modeling Specialty Section
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

Methods for quantitative risk assessment most commonly employ uncertainty factors to account for species' differences and human heterogeneity, including differences associated with life stages, in both toxicokinetics and toxicodynamics. While this approach is generally considered sufficient to provide protection for more sensitive subpopulations and life stages, it is a very crude approach to risk assessment that does not take into consideration data that are increasingly available to address species' differences and population variability. Specifically for life stage-associated differences, it is commonly assumed that infants and children are more sensitive than adults, despite data showing that this is often not true. Further, it is increasingly recognized that differences in sensitivity can change very quickly after the neonatal period such that very young infants might be more sensitive, but older infants and children are less sensitive than adults. Alternatively, for an early-life stage compared to adults, there can be increased sensitivity to one endpoint/target organ while there is decreased sensitivity to another, or the differential sensitivity can be related to dose. These differences are particularly important to understand in pharmaceutical development, where dosing must carefully consider both efficacy and safety over different life stages. The immaturity of key physiological processes associated with the toxicokinetic/toxicodynamic handling of xenobiotics is an important factor contributing to the differential susceptibility associated with early-life exposures; this is made more challenging by the rapid changes that occur in both growth and maturation throughout infancy and childhood. PBPK modeling provides an important tool to describe these key maturational processes such that they are explicitly considered in the risk assessment process. While application of these models generally confirms the adequacy of current default UFs for providing protection for early-life stages, it provides an opportunity to refine this assumption while significantly increasing our confidence in the resulting analysis.

Differential Physiology and Sensitivity of Infants and Children. Abby Collier, University of British Columbia, Vancouver, BC, Canada.

Age-Specific PBPK Models. John Troutman, Procter & Gamble, Cincinnati, OH.

Advances in Extrapolation to Help Inform Pharmacokinetics and Pharmacodynamics of Chemicals and Drugs in Infants and Children. Jeffrey Fisher, US FDA, Jefferson, AR.

Life Stage Physiologically-Based Pharmacokinetic (PBPK) Model Applications to Screen Environmental Hazards. Hisham El-Masri, US EPA, Research Triangle Park, NC.

PBPK Modeling and Simulation in Drug Development: A Focus on Pediatrics. Andrea Edgington, University of Waterloo, Waterloo, ON, Canada.

“Breaking Bad”: Cardiovascular Autophagy Gone Rogue: A Putative Mechanism of Toxicity and a Drug Target in Disease

Wednesday, March 16, 2:00 PM to 4:45 PM

Chairperson(s): Leslie C. Thompson, US EPA, Research Triangle Park, NC; and Tammy R. Dugas, Louisiana State University, Baton Rouge, LA.

Endorser(s):

**Cardiovascular Toxicology Specialty Section
Mechanisms Specialty Section
Regulatory and Safety Evaluation Specialty Section**

Christian de Duve coined the word “autophagy” in 1963 during his studies of the lysosome. In the 1970s autophagy was identified as a toxicological mechanism in acute liver damage caused by dimethylnitrosamine, and in 1983 rubomycin injection was used to generate a model of myocardial insufficiency in rats by impairing autophagic function in the heart. Autophagy is a tightly regulated process within cells that includes 1) molecular marking of damaged or dysfunctional cellular constituents; and 2) degrading/recycling those marked cellular constituents. Essentially autophagy is a waste management system for cells. By cleaning up worn, aged, and damaged cellular constituents, autophagy helps maintain overall cellular health, function, and efficiency. Disruption of autophagy can have adverse effects on cardiovascular function, and impaired autophagy has been implicated in cardiovascular pathologies and toxicity responses to various pharmaceuticals and environmental toxicants. Abnormal autophagic processes have been well documented in cardiovascular disease and are increasingly being targeted for therapeutic approaches. Thus, autophagy in the cardiovascular system is emerging as an important toxicological and therapeutic endpoint. This session will highlight the clinical consequences of impaired autophagy on normal cardiovascular function, discuss emerging evidence linking alterations in autophagy to cardiotoxicity responses to antineoplastic agents, and examine autophagic consequences in vascular endothelial cells following treatment with drugs used to treat HIV. Finally, this session will highlight evidence that proposes targeting autophagy as a therapeutic strategy in different vascular diseases. Namely, evidence will be presented describing targeted increase in autophagy to improve endothelial cell-mediated diabetic vasculopathy and decrease smooth muscle proliferation in conditions of atherosclerosis and restenosis.

Clinical Perspective on Cardiovascular Autophagy. Monte S. Willis, University of North Carolina, Chapel Hill, NC.

Contributions of Mitophagy in Cumulative Doxorubicin-Induced Cardiomyopathy. Kendall B. Wallace, University of Minnesota, Duluth, MN.

Cycles of Injury and Repair via Mitophagy Associated with Chronic Exposures and Premature Senescence. Tammy R. Dugas, Louisiana State University, Baton Rouge, LA.

Autophagy As a Drug Target in Diabetic Vascular Disease. Jessica L. Fetterman, Boston University, Boston, MA.

Verapamil, Autophagy, and Vascular Smooth Muscle Antiproliferation. Daniel J. Conklin, University of Louisville, Louisville, KY.

In Vitro Dosimetry of Engineered Nanomaterials: Too Complicated to Consider, Too Important to Ignore

Wednesday, March 16, 2:00 PM to 4:45 PM

Chairperson(s): Saber Hussain, US Air Force, Wright-Patterson AFB, OH; and Philip Demokritou, Harvard University School of Public Health, Cambridge, MA.

Endorser(s):

Nanotoxicology Specialty Section

Because of the potential public health risk arising from exposure to engineered nanomaterials (ENMs) through consumer applications, a thorough evaluation of their safety is essential. Owing to the fast pace of ENM generation, high-throughput *in vitro* methods for safety assessments are sorely needed, but to date have proven unreliable with limited predictive capabilities extending to *in vivo* models. One major contributor to the discrepancies that exist between these models is a failure to reconcile *in vitro* and *in vivo* dosages. Despite growing evidence of the importance of ENM dosimetry for accurate hazard assessments, few *in vitro* studies take it into consideration. This oversight is likely due to a lack of standardized, easy-to-use, and validated methodologies for dispersion preparation, characterization and *in vitro* dosimetry estimation. This workshop will highlight recent advancements that strengthen ENM dosimetry, including the development of aerosol lung deposition models, generation of pertinent *in vitro* exposure mechanisms, and integrated approaches for calculating and predicting relevant dosages for both *in vitro* and *in vivo* nanotoxicological examinations. It will also highlight several mature, sophisticated computational tools and experimental methods for obtaining dosimetry information *in vivo* and extrapolating those findings to *in vitro* cellular systems with specific examples related to “real world” ENM exposures. In addition to discussing the current state of the art regarding ENM dosimetry, discussions will center on the need and means for future development of this area.

Introduction. Saber Hussain, US Air Force, Wright-Patterson AFB, OH.

Emerging Tools and Approaches for Bridging the Gap between Exposure and In Vitro/In Vivo Dosimetry of Engineered Nanomaterials for Nanosafety Assessment. Phil Demokritou, Harvard University School of Public Health, Cambridge, MA.

In Vitro Aerosol Exposure Systems: Challenges in Dosimetry and Strategic Solution. Trevor Tilly, Air Force Research Lab, Wright-Patterson AFB, OH.

Workshops

Tools, Frameworks, and Approaches for Translation of Nanomaterial Exposure, Doses, and Responses between *In Vitro* and *In Vivo* Systems for Safety Assessment. Justin Teeguarden, Pacific Northwest National Laboratory, Richland, WA.

Advanced Computational Modeling for *In Vitro* Nanomaterial Dosimetry. Glen Deloid, Harvard University, Cambridge, MA.

***In Vitro* Dosimetry Modeling Will Be a Critical Step Toward Efficient Assessment of Engineered Nanomaterials for Environmental Health and Safety Implications.** William K. Boyes, US EPA, Research Triangle Park, NC.

Medical Device Biomaterials: Challenges in Assessing the Toxicity and Biocompatibility of Nanomaterials, Bioabsorbables, and Tissue Scaffolds

Wednesday, March 16, 2:00 PM to 4:45 PM

Chairperson(s): Niranjan S. Goud, Boston Scientific Corporation, Spencer, IN; and Peter L. Goering, US FDA, Silver Spring, MD.

Endorser(s):

**Association of Scientists of Indian Origin Special Interest Group
Medical Device and Combination Product Specialty Section
Nanotoxicology Specialty Section**

During the last two decades, there has been an increase in the use of medical devices for various diagnostic and treatment conditions in the healthcare sector. To meet this growing demand, more new and novel materials/chemicals involving cutting-edge technologies are being used in developing those devices and advanced biomaterials. The first speaker will begin the discussion on the toxicological impact of such device materials on patient health. Sometimes, while short-term biocompatibility studies utilizing ASTM and ISO 10993 methods may show passing results, but the long-term implant studies may fail. Given the complex characteristics of these new medical devices, the host defense system, including inflammation (innate immunity), acquired immunity, and foreign body reactions must be considered in determining biocompatibility (safety) and efficacy (function). Relationship of surface chemistries to reduction or enhancement of adverse response to the activity of macrophages, lymphocytes, and giant cells will be explored. The next talk will focus on how nano particles are being used for localization and treatment of cancer. The role of nanocomposite materials and stem cells in the development of artificial human organs such as trachea, facial organs, coronary grafts, and heart valves will be discussed. The current status on potential cytotoxicity of nanoparticles will be reviewed and how results from testing of ultra-high concentrations (which are in no way related to the actual doses used in clinic) are creating unnecessary alarm in the public. Discrepancies between *in vitro* and *in vivo* results involving nanomaterials will be described along with the need for a unifying protocol for reliable and realistic toxicity studies. The third speaker will provide insights into a fascinating field of 3-D polymer scaffolds for tissue engineering. Experimental data will be presented on the use of stereolithography-based fabrication with polymers (polylactic acid, polypropylene fumarate, and chitosan, etc.) to simulate internal structure of hepatic lobule and liver vasculature for tissue regeneration, wound healing, and personalized medicine. But

these technologies have their own unique challenges, such as sterility, presence of contaminants, bioabsorbable polymers, or monomers, and toxicity of photoinitiator compounds. There will be a discussion on how careful optimization of resin formulation can lead to elimination of cytotoxicity without compromising the accuracy and high resolution of fabrication. Next, the focus will be shifted from materials to fully processed and sterilized devices. Examples of how the presence of detergents, metallic ions, or sterilization residues from processing steps during manufacture can result in biocompatibility test failures. There will be discussion on case studies with anomalous test results involving cytotoxicity, hemocompatibility, and systemic toxicity, and their impact on patient health. Finally, the last speaker from notified body DEKRA will provide an overview of the regulatory approval process for marketing of medical devices in different EU countries and compliance with the Medical Device Directive. The role of European Medicines Agency in the review of devices containing drugs, pharmaceuticals, biologics, or biotechnology products. This will be followed by a discussion on the recently released guidance by the European Commission's SCENIHR to assess human health risks of medical devices containing nanomaterials. In summary, this workshop will provide an overview of toxicity issues concerning nanomaterials, bioabsorbables, 3-D tissue scaffolds, and synthetic organs, and strategies to overcome them. The role of device chemistry and host defense mechanisms in long-term test failures will be addressed, as well as examples of anomalous biocompatibility test results, with a discussion of their importance in patients' health, and European guidelines for medical device approvals with special emphasis on devices containing nanomaterials.

Biocompatibility and the Foreign Body Reaction to Medical Device Materials. James M. Anderson, Case Western Reserve University, Cleveland, OH.

Nanomaterials—Their Use in Biomedical Applications Including Development of Artificial Organs: Do the Benefits Outweigh the Risk? Alexander M. Seifalian, University College of London, London, United Kingdom.

Strategies in Stereolithography-Based Fabrication and Toxicity Evaluation of 3-D Polymer Scaffolds for Tissue Engineering. Shelby A. Skoog, US FDA, Silver Spring, MD.

Biocompatibility of Medical Devices—Anomalies in Test Results: Discussion on Their Relevance to Patient Safety. Niranjan S. Goud, Boston Scientific Corporation, Spencer, IN.

Regulatory Approval of Medical Devices in Europe—Recent Guidelines on Nanomaterials. Randy Scherer, DEKRA Certification B.V., Concord, CA.

THURSDAY

Beyond Benchmark Dose: Advancing Probabilistic and Bayesian Approaches in Hazard Characterization**Thursday, March 17, 9:30 AM to 12:15 PM**

🔥 Recent Advances in Safety Assessment

Chairperson(s): Nancy B. Beck, American Chemistry Council, Washington, DC; and Annie M. Jarabek, US EPA, Research Triangle Park, NC.

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

The National Academies (NRC) and other expert review bodies have frequently recommended that hazard assessments use Bayesian or probabilistic approaches in evaluating uncertainty and/or variability in hazard characterization. Most recently, in a 2014 review of EPA's Integrated Risk Information System (IRIS) program, the NRC reiterated its suggestion to use Bayesian analyses to inform quantitative judgments about hazard and dose response. In this report, unlike other reports on the IRIS program, the NRC provided specific examples illustrating how such approaches could be incorporated. Similarly, the WHO/IPCS has also provided recent advice on using probabilistic approaches to characterize hazards in lieu of point estimates. In addition, computational approaches are progressing that provide for description of key events in a prognostic fashion that can facilitate the application of advances in systems biology as well as meta-analysis and data integration. Such computational approaches offer the promise of network analyses and leveraging of new data streams in a read-across fashion. This workshop session will explore the recent recommendations provided by both NAS and WHO and will illustrate with case studies how these approaches, as well as other probabilistic and Bayesian approaches, can be implemented to inform hazard assessments.

Setting the Stage: Recent Advice from the National Academies on Bayesian Analysis in Hazard Assessment. Yiliang Zhu, University of South Florida, Tampa, FL.

Bayesian Methods for Uncertainty Factor (UF) Application: Proof-of-Concept and Pitfalls. Ted W. Simon, Ted Simon LLC, Winston, GA.

Probabilistic Dose-Response Assessment: Basic Principles and General Approach Developed by the WHO/IPCS. Weihsueh A. Chiu, Texas A&M University, College Station, TX.

Leveraging High-Dimensional Data to Inform Probabilistic Dose-Response Estimates. David M. Reif, North Carolina State University, Raleigh, NC.

Consensus Modeling in Support of a Semi-Automated Read-Across Application. Richard Judson, US EPA, Research Triangle Park, NC.

Facilitated Discussion on Bayesian Approaches in Hazard Assessment. Annie M. Jarabek, US EPA, Research Triangle Park, NC.

Bringing More Science into the Process of Risk Assessment for Endogenous Chemicals with Exogenous Exposures**Thursday, March 17, 9:30 AM to 12:15 PM**

🔥 Recent Advances in Safety Assessment

Chairperson(s): William Farland, Colorado State University, Fort Collins, CO; and Angela Lynch, American Chemistry Council, Washington, DC.

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

The endogenous presence in the body of chemicals that also have exogenous exposures poses a challenge to risk assessment. Endogenous is defined as “produced internally in the body,” typically as a result of intermediary metabolic function. In current risk assessment practice, there is not a standard approach for addressing exposure to endogenous levels of chemicals or chemicals with non-anthropogenic background exposures such as those from common, natural dietary sources (“natural background”). Determination of what criteria to consider when evaluating an exogenous chemical with endogenous exposure, and how best to incorporate such information in risk assessment practices is important to all stakeholders. The task of exploring an improved risk assessment approach requires that various disciplines including physiology, toxicology, and risk assessment come together to consider key issues and methodological approaches. The objectives of this workshop include framing important questions to ask when designing and conducting such a risk assessment, assessing what is known about example endogenous chemicals including normal function and homeostatic control, presenting common modes of action (MOAs) where total dose can be considered, and evaluating current risk assessment practices for such chemicals. The workshop will evaluate opportunities for improvement of risk assessment methodology with consideration of more data and improved technologies. The workshop will also engage the toxicology community in a discussion to help define an improved approach to incorporate this knowledge into the risk assessment process for endogenous exposures.

Session Overview and Framing the Issue Through Problem Formulation: Risk Assessment Considerations When Assessing Endogenous and Exogenous Exposures to the Same Chemical. William Farland, Colorado State University, Fort Collins, CO.

What Understanding Loss of Normal Homeostatic Control of Endogenous Toxicants and Their Pathways Tells Us about Risk of Exposure. Justin Teeguarden, Pacific Northwest National Laboratory, Richland, WA.

Understanding and Assessing Modes of Action from Endogenous and Exogenous Exposure: DNA Adducts, DNA-Protein Crosslinks and Mutagenicity. James Swenberg, University of North Carolina at Chapel Hill, Chapel Hill, NC.

The Role of Endogenous Oxidative Stress in Understanding and Assessing the Mode of Action of Exogenous Exposure to Toxic Agents. James Klaunig, Indiana University, Bloomington, IN.

Workshops

Factoring Endogenous Exposures Into the Risk Assessment Process: Current Approaches and Future Challenges.

Gary Ginsberg, Connecticut Department of Public Health, Hartford, CT.

Panel Discussion/Q&A. Lynn H. Pottenger, The Dow Chemical Company, Midland, MI.

Developmental Immunotoxicology—Are We Adequately Evaluating Safety?

Thursday, March 17, 9:30 AM to 12:15 PM

 **Developmental Toxicity: Mechanisms and Evaluation**

Chairperson(s): Laine Peyton Myers, US FDA, Silver Spring, MD; and Gary R. Burleson, Burleson Research Technologies, Inc., Morrisville, NC.

Endorser(s):

Biotechnology Specialty Section
Drug Discovery Toxicology Specialty Section
Immunotoxicology Specialty Section

The developing immune system has been shown to be more vulnerable to many xenobiotics, both environmental chemicals and pharmaceutical agents, than the adult immune system. Care must be taken to select different windows of susceptibility with a thorough knowledge of the differences in the stage of critical developmental windows between humans and rodents. Sensitivity differences are critical in evaluating therapeutics to be used for pregnant females as well as for drugs prescribed for juveniles. Knowledge of the critical windows of exposure will allow an evaluation of immunotoxicity assessments important for both developmental and juvenile immunotoxicological testing. Pediatric investigation plans (PIP) are now required for both the European and the US FDA regulatory agencies and the proposed strategy must be defined in the PIP. While there is no set way to perform a thorough evaluation, assessment of immunotoxicology should consider the known mechanisms of action of the agent, observations in adult studies, and the developmental age of the intended patient population relative to immune system development.

Developmental Immunotoxicology—Introduction. Laine Peyton Myers, US FDA, Silver Spring, MD.

Developmental Immunotoxicology—The Role of the Microbiome. Rodney R. Dietert, Cornell University, Ithaca, NY.

Regulatory Concerns for Developmental Immunotoxicology. Richard Houghtling, US FDA, Silver Spring, MD.

Approaches for the Evaluation of Juvenile Toxicology. Leigh Ann Burns Naas, Gilead Sciences Inc., Foster City, CA.

Current Paradigm for Evaluation of Developmental and Juvenile Immunotoxicity Evaluations—Testing and Limitations. Gary R. Burleson, Burleson Research Technologies, Inc., Morrisville, NC.

Potential Health and Environmental Effects of Unconventional Hydraulic Fracturing

Thursday, March 17, 9:30 AM to 12:15 PM

♥ **Health and Environmental Impacts of Man-Made and Naturally Released Toxicants**

Chairperson(s): Travis Lee Knuckles, West Virginia University, Morgantown, WV; and Judith Zelikoff, New York University Medical Center, Tuxedo, NY.

Endorser(s):

Ethical, Legal, and Social Issues Specialty Section
Mixtures Specialty Section
Occupational and Public Health Specialty Section

Unconventional gas well development in the Marcellus Shale geological formation has reached an all-time high in recent years. As such, many rural communities and regions are experiencing increased industrial activities and possibly air pollutant exposures from shale gas extraction activities. The burgeoning development of unconventional gas well sites has the potential to contribute to poor outdoor and indoor air and water quality. In particular, concentrations of particulate matter (PM) in the fine (<2.5 μm , PM_{2.5}) and ultrafine (<0.1 μm , PM_{0.1}) size ranges and volatile organic compounds (VOCs) may be increased in areas surrounding drilling operations. Furthermore, water quality issues have been reported in areas of hydraulic fracturing activity. However, potential exposures to complex mixtures of toxicants and the health effects on workers and on nearby residents are poorly understood. This multi-faceted symposium will begin with a discussion on the basics of hydraulic fracturing and the potential occupational exposures. Next will be a presentation on the regulatory policies and proposals that are currently in place at the state and federal levels. The third presentation will explore the potential mechanisms of exposure to the surrounding communities. A talk on air and water chemistry and the exposome will follow, and the workshop will conclude with relevant findings in animal models on the toxicological impacts of air and water samples collected on/nearby a drilling site. This cutting-edge presentation will provide the audience with a chance to better understand unconventional gas and oil drilling and reach their own conclusions on this passionate topic.

Overview of Unconventional Oil and Gas Exploration and Production and Possible Occupational Exposures. John Snawder, National Institute for Occupational Safety and Health, Cincinnati, OH.

Current State and Federal Regulatory Policies and Proposals Regarding Unconventional Natural Gas Drilling, and the Environmental Impacts of Drill Cuttings. Terry Polen, West Virginia Department of Environmental Protection, Charleston, WV.

An Approach to Studying Potential Acute and Chronic Disease Associated with Unconventional Natural Gas Development Operations. Michael McCawley, West Virginia University, Morgantown, WV.

Hydraulic Fracturing, Chemical Constituents and the Exposome. Beizhan Yan, Columbia University, Palisades, NY.

Workshops

Wide-Ranging Toxicological Effects of Produced Water from Hydraulic Fracturing in a Mouse Model. Judith Zelikoff, New York University Medical Center, Tuxedo, NY.

Panel Discussion/Q&A. Travis Lee Knuckles, West Virginia University, Morgantown, WV.

Which Human Cell Lines Should I Use? Choosing the Appropriate Biological Systems for High-Throughput Toxicity Testing

Thursday, March 17, 9:30 AM to 12:15 PM

🔥 Recent Advances in Safety Assessment

Chairperson(s): Nisha S. Sipes, NTP/NIEHS, Research Triangle Park, NC; and Falgun Shah, Pfizer, Cambridge, MA.

Endorser(s):

In Vitro and Alternative Methods Specialty Section
Molecular and Systems Biology Specialty Section
Women in Toxicology Special Interest Group

The advent of toxicogenomics, proteomics, and high-throughput screening has provided researchers with massive amounts of information to predict *in vivo* toxicity. Recent examples of such cross-disciplinary initiatives for toxicity prediction include Tox21, ToxCast, QSTAR, and L1000. Retrospectively, to better make sense of *in vitro* to *in vivo* correlation, not only is it important to choose an adequate study design, for example, compound sets and their curated annotations, experimental dose, and time points, but also the choice of suitable cell systems that is relevant to the toxicity phenotypes of interest. Cells have different gene and protein expression patterns, metabolic capabilities, and differential perturbations to compound exposure. Approaches to address the *in vivo* toxicity predictions must address the correct cell type(s) for

the problem in question. Ultimately, there is no one universal cell line that is predictive of general or all end-organ toxicities; however, it is important to know which combination is perhaps the most predictive for the given phenotype(s) of interest. The purpose of this workshop is to bring experts from pharmaceutical and biotech industries, academic institutions, and government agencies together to discuss the selection and use of human cell models relevant to specific toxicity predictions. Discussions will encompass a broad range of toxicities (cardiotoxicity, drug-induced liver injury), chemicals (pharmaceuticals, environmental), and cell types (cell lines, primary, stem cells). Speakers will also discuss objectives, approaches, technologies, knowledge gaps, and suggestions for future research. This workshop will be of high interest to a broad audience interested in *in vitro* methods to elucidate and predict toxicological outcomes.

Workshop Introduction—Why Do We Need Different Cell Lines? Falgun Shah, Pfizer, Cambridge, MA.

Strategies for Choosing Biological Diversity for High-Throughput Toxicity Testing. Nisha S. Sipes, NTP/NIEHS, Research Triangle Park, NC.

Selecting Cell Types that Provide Transcriptomic Data Over a Broad Range of Modes of Action. George Daston, Procter & Gamble, Cincinnati, OH.

Defining Appropriate *In Vitro* Model Systems for Assessing Toxicity in Early-Product Development. Yvonne P. Dragan, Takeda, Cambridge, MA.

High-Throughput Toxicity Testing—What Do Primary Human Cell-Based Assays Provide? Ellen L. Berg, BioSeek, a division of DiscoverRx, South San Francisco, CA.

Constructing the LINCS Reference Panel of Cell Types to Characterize Small-Molecule Pleiotropy. Aravind Subramanian, Broad Institute, Cambridge, MA.



Roundtables

MONDAY

Is a “Thresholdable” Carcinogen Still a Delaney Carcinogen?

Monday, March 14, 12:30 PM to 1:50 PM

 Recent Advances in Safety Assessment

Chairperson(s): Suzanne Compton Fitzpatrick, US FDA, College Park, MD; and A. Wallace Hayes, Harvard School of Public Health, Andover, MA.

Endorser(s):

**Food Safety Specialty Section
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section**

The 1958 Food Additives Amendment to the Food, Drugs, and Cosmetic Act was a response to concerns about the safety of new food additives. Congressman Delaney believed that there was a connection between increased uses of food chemicals and the rapid increase in reported cancer cases. The Delaney Clause was a provision in the amendment that stated that no food additive shall be deemed to be safe if found to induce cancer when ingested by man or laboratory animals. It applies to all food additives, as well as pesticides used on food crops and veterinary drugs given to food animals. At the time of its enactment, the Delaney Clause may have been a reasonable standard because the comparatively crude scientific detection technology of the time precluded discovery of tiny amounts of chemicals. Additionally the mechanisms by which chemicals induce cancer were not well understood, and it was assumed that even one molecule of a carcinogen could cause harm. The Delaney Clause has been a source of controversy since its enactment. This Roundtable will debate the relevance of the Delaney Clause to the 21st century regulatory issues that US FDA and US EPA must address. Dr. Keefe from US FDA will present the issues, including the role of Delaney in the current regulatory paradigm. Dr. Hayes will moderate the debate. Some pre-formulated questions will be developed to help guide and stimulate the discussion. Dr. Dourson and Dr. Williams are both highly respected risk assessors. Each debater will present some initial arguments followed by a moderated and lively debate. The audience will be encouraged to participate.

Defining the Question. Dennis Keefe, US FDA, College Park, MD.

No, “Thresholdable” Carcinogens Should Not Be Considered Delaney Carcinogens. Gary Williams, New York Medical College, Valhalla, NY.

Yes, “Thresholdable” Carcinogens Are Still Delaney Carcinogens. Michael Dourson, Toxicology Excellence for Risk Assessment, Cincinnati, OH.

Trichloroethylene Exposure and Development of Fetal Cardiac Malformations: What Do the Data Tell Us About Inhalation Exposures Resulting from Vapor Intrusion and Potential Health Risks to Pregnant Women?

Monday, March 14, 12:30 PM to 1:50 PM

 Developmental Toxicity: Mechanisms and Evaluation

Chairperson(s): Laurie C. Haws, ToxStrategies Inc., Austin, TX; and Bob Sonawane, US EPA, Washington, DC.

Endorser(s):

**Reproductive and Developmental Toxicology Specialty Section
Risk Assessment Specialty Section
Women in Toxicology Special Interest Group**

In 2011 the US EPA developed a Reference Concentration (RfC) for trichloroethylene of 2.0 µg/m³ based on two co-critical studies. One of the co-critical studies reported a dose-dependent increase in fetal cardiac malformations (FCM) in pregnant rats exposed to TCE via drinking water throughout pregnancy. As a result of concerns about this specific endpoint, some EPA regions and states recently issued interim action levels and response recommendations for TCE exposures from vapor intrusion based on accelerated timeframes meant to be protective of the developing fetus during the 3-week period in the first trimester during which the fetal heart develops. These actions have stimulated substantial debate about this particular endpoint within the scientific and regulatory communities, with some arguing that shortcomings of the *in utero* rat study should preclude it from being used as a co-critical study in the TCE inhalation risk assessment, while others argue that the overall weight of the evidence supports the conclusion that FCM is a sensitive adverse endpoint for TCE inhalation exposure, thereby justifying the use of the *in utero* rat study as a co-critical study. This session is intended to stimulate thought-provoking and open dialogue with members of the audience during a moderated panel discussion immediately following the scientific presentations. The moderated panel discussion will incorporate state-of-the-art tools in live audience polling to stimulate discussions. The goal of the roundtable is to identify the specific areas of agreement and/or disagreement and uncertainty regarding the toxicological evidence supporting the association between inhalation exposures to TCE and the potential for FCM and, through discussion, to develop strategies to help bring clarity to these areas.

Introduction. Laurie C. Haws, ToxStrategies Inc., Austin, TX.

Developing Interim Action Levels and Response Regulations for TCE Exposures from Vapor Intrusion. Dan Stralka, US EPA, San Francisco, CA.

Evidence Supporting Fetal Cardiac Malformations As a Sensitive Adverse Effect for Inhalation Exposures to TCE. Susan Makris, US EPA, Washington, DC.

Do Toxicological and Epidemiological Data Support Concerns About Pregnant Women Being Exposed to TCE via Inhalation? John DeSesso, Exponent Inc., Alexandria, VA.

Panel Discussion/Q&A. Sean Hays, Summit Toxicology, LLP; SciPinion, LLC, Allenspark, CO.

Roundtables

WEDNESDAY

Combination Toxicology: Are We Testing the Right Things?

Wednesday, March 16, 12:30 PM to 1:50 PM

Chairperson(s): Leigh Ann Burns Naas, Gilead Sciences Inc., Foster City, CA; and Helen Haggerty, Bristol-Myers Squibb Company, New Brunswick, NJ.

Endorser(s):

Biotechnology Specialty Section

Immunotoxicology Specialty Section

Regulatory and Safety Evaluation Specialty Section

Whether it is to increase efficacy by targeting multiple pathways for the same disease or to improve safety by being able to lower doses of one or more drugs, the use of combinations of drugs in clinical development is increasing. 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 toxicology profiles, extent of toxicology characterization of the individual agents and their margins of safety, human experience with the individual agents, stage of development, etc. Notably, combination testing of drugs intended for advanced oncology indications is typically not warranted. Rather, sponsors are encouraged to obtain toxicology-related endpoints from pharmacology studies to inform the need for additional testing. This leaves open the possibility that unexpected adverse events associated with targeted, novel agents could be observed clinically. The objective of this deliberately provocative session is to provide a forum to begin to discuss the possibility that the current testing paradigms may be less useful than originally envisioned or may not be providing sufficient safety evaluation for the clinical assessment of combination drugs. The session will consider examples in which testing under existing guidance has had limited to no clinical impact, as well as examples in which potential safety issues were identified in situations where testing may not have been warranted under existing guidance.

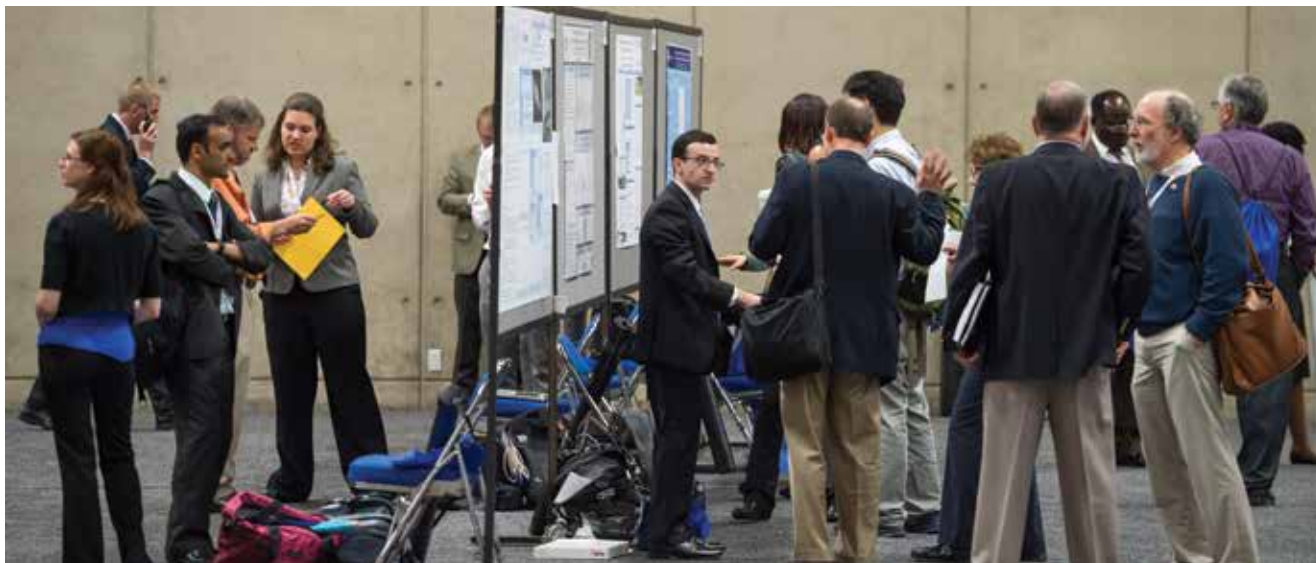
A proposal for a rational paradigm on how to address potential safety liabilities of particular drug combinations, and a framework for deciding when and how to interrogate *in vitro* or *in vivo* preclinical models in addressing combination safety will be presented by the third speaker. Examples presented will discuss incorporating safety criteria that will minimize combination toxicities for a particular target, exploring of potential synergistic toxicities in the combination of two redundant targets, and developing a preclinical model for dose-limiting clinical combination toxicity and using this model to evaluate whether an alternative target would mitigate the toxicity. The final speaker will provide a regulatory perspective on the adequacy of the current testing for oncology indications including the rationale for existing regulatory guidance. The following questions will be posed during the roundtable to facilitate the initial discussion: Is the current testing paradigm providing the appropriate investigation and adding to our understanding of the potential safety concerns for combination products? What is the most appropriate dose of each agent to test in order to adequately characterize the combination safety and protect patients? Given the limitations often encountered with crossreactivity and different animal models of disease in oncology that may impact the ability to draw concrete conclusions from these efficacy models, should greater consideration be given to evaluating the nonclinical safety of combinations of oncology drugs? If yes, is an otherwise healthy animal the appropriate model?

Non-Oncology Indications—What Have We Learned and What Impact Did It Have? Leigh Ann Burns Naas, Gilead Sciences Inc., Foster City, CA.

Combinations in Immuno-Oncology: To Test or Not To Test. Helen Haggerty, Bristol-Myers Squibb Company, New Brunswick, NJ.

Optimizing for Safe Combinations in the Discovery Space. Dolores Diaz, Genentech, South San Francisco, CA.

Regulatory Perspective on the Adequacy of Current Testing of Anticancer Therapeutic Combinations. Todd R. Palmby, US FDA, Silver Spring, MD.



Historical Highlight

MONDAY

Toxicologic Legacies of Major 21st Century Man-Made/Natural Disasters

Monday, March 14, 2:00 PM to 4:45 PM

♥ Health and Environmental Impacts of Man-Made and Naturally Released Toxicants

Chairperson(s): Mitchell D. Cohen, NYU School of Medicine/ Department of Environmental Medicine, Tuxedo, NY; and Mitsuaki Yoshida, Hirosaki University (IREM/HU), Hirosaki, Japan.

Endorser(s):

**Immunotoxicology Specialty Section
Inhalation and Respiratory Specialty Section**

Just 16 years into the 21st century, there have been a series of major man-made/natural disasters to befall the world, and each has engendered its own particular toxicologic legacy. In 2015–2016, the anniversaries of the World Trade Center disaster (15-year), the landing of Hurricanes Katrina and Rita (10-year), and the tsunami-induced disaster at the Fukushima Daiichi Nuclear Plant (5-year) will be upon us. Similarly, it will be 8 years since the great California wildfires that lasted four months and consumed >1.5 million acres. Each of these events gave rise to adverse health effects among those affected by the disasters, and many of these pathologies are still (or are becoming increasingly) evident. Over the years, clinical and laboratory-based studies have allowed the basis for many of the documented pulmonary/immuno-toxicologic effects from exposures to toxicants generated in each disaster to become clearer. The purpose of this session is to bring together experts to discuss the pulmonary/immuno-toxicologic

impacts on human health from each event; a final talk will provide attendees with information about the new NIH/NIEHS Disaster Research Response (DR2) Project and provide recommendations as to how such disasters like those covered in this session should be evaluated (i.e., what to do before, during, after) to mitigate toxicologic risks to those individuals that might be in potentially affected areas. It is expected that this session will provide attendees with the most up-to-date toxicology-related information on each of these major disasters. Accordingly, this will allow for development of better preparation paradigms to mitigate the risks to human health in the event any of these types of disasters occur again.

Introduction. Mitchell D. Cohen, NYU School of Medicine/ Department of Environmental Medicine, Tuxedo, NY.

Pulmonary/Immunotoxicologic Impacts of the WTC Disaster.

Mitchell D. Cohen, NYU School of Medicine/Department of Environmental Medicine, Tuxedo, NY.

Immuno-Toxicologic Impacts of the Fukushima Disaster.

Mitsuaki Yoshida, Hirosaki University (IREM/HU), Hirosaki, Japan.

Great California Wildfires of 2008: A Bigger Problem Than Burned Trees. Jerold A. Last, University of California Davis Medical School, Davis, CA.

Adverse Respiratory Impacts of Hurricanes Katrina and Rita.

Roy J. Rando, Tulane University, New Orleans, LA.

Integrating Health and Toxicology Research Into Disaster Responses: The New NIH Disaster Research Response (DR2) Project. Aubrey Miller, NIEHS/NIH, Bethesda, MD.

Moderated Discussion Among the Participants and Attendees.

Mitsuaki Yoshida, Hirosaki University (IREM/HU), Hirosaki, Japan.



Informational Sessions

WEDNESDAY

Tox21 Challenge To Build Predictive Models of Nuclear Receptor and Stress Response Pathways As Mediated by Exposure to Environmental Toxicants and Drugs**Wednesday, March 16, 9:30 AM to 12:15 PM**◆ **Molecular Toxicology: Mechanistic Insights and Hazard Assessment****Chairperson(s):** Menghang Xia, NCATS/NIH, Bethesda, MD; and Ruili Huang, NCATS/NIH, Bethesda, MD.**Endorser(s):****American Association of Chinese in Toxicology
Special Interest Group
Biological Modeling Specialty Section
In Vitro and Alternative Methods Specialty Section**

The Tox21 program, a collaboration between the National Institute of Environmental Health Sciences (NIEHS)/National Toxicology Program (NTP), the U.S. Environmental Protection Agency's (EPA) National Center for Computational Toxicology (NCCT), the National Institutes of Health (NIH) National Center for Advancing Translational Sciences (NCATS), and the U.S. Food and Drug Administration (FDA), has generated quantitative high-throughput screening (qHTS) data (>50 million data points) on a library of 10K compounds, including environmental chemicals and drugs, against a panel of nuclear receptor and stress response pathway assays during its production phase (phase II). NCATS organized a Challenge that asked a "crowd" of researchers to use these data as the training set for this modeling challenge to elucidate the extent to which the interference of biochemical and cellular pathways by compounds can be inferred from chemical structure data. This Challenge represents a groundbreaking new direction for toxicity testing and is intended to help improve the understanding of how chemicals could disrupt biological pathways and result in toxicity. Specifically, the computational models generated from this Challenge can be applied to predict the potential of those environmental chemicals with limited information to disrupt cellular nuclear receptor and stress response pathways. The computational models built within this Challenge are expected to improve the community's ability to prioritize novel chemicals with respect to potential concern to human health. The first presentation will give an overview of the Tox21 program, including the selection and validation of qHTS assays. The second presentation will summarize the Challenge in terms of participation (378 submissions from 18 different countries worldwide), data sets, the scoring process, and the performance of the computational models. The third to sixth presentations are from the Challenge winners who will discuss the specific methods they employed to develop the winning models.

Overview of In Vitro Assay Selection for the Tox21 HTS Program.
Menghang Xia, NCATS/NIH, Bethesda, MD.**Overview of the Tox21 Phase II Data and the Modeling Challenge.** Ruili Huang, NCATS/NIH, Bethesda, MD.**DeepTox: Toxicity Prediction Using Deep Learning.**
Günter Klambauer, Johannes Kepler University, Linz, Austria.**Consensus Approach for Modeling HTS Assays Using In Silico Descriptors.** Ahmed Abdelaziz Sayed, Technical University of Munich, Munich, Germany.**Identifying Biological Pathway-Interrupting Toxins Using Multi-Tree Ensembles.** Gergo Barta, Budapest University of Technology and Economics, Budapest, Hungary.**Construction of Discrimination Models for Identifying Compounds That Activate Toxicity-Related Proteins Based on the Rigorous Selection of Random Forest Models.** Yoshihiro Uesawa, Meiji Pharmaceutical University, Meiji, Japan.**Updating FDA's Redbook: The Importance of Stakeholder Involvement****Wednesday, March 16, 12:30 PM to 1:50 PM**🔥 **Recent Advances in Safety Assessment****Chairperson(s):** Dennis Keefe, US FDA, College Park, MD; and Yu Janet Zang, US FDA, College Park, MD.**Endorser(s):****Food Safety Specialty Section
Regulatory and Safety Evaluation Specialty Section**

The US Food and Drug Administration (US FDA) is updating its guidance titled "Toxicological Principles for the Safety Assessment of Food Ingredients," known less formally as the "Redbook." US FDA proposes to expand the scope of the Redbook to include chemical safety assessments for all products over which US FDA's Center for Food Safety and Applied Nutrition has statutory authority, including regulatory contexts such as food additives, food contact substances, dietary supplement ingredients, food contaminants, and cosmetics. This information session will introduce the proposal and engage the audience in a discussion as to how to best facilitate stakeholder involvement. The introductory presentation will give an overview about the agency's considerations underlying this proposal. With the increase in public awareness of food safety issues, US FDA must ensure its toxicology toolbox keeps pace with advances in science and technology. The time is right for US FDA to ask the question of whether or not the guidance in the Redbook used in the assessment of food ingredient safety represents an articulation and application of the best science to garner an understanding of the toxicity profile of food ingredients. US FDA recognizes the importance of stakeholder involvement in updating the Redbook and will outline its strategies for ensuring transparency and the inclusiveness of all interested parties in this endeavor. The second presentation will discuss the process by which US FDA plans to update the Redbook. The updated project is complex and large in scope. US FDA must ensure that actionable guidance, developed with extensive input from stakeholders, begins to become available as soon as reasonably possible. At the same time, stakeholders must have adequate information to understand the overall direction of the project and the context within which individual sections of the guidance will function. US FDA's plans for a "roadmap" of the overall project in conjunction with prioritization of individual sections for publication will be discussed. The third presentation will emphasize that guidance on methodologies to assess food ingredient safety must include the most up-to-date scientific approaches that will most accurately assess the safety. New knowledge and toxicological

Informational Sessions

approaches have the potential to make risk assessment more mechanistically based. However, whether these new approaches are ready to translate into changes in regulatory policies that govern human risk assessments needs to be thoroughly evaluated. Criteria for when a particular new toxicology method is validated sufficiently that it may be considered for incorporation into guidance will be discussed. The last presentation will share highlights of the International Life Sciences Institute (ILSI) North America's recommendations for Redbook enhancement from a stakeholder's perspective. Based on work undertaken by the ILSI organization, this presentation will discuss components of the Redbook that should receive the highest priority for review, new topics that are currently not addressed and should be considered for incorporation into the Redbook, and aspects of how the Redbook can be updated to more fully support the development and submission of safety assessments for substances introduced into food. As a stakeholder, ILSI believes this transparent and iterative process of the Redbook revision offers an opportunity for the US FDA to demonstrate global leadership and provide a model for global adoption of safety assessment for substances.

Why Now for the Redbook? Dennis Keefe, US FDA, College Park, MD.

Updating FDA's Redbook: The Roadmap. Jeremiah Fasano, US FDA, College Park, MD.

Integrating New Emerging Science Into the Risk Assessment Paradigm. A. Wallace Hayes, Harvard School of Public Health, Andover, MA.

Scientific Stakeholder Perspective: ILSI North America. Alison Krester, ILSI North America, Washington, DC.

Why Did the Scientific Program Committee Reject My Proposal? Developing a Good Idea Into an Accepted SOT Session

Wednesday, March 16, 12:30 PM to 1:50 PM

Chairperson(s): John B. Morris, University of Connecticut, Storrs, CT; and Patricia E. Ganey, Michigan State University, East Lansing, MI.

Endorser(s):
Scientific Program Committee

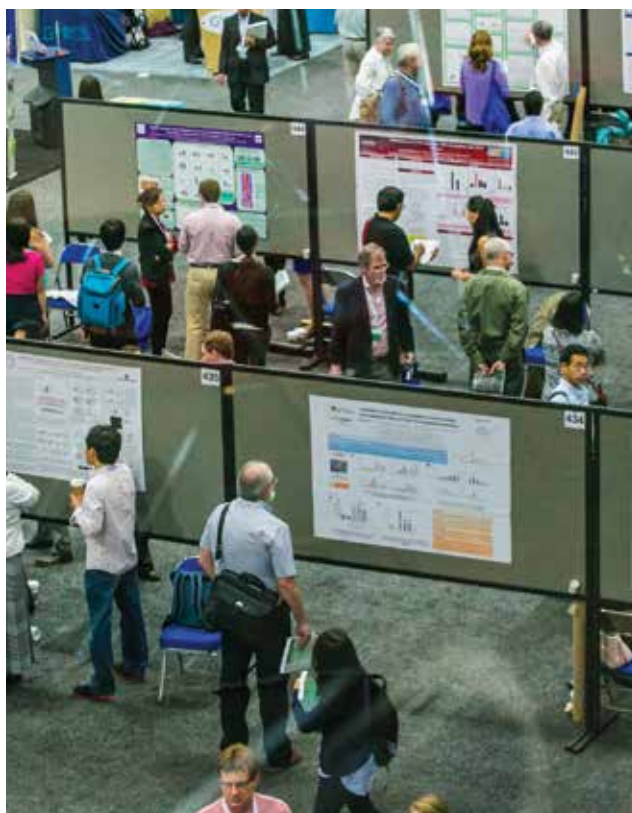
The scientific sessions at the Annual Meeting are selected from proposals submitted by the membership. In this way the Scientific Program Committee (SPC) ensures the Annual Meeting Program is responsive to the overall membership needs. Every year, many more proposals for sessions are received than could possibly be scheduled in the Annual Meeting. Thus, less than one-half of the proposals submitted for scientific sessions (symposia, workshops, informational sessions, roundtable sessions, regional interest sessions, and historical highlights) are accepted. Although many of the rejected proposals focus on a highly pertinent topic, they ultimately fail because of weaknesses in critical aspects of the submission. The SPC, which carefully considers input from SOT Specialty Sections, Special Interest Groups, and Committees (i.e., "component groups"), is responsible for selection of the scientific sessions that are presented at the Annual Meeting. This informational session is being hosted by the SPC with the objective to help members develop high-quality proposals for these scientific sessions. Participants will learn about the process by which proposals are selected to gain an appreciation for the value of working with one or more component groups during the development stage. Aspects of proposals that are critical to acceptance (thorough development of abstracts, balance among speakers, etc.), as well as those that can reduce enthusiasm, will be discussed. The session will conclude with a 20-minute question and answer period during which session attendees will be encouraged to address the speakers, all of whom are members of the SPC, in an informal setting. This session supplements the "Best Practices—Proposal Submission and Review" webinar hosted by SOT for component groups at the beginning of March.

Introduction. John B. Morris, University of Connecticut, Storrs, CT.

Another Year, Another Rejection: The Anatomy of a Bad Proposal. Mary Beth Genter, University of Cincinnati, Cincinnati, OH.

Constructing a Competitive Proposal: Increasing the Likelihood of Acceptance. Barry S. McIntyre, NIEHS, Research Triangle Park, NC.

Panel Discussion. Lisa M. Sweeney, Naval Medical Research Unit Dayton, Kettering, OH; Henry M. Jackson Foundation, Bethesda, MD; and Patricia E. Ganey, Michigan State University, East Lansing, MI.



Education-Career Development Sessions

WEDNESDAY

The Evolution of the Postdoc: Transitioning from Trainee to Professional in the Modern Era

Wednesday, March 16, 12:30 PM to 1:50 PM

Chairperson(s): Karilyn E. Sant, University of Massachusetts, Amherst, MA; and Samantha Snow, US EPA, Research Triangle Park, NC.

Endorser(s):

Career and Resource Development Committee
Graduate Student Leadership Committee
Postdoctoral Assembly

The postdoctoral experience has changed considerably over the past decade. The number of postdocs in the United States has been consistently growing, as has the time spent in this transitional position. The average age at which scientists are appointed to their first faculty job and awarded their first NIH grant has been increasing. This “hyper-competitive” culture in biomedical research has resulted in several publications and reports by the National Academies and the National Postdoctoral Association that focused on the best practices needed to improve the quality of the postdoctoral experience. This session is designed to bring leaders from across various research sectors to discuss what it means to currently be a postdoc in an academic, government, and industry setting. Speakers will focus on (1) the modern state of postdocs in their sector; (2) the advantages/disadvantages of pursuing a postdoctoral fellowship in their sector; (3) the postdoc as a mentored position; and (4) how we move forward to produce a high-quality, sustainable workforce. Each speaker will discuss how their sector is addressing the current needs of postdocs and the workforce, and will provide the audience with their thoughts on how to navigate to different career paths. Speakers will also address how a postdoc in their sector may help produce a diversified workforce. This discussion will be highly relevant to all student and postdoctoral attendees, as well as senior scientists currently mentoring trainees. This career development session will inspire toxicologists to think critically about their training and to develop an improved roadmap to navigate to their ideal careers.

Challenges, Opportunities, and Future Directions of the Traditional Academic Postdoc in Toxicology. Ilona Jaspers, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Postdoc Training: Thinking Beyond the Bench. Linda Birnbaum, NIEHS, Research Triangle Park, NC.

Pfizer’s Postdoctoral Program: An Example of an Industry’s Approach to Ensuring a High-Quality Postdoctoral Experience. Jon Cook, Pfizer, Inc., Groton, CT.

Institutional Transformation Strategies for Acceptance of Multiple Career Pathways As Successful Outcomes for Trainees in the Biomedical Research Workforce. Ambika Mathur, Wayne State University, Detroit, MI.

“Talksicology”: Effective Oral Presentation Techniques

Wednesday, March 16, 5:00 PM to 6:20 PM

Chairperson(s): Barbara L. F. Kaplan, Mississippi State University, Mississippi State, MS; and Richard Pollenz, University of South Florida, Tampa, FL.

Endorser(s):

Career and Resource Development Committee
Education Committee
Postdoctoral Assembly

Effective dissemination of research findings in seminars, interviews, scientific meetings or to the public has always been a critical skill for toxicologists. While effective oral presentation skills are formally taught in most training programs, gaps in the training exist and many programs do not measure success or offer direct evidence of effectiveness. The main goal of this workshop is to provide attendees with an opportunity to assess effectiveness, and improve their own presentations and oral communication skills. The session is designed to be engaging and interactive. The first part of the workshop will be the analysis of a “flawed” presentation in real time in which the audience will use smart phone-based technology (PollEverywhere) to rate and discuss the presentation. This exercise will be followed by short sessions from three experts for oral presentations specific to 1) a research seminar, 2) an interview, and 3) a situation in which the scientists must communicate to the media or lay public. Effective oral communication during poster presentations will also be presented. This workshop will be applicable for anyone wishing to enhance oral communication skills and is particularly pertinent to developing scientists who want to improve in this craft.

Introduction. Barbara L. F. Kaplan, Mississippi State University, Mississippi State, MS.

How Not to Engage the Audience. Richard Pollenz, University of South Florida, Tampa, FL.

Make an Impact with Your Research Seminar. Barbara L. F. Kaplan, Mississippi State University, Mississippi State, MS.

Presenting Your Research, Presenting Yourself. Lois Lehman-McKeeman, Bristol-Myers Squibb Co., Princeton, NJ.

Effectively Delivering Complex Messages to Non-Technical Audiences That Have a Short Attention Span. Steven J. Hermansky, ConAgra Foods, Omaha, NE.

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Regional Interest Session

MONDAY

The Toxicological Implications of the Gulf Oil Spill: Research Accomplishments and Research Needs**Monday, March 14, 9:30 AM to 12:15 PM**♥ **Health and Environmental Impacts of Man-Made and Naturally Released Toxicants****Chairperson(s):** Bernard Goldstein, University of Pittsburgh, Pittsburgh, PA; and Maureen Lichtveld, Tulane University, New Orleans, LA.**Endorser(s):**
Risk Assessment Specialty Section

This session will focus on existing toxicological research concerning the impact of the Gulf Oil Spill on human health, discuss the many remaining uncertainties requiring toxicological research, and review the availability to toxicological scientists of the more than \$1 billion that has or will be spent in different programs on research related to preventing and to understanding the potential impact of future oil spills affecting American coastal waters and communities. More than five years ago the Deepwater Horizon explosion released millions of barrels of oil into the Gulf of Mexico over a five-month period. The chemical and physical characteristics of this crude oil changed over time because of its interaction with sea, shore, and sun. Much of it was burned at sea, releasing combustion products. An unprecedented amount of a chemical dispersant sprayed on the oil spill added to the potential toxicological implications. The potential impact on seafood safety also has been a significant issue with concern both about health effects to those ingesting seafood as well as the economic and social implications to Gulf communities dependent on gathering seafood. After the spill, a Society of Toxicology Working Group developed a two page description of the toxicological implications aimed broadly at the public and at decision makers: www.toxicology.org/pubs/docs/pr/toxtopics/deepwater_oil_spill.pdf. This serves as a baseline for the proposed seminar that will be co-chaired by Maureen Lichtveld, the chair of the Department of Global Environmental Health Sciences at Tulane University School of Public Health and Tropical Medicine, who has been actively involved in the oil spill response, and Bernard Goldstein of the University of Pittsburgh, who has reviewed the subject with Dr. Lichtveld (*New Engl J Med* 364:1334–1348, 2011) and has been significantly involved in three of the programs funding oil spill activities. Dr. Goldstein was also involved in the SOT Communications Strategy that led to the SOT Working Group document.

The opening presentation will be delivered by Linda Birnbaum, director of the NIEHS, who will provide an overview of the NIEHS response that has led to funding for the large majority of oil spill toxicological research and for future research needs. This will be followed by scientists directly involved in research related to the oil spill. Cornelius Elferink of the University of Texas Medical Branch will present studies related to petrogenic PAH contamination in Gulf seafood and its implications to local seafood consumers, including use of a PAH assay dependent on aryl hydrocarbon receptor responsiveness. Jeffrey Wickliffe will present information from the NIEHS consortia (Tulane, Texas Medical Branch, University of Florida and Louisiana State University) relevant to assessing the risks of seafood contamination. Maureen Lichtveld will discuss the utilization of toxicological research in epidemiological studies evaluating the impact of the oil spill and other Gulf area stressors on the health of vulnerable populations. Last, Bernard Goldstein will build upon the previous presentations, discuss the extent to which toxicological research has provided answers to the questions about potential human health impacts raised by the SOT Working Group, and describe the many active research initiatives providing funding for oil spill research and critique the extent to which toxicological research has been included.

Gulf Oil Spill Response: Health Research, Community-Academic Partnerships, Lessons Learned, and Future Preparedness.

Linda S. Birnbaum, NIEHS, Research Triangle Park, NC.

A Toxicological Assessment of Petrogenic PAH Contamination in Gulf Seafood Following the Deepwater Horizon Oil Disaster.

Cornelis J. Elferink, University of Texas Medical Branch, Galveston, TX.

Human Health Risk Assessments Regarding Consumption of Fish and Shellfish From the Northern Gulf of Mexico Following the Deepwater Horizon Accident: Results Across Three Academic Research Consortia.

Jeffrey Wickliffe, Tulane University, New Orleans, LA.

Linking Bench to Trench: Embedding Toxicological Science in Environmental Epidemiologic Studies to Unravel Complex Health Threats in Gulf Coast Reproductive-Age Women and Infants.

Maureen Lichtveld, Tulane University, New Orleans, LA.

Opportunities and Needs for Toxicological Research Related to the Gulf Oil Spill.

Bernard Goldstein, University of Pittsburgh, Pittsburgh, PA.

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ReachBio

Ricerca Biosciences LLC

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Royal Society of Chemistry

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Science/AAAS

SciKon Innovation, Inc.

SCIREQ, Inc. (Scientific Respiratory Equipment)

Seahorse Bioscience

SenzaGen AB

Sequani Limited

Seventh Wave

Shanghai InnoStar Biotech Co., Ltd (InnoStar)

Shanghai Institute of Materia Medica, Chinese Academy of Sciences

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Exhibitor-Hosted Sessions

MONDAY

US EPA and Unilever Present New Research Collaboration to Advance Nonanimal Approaches for Chemical Risk Assessment

Monday, March 14, 9:00 AM to 10:00 AM

Presented by:

US Environmental Protection Agency

US EPA and Unilever will present progress on a research collaboration to develop ground-breaking scientific approaches to better assess the safety of chemicals found in some consumer products without using animal data. US EPA and Unilever are developing a series of case studies based on chemicals of mutual interest.

Advantages in Utilizing an Integrated *In Silico* Solution for ICH M7 Expert Review

Monday, March 14, 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 their views on the benefits of utilizing an integrated *in silico* solution to comply with the ICH M7 guidelines.

Continuing Advancements for *In Vitro* and *In Vivo* Medical Device Hemocompatibility Testing

Monday, March 14, 10:30 AM to 11:30 AM

Presented by:

American Preclinical Services

The *in vivo* thrombogenicity test is a method for screening blood contacting medical devices for thrombogenicity. The results are used to aid in the generation of safety data. The *in vivo* test is a screening designed to determine the thrombogenicity in comparison to a predicate device already on the market.

Essential Elements and Considerations for Neurotoxicity Study Designs: Excerpts from the presentation given to the US FDA on September 16, 2015

Monday, March 14, 10:30 AM to 11:30 AM

Presented by:

NeuroScience Associates, Inc.

As the session title suggests, the focus of this presentation and discussion will be essential elements for thorough assessment of neurotoxic effects of any insult to the brain. The presentation given here summarizes the presentation given by Dr. Switzer, at the US FDA on September 16, 2015.

Key Considerations in the Safety Evaluation of Drugs Targeting Immune Checkpoints

Monday, March 14, 10:30 AM to 11:30 AM

Presented by:

Envigo

Checkpoint inhibitors are a new and exciting class of therapeutics. As with any drug that targets the immune system, careful consideration in the design and execution of study programs are required. The session is aimed at safety assessment professionals keen to learn more about the subject matter.





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Exhibitor-Hosted Sessions

Biomarker Immunoassays: To Validate, or Not to Validate, That Is the Question

Monday, March 14, 1:30 PM to 2:30 PM

Presented by:
Charles River

The increased reliance on biomarkers to evaluate the toxicity and/or efficacy of new drugs during preclinical toxicology studies has driven routine validation of new analysis methods. Use of commercial immunoassay kits offers advantages, as the methods are usually functional. Some, however, require optimization of the methodology to suit regulatory compliance.

Do You See What Eye See? Ocular Distribution for Exposure Assessment

Monday, March 14, 1:30 PM to 2:30 PM

Presented by:
MPI Research

We use our eyes to understand the world around us, which is why diseases that distort or destroy our vision can be so devastating. This seminar will discuss a variety of *in vivo* and *ex vivo* biodistribution modalities to help you “see” your compound in the ocular space.

ICH M7—Dealing with Genotoxic Impurities

Monday, March 14, 1:30 PM to 2:30 PM

Presented by:
BioReliance

BioReliance will provide an overview of this legislation and go into detail on what are genotoxic impurities and why be concerned. We will then elucidate on what approaches and specific assays are acceptable per the guideline and BioReliance’s experience and recommendations on the proper assay designs.

CASE Ultra: Combining Statistical and Rule Based Methodologies

Monday, March 14, 3:00 PM to 4:00 PM

Presented by:
MultiCASE Inc

MultiCASE Inc, the leading provider of *in silico* toxicology solutions for chemical and pharmaceutical industries, will share its experience in implementing and combining statistical and expert rule-based methodologies for better performance and regulatory acceptance. Highlights, interpretation scenarios, and case studies will be presented.

Cryopreserved Human Enterocytes and Hepatocytes for the Evaluation of Adverse Drug Properties

Monday, March 14, 3:00 PM to 4:00 PM

Presented by:
In Vitro ADMET Laboratories LLC

Orally administered xenobiotics are subjected in intestinal metabolism/absorption and hepatic metabolism/systemic circulation. The isolation and characterization of human and animal enterocytes, and the application of enterocytes in conjunction with hepatocytes to define adverse drug properties including metabolism, drug-drug interactions, and toxicity will be described.

The Miniature Swine As a Model in Translational Medicine: Clinical and Pathology Evaluations

Monday, March 14, 3:00 PM to 4:00 PM

Presented by:
Sinclair Research Center

The use of miniature swine as a nonrodent species in safety assessments has continued to expand, and they are becoming routinely used as a model for human diseases. The specific features of the miniature swine, their impact on pharmacotoxicology, and clinical and anatomic pathology data will be presented.



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SOT Exhibitor Hosted Session

Continuing advancements for *in-vitro* and *in-vivo* medical device hemocompatibility testing

Presented by Kent Grove

March 14, 2016 - 10:30 am
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Exhibitor-Hosted Sessions

Multiplexed Assays for Flow Cytometry: Case Example of Mode of Action Determination for Genotoxic Agents

Monday, March 14, 3:00 PM to 4:00 PM

Presented by:
Litron Laboratories

The MultiFlow™ family of kits enables fast, reliable, high-throughput, high-content flow cytometry-based analyses. The MultiFlow DNA Damage kit—p53, γH2AX, phospho-histone H3 is a multiplexed, add-and-read assay that provides classification of compounds based on genotoxic mode of action. Information on related kits will also be provided.

TUESDAY

Advances in the Use of Bioprinted 3D Human Liver Tissues for the Assessment of Drug Induced Liver Toxicity

Tuesday, March 15, 9:00 AM to 10:00 AM

Presented by:
Organovo

3D bioprinted tissues exhibit architectural and functional features that mimic key aspects of a natural tissue environment, allowing for generation of clinically translatable toxicity data from biochemical, genomic, metabolic and histologic endpoints. Several case studies using bioprinted liver tissues for toxicity testing will be presented.

Dealing with Uncertainty: Science based Solutions to the Challenges of Worldwide Agrochemical Registration

Tuesday, March 15, 9:00 AM to 10:00 AM

Presented by:
Envigo

The session will discuss the roadmap for successful registration and registration of agrochemical products. Case studies will be discussed which highlight the relevant human and environmental safety studies conducted in support of regulatory submissions, the submission process itself in different jurisdictions and how to plan for a successful registration.

Efficiently Generating Reliable Toxicological Data on Protein Therapeutics

Tuesday, March 15, 9:00 AM to 10:00 AM

Presented by:
Altasciences

The complex nature of protein/peptide therapeutics can affect the integrity of toxicokinetic data and how it should be interpreted. Through case studies, this session will demonstrate how concerns directly relevant to the generation of toxico/pharmacokinetic and pharmacodynamic data can be addressed by innovative and proactive bioanalytical method development.

Ocular Gene and Cell Therapy Safety Studies: Critical Ophthalmology Endpoints to Consider

Tuesday, March 15, 9:00 AM to 10:00 AM

Presented by:
MPI Research

Gene and cell therapies are making significant advances in preclinical and clinical development for management of various diseases in ophthalmology. Familiarization with current ocular therapeutic strategies, common intraocular dosing routes, and eye-specific safety endpoint assessments will help you successfully develop your IND-enabling study designs.

Combining Real-Time Measurement of Cell Viability and Extraction of RNA from the Same 3D Spheroids

Tuesday, March 15, 10:30 AM to 11:30 AM

Presented by:
Promega Corporation

Promega developed a new luminescent assay technology to measure viable cell number in real time. We'll describe an efficient experimental approach to use the same 3D spheroids for measuring the real-time onset of cytotoxicity and extracting RNA to detect changes in gene expression associated with events leading to cytotoxicity.



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Exhibitor-Hosted Sessions

Conducting Aerosol and Vapor Inhalation Studies Using Highly Hazardous Chemical Agents: A Case Study of Sulfur Mustard (HD) Vapor Inhalation to Swine**Tuesday, March 15, 10:30 AM to 11:30 AM****Presented by:**
Battelle

In animal models it's critical to have stable aerosol or vapor concentration control for inhalation testing of highly hazardous compounds delivered inhalation in order to evaluate potential treatments. The considerations taken to meet these requirements and a case example system to deliver HD vapor to swine will be discussed.

Corning HepatoCells and 3D Organotypic Spheroid Culture Systems for Predicting Drug Induced Liver Toxicity**Tuesday, March 15, 10:30 AM to 11:30 AM****Presented by:**
Corning Life Sciences

This session will introduce Corning HepatoCells, a renewable human hepatocyte-like cell for ADME/Tox studies. Data will be presented demonstrating HepatoCells ability to detect a wider range of known toxins compared to other liver cell models such as HepG2, as well as the improvement in sensitivity with 3D organotypic spheroid cultures.

Inflammation—Discovery to Toxicology**Tuesday, March 15, 10:30 AM to 11:30 AM****Presented by:**
Charles River

Recent advances in immunology and knowledge of mechanisms involved in inflammation raise hope for developing more effective treatments of autoimmune diseases, including arthritis. This session will briefly explore recent advances in inflammation, and highlight the importance of selecting appropriate *in vitro* and *in vivo* models for research.

The Next Generation of Cardiomyocyte Contractility, Cell Migration, and Cell Viability Assays using the Sony SI8000 Live Cell Imaging Platform**Tuesday, March 15, 12:00 Noon to 1:00 PM****Presented by:**
Sony Biotechnology Inc.

The Sony SI8000 Cell Motion Imaging System combines high-speed video microscopy with a motion vector algorithm to quantify cell motion. This new platform provides high resolution cardiomyocyte contractility analysis making it ideal for toxicology screening. Easily adapt the platform to assays such as cell migration, cell death, and viability assays.

Can We Learn More from Our Göttingen Minipig Toxicology Studies?**Tuesday, March 15, 1:30 PM to 2:30 PM****Presented by:**
Ellegaard Göttingen Minipigs and CiToxLAB Scantox

Strategies to evaluate cardiovascular, respiratory, and central nervous system pharmacology using the Göttingen minipig will be presented.

Complete CV Assessment, *In Vitro* through *In Vivo***Tuesday, March 15, 1:30 PM to 2:30 PM****Presented by:**
ChanTest and Charles River

This presentation will describe complete preclinical cardiovascular assessment, including *in vitro*, *in silico*, and *in vivo* assessments, and introduce arrhythmia detection. We will discuss both prospective and retrospective cases, highlighting the added sensitivity of PK/PD modeling. The forum will also showcase the latest approaches in socialized telemetry.

XposeALI—Setting a New Standard for ALI Cell Exposures**Tuesday, March 15, 1:30 PM to 2:30 PM****Presented by:**
Inhalation Sciences Sweden AB

Combining PreciseInhale and its module for ALI cell exposures, XposeALI, provides new possibilities for researchers to study inflammatory and toxic effects of cells exposed to airborne particles. Listen to Dr. Per Gerde describe his ground breaking technology and Dr. Lena Palmberg (Karolinska Institute) explain its possibilities when studying nano particles.



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Exhibitor-Hosted Sessions

Practical Application of a Human Stem Cell Assay for Developmental Toxicity Testing

Tuesday, March 15, 3:00 PM to 4:00 PM

Presented by:
Stemina Biomarker Discovery

DevTOX quickPredict is a reliable, human stem cell screen for developmental toxicity. Using two structurally related compound series, we will demonstrate practical application of our assay for series ranking and enhancing read across and weight of evidence approaches for toxicity assessment. Additionally, ongoing collaborations and validation efforts will be discussed.

Implementation of ICH M7 Recommended (Q)SAR Analyses

Tuesday, March 15, 4:30 PM to 5:30 PM

Presented by:
Leadscope Inc., Lhasa Limited, and MultiCASE Inc.

This session outlines principles to consider when generating a (Q)SAR assessment consistent with the ICH M7 guideline. Presentations will cover when an expert opinion might be beneficial, what it may contain, and how the prediction results and accompanying opinions may be documented.

WEDNESDAY

In Vitro Toxicology and Integrated Toxicology—What Are These?

Wednesday, March 16, 9:00 AM to 10:00 AM

Presented by:
Charles River

In vitro toxicology tests utilize mammalian tissues. Acceptance and regulatory demand for these is increasing with validation testing leading to OECD guidelines. AOPs provide mechanistic approaches that can lead to test banks. These are part of integrated testing strategies allowing products to be brought to market more rapidly and safely.

Key Considerations in the Safety Evaluation of Novel Therapeutic Modalities for Oncology

Wednesday, March 16, 10:30 AM to 11:30 AM

Presented by:
Envigo

The session will address the development of novel cancer drugs, how the drug development landscape is changing. This educational, interactive forum will highlight recent advances in novel cancer therapies including ADCs. Preclinical and regulatory considerations will be discussed, and case studies shared highlighting developments in the field.

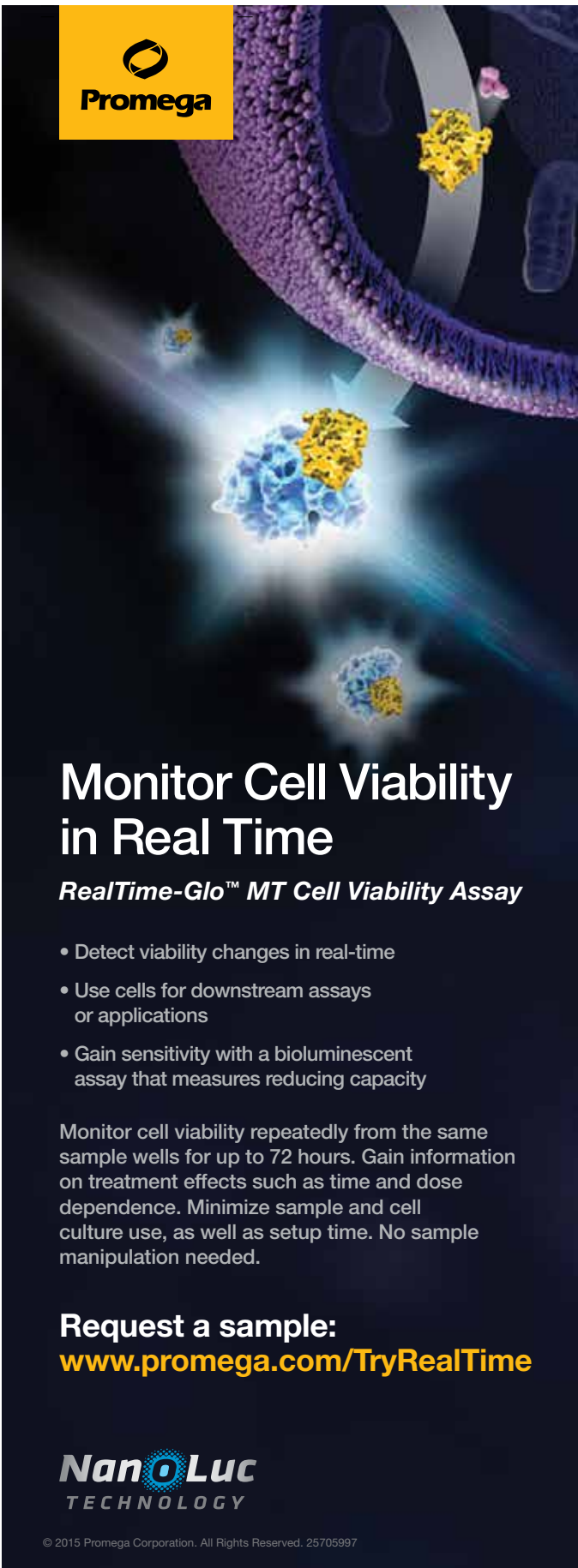
Behavioral and Neurological Assessments in the Miniature Swine

Wednesday, March 16, 4:30 PM to 5:30 PM

Presented by:
Sinclair Research Center

The miniature swine are becoming routinely used in toxicology as a nonrodent species for neurobehavioral and neurotoxicology assessments, as well as a model for human neurological and neurodegenerative diseases. The important behavioral and neurological features of the miniature swine will be presented in the perspective of drug safety evaluations.





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Society of Toxicology

56th Annual Meeting and ToxExpo™

Baltimore, Maryland

March 12–16, 2017
Baltimore Convention Center



2017 Annual Meeting Session Proposal Deadline: April 30, 2016

Why Submit a Proposal?

1. To present new developments in toxicology
2. To provide attendees with an opportunity to learn about state-of-the-art technology and how it applies to toxicological research
3. To provide attendees with an opportunity to learn about the emerging fields and how they apply to toxicology

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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Support Opportunities

Annual Meeting support serves as visible evidence of an organization's commitment to the Society's mission of "creating a safer and healthier world by advancing the science and increasing the impact of toxicology." Moreover, support provides an opportunity for private, public, and not-for-profit organizations to increase overall awareness of their services and programs to SOT members and Annual Meeting attendees. Supporters are acknowledged in pre- and postmeeting newsletters, publications including the *Preliminary Program*, the *Program*, *ToxExpo Directory* and in the Mobile Event App. Supporters are also recognized via signage prominently displayed throughout the meeting, including in scientific session rooms. Supporters at the Silver Level and above receive invitations to the SOT President's Reception, an invitation-only event for those who have generously contributed to the Society.

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Five levels of support are available:

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