Dear Colleagues:

The planning for the 2021 SOT Annual Meeting and ToxExpo has been unique. SOT Council, the Scientific Program Committee, and an Annual Meeting Task Force, all aided by our hardworking headquarters team, explored how to take a 6,000+ attendee event online and still maintain scientific discourse, time for personal connections and networking, access to service and product providers, and opportunities for professional development. It has been quite an undertaking, but I am confident that you will be pleased with the results.

What’s the Same in 2021?

You can expect the same level of scientific quality as with past SOT annual meetings. The 65+ Featured and Scientific Sessions were already approved and scheduled before we made the decision to go virtual. You also will have chances to interact with speakers and presenters through chats and question-and-answer times.

In addition, SOT is busy programming social events and activities, such as Regional Chapter, Special Interest Group, and Specialty Section meetings and receptions; student- and postdoc-focused opportunities; and more.

The 2021 SOT Award recipients will be recognized and honored during the Virtual Annual Meeting as well, including delivery of Award Lectures.

Finally, the Virtual ToxExpo will allow attendees to interact with service and product providers to develop collaborations and relationships that benefit toxicology.

What’s New in 2021?

Of course, having an online venue for the meeting is entirely new, but our virtual platform is not just a cookie-cutter environment. We are using customized features and multiple types of technology to provide a quality and engaging experience for SOT meeting participants.

To accommodate the worldwide attendance that occurs during an SOT meeting, we are reducing the hours of each meeting day but expanding the number of days to allow for the presentation of a full scientific program; we also will be making all sessions available for on-demand viewing. Taking place from Friday, March 12, to Friday, March 26, 2021, the Virtual Annual Meeting will feature approximately five hours of activity from 10:00 am to 4:00 pm (EDT, UTC -4) each day, including Scientific Sessions, virtual exhibits, and more. Fridays have been reserved for Continuing Education courses, which should permit participants to attend more courses than would be possible during a typical SOT meeting. Events that usually occur before or after hours, such as Component Group receptions, will continue to occur outside the main meeting time frame each day.

While many of the Scientific Sessions will be formatted and presented in familiar ways, the 2021 posters will have a new twist. Poster presenters will be able to pair an audio recording with their poster, allowing anyone who visits the poster outside the author-attended Poster Session to gain additional insight.

To capture the impromptu conversations that often happen in hallways and lobbies during an in-person event, the Virtual Meeting will utilize networking lounges to allow attendees to take a break from the scientific program and engage in social interactions. There will be multiple lounges as part of the platform, and each will be themed around topics or activities of interest. These areas also will allow attendees to enter private rooms to conduct short meetings and exchanges.

Over the next few months, we will provide many sneak peeks into the Virtual Meeting platform (the Poster Session sneak peek is available now), will announce new events and activities, and will unveil more details about those already scheduled.

I hope you will join SOT in March 2021 for the opportunity to explore influential research and interact with the amazing SOT community in a new way.

Sincerely,

George P. Daston
PhD
2020–2021 SOT President
Dear Colleagues:

As is fitting for a year in which effective science communication has proven to be a critical need, I am excited to announce that the 2021 Opening Plenary Session speaker is Laura Lindenfeld, PhD, the Executive Director of the Alan Alda Center for Communicating Science at Stony Brook University. In her presentation, titled “Blending Art and Science to Master Science Communication,” Dr. Lindenfeld will introduce the SOT Virtual Meeting attendees to the science underlying the art of the Alda Center’s unique approach to science communication. Science communication is a priority of the SOT Strategic Plan, and I anticipate that Dr. Lindenfeld’s presentation will serve as the flagship for additional resources that SOT will provide for members wishing to master effective communication of our science. Don’t miss the start of the Virtual 2021 Annual Meeting and Dr. Lindenfeld’s presentation on Monday, March 15, at 10:00 am (EDT, UTC -4).

I also am pleased to confirm that the Virtual 2021 Annual Meeting will continue our partnerships with the Medical Research Council (MRC), EUROTOX, and the Japanese Society of Toxicology (JSOT) to present unique topics and discussions:

- **SOT/EUROTOX Debate: “Individualized Toxicity Is the Future of Risk Assessment”**
  Wednesday, March 17, 10:00 am (EDT, UTC -4)
  Debaters: Syril D. Pettit, HESI; and Alan R. Boobis, Imperial College London

- **EUROTOX Bo Holmstedt Memorial Award Lecture: “Understanding Three Fundamental Quantitative Principles Is a Prerequisite for Improving Toxicological Science and Risk Assessment”**
  Monday, March 22, 10:00 am (EDT, UTC -4)
  Lecturer: Wout Slob, Rijksinstituut voor Volksgezondheid en Milieu (RIVM), Netherlands

- **MRC Keynote Lecture: “Using Luciferase-Based Mouse Reporter Lines to Detect and Track Epigenetic Changes Induced by Environmental Exposures”**
  Tuesday, March 23, 10:00 am (EDT, UTC -4)
  Lecturer: Dame Amanda Fisher, MRC London Institute of Medical Science

- **SOT and JSOT Symposium: “Oxidative Stress in Multiple Manifestations of Toxicity”**
  Wednesday, March 24, 5:30 pm (EDT, UTC -4)
  Speakers: Yoshito Kumagai, University of Tsukuba, Japan; Yoshiro Saito, Tohoku University, Japan; Alicia R. Timme-Laragy, University of Massachusetts Amherst; and Dean P. Jones, Emory University

The SOT Award Lectures and other Featured Sessions will be announced later this month and into February 2021.

In addition, SOT looks forward to presenting the Symposium Session “Environmental Risk Assessment of PFAS” alongside its new partner, the Society of Environmental Toxicology and Chemistry (SETAC). This session, on Tuesday, March 23, at 2:45 pm (EDT, UTC -4), will mirror a Special Session on the same topic and with the same speakers that took place during the SETAC SciCon, in November 2020.

Register now to join SOT for these Featured Sessions, as well as the 60+ additional Scientific Sessions, networking opportunities, and more taking place as part of the Virtual 2021 SOT Annual Meeting and ToxExpo.

Sincerely,

Myrtle Davis, DVM, PhD, ATS
2020–2021 SOT Vice President and Scientific Program Committee Chair

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Up-to-date info at [www.toxicology.org/2021](http://www.toxicology.org/2021) | #2021SOT | #ToxExpo
Use the SOT Online Planner to Review the Latest Virtual 2021 Annual Meeting Schedule and Plan Your Virtual Meeting Attendance

Key Features of the Online Planner

- Your personalized schedule
- All abstracts and author blocks
- All presenters
- Access to Exhibitors and Planner Tutorials

Ways to Customize Your View of the 2021 Schedule

- Close menu to increase viewing window size
- Search by key word, presenter name, and more

- Access your bookmarked events
- View your notes about events
- Review your personalized schedule
- View the events on a specific day
- Filter the schedule by event type
Use the Online Planner and Build a Customized Meeting Schedule

Online Planner Tips and Tricks

- Use the email/password from your Annual Meeting registration to unlock the customizable features of the Online Planner.
- Add event to your schedule.
- Bookmark event to find easily in future.
- Select to view more information on the event.
- Share event info via email or social media.
- Add event to your schedule.
- Bookmark event to find easily in future.
- Add notes before, during, or after the event.
Virtual Program Preview

Session Types (Listed by date, then time, then session type)

- Continuing Education Courses
- Education-Career Development Sessions
- Featured Sessions
- Informational Sessions
- Poster Sessions
- Roundtable Sessions
- Symposium Sessions
- Workshop Sessions

For the most up-to-date information on all Annual Meeting sessions, events, and activities, consult the Online Planner on the Annual Meeting website.

Friday, March 12

9:30 AM to 10:30 AM
CONTINUING EDUCATION COURSE  CE
CE01 Chemical Probes: New Tools to Identify Molecular Targets
Abstract#: 1001

10:00 AM to 1:45 PM
CONTINUING EDUCATION COURSE  CE
CE05 Less Is More: Sustainable Product Development Requires More Toxicological Considerations
Abstract#: 1005

11:00 AM to 2:45 PM
CONTINUING EDUCATION COURSES  CE
CE02 Advances in Single Cell Genomic Analyses for Toxicological Testing
Abstract#: 1002
CE03 Applications of In Vitro and In Silico New Approach Methodologies for Predictive and Mechanistic Thyroid Toxicity Testing
Abstract#: 1003
CE04 Concepts and Approaches for Current and Future Metals Toxicological Research
Abstract#: 1004

Monday, March 15

10:00 AM to 11:00 AM
PLENARY SESSION  FS
Blending Art and Science to Master Science Communication
Speaker: Laura Lindenfeld, Alan Alda Center for Communicating Science, Stony Brook University, Stony Brook, NY.

11:00 AM to 4:00 PM
NETWORKING LOUNGES
- Enter these spaces to chat with other attendees, leave notes, or enter private rooms for short meetings.

TOXEXPO EXHIBITS
- Visit the Virtual Exhibit Hall for product, service, and career insights.

Don’t Be Late
Please note that the listed times for the Continuing Education courses on Friday, March 12, reflect US Eastern Standard Time (UTC -5). Events from Monday, March 15, through Friday, March 26, will occur during US Eastern Daylight Time (UTC -4). For additional information on how this time translates to other time zones, please see the World Map on page 23, which reflects time comparisons for UTC -4.

On-Demand Viewing
After a Featured or Scientific Session is presented on its assigned date and time, the session will become available for on-demand viewing through the Virtual Meeting platform.
11:15 AM to 2:00 PM

**SYMPOSIUM SESSIONS**

- Environmental Influences on Placental Origins of Development
  - Abstract#: 1015–1019
- Impaired Brain Barrier Systems: Relationship to Chemical-Induced Neurotoxicities
  - Abstract#: 1020–1025
- Industrial Applications of Artificial Intelligence in Toxicology
  - Abstract#: 1026–1030

**WORKSHOP SESSIONS**

- A Future Framework for Application of In Vitro Metabolism and QIVIVE Models to Inform Risk Assessment
  - Abstract#: 1031–1036
- Chemical-Induced Mouse Lung Tumors: Mode of Action, Relevance, and Risk Assessment
  - Abstract#: 1037–1042
- Establishing Quality, Safety, and Regulatory Principles for Probiotics: More Than Just a Gut Check
  - Abstract#: 1043–1047
- Standardization of In Vitro Inhalation Exposure for Regulatory Acceptance
  - Abstract#: 1048–1053
- Using Human Genetics to Aid in Safety Assessment of Therapeutics
  - Abstract#: 1054–1060

2:45 PM to 4:05 PM

**INFORMATIONAL SESSIONS**

- Turning Over a New Leaf: An Update on the Clinical Toxicology of Synthetic Cannabinoids
  - Abstract#: 1061
- Understanding the Spread and Toxicological, Environmental, and Public Health Impact of the COVID-19 Pandemic on the African Continent
  - Abstract#: 1062

Tuesday, March 16

10:00 AM to 11:00 AM

**LEADING EDGE IN BASIC SCIENCE AWARD LECTURE**

- To be announced January 2021

11:00 AM to 4:00 PM

**NETWORKING LOUNGES**

- Enter these spaces to chat with other attendees, leave notes, or enter private rooms for short meetings.

**TOXEXPO EXHIBITS**

- Visit the Virtual Exhibit Hall for product, service, and career insights.

11:15 AM to 2:00 PM

**SYMPOSIUM SESSIONS**

- Developmental Toxicity Hazard Assessment without Animals: Pathways and Prospects
  - Abstract#: 1063–1069
- From Inhaled Particles to Neurodegeneration and Toxicity: Evidence from Studies in Volunteers, Experimental Animals, and Cell-Based Systems
  - Abstract#: 1070–1076
- Novel Emerging Treatments for Acetaminophen Toxicity
  - Abstract#: 1077–1082
- Pairing Adverse Outcome Pathway Discovery with Advances in Gene Editing to Solve Toxicity Mechanisms
  - Abstract#: 1083–1088

**WORKSHOP SESSIONS**

- Improving Our Understanding of Toxicant Metabolism and Cytochrome P450s Using Novel Knockout Models and High-Throughput Methods
  - Abstract#: 1089–1094
- New Approach Methodologies for Exposure: Advancing Chemical Risk Assessment
  - Abstract#: 1095–1100
- Precision-Cut Lung Slices: A Versatile Tool for Pulmonary Toxicology
  - Abstract#: 1101–1106

Platform Sessions

These 90- or 165-minute sessions are composed of 15-minute oral presentations that cover new areas, concepts, or data. The topics and presentations for these sessions, as well as the session days and times, will be announced by February 2021.
11:15 AM to 1:00 PM
POSTER SESSIONS
• Carcinogenicity
• Epidemiology and Public Health
• Mixtures

1:00 PM to 2:45 PM
POSTER SESSIONS
• Food Safety/Nutrition
• Metals

2:45 PM to 4:15 PM
SYMPOSIUM SESSION
• Evolving Technologies for Determination of Biotherapeutic Specificity

WORKSHOP SESSION
• The Methodological Road toward Single Cell High-Throughput Transcriptomics (scHTTr)

Wednesday, March 17
10:00 AM to 11:15 AM
SOT/EUROTOX DEBATE

Individualized Toxicity Is the Future of Risk Assessment

SOT Debater: Syril D. Pettit, HESI, Washington, DC.

EUROTOX Debater: Alan R. Boobis, Imperial College London, United Kingdom.

11:00 AM to 4:00 PM
NETWORKING LOUNGES
• Enter these spaces to chat with other attendees, leave notes, or enter private rooms for short meetings.

TOXEXPO EXHIBITS
• Visit the Virtual Exhibit Hall for product, service, and career insights.

11:15 AM to 1:00 PM
POSTER SESSIONS
• Biotransformation/Cytochrome P450
• Kidney
• Liver: In Vitro
• Liver: In Vivo
Virtual Program Preview—Wednesday, March 17/Thursday, March 18

11:30 AM to 2:15 PM

SYMPOSIUM SESSIONS

- Challenges and New Approaches in Characterizing Toxicity within the Military
  Abstract#: 1115–1120
- Identifying and Communicating Adverse Neurological Outcomes from Parental Cannabis Use
  Abstract#: 1121–1126
- It Is Not Just Air: Exposure to Indoor Air Pollution, Diagnostic Tools, and Evaluation of Health Effects
  Abstract#: 1127–1132
- Mind the Gap: Finding Practical Ways to Fast-Track the Future of Animal-Free Toxicology Testing
  Abstract#: 1133–1137
- Opportunities and Challenges in Utilization of Toxicokinetic Data in Dose-Level Selection for Repeated-Dose Toxicity Studies
  Abstract#: 1138–1143
- Testing the Waters: How the Zebrafish, Xenopus, and Medaka Models Are Advancing Our Understanding of Reproductive and Developmental Toxicity
  Abstract#: 1144–1149
- The Power of Integrating Computational Toxicology with Multiparametric In Vitro Assay Systems
  Abstract#: 1150–1155

1:00 PM to 2:45 PM

POSTER SESSIONS

- Nanotoxicology: In Vitro
- Nanotoxicology: In Vivo
- Nanotoxicology: Methodologies and Assessments
- Systems Biology

2:45 PM to 4:15 PM

SYMPOSIUM SESSIONS

- Across the Life Span: Emerging Mechanisms of Prenatal and Transgenerational Toxicity
  Abstract#: 1156–1159
- Nonclinical Safety Toxicology Strategies for the Development of Novel Ocular Biotherapeutics
  Abstract#: 1160–1165

2:45 PM to 4:05 PM

EDUCATION–CAREER DEVELOPMENT SESSION

- Innovation in Toxicology Training during Summer Undergraduate Internships
  Abstract#: 1166

Thursday, March 18

10:00 AM to 11:00 AM

DISTINGUISHED TOXICOLOGY SCHOLAR AWARD LECTURE

- To be announced January 2021

11:00 AM to 4:00 PM

NETWORKING LOUNGES

- Enter these spaces to chat with other attendees, leave notes, or enter private rooms for short meetings.

TOXEXPO EXHIBITS

- Visit the Virtual Exhibit Hall for product, service, and career insights.

11:15 AM to 2:00 PM

SYMPOSIUM SESSIONS

- Challenges and Opportunities in Applying Quantitative and Translational Systems Toxicology Models to Drug Safety Testing
  Abstract#: 1167–1171
- Closing the Data Gap: Assessing Population Variability Using Next-Generation Tools in Toxicology
  Abstract#: 1172–1176
- Hereditary Disorders of Manganese Metabolism: Mechanisms, Clinical Presentation, and Neurotoxicity
  Abstract#: 1177–1182

11:15 AM to 12:45 PM

WORKSHOP SESSION

- Are Aircraft Cabin Fume Releases a Cause for Toxicological Concern?
  Abstract#: 1183–1186

11:00 AM to 11:30 AM

Exibitor-Hosted Sessions

These commercially supported educational sessions will occur throughout the Virtual Annual Meeting and ToxExpo concurrently with 80- and 90-minute Scientific Sessions. As these sessions are scheduled, the Online Planner on the Annual Meeting website will be updated with the day, time, and other event details.
11:15 AM to 2:00 PM
WORKSHOP SESSIONS

- Navigating Your Health and Wellness through Graduate School and Early Careers
  \textit{Abstract#: 1187–1194}
- New Approach Methods for Cancer Risk Assessment
  \textit{Abstract#: 1195–1200}
- The Need for Protocol Harmonization in the Advancement of Zebrafish as a Model for Toxicological Screening: Global Perspectives and Recent Advancements
  \textit{Abstract#: 1201–1206}

11:15 AM to 1:00 PM
POSTER SESSIONS

- Cardiovascular Toxicology/Hemodynamics
- Chemical Threats and Bioterrorism
- Ocular Toxicology

1:00 PM to 2:45 PM
POSTER SESSIONS

- Air Pollution Toxicology I
- Air Pollution Toxicology II
- Ecotoxicology
- Epigenetics
- Regulation/Policy

2:45 PM to 3:45 PM
MERIT AWARD LECTURE

Unraveling the Molecular Mechanisms of Cannabinoid-Mediated Immune Modulation and Cannabinoid Receptor 2 as a Putative Therapeutic Target

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

2:45 PM to 4:15 PM
WORKSHOP SESSION

- Revising Biology: Alternative Splicing in Toxicology
  \textit{Abstract#: 1207–1210}

2:45 PM to 4:05 PM
ROUNDTABLE SESSION

- The Future of Uncertainty Factors with \textit{In Vitro} Studies Using Human Cells
  \textit{Abstract#: 1211}

Friday, March 19

9:30 AM to 10:30 AM
CONTINUING EDUCATION COURSE

CE06 Insider Secrets for Design and Analysis of Defined-Mixture Experiments
  \textit{Abstract#: 1006}

11:00 AM to 2:45 PM
CONTINUING EDUCATION COURSES

CE07 Development, Toxicology, and Pathology of the Female Reproductive Tract: Interpretation of Findings from the Pathologist and Regulatory Perspectives
  \textit{Abstract#: 1007}

CE08 Guidelines for Developing and Implementing Organ-on-a-Chip/Microphysiological Systems for Toxicity Evaluation of Drug Candidates in Drug Development
  \textit{Abstract#: 1008}

CE09 Navigating New Modalities: A Preclinical Roadmap for Developing Novel Oligonucleotide Safety Strategy
  \textit{Abstract#: 1009}

CE10 Rapid Chemical Assessment Using Open Computational Methods
  \textit{Abstract#: 1010}
Monday, March 22

10:00 AM to 11:00 AM
EUROTOX BO HOLMSTEDT MEMORIAL AWARD LECTURE

Understanding Three Fundamental Quantitative Principles Is a Prerequisite for Improving Toxicological Science and Risk Assessment

Lecturer: Wout Slob, Rijksinstituut voor Volksgezondheid en Milieu (RIVM), Netherlands.

11:00 AM to 4:00 PM
NETWORKING LOUNGES
- Enter these spaces to chat with other attendees, leave notes, or enter private rooms for short meetings.

TOXEXPO EXHIBITS
- Visit the Virtual Exhibit Hall for product, service, and career insights.

11:15 AM to 2:00 PM
SYMPOSIUM SESSION
- Applications of Novel High-Throughput Approaches for Mechanism-Based Chemical Safety Assessment
  Abstract#: 1212–1217

WORKSHOP SESSIONS
- New Approaches for the Identification and Evaluation of Chemical Respiratory Sensitizers
  Abstract#: 1218–1223

- Tackling the Potential Human Health Impacts of Microplastics and Nanoplastics: Challenges for Toxicologists in the Assessment of Real-World Complex Mixtures
  Abstract#: 1224–1230

- Thresholds of Toxicological Concern: Reassessing the Basis and Expanding the Horizon
  Abstract#: 1231–1236

11:15 AM to 1:00 PM
POSTER SESSIONS
- Biological Modeling
- Endocrine Toxicology
- Immunotoxicity
- Neurotoxicity: Developmental
- Neurotoxicity: General
- Reproductive and Developmental Toxicology I

1:00 PM to 2:45 PM
POSTER SESSIONS
- Bioinformatics
- Computational Toxicology I
- Risk Assessment
- Tobacco and ENDS Toxicology

2:45 PM to 3:45 PM
TRANSLATIONAL IMPACT AWARD LECTURE
- To be announced January 2021

2:45 PM to 4:15 PM
WORKSHOP SESSION
- The Community Exposome: Effects of Environmental Contamination on Health Disparities and Marginalized Populations through the Lens of a Toxicologist
  Abstract#: 1237–1241

2:45 PM to 4:05 PM
INFORMATIONAL SESSION
- Toxicology for Chemists: Preparing Chemists to Design Safer Products through Smarter Molecular Design
  Abstract#: 1242

Regional Chapter and Special Interest Group Events
The SOT Regional Chapters and Special Interest Groups can host social events from Monday, March 22, to Thursday, March 25, before 9:45 am or after 4:15 pm. These events will use dedicated Zoom rooms with all the accompanying Zoom technology, such as video chats, text messaging, virtual backgrounds, and slide presentations. The schedule for these events will be available by February 2021.
**Tuesday, March 23**

**10:00 AM to 11:00 AM**

**PLENARY KEYNOTE MEDICAL RESEARCH COUNCIL (MRC) LECTURE 🎤**

Using Luciferase-Based Mouse Reporter Lines to Detect and Track Epigenetic Changes Induced by Environmental Exposures

*Lecturer: Dame Amanda Fisher, MRC London Institute of Medical Sciences, United Kingdom.*

**11:00 AM to 4:00 PM**

**NETWORKING LOUNGES**

- Enter these spaces to chat with other attendees, leave notes, or enter private rooms for short meetings.

**TOXEXPO EXHIBITS**

- Visit the Virtual Exhibit Hall for product, service, and career insights.

**11:15 AM to 2:00 PM**

**SYMPOSIUM SESSION 🎤**

- Opportunities for Human-Induced Pluripotent Stem Cell–Derived Neurons in *In Vitro* Neurotoxicity Safety Testing
  
  *Abstract#: 1243–1247*

**WORKSHOP SESSIONS 🎤**

- Bile Acids Profiling as Biomarkers for Hepatobiliary Toxicity and Disease
  
  *Abstract#: 1248–1251*

- Molecular-Based Points of Departure as the New Basis for Chemical Risk Assessment: Are We Ready?
  
  *Abstract#: 1252–1257*

- Paving the Way for Greater Data Sharing to Advance Biomarker and Drug Development: Industry, Academia, and Regulatory Insights
  
  *Abstract#: 1258–1263*

**INFORMATIONAL SESSION 🎤**

- Strategies to Increase Global Awareness of Toxicology: Focus on Developing Countries
  
  *Abstract#: 1264*

**11:15 AM to 1:00 PM**

**POSTER SESSIONS 🎤**

- Exposure Assessment/Biomonitoring
- Neurodegenerative Disease
- PFAS
- POPs
- Reproductive and Developmental Toxicology II
- Safety Evaluation of Nonpharmaceutical Products

**1:00 PM to 2:45 PM**

**POSTER SESSIONS 🎤**

- Alternatives to Mammalian Models I
- Cell Death Mechanisms
- Computational Toxicology II
- DNA Damage and Repair
- Respiratory Toxicology
- Skin and Dermal Toxicity

**2:45 PM to 3:45 PM**

**MERIT AWARD LECTURE 🎤**

- To be announced January 2021

**2:45 PM to 4:05 PM**

**SYMPOSIUM SESSION 🎤**

- SETAC-SOT Session: Environmental Risk Assessment of PFAS
  
  *Abstract#: 1265–1268*

**INFORMATIONAL SESSION 🎤**

- Safety Assessment of Devices Used in Assisted Reproduction Technology: Mouse Embryo Assay
  
  *Abstract#: 1269*

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**Honoring Award Recipients**

The 2021 SOT Award recipients will be honored during the Virtual Annual Meeting. The SOT Awards Committee is determining the details regarding when and how this recognition will occur and will announce the details in early 2021. In addition, the SOT Component Groups will announce and honor their award recipients throughout the meeting.
Wednesday, March 24

10:00 AM to 11:00 AM
FEATURED SESSION

• To be announced January 2021

11:00 AM to 4:00 PM
NETWORKING LOUNGES

• Enter these spaces to chat with other attendees, leave notes, or enter private rooms for short meetings.

TOXEXPO EXHIBITS

• Visit the Virtual Exhibit Hall for product, service, and career insights.

11:15 AM to 1:00 PM
POSTER SESSIONS

• Alternatives to Mammalian Models II
• Biomarkers
• Clinical and Translational Toxicology
• COVID-19 Issues
• Medical Devices
• Stem Cell Biology and Toxicology

11:45 AM to 2:30 PM
SYMPOSIUM SESSIONS

• Application of Computational Genomic Approaches to Address Toxicity Mechanisms and Prediction
  Abstract#: 1270–1275
• Botanical Mixtures: Predictive Approaches to Evaluating Pregnancy, and Reproductive and Developmental Health
  Abstract#: 1276–1281

WORKSHOP SESSIONS

• Applicability Domains and Future of Nonanimal Tests for Skin Sensitization
  Abstract#: 1282–1287
• The Scientific Challenges in Regulating Organohalogen Flame Retardants (OFRs) as a Class in Consumer Products
  Abstract#: 1288–1293

1:00 PM to 2:45 PM
POSTER SESSIONS

• Disposition/Pharmacokinetics
• Education, Ethical, Legal, and Social Issues
• Neurotoxicity: Metals
• Neurotoxicity: Pesticides
• Pesticides
• Safety Assessment: Pharmaceutical—Drug Discovery

3:00 PM to 4:30 PM
SOT ANNUAL BUSINESS MEETING

• SOT members are encouraged to attend.

5:30 PM to 8:15 PM
SOCIETY OF TOXICOLOGY AND JAPANESE SOCIETY OF TOXICOLOGY SYMPOSIUM

Oxidative Stress in Multiple Manifestations of Toxicity

JSOT Speaker:
Yoshito Kumagai, University of Tsukuba, Tsukuba, Japan.

JSOT Speaker:
Yoshiro Saito, Tohoku University, Sendai, Japan.

SOT Speaker:
Alicia R. Timme-Laragy, University of Massachusetts Amherst, Amherst, MA.

SOT Speaker:
Dean P. Jones, Emory University School of Medicine, Atlanta, GA.

Student and Postdoc Events

Activities catered toward undergraduate students, graduate students, and postdocs are being planned for the Virtual Annual Meeting by various SOT Committees. These events will focus on career development, networking, mentoring, and more. Details on these activities will be available in early 2021.
Thursday, March 25

10:00 AM to 11:00 AM
FEATURED SESSION
• To be announced January 2021

11:00 AM to 4:00 PM
NETWORKING LOUNGES
• Enter these spaces to chat with other attendees, leave notes, or enter private rooms for short meetings.

TOXEXPO EXHIBITS
• Visit the Virtual Exhibit Hall for product, service, and career insights.

11:15 AM to 1:00 PM
POSTER SESSIONS
• Animal Models
• Autoimmunity/Hypersensitivity
• Inflammation
• Natural Products
• Oxidative Injury and Redox Biology
• Receptors

11:30 AM to 2:15 PM
SYMPOSIUM SESSIONS
• Controlling the Message: Safely Navigating the Development of Novel Oligonucleotide Therapeutics
  Abstract#: 1294–1298
• From Conception to Cane: Unique Life-Stage Considerations for Reproductive Toxicity
  Abstract#: 1299–1303

Friday, March 26

11:00 AM to 4:00 PM
CONTINUING EDUCATION COURSES
CE11 Establishing Confidence in Organ-on-a-Chip Systems for Toxicity Testing: Lung-on-a-Chip as an Example
  Abstract#: 1011
CE12 Risk Assessment, DART, and Endocrine Disruption: A World View
  Abstract#: 1012
CE13 Timing Is Everything: Role of Aging in Immune Responses and Toxicological Implications
  Abstract#: 1013
CE14 Understanding Tox21/ToxCast High-Throughput Screening Data and Applications to Modeling
  Abstract#: 1014

Volunteer with SOT
A new Volunteer section in ToXchange gives SOT members the opportunity to express their interest in a wide variety of service positions within the Society, including leadership positions.

Explore the opportunities today!
www.toxicology.org/volunteer
Pledge Your 2021 Support

Supporters Make the Annual Meeting Affordable for Everyone
Contributions keep registration fees low, enabling scientists at all career levels to attend.

Make your contribution today!
Supporters receive prominent recognition as part of the Virtual SOT Annual Meeting and ToxExpo.*
www.toxicology.org/support

*Benefits vary by level of support.
The Virtual 2021 Annual Meeting and ToxExpo will feature 70+ Scientific Sessions and courses, alongside poster presentations, virtual exhibits, networking lounges, and more. Presentations, digital chats, and social activities will be presented live, semi-live, and on demand for flexible attendance and participation. Essentially, attendees will experience all the content traditionally associated with the SOT meeting without travel and hotel costs. Select activities, such as Continuing Education courses, are available for small add-on fees: see the "Registration Fees and Types" web page on the Annual Meeting website for add-on fee information.

### 2020 Registration Rollovers

If you rolled your 2020 Annual Meeting and ToxExpo registration to the 2021 meeting, those rollovers will still apply for the Virtual 2021 Annual Meeting and ToxExpo. SOT staff is processing all rollover-related registrations in December 2020. If you do not receive a registration confirmation email by January 1, 2021, please contact the SOT Registration Department by email or call 703.438.3115.

### Registration Fees

<table>
<thead>
<tr>
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<th>Early-Bird (By Jan. 22)</th>
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Register Now
How to Register

Online Registration
SOT members and nonmembers paying by credit card may use the SOT Online Registration System. The Online Registration System is available 24-7 and will remain open throughout the meeting. Online registrants will receive an electronic confirmation after registering. If you do not, please contact the SOT Registration Department by email or call 703.438.3115.

Fax or Mail Registration
To pay by check, government purchase order, money order, or credit card, register by mailing the Registration Form to SOT Headquarters. Fax registrations must be accompanied by credit card payment. Forms will be date-stamped as they arrive. This is your date of registration. A registration confirmation will be provided via email; if you do not receive confirmation within two weeks, please contact the SOT Registration Department by email or call 703.438.3115.

DO NOT mail your Registration Form to SOT if it will arrive after March 10, 2021. SOT will accept hard copy Registration Forms until March 11; only online registrations will be accepted from March 11 until the close of the meeting.

Payment Reminders
Company or personal checks must be in US currency and should list all registrants in the check memo area or on the check stub. Please address payment to “Society of Toxicology.”

Government purchase orders must be drawn from the US Department of the Treasury.

SOT accepts American Express, Diner’s Club, Discover, MasterCard, or Visa. Fax registrations will be accepted only if a credit card number is clearly listed in the appropriate area.

Attendees from Developing Countries
Registrants residing in a developing country are eligible for a reduced registration for the 2021 Virtual Annual Meeting. Please contact the SOT Registration Department for details.

Exhibitor Registration
Exhibitors should register using the Exhibitor Service Center on the ToxExpo website. For assistance with exhibitor registration, please contact Will Low by email or call 703.438.3115.

Media Registration
Accredited and vetted representatives of media organizations receive complimentary registration for the meeting. To request press registration or for more information, please contact Michelle Werts by email or call 703.438.3115.

Undergraduate and High School Student Registration
Registration is free for undergraduate and high school students. To register, complete and return the Registration Form along with a copy of your student ID to the SOT Registration Department.
Cancellation, Refund, and Registration Policies

All requests for cancellations and/or refunds must be received in writing at SOT Headquarters by February 19, 2021. These refunds will be processed, less a $50 fee, after the SOT Annual Meeting and ToxExpo. Refund requests received after February 19, 2021, will not be processed.

By registering for the 2021 SOT Annual Meeting and ToxExpo, you are agreeing to the terms and conditions of the Annual Meeting Policies.

Virtual 2021 SOT Annual Meeting Policies

Attendee Qualifications

The Society of Toxicology (SOT) reserves the right to review applications for participation in the SOT Annual Meeting and ToxExpo to confirm that the applicant meets the SOT attendance qualifications. The Society may reject a registration by any individual or organization or withdraw registration privileges at any time if the individual or organization is found to be inconsistent with the Society’s principles and interests.

Individuals

Participation 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.

Organizations

Participation is available only to bona fide organizations with public policy positions and business practices that are generally consistent with the SOT mission, goals, and reputation, as well as its policies and principles, as determined by the Society.

SOT Code of Conduct

The Society of Toxicology is committed to providing a safe and productive environment for all of its meetings; one that fosters open dialogue, the free exchange of scientific ideas, the promotion of equal opportunity, and is free of any sort of harassment, coercion, and discrimination. All meeting participants are expected to treat others with respect and consideration, follow virtual platform rules, and alert Society of Toxicology staff or officers of instances of harassment, coercion, or discrimination. The Society of Toxicology is fully cognizant that there are areas of our science that are controversial. Our meetings can and should serve as an effective forum to consider and debate scientifically-relevant viewpoints in an orderly, respectful and fair manner. The policies herein apply to all meeting attendees, speakers, exhibitors, guests, staff, contractors, and volunteers.

What Is Harassment?

Harassment includes speech or behavior that is not welcome or is personally offensive, whether it is based on ethnicity, race, gender, religion, age, body size, disability, veteran status, marital status, sexual orientation, gender identity, or other reason not related to scientific merit.

Behavior acceptable to one person may not be acceptable to others. As such, meeting attendees must use discretion to ensure that respect is clearly communicated. Harassment expressed in a joking manner still constitutes unacceptable behavior. Retaliation for reporting harassment is a violation of this policy, as is reporting an incident in bad faith.

(Annual Meeting Policies continued on next page)
Reporting Harassment

The Society of Toxicology is committed to providing a safe environment for everyone at any of its meetings. If an individual experiences or witnesses harassment of any kind, they should contact Society of Toxicology staff at SOTHQ@toxicology.org or 703.438.3115. All complaints will be treated seriously and responded to promptly.

If an individual wishes to file a formal grievance of harassment:

- The individual should notify meeting staff at SOTHQ@toxicology.org or 703.438.3115.
- Society of Toxicology staff will discuss any grievance first with the individual filing the grievance then with the alleged offender, seek counsel if the appropriate action is unclear, and report the incident and findings to the Society of Toxicology Council and legal counsel.
- The Society of Toxicology will consult with the individual filing the grievance before taking any action.

The Society of Toxicology reserves the right to remove an individual from a meeting without warning or refund of any expenses, to prohibit attendance at future Society of Toxicology meetings, and to notify the individual’s employer.

If there are questions related to this policy, please contact the Society of Toxicology Executive Director at SOTHQ@toxicology.org or 703.438.3115.

Attendance Terms and Conditions

By registering for the Virtual SOT 60th Annual Meeting and ToxExpo, you are agreeing to abide by SOT Code of Conduct policy and to the following terms and conditions, granting SOT permission to:

- Reproduce, copy, and publish your image, voice, and any or all media taken as part of the Annual Meeting and ToxExpo.
- Share your contact information with organizations that the Society believes might have a product or service of interest to you. Limited data provided to third parties include name, title, affiliation, and business address. Your telephone and fax numbers and email will not be disclosed to third parties.
- Share your name and affiliation with ToxExpo exhibitors and Annual Meeting Supporters.
- Include you in the attendee list, which includes your name and affiliation, accessible to meeting registrants using the SOT Event App.
- Capturing, copying, or taking screenshots of any aspect of the Virtual Annual Meeting without the consent of the presenter(s)/author(s)/exhibitor(s)/etc., including but not limited to slide presentations, video presentations, audio presentations, Q&As, chats, exhibits, posters, and abstracts.
- Sharing derogatory, offensive, or inappropriate content in any format on the Virtual Meeting platform.

SOT Annual Meeting registrants are prohibited from:

- Including promotional materials, special offers, job offers, product announcements, or solicitation for services outside of the Virtual ToxExpo and/or other designated spaces. SOT reserves the right to remove such messages and potentially ban the sources of those solicitations.
- Causing a disruption to any virtual activity, session, or event.

These policies will be enforced by the Society. Those individuals who do not comply will be asked to leave the Virtual Meeting. To request an exemption from any of the Annual Meeting policies, written notification by the registrant must be submitted to SOT Headquarters before the start of the Annual Meeting and ToxExpo. If you have any questions regarding these policies, please contact the SOT Headquarters Office.

SOT Privacy Policy and Disclaimer

The SOT Annual Meeting and ToxExpo adheres to the Society’s general privacy policy and disclaimers.
Join the Society of Toxicology to engage with more than 8,000 members from 70+ countries and help advance toxicology research.

Member Benefits Include:

- Discounted Registration Rates for SOT-Hosted Meetings
- Access or Discounted Access to Toxicological Sciences, the Society’s Official Journal
- Exclusive Award Opportunities
- Travel Support for Students and Postdocs
- Career and Education Resources for All Career Levels—From Undergraduates to Senior Scientists

www.toxicology.org

SOT Membership = Annual Meeting Savings

Apply for SOT membership by December 31 to qualify for discounted registration fees for the Virtual 2021 Annual Meeting and ToxExpo. Approved new members will be notified in February 2021.
Here’s Why You Should Support SOT

By becoming an SOT Global Partner, organizations are:

- Supporting the premiere toxicology society in increasing the scientific impact of and advocating for the value of toxicology;
- Contributing to the success of the largest scientific meeting in toxicology and attracting scientists at all stages of their careers from around the globe;
- Promoting the importance of education and building for the future of toxicology; and
- Encouraging activities aligned with the prediction and prevention of toxicity and disease.

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 the Society through year-round support. You, too, can become among those organizations that demonstrate their commitment to the SOT mission of “creating a safer and healthier world by advancing the science and increasing the impact of toxicology.” Organizations interested in becoming an SOT Global Partner should contact SOT Headquarters.

AbbVie
North Chicago, Illinois

Alcon
Fort Worth, Texas

Biomere
Worcester, Massachusetts

Bristol-Myers Squibb
Pennington, New Jersey

Chevron Energy Technology Company
Houston, Texas

Colgate-Palmolive Company
Piscataway, New Jersey

Corteva Agriscience Haskell R&D Center
Newark, Delaware

Covance Inc.
Madison, Wisconsin

DuPont de Nemours, Inc.
Wilmington, Delaware

ExxonMobil Biomedical Sciences Inc.
Annandale, New Jersey

Genentech
South San Francisco, California

Gilead Sciences Inc.
Foster City, California

Novartis Pharma AG
Basel, Switzerland

Oxford University Press
Oxford, United Kingdom

Pfizer Inc.
Groton, Connecticut

Procter & Gamble
Mason, Ohio

Regeneron Pharmaceuticals Inc.
Tarrytown, New York

Sanofi
Bridgewater, New Jersey

Syngenta Crop Protection Inc.
Greensboro, North Carolina

As of December 4, 2020
About the Virtual Meeting

For 11 days in March 2021, SOT will present approximately five hours of scientific content every weekday from 10:00 am to 4:00 pm concurrently with opportunities for networking, exhibit visits, and social interactions. Just as when attending an in-person event, attendees have control of when and how they experience the meeting by using the fully customized web-based Virtual SOT Annual Meeting and ToxExpo platform. SOT has spared no effort in ensuring that the Virtual Meeting will deliver the robust scientific and interpersonal content that defines the SOT meeting each year.

Some of the events and virtual meeting experiences attendees can expect include:

» **65+ Featured and Scientific Sessions**—All sessions will be presented semi-live, meaning the presentations are prerecorded but the presenters will be available during the session to answer questions and engage with attendees to ensure comprehensive scientific exchange. In addition, all sessions will be available on demand after the session’s scheduled day and time for flexible viewing options.

» **90+ Poster Sessions**—Author-attended Poster Sessions will occur concurrently with other Scientific Sessions and will feature poster presenters engaging in digital chats with attendees to foster connection in much the same way such engagement would occur in person. Posters also will be displayed in the Poster Gallery throughout the meeting, and authors are encouraged to upload audio recordings about their posters to accompany these displays.

» **Networking Lounges**—These special locations can be visited at any time and offer opportunities for digital chats with fellow attendees, as well as the ability to enter a private Zoom room for virtual face-to-face interactions.

» **ToxExpo Exhibits**—Available throughout the meeting, the ToxExpo exhibits will include chat features, videos, exhibitor resources, and more to allow attendees and exhibitors to discuss the latest offerings in toxicology technology and services.

» **Social Events**—The SOT Committees, Regional Chapters, Special Interest Groups, Specialty Sections, and others are planning virtual social activities to occur before or after the day’s Scientific Sessions.

Contribute to Your Journal

Reproducible, Transparent, Impactful, Rigorous, Timely
Annual Meeting Publications

The 2021 SOT Online Planner is the most up-to-date source of information regarding the Virtual 2021 SOT Annual Meeting and ToxExpo. Instructions on how to use the Online Planner are available on page 3. Similar to previous years, the 2021 Annual Meeting publications are available exclusively in digital format as PDFs.

- **SOT Online Planner**—allows desktop and laptop users to browse the complete meeting calendar and build customized schedules that will sync with the SOT Event App (available now)
- **SOT Awards Program PDF**—recognizes the 2021 SOT Award recipients and 2020 Endowment Award recipients (coming December 2020)
- **Program Overview PDF**—provides a quick, day-by-day reference of the Scientific Sessions and activities occurring during the Annual Meeting (coming January 2021)
- **Platform and Poster Session Supplement PDF**—contains the schedule, abstract titles, author information, and more for all the Platform and Poster Sessions (coming February 2021)
- **SOT Event App**—provides up-to-date information on the Annual Meeting and ToxExpo and is your all-in-one resource for the complete schedule, abstract details, and more (coming February 2021)
- **The Toxicologist PDF**—compiles all abstracts accepted for the Annual Meeting and is an official supplementary issue of Toxicological Sciences, the Society’s official journal (coming February 2021)

SOT on Social Media

#2021SOT and #ToxExpo are the official hashtags for the Virtual 2021 SOT Annual Meeting and ToxExpo. Please use them to share ideas, content, and reactions to Annual Meeting and ToxExpo events and activities when posting to your social media accounts. Also, follow and engage with SOT on Facebook, Instagram (@SOToxicology), LinkedIn, and Twitter (@SOToxicology), as well as the official SOT journal, Toxicological Sciences, on Instagram (@ToxSpotlight) and Twitter (@ToxSci).
World Time Zones for the Virtual Meeting

Events on Friday, March 12, are occurring at UTC -5. Beginning Sunday, March 14, the official meeting time zone is UTC -4.

Virtual SOT Meeting Time Zone

UTC -4
Cartagena, Colombia
Montréal
New York
San Juan, Puerto Rico
10:00 AM

UTC -3
São Paulo
11:00 AM

UTC +1
Berlin
Lagos, Nigeria
Stockholm
3:00 PM

UTC +3
Ankara, Turkey
Riyadh, Saudi Arabia
5:00 PM

UTC +8
Shanghai
10:00 PM

UTC +11
Sydney
1:00 AM Next Day

Up-to-date info at www.toxicology.org/2021 | #2021SOT | #ToxExpo
Beyond the scientific program, the Virtual Annual Meeting and ToxExpo will feature many of the social, networking, and professional development events that are an integral part of the SOT experience.

In addition to the informal networking lounges, which attendees can enter at any time, the meeting will include activities programmed by the Committee on Diversity Initiatives (CDI), Education and Career Development Committee (ECDC), Faculty United for Toxicology Undergraduate Recruitment and Education (FUTURE) Committee, Graduate Student Leadership Committee (GSLC), Postdoctoral Assembly (PDA), Regional Chapters, Special Interest Groups, and Specialty Sections. Details regarding these events and the schedule are still being developed, but SOT hopes to announce the full slate of additional programming in early 2021.

**Awards**

The 2021 SOT Award recipients will be announced in December 2020 and will be honored during the Virtual Annual Meeting. Similarly, other groups that bestow awards, such as the Component Groups, will be announcing and recognizing their award recipients throughout the meeting.

**Component Groups**

The Component Group annual business meetings and social events will occur throughout the Virtual Meeting and will include award presentations, networking time, and more. These events will take place before 9:45 am (US EDT, UTC -4) or after 4:15 pm (US EDT, UTC -4). Specialty Section–hosted activities will take place March 15–17, 2021, while Regional Chapters and Special Interest Groups will host events the following week from March 22 to March 25.

**Fun Run and Tox Showdown**

These attendee-favorite activities are going virtual with the rest of the meeting in 2021, so be on the lookout for announcements on how to participate.

**Graduate Students and Postdocs**

The GSLC and PDA are developing programs focused on providing networking, skill development, and other services to student and postdoc meeting participants. For instance, the GSLC Chat with an Expert program will allow graduate students to engage in candid career-based conversations with SOT member.

**Undergraduate Students**

Introducing undergraduate students to toxicology and featuring their research are valuable activities during all SOT annual meetings and have inspired amazing scientists to become toxicologists. Programs planned by CDI and FUTURE for undergraduate award recipients and attendees will provide small group interactions, investigations in toxicology topics, exploration of graduate school, and an overview of career options.

**Undergraduate Educators**

The SOT Undergraduate Educator Network will convene to focus on topics and resources of interest to those supporting the education of undergraduates.
Undergraduates at the SOT Annual Meeting

Free registration available for all undergraduate students

Complimentary undergraduate registration provides access to all the Virtual SOT Annual Meeting programming. In addition, undergraduates are invited to participate in special activities designed for them. Students will learn more about toxicology and gain insights into science and career opportunities. Plus, they will learn about graduate toxicology programs and tips for submitting successful applications.

SOT Engages Undergraduates in Toxicology

- SOT Undergraduate Student Affiliate status, providing access to toxicology news and resources
- Abstract and other award opportunities through SOT and its Regional Chapters, Special Interest Groups, and Specialty Sections
- Internships and research experiences in SOT members' labs
- Regional Chapter meetings, including networking, presentation, and award opportunities

www.toxicology.org/undergraduate
Continuing Education

The Continuing Education (CE) Program offers a wide range of courses that cover established knowledge and new developments in toxicology and related disciplines. General courses are intended to provide a broad overview of an area or to assist individuals in learning new techniques or approaches, while courses based on more specialized topics are intended to be of interest to individuals with previous knowledge of the subject who are already working in the field.

SOT CE courses can be applied toward numerous certifying and licensing board requirements in the United States and around the world. Please be sure to review the specific requirements of your licensing board or certification for details.

A Virtual Annual Meeting registration and accompany CE course registration(s) are required to attend a CE course.

FRIDAY, MARCH 12

9:30 AM–10:30 AM (EST)
• CE01: Chemical Probes: New Tools to Identify Molecular Targets

10:00 AM–1:45 PM (EST)
• CE05: Less Is More: Sustainable Product Development Requires More Toxicological Considerations

11:00 AM–2:45 PM (EST)
• CE02: Advances in Single Cell Genomic Analyses for Toxicological Testing
• CE03: Applications of In Vitro and In Silico New Approach Methodologies for Predictive and Mechanistic Thyroid Toxicity Testing
• CE04: Concepts and Approaches for Current and Future Metals Toxicological Research

FRIDAY, MARCH 19

9:30 AM–10:30 AM (EST)
• CE06: Insider Secrets for Design and Analysis of Defined-Mixture Experiments

11:00 AM–2:45 PM (EDT)
• CE07: Development, Toxicology, and Pathology of the Female Reproductive Tract: Interpretation of Findings from the Pathologist and Regulatory Perspectives
• CE08: Guidelines for Developing and Implementing Organ-on-a-Chip/Microphysiological Systems for Toxicity Evaluation of Drug Candidates in Drug Development
• CE09: Navigating New Modalities: A Preclinical Roadmap for Developing Novel Oligonucleotide Safety Strategy
• CE10: Rapid Chemical Assessment Using Open Computational Methods

FRIDAY, MARCH 26

11:00 AM–2:45 PM (EDT)
• CE11: Establishing Confidence in Organ-on-a-Chip Systems for Toxicity Testing: Lung-on-a-Chip as an Example
• CE12: Risk Assessment, DART, and Endocrine Disruption: A World View
• CE13: Timing Is Everything: Role of Aging in Immune Responses and Toxicological Implications
• CE14: Understanding Tox21/ToxCast High-Throughput Screening Data and Applications to Modeling
Continuing Education Courses—Friday, March 12

Please note that the listed times for CE courses taking place on Friday, March 12, reflect the US Eastern Standard Time (UTC -5).

Friday, March 12, 9:30 AM to 10:30 AM

**Continuing Education Course CE01: Chemical Probes: New Tools to Identify Molecular Targets**

**Chair(s):** Jordan N. Smith, Pacific Northwest National Laboratory; and Aaron T. Wright, Pacific Northwest National Laboratory.

**Primary Endorser:** Mechanisms Specialty Section

**Other Endorser(s):** Drug Discovery Toxicology Specialty Section

Chemical biology is an emerging scientific discipline that utilizes synthetic chemical probes to functionally identify and measure reactive biological molecules. Researchers design and synthesize small molecule chemical probes to functionally target and covalently label enzymes, receptors, and nucleic acids based on catalytic activities or selective affinities. Using fluorescent or mass spectrometry–based readouts, chemical probe platforms facilitate rapid and quantitative screening of cells, tissues, and biological fluids from microbes, animal models, and humans. Compared with conventional transcriptomics and proteomics, chemical probes provide measurements of functional activity rather than total abundance of transcripts, proteins, or nucleic acids. As such, chemical probes have recently gained popularity among research toxicologists and drug developers as tools to measure enzymatic activity important in metabolism and identify novel molecular binding targets of toxicants and drugs.

This course will highlight innovative methods using chemical probes in the field of toxicology. The first presenter will cover how chemical probes can measure enzyme activity and resulting consequences of enzyme variability, induction, and ontogeny and impacts on chemical metabolism. The next presenter will demonstrate how chemical probes can be used to identify novel targets of organophosphates beyond acetylcholinesterase inhibition. Finally, the last presenter will discuss how chemical probes can reveal chemically induced damage to DNA and resulting mutations.

**Abstract #**

#1001  
**Activity-Based Protein Profiling to Better Understand, Measure, and Translate Metabolism.**  
Jordan N. Smith, Pacific Northwest National Laboratory, Richland, WA.

**Activity-Based Protein Profiling for Identifying and Translating Organophosphate Targets across Animal Models.**  
Vivian S. Lin, Pacific Northwest National Laboratory, Richland, WA.

**Next-Generation DNA Damage Sequencing.**  
Shana J. Sturla, Eidgenössische Technische Hochschule Zürich, Zurich, Switzerland.

Friday, March 12, 11:00 AM to 2:45 PM

**Continuing Education Course CE02: Advances in Single Cell Genomic Analyses for Toxicological Testing**

**Chair(s):** Justin Colacino, University of Michigan; and Sudin Bhattacharya, Michigan State University.

**Primary Endorser:** Molecular and Systems Biology Specialty Section

**Other Endorser(s):** Computational Toxicology Specialty Section; Mixtures Specialty Section

In recent years, single cell genomic analyses have provided a foundational new understanding of development and disease. While these novel and exciting technologies are being adopted across many fields in biology, their usage in the toxicological sciences is not yet widespread. This Continuing Education course will highlight the applications and current best practices for single cell genomics analyses in toxicology. The lectures will describe experimental design and analytic considerations for single cell experiments, define best practices...
and an overview of analytic methods for single cell RNA-sequencing and single cell chromatin profiling with ATAC-seq, and identify the state-of-the-art computational methods for integrated single cell multi-omics analyses and new machine-learning techniques to best apply single cell technologies in toxicology studies. The content of the course will benefit researchers from industry, government, and academia who evaluate mechanisms of action and safety of experimental compounds, consumer products, and environmental exposures and want to learn more about emerging technologies in this rapidly evolving area.

Abstract #

#1002

**Experimental Considerations and Best Practices for Single Cell Analyses in Toxicology.** Justin Colacino, University of Michigan, Ann Arbor, MI.

**Application of Single Cell Transcriptomics to Mechanistic Toxicology.** Peer Karmaus, NIEHS, Research Triangle Park, NC.

**Epigenetic Profiling and Chromatin Confirmation Analysis with Single Cell ATAC-Seq.** Poudyal Rosha, 10x Genomics, Pleasanton, CA.

**A Practical Guide for Single Cell Data Analysis.** Lana Garmire, University of Michigan, Ann Arbor, MI.

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**Friday, March 12, 11:00 AM to 2:45 PM**

**Continuing Education Course CE03: Applications of In Vitro and In Silico New Approach Methodologies for Predictive and Mechanistic Thyroid Toxicity Testing**

**Chair(s):** Jessica LaRocca, Corteva Agriscience; and Edward LeCluyse, LifeNet Health.

**Primary Endorser:** Mechanisms Specialty Section

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

Understanding disruption of thyroid signaling pathways and thyroid homeostasis following exposure to environmental, agricultural, and industrial chemicals is both an evolving and an increasingly important challenge in the global regulatory community. This session will focus on innovative new approach methodologies (NAMs), such as 3D microtissues, organ-on-a-chip, hepatic thyroxine clearance models, and computational approaches, that are being developed for predictive and mechanistic thyroid toxicology testing approaches. There is currently a heavy reliance on traditional animal testing approaches to evaluate the potential for a chemical to induce adverse thyroid effects, which are time and resource intensive. In fact, several in vivo guideline studies were recently updated to include additional thyroid-related apical endpoints, such as thyroxine and thyroid-stimulating hormone measurements. There is an opportunity to harness new transformative approaches, such as in silico screening and organotypic in vitro models, to replace animal-intensive testing programs to identify thyroid disrupting toxicants and elucidate the mode of action and human relevance. Embracing NAMs can both provide valuable information to aid in molecule design from a predictive safety standpoint and provide guidance for targeted toxicological testing strategies. With continual progress in screening assays for thyroid hormone disruption as demonstrated by recent publications and new releases of data, and with endocrine-disruptor identification in the EU being dependent on such assays to identify points of chemical interaction with the thyroid pathway, this session will provide a timely update on the data and tools available for rapidly evaluating in vitro activity relevant to the thyroid adverse outcome pathway network. To this end, experts from industry, the United States government, and the European Commission will discuss the current state-of-the-science and how these approaches are being utilized for predictive and mechanistic studies as well as regulatory toxicology applications. Each speaker will discuss opportunities for NAMs to be integrated in chemical safety evaluation. After the presentations, a Q&A will engage attendees to enable deeper understanding of the current state-of-the-art approaches for addressing chemical-induced thyroid-related bioactivities. The target audience would be those interested in understanding how these tools are being leveraged in real-world regulatory testing paradigms. They also will gain insight into the strengths, limitations, and future development opportunities of in vitro, in silico, and alternative models for predictive and mechanistic thyroid toxicity assessments.
Abstract #

**#1003**

**Integration of In Vitro and Aquatic Embryo Models to Predict Direct and Indirect Thyroid Toxicity Modes of Action.** Jessica LaRocca, Corteva Agriscience, Indianapolis, IN.

**Development of Novel In Vitro Assay Technologies for Human Thyroid Screening.** Chad Deisenroth, US EPA/CCTE, Research Triangle Park, NC.

**Mechanistic Nonanimal Methods for the Detection of Thyroid Disruptors in the EU Regulatory Context.** Sharon Munn, European Commission, Lombardy, Italy.

**In Vitro Methods to Address Species Differences in Liver-Mediated Thyroid Toxicity.** Remi Bars, Bayer SAS, Valbonne, France.

**State-of-the-Science: ToxCast and Tox21 Assays and Approaches to Screening for Potential Thyroid Hormone Disruption.** Katie Paul-Friedman, US EPA/CCTE, Research Triangle Park, NC.

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**Friday, March 12, 11:00 AM to 2:45 PM**

**Continuing Education Course CE04: Concepts and Approaches for Current and Future Metals Toxicological Research**

Chair(s): Wei Zheng, Purdue University; and Edward Levin, Duke University.

Primary Endorser: Metals Specialty Section

Other Endorser(s): Mechanisms Specialty Section; Neurotoxicology Specialty Section

Advancement of metal toxicology, from a historical perspective, relies on innovation in science and technology. Discovery of atomic absorption spectrophotometry in the 19th century made it possible to quantify metals in the environment and human body, representing a turning point in understanding metals' effects on human health. Since then, a variety of animal models have been developed—ranging from drosophila, *C. elegans*, and zebrafish to rodents and nonhuman primates—for *in vivo* metal toxicity evaluation. Recent advances in specific fluorescent metal-binding ligands have further allowed tracing of the subcellular trafficking of metals by live imaging in cells and tissues. For mechanistic investigation, the CRISPR technology permits impeccable gene editing, lending itself to an effective, precise, and affordable method for identification of modes of metal toxicity. Moreover, big data algorithms and artificial intelligence (AI) offer advantages not only by the machine learning for fast processing of existing data, but more importantly through learning, it maximizes the chances of successful choices for better prediction of metal's health impact. Achievements notwithstanding, application of these technologies—especially AI in infotechnology and CRISPR in biotechnology, two leading technology breakthroughs—in basic metal toxicological research remains in its infancy. This basic course is designed to introduce essential concepts and new technologies in the metal toxicity research field. The first lecture will review the history of metal toxicology in the context of historical technology advancement, followed by identifying gaps in the field and the future direction of trace element research. The second lecture will introduce the principles in metal quantification, with a focus on using genetic- and protein-based biomarkers for assessment of metals in cells and tissues; the speaker also will discuss fluorescent reporters and high-tech imaging and spectroscopy in metal research. The third lecture will discuss the concepts, general approaches, and applications of CRISPR for precise mechanistic study of metal toxicity; the speaker will teach this revolutionary technology from his own experience on the ideal procedure for investigation of metal-induced neurotoxicities. The fourth lecture will focus on the essential framework and considerations for choosing the most informative animal model to study modes of metal toxicity, neurotoxic risk, and therapeutic treatment. Finally, the last lecture will introduce the basic concept and general practice of AI in health research, followed by integrative examples of how to use AI to interpret chemical toxicities as well as the policy regulation. Each lecture captures the most up-to-date knowledge and development in the field and discusses the concepts and technologies with details specific to metals that have particular human environmental and occupational health relevance, such as lead (Pb), manganese (Mn), cadmium (Cd), arsenic (As), silver (Ag), and mercury (Hg). The course will benefit those who desire to learn basic knowledge on technologies for mechanistic interpretation, novel concepts of machine-assisted prediction of metal or chemical toxicities, and technical approaches in utilizing widely available CRISPR and cellular imaging technologies that can be used to support research in metal toxicology. As the course introduces these techniques that are equally applicable to other fields, such as neurotoxicology, nanotoxicology, carcinogenesis, risk assessment, and occupational health, researchers engaged in these wider aspects of toxicological sciences shall benefit by attending this basic course and learning the knowledge beyond metals.
Abstract #

#1004 Brief History of Metal Toxicology: Propelled by Discovery and Technology Innovation. Wei Zheng, Purdue University, West Lafayette, IN.

Concepts and Applications of Metal Detection and Measurement Technology for Cellular, Tissue, and Organism Exposure Assessments. Aaron Bowman, Purdue University, West Lafayette, IN.

Introduction of CRISPR Technology and Its Uses in Studying Metal Neurotoxicity. Somshuvra Mukhopadhyay, University of Texas at Austin, Austin, TX.

Basic Considerations for Choosing Optimal Animal Models for Assessing Metal-Induced Neurobehavioral Toxicity. Edward Levin, Duke University, Durham, NC.

Artificial Intelligence in Regulatory Toxicology: Concept, Strategy, and Possible Application in Metal Toxicity Assessment. Weida Tong, US FDA/NCTR, Little Rock, AR.

Friday, March 12, 10:00 AM to 1:45 PM

Continuing Education Course CE05: Less Is More: Sustainable Product Development Requires More Toxicological Considerations

Chair(s): Mansi Krishan, Becton, Dickinson and Company; and Brittany Baisch, Henkel Corporation.

Primary Endorser: Sustainable Chemicals through Contemporary Toxicology Specialty Section

Other Endorser(s): Ethical, Legal, Forensics, and Societal Issues Specialty Section; Women in Toxicology Special Interest Group

Developing sustainable products with less impact on the environment and human health requires additional considerations and legwork by toxicologists. Performing the appropriate risk assessments for consumer product goods and pharmaceuticals is of paramount importance, but there are many added layers if the product has sustainable attributes. Sustainable products are those that address current-day challenges of depletion of natural resources, high energy consumption, and release of chemicals and waste into the environment. Furthermore, sustainable products also are those for which consumers hold high expectations of having more transparency about the ingredients and containing fewer ingredients overall, yet also anticipate a certain level of satisfaction and product performance. Global regulatory agencies, academicians, product developers, and manufacturers have been working toward developing such sustainable, innovative, safe, efficacious, and cost-effective solutions for consumers. With advances in substituting existing substances and processes with greener alternatives, there is a need for holistic methodologies that ensure that the substituted products and processes leave a smaller environmental footprint throughout their life cycle. Toxicologists must integrate all these considerations into their product safety risk assessments. The Organisation for Economic Co-operation and Development (OECD) publication Fostering Innovation for Green Growth highlights how the chemical industry and chemical management serve as examples of a scientific discipline that influences innovation in green technologies. As the demand for sustainable products increases, there is a need to integrate the elements of green and sustainable chemistry, such as green engineering, with toxicology early in the product development process. The field of “green toxicology” expands on the principles of green chemistry to develop products that not only are safe for use but also result in reduced human exposure, waste, or environmental impact; address climate change; and are not resource intensive. The US Environmental Protection Agency (US EPA) Toxics Release Inventory and Safer Choice Program and US Department of Agriculture Biobased certifications highlight the shift toward ingredient safety and transparency, as well as the incorporation of 21st-century toxicological principles and advances with green chemistry to develop sustainable alternatives. This shift emphasizes the need for toxicologists to provide guidance on the requirements in the development of sustainable alternatives, how to perform substitutions, how to conduct risk assessments on alternatives, and how to meet sustainability-related certifications and claims. This CE course will provide an overview of the role of the safety assessment toxicologist in bringing sustainable solutions to the market, with case studies from different sectors. The speakers will present (1) the key principles of green chemistry and how they intersect with toxicology, and key opportunities for toxicologists to be engaged with the selection of more sustainable ingredients; (2) US EPA programs such as the Toxics Release Inventory and Safer Choice, the national analyses that demonstrate the use of databases and assessment tools by toxicologists to identify and prioritize specific chemicals that, if replaced, can reduce the impact on waste streams in various industries; (3) the importance of understanding consumer expectations and how regulatory toxicology, external certifications, and safety-related product claims converge to inform the safety assessment of a sustainable product, demonstrated with a laundry detergent case study; (4) strategies for the application of in silico, in vitro, and
targeted in vivo tests within the stage gate development process to satisfy regional and pseudo-regulatory requirements from retailers to produce more sustainable personal care products; and (5) the toxicological assessment considerations in the design and manufacturing of pharmaceuticals. Attendees of this CE course will be equipped to apply the key principles of green toxicology, use different tools and approaches, and navigate certifications to build safety assessments for sustainable products, particularly for consumer products and pharmaceuticals. In addition, this CE course provides the opportunity for attendees to learn about a transdisciplinary field, capitalize on scientific advancements in safety assessment, and discover the robust role of toxicologists in innovating sustainable products and practicing product stewardship.

Abstract #
#1005

Green Toxicology Approaches toward Sustainable Environmental Quality. Bryan W. Brooks, Baylor University, Waco, TX.


Sustainability Adds Complexity to Product Safety Assessments: A Laundry Detergent Case Study. Brittany Baisch, Henkel Corporation, Trumbull, CT.

Sustainable Personal Care Ingredients and New Product Development—How to Optimize Safety Assessments That Meet Regional Requirements. Pamela J. Spencer, ANGUS Chemical Company, Buffalo Grove, IL.

Integration of New Testing Methods and Strategies in Pharmaceutical Product Development toward Green Toxicology: Where Are We Today? Brinda Mahadevan, Consultant, Columbus, OH.

Continuing Education Courses—Friday, March 19

Please note that the listed times for CE courses taking place on Friday, March 19, and Friday, March 26, reflect the US Eastern Daylight Time (UTC -4).

Friday, March 19, 9:30 AM to 10:30 AM

Continuing Education Course CE06: Insider Secrets for Design and Analysis of Defined-Mixture Experiments

Chair(s): Jane Ellen Simmons, US EPA/CPHEA; and Richard Hertzberg, Emory University.

Primary Endorser: Mixtures Specialty Section

Other Endorser(s): Risk Assessment Specialty Section; Women in Toxicology Special Interest Group

Design, conduct, analysis, and interpretation of mixtures experiments are daunting challenges. Frequently, defined-mixture experiments investigate whether the response of a mixture is predictable from the dose-responses curves of the component chemicals. Experimental toxicologists have found that guideline study designs, while extremely valuable for intended purposes, are often not useful for investigation of consistency or lack of consistency with various definitions and forms of additivity (e.g., dose/concentration addition, response addition). Not typically taught in toxicology courses, individuals seeking knowledge on experimental design for mixtures generally sort through sometimes bewildering literature, where sources seemingly, or actually, contradict one another. There is a long history of poorly designed and analyzed studies; the ability to use available literature to understand the potential for nonadditive interactions is hampered by these design and analysis issues. This course will shed light on the poorly illuminated topic of mixture experimental design. Attendees will leave the course informed on fundamental factors and important elements to consider when constructing defined-mixture experiments. Benefits of incorporating multidisciplinary expertise (the essential trio) will be discussed. The advantages of working with a qualified data analyst before executing the experiment will be contrasted with the inefficiency of statistical consultation only after data are in hand. Areas of focus will be the low-dose/low-effect region, particularly important when concerned with environmental agents; designs useful when higher-dose regions are of interest, such as combinations of pharmaceutical agents; and ensuring utility of results for risk assessment, risk management, and regulatory decision-making. Both frequently used and less common
but important designs with associated analysis strategies will be covered, as will those that allow insight into biologically interpretable dose-response models. Key factors requiring consideration during construction of the design will be emphasized, including power, overall experimental size, dose level spacing, and placement of experiment units within dose groups. The design impact(s) of testing for greater-than additive versus less-than additive outcomes will be covered. The concepts and strategies covered apply to traditional in vivo, traditional in vitro (e.g., Salmonella mutational assays), and new approach methodology (NAM) experiments. Attendees will be provided a curated, annotated bibliography for future reference. Example mixtures covered in the course and/or the annotated bibliography include mixtures of chemicals known or thought to act either by a common mechanism/mode of action/adverse outcome pathway or by dissimilar mechanisms/modes/pathways. While design and statistical considerations will be illustrated with mixtures relevant to occupational, pharmaceutical, and environmental exposures, the concepts are broadly and generally applicable. At the conclusion of the course, attendees will be better equipped to answer the perennially vexing question: What is the optimal defined-mixture experiment for my goals? Attendees will acquire a foundation of knowledge equipping them to participate more fully in selection or construction of experiments suitable to the goal(s) of the study, yielding data that meet the criteria for appropriate statistical analyses. In addition to toxicologists interested in defined-mixture experiments, this course will be of value to those who evaluate or use the results of such experiments. Because of the multidisciplinary collaboration required for fit-for-purpose, high-quality defined-mixture experimentation, the presentation will be given jointly (in true mixtures fashion).

Abstract #

#1006  Toxicology and Experimenter Perspective. Jane Ellen Simmons, US EPA/CPHEA, Research Triangle Park, NC.
Statistical and Risk Assessment Perspective. Richard Hertzberg, Emory University, Atlanta, GA.

Friday, March 19, 11:00 AM to 2:45 PM

Continuing Education Course CE07: Development, Toxicology, and Pathology of the Female Reproductive Tract: Interpretation of Findings from the Pathologist and Regulatory Perspectives

Chair(s): AtLee Watson, Integrated Laboratory Systems Inc.; and Aileen Keating, Iowa State University.
Primary Endorser: Reproductive and Developmental Toxicology Specialty Section
Other Endorser(s): Regulatory and Safety Evaluation Specialty Section

The development, maturation, and function of the female reproductive system is a complex, dynamic process in humans and laboratory animals and is sensitive to perturbation following exposure to a range of environmental and pharmacological agents. As a result, preclinical studies involving therapeutics intended for use in the female population or agents with potential widespread human exposure often require toxicologic and histopathologic assessments of female reproductive endpoints to demonstrate safety. Evaluation of these endpoints in laboratory animals necessitates an understanding of considerations that include developmental timing, concordance of clinical and histopathological correlates, species differences, and the translational relevance of animal findings to the broader human population. The objective for this advanced CE course is to provide attendees with an overview of the development and maturation of the female reproductive system, study design considerations, and pathology and regulatory perspectives to facilitate interpretation of abnormal findings observed in in vivo animal studies. Speakers from academia, industry, and government (research and regulatory) with expertise in the fields of female reproductive and developmental toxicology will provide attendees with (1) a concise review of the development of the female reproductive tract, highlighting species differences and known targets; (2) current toxicologic and histopathologic methods to assess effects on female reproductive function and cyclicity; (3) distinct mechanisms of toxicity in adult female rats, including the onset of sexual maturity, cycling, and reproductive senescence; and (4) a regulatory perspective that will cover recent draft guidance from the US Food and Drug Administration and other regulatory bodies and include relevant case examples to illustrate specific issues encountered when reviewing preclinical toxicity packages for small molecules and biologics. Note: this course will complement the CE course “The Male Reproductive Tract: Development, Toxicology, and Pathology,” presented as part of the scientific program during the 2020 SOT Virtual Meeting. The course “The Male Reproductive Tract: Development, Toxicology, and Pathology” is available as part of SOT CEd-Tox, the Society's online continuing education course program.
Abstract #

#1007

**Unscrambling Female Reproductive Toxicology.** Aileen Keating, Iowa State University, Ames, IA.

**Methods and Approaches to Evaluate the Female Reproductive Tract.** Darlene Dixon, NIEHS/NTP, Research Triangle Park, NC.

**Mechanisms and Patterns of Toxicity in the Female Reproductive System: A Pathologist's Perspective.** Justin Vidal, Charles River, Mattawan, WI.

**Regulatory Considerations for Reproductive Toxicity Testing of Pharmaceuticals.** Andrew McDougal, US FDA/CDER, Silver Spring, MD.

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**Friday, March 19, 11:00 AM to 2:45 PM**

**Continuing Education Course CE08: Guidelines for Developing and Implementing Organ-on-a-Chip/Microphysiological Systems for Toxicity Evaluation of Drug Candidates in Drug Development**

**Chair(s):** Jason Ekert, GlaxoSmithKline plc; and Anthony Bahinski, GlaxoSmithKline plc.

**Primary Endorser: In Vitro and Alternative Methods Specialty Section**

**Other Endorser(s):** Drug Discovery Toxicology Specialty Section; Mechanisms Specialty Section

Drug failures in clinical trials are mainly due to the poor translational relevance and clinical predictive power of existing preclinical models, which include human cell-based in vitro and animal models. Microphysiological systems (MPS) (or organs-on-chips [OOC]) bring together advances in stem cell/organoid biology, biomaterials, tissue engineering, and biosensors to generate healthy and diseased models, where these human organ biomimetics more closely model the organ's physiology and pathophysiology. There is a clear need to enhance predictability of toxicities that may be encountered in human subjects. Human MPS models may assist to better identify early potential toxicity and elucidate the mechanism of toxicity once identified. The goal of the course will be to outline general principles and considerations of the appropriate use of OOC/MPS models in drug development for safety evaluation and highlight advantages/limitations in the current models. The first talk will give an overview and history of HOOC/MPS. The tissue chip developer will discuss how to leverage MPS technology for generating toxicity assays and will give several examples of systems that have been used to evaluate toxicological events. The second presentation will focus on the characterization and validation of linked organ chip systems that could be utilized for PK/PD modeling and for a predictive way to model human drug toxicity. The third presentation will give insights and recommendations from a pharma perspective when implementing 3D/MPS for early toxicology testing and for later-stage toxicology investigations in a drug discovery setting. The final presentation will be given from a regulatory perspective that will inform the audience about performance criteria, standardizing the evaluation of MPS, and the importance of utilizing human cellular material and will present cardiac and liver MPS case studies. This course should be of broad interest to laboratories considering using 3D/OOC/MPS platforms as a mechanistic approach to predicting and understanding human organ system toxicities.

Abstract #

#1008

**Organ-on-a-Chip/Microphysiological Systems to Improve Culture and Assaying of In Vitro Tissue for Toxicological Testing.** Joseph Charast, Charles Stark Draper Laboratory Inc., Cambridge, MA.

**Quantitative Prediction of Human Pharmacokinetic Responses to Drugs via Fluidically Coupled Vascularized Organ Chips.** Rachelle Prantil-Baun, Wyss Institute for Biologically Inspired Engineering at Harvard University, Cambridge, MA.

**Considerations When Developing and Implementing 3D/MPS Models for Safety Testing and Investigative Toxicology in Pharmaceutical Drug Development.** Jason Ekert, GlaxoSmithKline plc, Collegeville, PA.

**Evaluation of Cardiac and Hepatic Cellular Microsystems for Drug Development.** Alexandre Ribeiro, US FDA/CDER, Silver Spring, MD.
New chemical modalities (such as RNA-based or oligonucleotide gene therapies) represent a paradigm shift in drug discovery and toxicology. While these molecules were initially developed as therapeutics more than 30 years ago, novel sequences, chemistries, and delivery mechanisms have introduced unknown safety risks that require toxicologists to expand beyond the traditional small molecule chemical space and think more broadly when assessing potential hazards and how toxicological effects will impact meaningful therapies for patients. This Continuing Education course will serve as a roadmap for how to approach evaluating safety concerns for novel oligonucleotides starting in early drug discovery phases through regulatory development, and will detail approaches to design oligonucleotide-based gene therapies with safety in mind. The course will begin with an overview that explores the advances of oligonucleotide platforms over the last three decades and outlines the obstacles faced by toxicologists to evaluate safety for novel oligonucleotide sequences. Our first speaker will delve into chemical and structural sequence alterations associated with toxicity as well as share a case study that highlights the importance of sequence selection for optimizing tolerability. The next speaker will explore several studies that emphasize the importance of in vitro assays for predicting oligonucleotide-dependent toxicity and the utility of 3D microphysiological systems for de-risking oligonucleotide platforms. The third speaker will focus on available preclinical in vivo models for oligonucleotide toxicity studies and concerns regarding cross-species differences in response. The fourth speaker will discuss the preclinical and clinical oligonucleotide therapy landscape and findings from a meta-analysis study detailing the main adverse events driving attrition of oligonucleotide candidates in the clinic. The final speaker will conclude the course with discussion of regulatory approaches for novel oligonucleotide gene therapies and the advantage of pre-IND discussions to ensure successful development of novel compounds. Navigating a new chemical modality space can be challenging, especially when no defined regulatory pathway exists; therefore, this course offers a guide for the development of novel RNA-based therapeutic platforms from chemical toxicology through drug development. As experts in their field, the speakers offer key insights into drug discovery and toxicological parameters that are essential for successful development of oligonucleotide therapy platforms and will aid in advancing our understanding of unforeseen drug-induced toxicological endpoints for improved human health and safety.

Abstract #

#1009

**Strategic Thinking in Early Drug Discovery for RNA-Based Therapeutics.** Lauren Lewis, Takeda Pharmaceutical Company Limited, Cambridge, MA.

**Chemical Toxicology Approaches to Selecting Oligonucleotides.** Andrew Burdick, Pfizer Inc., Cambridge, MA.

**In Vitro Approaches for Oligonucleotide Safety Profiling.** Sebastien Burel, Ionis Pharmaceuticals, Cambridge, MA.

**Preclinical Toxicity Models for Oligonucleotide Development.** Patrik Andersson, AstraZeneca, Gothenburg, Sweden.

**Drawing Strategies from Tragedies: A Meta-Analysis of Clinical Trial Data on Oligonucleotides.** Samantha Faber, Takeda Pharmaceutical Company Limited, Cambridge, MA.

**Regulatory Aspects Involved in Developing INDs for Novel Oligonucleotides and Strategies for Product Development.** James Wild, US FDA/CDER, Silver Spring, MD.
Traditional chemical assessments are time-intensive, manual efforts requiring large amounts of human and experimental data. There are times, though, when a quick assessment of health impacts for a chemical is needed. Literature-based chemical assessments paired with computational and open-access (free) software applications (tools) can provide a quick, evidence-based solution. Human expertise supported by these tools can allow you to go from zero information to a preliminary hazard level without setting foot in the lab. Many freely available tools and workflows exist to support this process without adding on the cost for new software.

This course will provide an overview of the types of chemical health safety assessments and their information requirements, setting the stage for how tools can support rapid chemical evaluations. It will close with an example of how structured data extractions are deposited into US Environmental Protection Agency (US EPA) dashboards.

The format of the course follows the risk assessment process, as follows:

- Identifying chemical information using literature search: No/little information on a chemical? Learn how to conduct a literature search for chemical data. Focus will be on search strategy, identifying studies with information of interest, and results prioritization.
- Expanding the dataset using chemical similarity: Are the data for the chemical of interest limited, but rich for a structurally similar neighbor? Learn how to expand your chemical search for data-poor chemicals using structural similarity or apply new approach methods in chemical assessment while considering other key data.
- Using in vitro evidence for toxicokinetic modeling: Is the evidence so limited (i.e., no information available at all) that a purely in vitro/in silico approach should be considered? Learn how to use in vitro to in vivo extrapolation to calculate in vivo measurements, even ones tailored to susceptible populations. This will help you go from internal concentrations (or close estimates) to external/applied exposure concentrations/doses.
- Calculation of point of departure: Use the concentration response information from various data sources, including in vitro, in vivo, and in silico, to develop the point of departure (POD). You’ll need the POD to develop toxicity reference values that you can use to estimate safe exposure levels.

Course materials will include listing of additional resources, a walk-through of highlighted tools discussed, and example datasets. At the end of this course, participants will be able to:

- Explore and prioritize data needed for rapid chemical assessment
- Expand searches for data-poor chemicals using chemical analog toxicity information
- Extrapolate in vitro bioactivity to in vivo exposure scenarios
- Apply approaches for calculating POD

**Abstract #

#1010 Welcome and Introduction.** Michelle Angrish, US EPA, Durham, NC.

**Identifying Data on Your Chemical.** Neepa Choksi, Integrated Laboratory Systems Inc., Durham, NC.

**httk and HTK-Pop: Open-Source Software for Simulation of Population Variability in High-Throughput Toxicokinetic Modeling for In Vitro to In Vivo Extrapolation and Rapid Chemical Prioritization.**
Caroline Ring, US EPA/CCTE, Research Triangle Park, NC.

**Open-Source Approaches to Calculating a Point of Departure.** Lyle Burgoon, Raptor Pharm & Tox Ltd., Apex, NC.
Use of Specialized Software to Improve the Efficiency of Conducting Chemical Assessments and Interoperability with the US EPA CompTox Chemicals Dashboard.  
Kristina Thayer, US EPA, Durham, NC.

Use of Specialized Software to Improve the Efficiency of Conducting Chemical Assessments and Interoperability with the US EPA CompTox Chemicals Dashboard.  
Antony Williams, US EPA, Durham, NC.

Continuing Education Courses—Friday, March 26

Please note that the listed times for CE courses taking place on Friday, March 19, and Friday, March 26, reflect the US Eastern Daylight Time (UTC -4).

Friday, March 26, 11:00 AM to 2:45 PM

Continuing Education Course CE11: Establishing Confidence in Organ-on-a-Chip Systems for Toxicity Testing: Lung-on-a-Chip as an Example

Chair(s): Robert Moyer, Battelle Memorial Institute; and Jennifer Harris, Los Alamos National Laboratory.
Primary Endorser: In Vitro and Alternative Methods Specialty Section
Other Endorser(s): Drug Discovery Toxicology Specialty Section; Inhalation and Respiratory Specialty Section

Over the past several decades, there has been a disturbing trend of declining efficiency in drug research and development. This trend has led to unsustainable cost growth for pharmaceutical research and highlights a significant risk for the development of new drugs. One of the most compelling explanations is that the conventional "brute force" methods of drug discovery are reaching a point of diminishing returns. Animal tests are too slow and expensive to keep pace with increasing demands for innovation and often fail to predict human responses because traditional animal models frequently do not accurately mimic human physiology. Organ-on-a-chip systems have the potential to address these concerns and meet the growing need for rapid, affordable, and replicable preclinical models. They offer the benefits of using human cells to recreate functions of living human organs, thus bridging the gap between extensively studied animal models and human clinical trials. As with any model, some level of confidence in the results provided is necessary for the successful implementation of organ-on-a-chip models, and widespread agreement in the field on approaches for the validation of organs-on-a-chip will be essential. This course will present considerations for the validation of organ-on-a-chip models for toxicity assessment from the perspectives of regulatory, industry, and academic stakeholders, with lung-on-a-chip as an example. The course Co-Chairs will begin the session with a brief introduction of the topic and the speakers. The first two speakers will be representatives of US government agencies. The first speaker, a representative from the US Food and Drug Administration, will discuss regulatory compliance and application requirements that significantly impact the use of organs-on-a-chip technologies for drug discovery and development. She also will describe current thinking on use of nonanimal alternatives in efficacy and toxicology testing. The second speaker, representing NIEHS and ICCVAM, will focus on the challenges and lessons learned from past and current validation efforts. The next three speakers, including representatives from academia, government, and industry, will present the perspectives of laboratories that conduct organ-on-a-chip research, development, and validation efforts. The third speaker will present the development and validation of a multi-organoid “body-on-a-chip” platform for testing drug toxicity and developing countermeasures for toxic agents. Next, the fourth speaker will describe the applications for and validation efforts with a multi-bioreactor platform that recapitulates bronchiolar and alveolar aspects of the human lung. Finally, the last talk will be a collaborative presentation describing the design and validation of a breathing lung-on-a-chip that integrates reliable and reproducible application of test aerosols at the air-liquid interface. This course includes a diverse group of speakers and topics that will translate well to the target audience of scientists and practicing toxicologists. Attendees from academic institutions, government, and industry alike will be well represented and have sincere interest in the overall discussion. Attendees will leave the session with a greater understanding of the regulatory considerations, lessons learned, and potential next steps for the validation of organ-on-a-chip systems for toxicity testing.
Protection of humans from excessive exposures to chemicals and pharmaceuticals associated with toxicity can be managed through risk assessment. Developmental and Reproductive Toxicity/Endocrine Disruption (DART/ED) hazard identification (ID) is a critical component of the risk assessment process. DART/ED hazard ID also is used independent of exposure assessment considerations to label compounds with DART or ED properties and, in some cases, limit or prevent sales in certain geographies. Although risk assessment or hazard ID applications can differ across sectors and geographies, scientists often collaborate on best practices for methods and interpreting endpoints within DART and endocrine-specific toxicity studies. This course will therefore provide a view of the regulatory landscape for DART/ED assessments, focusing on specific case studies as examples of applying DART/ED data to the end goal of protection of human health through risk assessment. The first talk will focus on the application of DART data for regulatory decision-making in the pharmaceutical sector. The second talk will then cover specific pharmaceutical case studies with DART data from nonclinical studies and the determination of human risk. The third talk will give an overview of endocrine disruption and how DART data apply to ED-specific requirements for chemicals across geographies, with examples of regulatory decisions based on existing datasets. The fourth talk will provide an overview of the US perspective on application of DART and ED data to the risk assessment process for chemicals, with a specific example focused on thyroid assessments. Finally, the fifth talk will introduce alternative approaches for DART/ED assessments and the vision for application of alternative approaches to regulatory decision-making. This will be a crash course on the current regulatory approach to use of DART/ED data, with a view to the future, considering alternatives to animal testing approaches. As such, this course will offer broad appeal to audience members of different backgrounds and may be of interest to trainees interested in a career in regulatory toxicology.

Abstract #
#1012

Introduction. Bethany Hannas, Corteva Agriscience, Newark, DE.

DART in Risk Assessment for Pharmaceuticals. Ilona Bebenek, US FDA/CDER, Silver Spring, MD.

Case Studies of Regulatory Decision-Making Based on DART Data for Pharmaceuticals. Natasha Catlin, Pfizer Inc., Groton, CT.

Sufficiency of Pesticides DART Data Package for Endocrine Disruption Assessments: A Global Perspective on Regulatory Requirements for Human Health. Bethany Hannas, Corteva Agriscience, Newark, DE.

Thyroid Hormone Assessment: Implications for Developmental and Reproductive Toxicology. Elizabeth Mendez, US EPA, Washington, DC.

Application of Alternative Approaches for DART/ED to Regulatory Decisions. George Daston, Procter & Gamble, Mason, OH.
CE

Continuing Education Course CE13: Timing Is Everything: Role of Aging in Immune Responses and Toxicological Implications

Chair(s): Emanuela Corsini, Università degli Studi di Milano, Italy; and Florence Burleson, Burleson Research Technologies.

Primary Endorser: Immunotoxicology Specialty Section

Two major features in the process of aging of the human immune system are immunosenescence and inflammaging. Immunosenescence refers to the gradual deterioration of the immune system by natural age advancement and is one of the potential reasons for the increase in the incidence of infections. The term “inflammaging” was coined to combine the processes of inflammation and aging, since chronic, low-grade, systemic inflammation is associated with aging, contributing significantly to age-related diseases and mortality risk in the elderly. With age, the immune system undergoes adaptations and modifications, with important consequences for both communicable and noncommunicable diseases, for which the contribution of chemical exposure is not fully understood. This Continuing Education course aims to cover mechanisms of inflammaging and immunosenescence, their consequences, and implications in terms of response to vaccination, drugs, and immunotoxic compounds, which is timely and relevant in the era of COVID-19.

The first speaker will introduce the audience to the current understanding of the biology underlying immunosenescence and inflammaging, and their contribution to age-related diseases. The second speaker will cover the problems associated with an effective vaccination and discuss how the understanding of immunosenescence will help in the design of more effective vaccines for the elderly. The third speaker will discuss the merits of animal models and their usefulness in the study of immunosenescence and drug-induced liability in a growing older population. Finally, the last speaker will cover the role of age in chemical-induced immunotoxicity and how the understanding of the mechanism of action underlying chemical toxicity is central to define an increased risk—or not—in the elderly. Overall, this course aims to contribute to the understanding of physiological aging in the response to vaccines, drugs, and chemicals, which is considered of fundamental importance in light of an increasingly older population.

Abstract #

#1013

Role of Immunosenescence in the Development of Age-Related Diseases. Tamas Fulop, Université de Sherbrooke, Sherbrooke, QC, Canada.


Impact of Immunosenescence on Immunotoxicity: From Mechanistic Understanding to Susceptibility to Immunotoxicants. Emanuela Corsini, Università degli Studi di Milano, Milan, Italy.

CE

Continuing Education Course CE14: Understanding Tox21/ToxCast High-Throughput Screening Data and Application to Modeling

Chair(s): Ruili Huang, NIH/NCATS; and Menghang Xia, NIH/NCATS.

Primary Endorser: Women in Toxicology Special Interest Group

There is a large number of chemicals in the environment that lack adequate toxicological characterization necessary for the assessment of their exposure risk and subsequent regulatory decision-making. In order to generate toxicity profiles effectively on large sets of compounds, the US Tox21 and US Environmental Protection Agency (US EPA) ToxCast programs have developed in vitro assays to test thousands of environmental compounds in a high-throughput screening (HTS) format. To date, more than 100 million data points have been generated from these screens and made publicly available. These datasets can aid in the identification of previously uncharacterized toxicants as well as the development of computational models for toxicity prediction. However, there are technical aspects and caveats associated with these HTS assays that are not well understood by the end users, creating a gap between data generation and data inter-
pretation. To bridge this gap, this Continuing Education course will provide an explanation and guidance on the understanding of Tox21/ToxCast HTS data to be applied more efficiently to toxicological modeling. The course will start with a presentation that describes various HTS assays used in the Tox21/ToxCast screening programs, followed by presentations describing different data processing methods and activity definitions dealing with biological and technological artifacts, a presentation comparing these data analysis methods, and finally a presentation on example applications to computational modeling. Live demos of the databases containing the results from different analysis pipelines will be included in some presentations. The content of this course will benefit researchers in the toxicology field, especially computational scientists who wish to develop models using the screening data and learn more about the assay technologies and data analysis methodologies.

Abstract 
#1014

**Application of Various Assay Technologies for Tox21 Screening.** Menghang Xia, NIH/NCATS, Rockville, MD.

**A Quantitative High-Throughput Screening Data Analysis Pipeline for Activity Profiling.** Ruili Huang, NIH/NCATS, Rockville, MD.

**Analyzing and Interpreting Tox21 Quantitative High-Throughput Screening (qHTS) Data from a Data Science Perspective.** Jui-Hua Hsieh, NIEHS/NTP, Durham, NC.

**An Update on the ToxCast Data Pipeline: New Features for Dataset Development.** Katie Paul-Friedman, US EPA/CCTE, Durham, NC.

**Concentration-Response Modeling in High-Throughput Transcriptomics.** Richard Judson, US EPA/CCTE, Durham, NC.

**Interpreting the Tox21 Data Analysis Methods toward a Consensus.** Agnes Karmaus, Integrated Laboratory Systems Inc., Durham, NC.

**Use of Tox21 Data for QSAR Modeling of Different Minimum Potency Levels for Aromatase Inhibition and PPAR-Gamma Activation in the H2020 FREIA Project.** Eva Wedebye, DTU Fødevareinstituttet, Danmarks Tekniske Universitet, Lyngby, Denmark.
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Featured Sessions

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

Opening Plenary Session: Blending Art and Science to Master Science Communication

**Speaker:** Laura Lindenfeld, Alan Alda Center for Communicating Science, Stony Brook University, Stony Brook, NY.

In this keynote, Dr. Lindenfeld will introduce participants to the Alda Center's unique approach to science communication. Building on the foundations of improvisational theater, which cultivates a stronger ability to relate and connect, the Alda Center leverages scientific research on science communication to empower scientists to connect with diverse audiences in clear and vivid ways.

Wednesday, March 17, 10:00 AM to 11:15 AM

SOT/EUROTOX Debate: Individual Toxicity Is the Future of Risk Assessment

**Chair(s):** Michael Aschner, Albert Einstein College of Medicine; and Félix D. Carvalho, Universidade do Porto, Portugal.

**SOT Debater:** Syril D. Pettit, HESI, Washington, DC.

**EUROTOX Debater:** Alan R. Boobis, Imperial College London, London, United Kingdom.

Each year, the SOT Annual Meeting includes a debate in which leading toxicologists advocate opposing sides of an issue of significant toxicological importance. The debate continues a tradition that originated in the early 1990s. This year, the debaters will address the proposition “individualized toxicity is the future of risk assessment.” As toxicologists, we seek to define safe operating parameters for the use of a substance in a population. The opportunity to use “real-world evidence” and personal data collection devices (human biomonitoring) to gather information on toxicity from individuals and small populations allows us to envision new ways to refine these parameters as they relate to individuals. Is the future of toxicology and risk assessment headed toward a paradigm that must include approaches for patients/individuals at a public health—protection scale? If so, is it possible (or even desirable) to view risk of small groups of individuals based on discrete risk factors? Can adverse outcome assessments for groups be improved by this approach? Can recent developments in machine learning and other computational methods be applied in toxicology as they are being applied in precision medicine? Does surveillance of a patient’s response via personalized adverse effect monitoring provide a means to qualify the exposure-response relationship that can be tailored to each patient? Would better profiling be helpful to avoid lethal errors? Does an integrated exposure reduce the number of assumptions that need to be made?

Please note that the listed times for all Featured Sessions reflect US Eastern Daylight Time (UTC -4).
when estimating exposure and thus help reduce the uncertainties in exposure science? Can we address the ethical and political aspects of its application? In addition to inclusion as a Featured Session at this meeting, this debate will again take place (with the debaters taking the reverse positions) in Copenhagen, Denmark, during the EUROTOX 2021 congress, September 26–29, 2021.

**Monday, March 22, 10:00 AM to 11:00 AM**

**EUROTOX Bo Holmstedt Memorial Award Lecture: Understanding Three Fundamental Quantitative Principles Is a Prerequisite for Improving Toxicological Science and Risk Assessment**

**Lecturer:** Wout Slob, Rijksinstituut voor Volksgezondheid en Milieu (RIVM), Netherlands.

Wout Slob, PhD, studied biology at Vrije Universiteit Amsterdam, with theoretical biology as his main subject. He obtained his PhD in 1987 with work on applying statistics in biological research, including log transformation and power analysis. Dr. Slob worked at RIVM from 1986 to 1995 as a consulting statistician. During that period, he gradually became more interested in toxicology and risk assessment. From 1996, he specialized in methods for risk assessment of substances, including dose-response modeling, exposure modeling, probabilistic risk analysis, and toxicokinetic modeling. As an expert in these quantitative methods, he played an important role in many international committees. Dr. Slob developed a software program for analyzing dose-response data (PROAST). This is used a lot, nationally and internationally, in the context of risk assessment as well as in the context of scientific research in general. From 2000 to 2010, Dr. Slob also was appointed as a professor for quantitative risk assessment at the Institute of Risk Assessment Sciences (IRAS) of Universiteit Utrecht.

**Tuesday, March 23, 10:00 AM to 11:00 AM**

**Plenary Keynote Medical Research Council (MRC) Lecture: Using Luciferase-Based Mouse Reporter Lines to Detect and Track Epigenetic Changes Induced by Environmental Exposures**

**Lecturer:** Dame Amanda Fisher, MRC London Institute of Medical Sciences, London, United Kingdom.

Professor Dame Amanda Fisher has contributed to many areas of biology, including the molecular discovery of HIV and the impact of chromatin and nuclear location for gene expression.

Imprinted genes are epigenetically regulated and show parent of origin-specific expression. These genes have important roles in embryonic growth and metabolism, and their deregulation impacts upon postnatal metabolism and behavior, as well as susceptibility to disease. We recently created a series of luciferase reporter mice that enable imprinted gene expression to be sensitively imaged throughout development in vivo and across successive generations of animals. Our experiments have shown that environmental factors encountered in utero can disrupt epigenetic control within developing embryos and permanently alter the expression of imprinted alleles in offspring. For example, transient exposure to chromatin-modifying drugs such as TSA or 5’Azacytidine provoke the misexpression of paternally inherited (and normally silent) Cdkn1c alleles. In utero exposure to a low-protein maternal diet also induces paternal Cdkn1c re-expression, which is not reversed when offspring resume a normal diet. In a second series of experiments, we have shown that in utero exposure to high-fat maternal diet provokes the de-repression of a different (maternally silenced) imprinted gene, Dlk1. Remarkably, our data indicate that the epigenetic impact of this exposure remains visible across three generations of offspring. These results illustrate how luciferase-based reporter mice can be used to uncover exposures that alter the epigenetic landscape, examine how this occurs, and explore specific vulnerabilities of the developing embryo.

Co-authors: Mathew Van de Pette, Chiara Prodani, Alessandro Sardini, Dominic Withers, Oliver Howes, Matthias Merkenschlager, Rosalind M. John, and Anne Ferguson-Smith. MRC London Institute of Medical Sciences, Hammersmith Hospital, Imperial College London.
The term *cannabinoid* encompasses a broad family of molecules, including plant (cannabis)-derived, synthetic, and endogenous compounds possessing diverse biological activities. Indeed, cannabis alone possesses over 100 structurally related cannabinoids, most of which have yet to be studied to any extent. The majority of attention during the past 50 years has focused on the primary psychotropic constituent in cannabis, $\Delta^2$-tetrahydrocannabinol, and very recently cannabidiol, both of which can influence immune function. A focus of the Kaminski laboratory has been on defining the profile of immune activity by cannabinoids and elucidating the molecular mechanisms mediating cannabinoid immune modulation. A significant advancement in the field came with the identification and cloning of two G-protein coupled cannabinoid receptors, CB1 and CB2, and the establishment of their expression on leukocytes. Identification of cannabinoid receptors quickly led to the discovery of endogenous cannabinoid receptor ligands, raising questions concerning their physiological role, including in immune regulation. An important backdrop to cannabinoid research has been the prevalence of cannabis use, with an estimated 37 million adult users in the US and likely increasing with recent trends toward legalization of recreational consumption. Likewise, medical use of cannabis and cannabidiol has also increased significantly, with many questions about the benefits remaining unanswered. Finally, expression of cannabinoid receptors within the immune system, coupled with the absence of CB2 within the CNS, provides a putative drug target for cannabinoid-mediated immune modulation devoid of psychotropic activity. This presentation will discuss the molecular mechanisms by which cannabinoids modulate the immune system, as well as putative health implications and CB2 as a putative therapeutic target for the treatment of inflammatory diseases. Dr. Kaminski was the recipient of the SOT Merit Award in 2020.
SOT and the Japanese Society of Toxicology (JSOT) are delighted to jointly sponsor a Symposium on a topic of mutual interest: oxidative stress in multiple manifestations of toxicity. Each society has selected from among its membership leaders in the field to provide their perspectives on recent advances in this area. The Symposium will highlight advances in research on the role of oxidative stress in adverse outcomes. Oxidative stress occurs when the products of oxidative processes exceed the cell’s capacity to handle them. The resulting imbalance causes damage to macromolecules, leading to cellular damage and eventually to a variety of disease states. The SOT/JSOT Symposium will explore multiple mechanisms and outcomes of oxidative stress.

**Nrf2 and CSE: Two Sides of the Same Coin in Protection against Electrophilic Stress as a Category of Oxidative Stress.**

Yoshito Kumagai, University of Tsukuba, Tsukuba, Japan.

We are exposed to numerous xenobiotic electrophiles on a daily basis through the environment, lifestyle, and dietary habits. These compounds are able to covalently modify protein thiols, resulting in formation of protein adducts associated with activation of redox signaling pathways and toxicity. However, it is well recognized that such reactive chemicals undergo conjugation with GSH produced by GCL in the absence and presence of GST, yielding their GSH adducts, which are in turn excreted into extracellular space through MRP. Several lines of evidence have indicated that Nrf2 is a key molecule in detoxification and excretion of xenobiotic electrophiles because Nrf2 cooperatively regulates gene expressions of GCL, GST, and MRP.

Cystathionine γ-lyase (CSE) catalyzes cysteine persulfide (CysSSH) derived from cystine as a substrate. Importantly, CysSSH interacts with GSH, yielding GSH sulfide, indicating that the formation of these reactive sulfur species (RSS) is due to the transfer of their intramolecular sulfane sulfur. In 2011, we identified bismethylmercury sulfide as a less toxic metabolite of methylmercury (MeHg) from livers of rats given MeHg and found that formation of this sulfur adduct is due to nonenzymatic reaction of MeHg with hydrogen sulfide and GSSH derived from CysSSH. Several lines of evidence suggest that other xenobiotic electrophiles could be captured by RSS as above. Consistent with this notion, we identified a variety of sulfur adducts of xenobiotic electrophiles and even endogenous ones. Of interest, exposure of cultured cells to sulfur adducts of either 1,4-naphthoquinone or cadmium did not cause activation of redox signaling pathways and cytotoxicity, suggesting RSS are novel molecules to regulate reactivity of electrophiles through formation of the sulfur adducts. The Symposium will introduce a mouse model that provided new insights into the response to electrophilic stress; while Nrf2 is recognized as an important transcription factor for detoxification of xenobiotic electrophiles, CSE is a crucial enzyme to repress their toxicity in a parallel mode.


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**Janus Face of Antioxidative Selenoprotein P: Friend or Foe?**

Yoshiro Saito, Tohoku University, Sendai, Japan.

An essential trace element, selenium (Se) has high toxicity, and the optimum range of Se between excess and deficiency is quite narrow. It has been thought that the essential biological role of Se is mediated by selenoproteins, possessing Se as selenocysteine (Sec), which is an analog of cysteine containing Se instead of sulfur.

Selenoproteins, such as glutathione peroxidase (GPx; remove reactive oxygen species) and thioredoxin reductase (TrxR), play a significant role in redox regulation and antioxidative defense, and its dysfunction leads to oxidative stress and its related diseases; however, recent evidence has demonstrated the undesired effects of excess selenoproteins. Selenoprotein P (SeP; encoded by SELENOP) is a Se-rich plasma protein synthesized primarily by the liver. SeP is a multifunctional protein possessing GPx-like phospholipid hydroperoxide reducing activity and Se-transport activity, playing an essential *in vivo* role to maintain selenoprotein levels in several tissues. SeP deficiency decreases selenoproteins in the brain and testis and results in oxidative stress. In addition, the binding properties of SeP for heavy metals have been discovered. Thus, SeP acts as an important redox regulator. However, in type 2 diabetes patients, SeP levels...
were high, and increased SeP impaired insulin signaling, promoting insulin resistance in the skeletal muscle\textsuperscript{3,4}. Furthermore, excess SeP disturbed the function of pancreatic β cells and inhibited insulin secretion\textsuperscript{5}. These studies indicate that excess SeP is a significant target of diabetes therapeutics. This presentation will address the role of SeP as a redox regulator \textit{in vivo}, and particularly its relevance to the brain and testis. Further, the molecular mechanisms of glucose metabolism disorder induced by excess SeP will be presented and the effectiveness of SeP-neutralizing antibody will be shown. Finally, a molecular mechanism of pancreatic toxicity of excess SeP in type 2 diabetes and a control mechanism operating via SeP and insulin between the liver and pancreas will be discussed\textsuperscript{6,7}.


The Wrong Place at the Wrong Time: Redox Stress in the Developing Embryo.
Alicia R. Timme-Laragy, University of Massachusetts Amherst, Amherst, MA.

Glutathione (GSH) is the most abundant endogenous cellular redox buffer and plays key roles in vertebrate embryonic development and organogenesis. The GSH system in the embryo changes in both quantity and redox potential at different stages of development in specific and dynamic ways that can define critical windows of susceptibility to chemical-induced redox stress. Further, the ability of the GSH system to respond to and recover from redox stress changes throughout development. Investigating changes in GSH during this vulnerable period of life has been challenging, as it has been difficult to obtain organ-specific data. The zebrafish embryo is transparent, develops externally to the mother, and is highly permeable to dyes and other small molecules. By applying the GSH dye monochlorobimane (MCB) to the zebrafish at different stages of development, we have demonstrated that this presents an unbiased tool with which to examine organ-specific changes to GSH utilization \textit{in vivo}. The brain and heart demonstrated the largest endogenous changes in MCB staining over four days of development, as well as dynamic responses to GSH modulation. The GI tract showed changes with redox-active toxicants perfluorooctanesulfonic acid (PFOS) and mono-(2-ethyl-hexyl)phthalate (MEHP) in a dose- and age-dependent manner that correlate with structural changes to the pancreas within that region; endocrine pancreas morphology is most sensitive to redox chemical–induced changes at 48 hours post fertilization. As numerous toxicants affect the glutathione system, understanding where and when this occurs in the embryo can help identify sensitive target tissues of redox-active toxicants, and MCB staining is a robust, sensitive method to detect these spatiotemporal changes in embryonic GSH.

Redox Metabolomics and Network Analysis of Oxidative Stress and Toxicity.
Dean P. Jones, Emory University, Atlanta, GA.

The redox metabolome, along with the redox proteome, transcriptome, and epigenome, provides an adaptive network to defend an organism from environmental stresses. Systematic study of the redox metabolome is challenging because the total number of ‘omics elements (>1018) is too large to allow targeted, hypothesis-driven research for each (>1018 experiments). Additionally, the environmental challenges are diverse and numerous. High-resolution metabolomics (HRM) takes advantage of ultra-high-resolution mass spectrometry and advanced computational methods to provide ‘omics-scale biomonitration of exposures and biologic responses in model systems and human research. Application of untargeted HRM to oxidative stress research has been difficult, however, owing to uncertainty about efficiency of trapping correct oxidation-reduction balance for oxidizable components. Two approaches are now available to overcome this limitation, enabling untargeted redox metabolomics studies of oxidative stress. One approach uses data-driven integrative ‘omics with xMWAS to link metabolite changes, as well as transcript and protein changes, to measured levels of specific oxidants, such as H2O2. Another uses xMWAS to link metabolite and other ‘omics data to measured thiol redox parameters, including GSH and related redox ratios and redox potential. Results from model systems show extensive redox networks associated with mitochondrial respiratory and antioxidant functions, interconnecting redox proteome, transcriptome, and redox metabolome. Results from human studies show major mitochondrial and lipid pathways varying with plasma GSH–related redox systems. These analytic capabilities create new opportunities to elucidate mechanisms of oxidative stress and toxicity in complex biologic systems.

Additional Featured Sessions
Other Featured Sessions, including additional Award Lectures, will be added to the 2021 Virtual Meeting schedule. Look for announcements in January 2021 regarding these new sessions.
About the Scientific Program Schedule

The program schedule layout is ordered by date and start time. Each Scientific Session listing includes a session abstract and list of speakers/featured presenters.

- **Session Type and Title:** Session type and title display in large white type within the dark blue and teal box.
- **Primary Endorser:** This notation identifies the SOT Committee, Regional Chapter, Special Interest Group, or Specialty Section that developed and/or recommended the session.
- **Other Endorser(s):** This notation identifies other SOT groups that endorsed the session.

More details and the most up-to-date information related to the 2021 Annual Meeting program schedule are available in the Online Planner on the SOT Annual Meeting website.

During the Virtual Annual Meeting, SOT will present approximately five hours of scientific content—from Symposium to Poster Sessions—every weekday from 10:00 am to 4:00 pm (EDT, UTC -4). Each Scientific Session will premiere on a specific day and time, with all speakers and Chairs present to answer questions and comments in real time while their pre-recorded presentations are shown. Upon the completion of a scheduled session, all associated presentations will be available on demand via the Virtual Meeting platform for the duration of the meeting. Most of the Scientific Sessions will be occurring concurrently with each other, so attendees will have many choices at any given time, including the opportunity to take part in networking events, social interactions, and exhibit exploration. SOT has spared no effort in ensuring that the Virtual Meeting will deliver the robust scientific and interpersonal content that defines the SOT meeting each year.

The following pages contain details on the nearly 60 Symposium, Workshop, Roundtable, Informational, and Education-Career Development Sessions scheduled for the Virtual Meeting. Information on the Platform and Poster Sessions will be available as a separate PDF in February 2021.
Scientific Sessions | Monday, March 15

Please note that the listed times for all Scientific Sessions reflect US Eastern Daylight Time (UTC -4).

Monday, March 15, 11:15 AM to 2:00 PM

Symposium Session: Environmental Influences on Placental Origins of Development

Chair(s): Lauren Aleksunes, Rutgers, The State University of New Jersey; and Thad Schug, NIEHS.

Primary Endorser: Reproductive and Developmental Toxicology Specialty Section

Other Endorser(s): Mechanisms Specialty Section

The placenta is one of the least understood human organs and is important, not only for the health of a woman and her fetus during pregnancy, but also for the lifelong health of both. The placenta connects the developing embryo/fetus to the uterine wall and functions as a barrier to mediate nutrient uptake, waste elimination, and gas exchange via the mother’s blood supply. It helps fights against internal infection, produces hormones to support pregnancy and metabolic activity, and transports environmental chemicals both within the placenta and to the fetus. Yet, our understanding of placental physiology, endocrinology, and toxicology is very limited. It is becoming clear that the placenta is more than a conduit between the mother and developing fetus. It is a physiologically active tissue, which has the potential to impact the health of the offspring and the mother. The structure, including size, shape and orientation, and function of the placenta not only affect the health of the mother, as seen in the development of insulin resistance, preeclampsia, gestational hypertension, and eclampsia, but also affect the fetus, causing premature birth, intrauterine growth restriction, and functional changes in the fetus including altered male reproductive development and neurodevelopment. The goal of this session will be to discuss how toxicant exposures affect placental structure and function and how these changes impact the health of the offspring and the mother and offspring.

This session will highlight placental research projects that use a combination of animal/cell models and noninvasive human placenta tissues or biomarkers from existing human studies to comparatively investigate placental exposures, and to gain a better mechanistic understanding of the effects of environmental exposures on early-stage placental health and the subsequent effects on the health of offspring.

Abstract #

#1015 11:15 AM Environmental Influences on Placental Origins of Development.  


#1017 12:00 Noon Impact of Nanoplastic Particles in the Maternal-Fetal Environment.  P. Stapleton. Rutgers, The State University of New Jersey, Piscataway, NJ.


#1019 1:20 PM Developing a High-Throughput Placenta-on-a-Chip.  K. Bircsak. MIMETAS, Gaithersburg, MD.
For a blood-borne endo- or xenobiotic to gain access to neurons, neuroglia, and cerebrospinal fluid (CSF), it must pass across a monolayer of “barrier” cells that are sealed by tight junctions between adjacent cells. The blood-brain barrier (BBB), structurally featured by cerebral capillary endothelial cells, separates the blood circulation from brain’s interstitial fluid, whereas the blood-CSF barrier (BCB), formed by choroidal epithelial cells in brain ventricles, discontinues the blood from the CSF. Rapid progress in the past decades, fueled by innovative neuroimaging technology, dynamic in vitro microfluidic models, and human-induced pluripotent stem cells (hiPSC), has established an indisputable role of brain barrier systems in the causation and progression of a variety of neurodegenerative diseases as well as chemical-, microbiota-, virus-, or external force-induced neurotoxicities. For example, the loss of the BBB’s tight junction integrity with the increased paracellular permeability is known to facilitate vasogenic edema, neuroinflammation, and increased mortality in ischemic stroke and traumatic brain injury. The revolving circle between BBB injury and cerebral amyloid angiopathy, which enhances each other’s severity, has been proposed in the lead-induce pathogenesis in Alzheimer’s disease. Furthermore, the concept of the early-life exposure leading to BBB/BCB disorders and the possible late-life neurological impairments has recently been established with the evidence from animal models, medical imaging analyses, and CSF biomarker studies. Yet, the knowledge gap still exists in toxicological understanding of brain barriers in brain development, transport, and metabolism of toxicants/metals in chemical- or external force-induced neurotoxicities. This Symposium invites internationally well-established researchers in this cutting-edge research field to discuss how the structural and functional damages in brain barrier systems can lead to detrimental neurotoxicities. The first speaker introduces the concept of blood-brain interfaces and categories of transport systems in brain barriers, and the recent data that support the lead-induced amyloid angiopathy due to disrupted amyloid transport in BBB. The second speaker expends the subject by introducing advanced neuroimaging technology in assessing the BBB permeability in an ischemic stroke model and how this technique can be applied to visualize the choroid plexus where the BCB is localized. The third speaker further focuses on the response of brain barrier systems to developmental injury leading to subsequent neuroinflammation and neurotoxicity. The fourth speaker continues the subject of developmental BBB, but with an emphasis on the recent discovery of TCDD activation of Ahr2 and the ensuing damage to cerebral vascular development. The last speaker addresses, beyond biochemical interactions at barriers, how external physical forces such as brain traumatic injury can alter the BBB structure, causing severe neurotoxic consequences. In addition, the speaker discusses the capability of metallic nanoparticles such as silver, gold, copper, and iron to produce the selective damage to BBB depending on their shape and size. The Symposium synthesizes a broad range of speakers’ unique experience in this critical niche area of neuroscience, in the hope to raise the awareness and thus promote the brain barrier research in toxicological sciences. The in-depth mechanisms uncovered by each speaker will provide new clues for potential amelioration and therapeutic intervention. This Symposium will be of interest to clinical and basic scientists engaged in toxicology research related to neurotoxicology, neurodegenerative diseases, development, metals and pesticides, and systems biology.

Abstract #

#1020 11:15 AM  Impaired Brain Barrier Systems: Relationship to Chemical-Induced Neurotoxicities.  W. Zheng. Purdue University, West Lafayette, IN.


Monday, March 15, 11:15 AM to 2:00 PM

Symposium Session: Industrial Applications of Artificial Intelligence in Toxicology

Chair(s): Catrin Hasselgren, Genentech Inc.; and Nigel Greene, AstraZeneca.

Primary Endorser: Computational Toxicology Specialty Section

Other Endorser(s): Drug Discovery Toxicology Specialty Section

Artificial intelligence (AI) is being touted as a solution to improve efficiencies in new product development. This is especially apparent in the chemical industries, where rising costs and greater regulations on environmental and consumer safety, as well as the desire or need to reduce the use of animals in testing, have led to major investments in AI. In the pharmaceutical industry, computational methods in toxicology have received recent attention with the adoption of the ICH M7 Guideline, which specifies using (Q)SAR methods to predict bacterial mutagenicity of drug impurities, but computational methods in toxicology have had a much broader impact than just this narrow application. This session will look at a variety of applications of AI in chemical development using pharmaceutical development as an example. The methods and use cases will demonstrate the diversity of computational uses that are dependent on real-world challenges toxicologists face. The first presenter will address how using large databases of in vivo data can be used to predict the outcomes of novel compounds using AI. The second presentation focuses on how artificial intelligence is aiding in the automated diagnosis of tissue damage resulting from chemical exposure. The third presentation will describe the use of graph convolutional networks to predict new indications for existing therapies, unwanted side effects of therapies, and address the concept of predicting the effects of combinations of drugs using real-world evidence. The final presentation will focus on predicting the pharmacokinetics of a drug molecule as well as its effects on a biological system using combinations of both structural and biological data including gene expression profiles.

Abstract #

#1026 11:15 AM Industrial Applications of Artificial Intelligence in Toxicology. C. Hasselgren. Genentech Inc., South San Francisco, CA.

#1027 11:20 AM Development of In Silico Models from In Vivo Drug Toxicity Data and Their Successful Application for Regulatory Submission. A. Amberg. Sanofi, Frankfurt, Germany. Sponsor: C. Hasselgren


#1029 12:40 PM Machine Learning for Prediction of Safe and Effective Drugs. M. Zitnik. Harvard University, Cambridge, MA. Sponsor: C. Hasselgren

#1030 1:20 PM Toward Integrated Compound Safety Assessment, in Particular the Use of 'Omics Data and Pharmacokinetics Information, in Toxicity and Safety Prediction. A. Bender. Cambridge University, Cambridge, United Kingdom.
Recent advancements of *in vitro* methodologies provide valuable insight into better ways to incorporate toxicokinetics and exposure in various decision-making contexts. One of the indisputable benefits of *in vitro* approaches is their capacity to increase chemical throughput compared with animal testing, allowing faster chemical screening and prioritization. However, with the advent of pressing global drivers to reduce and eliminate animal testing, understanding the utility of integrated *in vitro* approaches is critical. Often in chemical safety testing, when evaluating or extrapolating human kinetics from *in vivo* models, providing a comparison of effect levels from exposure scenarios has been challenging. Increasing evidence demonstrates we can move beyond the use of *in vitro* assays for compound prioritization and risk ranking potential to applications for quantitative exposure and risk estimates by using physiologically based pharmacokinetic (PBPK) models and quantitative *in vitro* to *in vivo* extrapolation (QIVIVE). The advantage of using *in vitro* approaches now extends to dose-response relationships, benchmark dose modeling, and elucidating complex metabolic pathways. By leveraging an understanding of toxicokinetics and dose-response relationships, QIVIVE converts *in vitro* bioactivity through reverse dosimetry to estimate human equivalent administered dose. The objective of this session is to demonstrate, through the use of integrated approaches, the application of *in vitro* metabolism and QIVIVE in various decision-making contexts. Key discussion points will include interpreting integrated data streams, building confidence in new approaches to inform quantitative risk assessment, applying weight of evidence to overcome assay uncertainty, and increasing uptake of new methodologies for regulatory application. Based on current findings, this session also will outline an initial framework to learn how *in vitro* technologies can be used to increase confidence in chemical safety and inform risk assessment. The session begins with a brief review of recent technological advances. Each speaker will then present a novel case study illustrating the benefits and complexities of adopting *in vitro* metabolism and QIVIVE models for chemical risk assessment.

**Abstract #**

#1031 11:15 AM  **A Future Framework for Application of *In Vitro* Metabolism and QIVIVE Models to Inform Risk Assessment.**

11:15 AM  **Introduction.**  *E. Haugabrooks.* Physicians Committee for Responsible Medicine, Washington, DC.

#1032 11:20 AM  **Strategies to Overcome the “Human Metabolism” Bottleneck in Regulatory Risk Assessment of the 21st Century.**  *S. Coecke.* European Commission Joint Research Centre, Ispra, Italy. Sponsor: *E. Haugabrooks*

#1033 11:50 AM  **Toxicokinetic Models for QIVIVE and Considerations of Uncertainty.**  *X. Chang.* Integrated Laboratory Systems Inc., Research Triangle Park, NC.

#1034 12:20 PM  **Practical Applications of QIVIVE (Quantitative *In Vitro* to *In Vivo* Extrapolation) and Associated Interpretive Opportunities.**  *K. Magurany.* NSF International, Ann Arbor, MI.

#1035 12:50 PM  **The Impact of *In Vitro* Metabolic Competency on Chemical Screening and Its Relevance to *In Vivo* Toxicity.**  *S. Marty.* Dow, Midland, MI.

#1036 1:20 PM  **Case Study Examples Establishing the Utility of QIVIVE and for Estimating Safe Human Exposures.**  *R. Clewell.* 21st Century Tox Consulting, Durham, NC.

1:50 PM  **Panel Discussion/Q&A.**
Chemically induced lung tumors are commonly reported in mouse carcinogenicity bioassays, and often in the absence of parallel tumor-igenicity in rats. Long-term bioassays need to be assessed for appropriateness of the dose, neither exceeding the Maximum Tolerated Dose (MTD) nor the Kinetically Based Maximum Dose (KMD). In addition, since mouse lung tumors are common (>1% incidence), the appropriate statistical significance is p<0.01. Numerous differences exist for mouse lung tumors compared with humans, including anatomy, respiratory rate, metabolism, tumor histogenesis, and metastatic frequency. The recent demonstration of the critical role of mouse CYP2F2 metabolism in mouse lung carcinogenicity (e.g. styrene, fluensulfone) indicates that this tumor response is not qualitatively or quantitatively relevant to humans. For non-DNA-reactive and nonmutagenic carcinogens, the mode of action involves direct mitogenicity (isoniazid, styrene, fluensulfone, permethrin) or cytotoxicity with regeneration (e.g., naphthalene). However, the possibility of mixed mitogenic and cytotoxic modes of action cannot always be excluded. Finally, human health risk assessment can be conducted based on these considerations/conclusions. This Workshop will comprise a series of presentations addressing (1) important considerations for assessing carcinogenic potential of chemicals due to increased mouse lung tumors; (2) distinct inter-species differences in lung and respiratory tract anatomy and cell types, as well as metabolism between mice, rats, and humans, and thus a possible mouse lung tumor screening strategy; (3) utility of genetically modified mouse strains as mode-of-action research tools to understand key metabolic drivers of mouse lung toxicity and tumors; (4) styrene mode of action as a case example of a potential qualitative difference in mode of action between mice, rats, and humans; and (5) perspective from the US Environmental Protection Agency (US EPA): key considerations for regulatory decision-making. The Workshop presentations and panel discussion will catalyze audience dialog of the key mode-of-action consideration of “how much (data) is enough” and a potential decision tree to support science-justified risk evaluations of the human relevance of mouse lung tumors.

**Abstract #**

#1037  11:15 AM  **Chemical-Induced Mouse Lung Tumors: Mode of Action, Relevance, and Risk Assessment.**

#1038  11:15 AM  **Introduction: Chemicals That Induce Lung Tumors in Mice but Not in Rats, and Biological Considerations for Evaluating Chemical Carcinogenic Potential.**  Z. Yan. Corteva Agriscience, Indianapolis, IN.

#1039  11:35 AM  **Assessment of Mouse Lung Tumorigenesis: Importance of Evaluating Mode of Action and Relevance to Humans.**  S. Cohen. University of Nebraska Medical Center, Omaha, NE.

#1040  12:05 PM  **Genetically Modified Mouse Models as a Means for Informing the Human Health Relevance of Mouse Lung Toxicants.**  X. Ding. University of Arizona, Tucson, AZ.

#1041  12:35 PM  **Styrene-Induced Lung Tumors: Lack of Quantitative or Possible Qualitative Relevance to Human Risk.**  J. Bus. Exponent, Midland, MI.


1:35 PM  **Panel Discussion/Q&A.**
Probiotics are among the most widely used specialty supplements in the United States, according to a recent consumer survey conducted by the Council for Responsible Nutrition. A continued increase in probiotic usage is expected as companies develop probiotic strains for uses beyond gut health to such usage as sports nutrition and upper respiratory health. Like many natural products used in dietary supplements, probiotics are presumed to be safe. This presumption of safety is not completely unfounded; there is global consumption of common probiotics, and data from large cohort studies indicate a lack of serious adverse events. However, as probiotic manufacturers are increasingly seeking to use new strains, species, or even novel probiotics (human commensals, but not currently found in the food supply), justification based on a significant history of use may be challenged. Furthermore, a number of clinicians have very recently publicly questioned the available safety and efficacy data supporting the widespread use of probiotics. Additionally, criticisms have been directed toward the dietary supplement industry for circumventing US Food and Drug Administration review of new dietary supplement products by utilizing the self-GRAS approach. There are efforts underway by a variety of stakeholders, including the United States Pharmacopeia (USP) and various probiotic and dietary supplement trade associations to develop best practices guidelines for assessing the quality and safety of probiotics. This session includes presentations on and industry approach to ensuring the safety of probiotics (and prebiotics/postbiotics), efforts underway to define quality and safety standards for probiotics by the USP, justification for continued regulation by industry through a self-GRAS path, and an overview of Health Canada’s approach to regulating probiotics as Natural Health Products.

Abstract #


#1044 11:15 AM An Industry Perspective on Assessing Safety of “-Biotics” as Dietary Supplements. A. Roe. Procter & Gamble, Cincinnati, OH.


#1047 1:10 PM Probiotic Safety in the Natural Health Product Context. M. Steller. Health Canada, Ottawa, ON, Canada. Sponsor: A. Roe

1:45 PM Panel Discussion/Q&A.
Workshop Session: Standardization of \textit{In Vitro} Inhalation Exposure for Regulatory Acceptance

\textbf{Chair(s):} Holger Behrsing, Institute for In Vitro Sciences Inc.; and Xuefei Cao, US FDA/NCTR.

\textbf{Primary Endorser:} Inhalation and Respiratory Specialty Section

\textbf{Other Endorser(s):} Exposure Specialty Section; \textit{In Vitro} and Alternative Methods Specialty Section

Human exposure to airborne substances occurs from a number of sources, including air pollution and the use of consumer products. As some of these exposures can have detrimental effects on health, exposure limits have been established and/or registration is required for their use based on a thorough understanding of their acute and chronic toxicity. Traditionally, animal models have been used for assessing the respiratory toxicity of chemicals inhaled as aerosols, vapors, or airborne dust. However, the fundamental differences in the anatomy, physiology, and biology of animals and humans, along with ethical issues raised with animal testing, have greatly promoted the use of human-relevant \textit{in vitro} methods. However, conducting \textit{in vitro} exposures in a manner simulating human inhalation exposure is technically challenging due to the unique variables related to the properties of the test articles, exposure dosimetry, and deposition dynamics within the respiratory tract, all of which influence the outcomes of the studies. Although workshops have been held to establish consensus on \textit{in vitro} methodologies for assessing inhaled substances, most discussions focused on cell-based lung models.

Methods for controlled generation and delivery of test articles in forms and at doses relevant to human inhalation exposure, which are paramount to the resulting toxic effects of the test substances, are less discussed. Furthermore, the standardization of \textit{in vitro} exposure methods that is required for their regulatory acceptance is also lacking. To stimulate discussions on this important aspect of \textit{in vitro} inhalation toxicology, subject-matter experts will present their approaches for exposing \textit{in vitro} human lung models to occupational chemicals, consumer products, and nanomaterials at the air-liquid interface (ALI). Specifically, Workshop speakers will present (1) an overview of the existing ALI exposure systems as well as the recommended practice for conducting analytical validation of these systems; (2) key considerations for selecting the appropriate \textit{in vitro} test system, exposure regimen, and toxicity endpoints for toxicity assessment of occupational and consumer product exposures; (3) an integrated \textit{in vitro} approach for safety evaluation of fragrance ingredients in consumer products; (4) a six-step methodology for selecting \textit{in vitro} doses reflecting \textit{in vivo} internal doses at the target organ burden for respiratory toxicity evaluation of nanomaterials; and (5) ongoing regulatory activities at the US Environmental Protection Agency’s Office of Pesticide Programs to evaluate \textit{in vitro} alternatives for inhalation risk assessment to support pesticide registrations. The audience will take home the basic experimental designs and practical considerations for testing a range of substances, the human relevancy of the approaches, and determination of exposure dosimetry. The roundtable discussion following these presentations will discuss elements that require standardization for regulatory acceptance and identify and prioritize common elements of the experimental approaches for conducting ALI exposures to airborne substances, regardless of their physiochemical properties, for further action. This Workshop will not only provide a comprehensive overview of methodologies for conducting \textit{in vitro} inhalation exposures, but also identify key knowledge gaps in standardization of \textit{in vitro} exposure methods for regulatory acceptance and develop a framework to ensure human relevancy of the \textit{in vitro} approaches.

\textbf{Abstract #}

\begin{tabular}{ll}
\#1048 & 11:15 AM \textbf{Standardization of \textit{In Vitro} Inhalation Exposure for Regulatory Acceptance.} \\
& 11:15 AM \textbf{Introduction.} \textit{H. Behrsing}. Institute for In Vitro Sciences Inc., Gaithersburg, MD. \\
\#1050 & 11:50 AM \textbf{Integrating New Approach Methodologies (NAMs) to Assess Risk to Human Health from Occupational and Consumer Exposures to Inhaled Toxicants.} \textit{S. Krieger}. Dow, Midland, MI. \\
\#1051 & 12:15 PM \textbf{Consumer Exposure to Fragrance Ingredients and Implementation of \textit{In Vitro} Risk Evaluations.} \textit{N. Sadekar}. Research Institute for Fragrance Materials, Woodcliff Lake, NJ.
\end{tabular}
Preclinical safety evaluation of pharmaceuticals relies mainly on studies in animal models. While the use of animals has made significant contributions to safety assessment, there remains uncertainty in the extrapolation of risk from animals to humans. This is particularly true for novel therapeutics that do not cross-react to animal orthologs and lack pharmacological activity in species used for toxicology studies. Therefore, development of human-centric approaches to predict drug safety in humans is essential. Human genetics research has discovered thousands of proteins associated with complex and rare diseases. Genome-wide association studies (GWAS) and studies of Mendelian disease have resulted in an increased understanding of the role of gene function and regulation in human conditions, which has been leveraged to discover and validate therapeutic targets. While the application of human genetics has been explored primarily as a method to identify potential drug targets and support their relevance to disease in humans, there is increasing interest in genetic data to predict safety liabilities. Human genetic variants can be used as a model to anticipate the lifelong modulation of therapeutic targets and predict the potential for on- and off-target adverse events. This approach is particularly useful for nonclinical safety evaluation of novel therapeutics that lack appropriate animal models that demonstrate pharmacological activity and may provide justification of the intrinsic safety profile of the target. The overall objective of this Workshop is to introduce human genetics and showcase its use and potential to inform safety signals of therapeutics. The Workshop will cover the following topics: (1) an overview of human genetic association studies, including GWAS and PheWAS, with the aim of providing a basic understanding of the methodologies and applications to drug discovery and development; (2) Case examples that illustrate the applications of human genetics in target discovery, to inform on- and off-target adverse events. The impact on drug safety evaluation and clinical utility will be discussed; (3) Utility of human genetics in identifying genetic risk factors contributing to adverse drug reactions from the large volume of health records as well as knowledge accumulated from drug development; and (4) Discussion on the challenges of and future perspectives on translating human genetic information to predict drug effects in preclinical and clinical development. This Workshop will be of interest to toxicologists engaged in preclinical and clinical safety evaluation during drug development and to human geneticists interested in preclinical applications and clinical translation.

Abstract #

#1054 11:15 AM Using Human Genetics to Aid in Safety Assessment of Therapeutics.


#1057 12:20 PM Observational Data for Pharmacogenomics Discovery. N. Tatonetti. Columbia University, New York, NY. Sponsor: J. Yuan

#1058 12:45 PM HLA and Predisposition to Serious Adverse Drug Reactions. M. Pirmohamed. University of Liverpool, Liverpool, United Kingdom. Sponsor: J. Yuan
#1059 1:15 PM  The Role of Genetics and Genomics in Predicting Drug-Induced Liver Injury.  M. Chen. US FDA/NCTR, Jefferson, AR.


### Monday, March 15, 2:45 PM to 4:05 PM

#### Informational Session: Turning Over a New Leaf: An Update on the Clinical Toxicology of Synthetic Cannabinoids

**Chair(s):** Sally Bradberry, West Midlands Poisons Unit, United Kingdom; and Jeffrey Brent, University of Colorado Denver.

**Primary Endorser:** Clinical and Translational Toxicology Specialty Section

**Other Endorser(s):** Neurotoxicology Specialty Section; Occupational and Public Health Specialty Section

Synthetic cannabinoid abuse is an important cause of avoidable physical and psychological ill health. Many unknowns remain, particularly in terms of understanding mechanisms of toxicity and potential long-term health effects. This session will review the chemistry of these psychoactive drugs, how their structure impacts both mechanisms and clinical features of toxicity, the challenges intoxication causes at both an individual and a public health level and the management strategies employed. The first speaker will describe the chemical heterogeneity of synthetic cannabinoids and its potential relevance to mechanisms and the risk of toxicity. He will explain the potential advantages and problems surrounding different nomenclature systems, including laboratory-generated serial designations, names used by recreational users, and an alpha-numeric systematic nomenclature. The second speaker will describe the US experience of synthetic cannabinoid use, emphasizing the diverse and unpredictable clinical presentations and complications, including stroke, myocardial infarction, acute kidney injury, rhabdomyolysis, and hyperthermia. He will address the important issue of the potential contamination of synthetic cannabinoids with other biologically active molecules. The final speaker will give a firsthand account of acute management of those intoxicated with synthetic cannabinoids. She will explain why the diagnosis of synthetic cannabinoid intoxication has demanded a new approach to drugs of abuse laboratory diagnostics and collaborative working between clinical and analytical colleagues. She will discuss the public health challenge of managing synthetic cannabinoid use in vulnerable groups and the evolving concerns related to long-term use of these agents.

**Abstract #**

#1061 2:45 PM  Turning Over a New Leaf: An Update on the Clinical Toxicology of Synthetic Cannabinoids.

2:45 PM  Introduction.  S. Bradberry. West Midlands Poisons Unit, Birmingham, United Kingdom.

2:50 PM  Synthetic Cannabinoids: Chemistry, Nomenclature, and Mechanisms.  S. Hill. National Poisons Information Service (Newcastle Unit), Newcastle, United Kingdom. Sponsor: S. Bradberry

3:15 PM  Clinical Presentation of Synthetic Cannabinoid Exposures and the US Experience.  J. Brent. University of Colorado Denver, Denver, CO.

3:35 PM  Synthetic Cannabinoid Abuse: Diagnosis and Management.  S. Bradberry. West Midlands Poisons Unit, Birmingham, United Kingdom.

3:50 PM  Panel Discussion/Q&A.
The COVID-19 pandemic is one of the most crucial global health calamities of the century spreading around the globe. This spread has been attributed to the transmissibility of the virus combined with scarcity of critical infrastructure and the unique challenges of sustaining population health and protecting the environment. The session is focused on the impact of COVID-19 (specifically toxicological, environmental, public health, and vulnerable indigenous populations) on the African continent given that the infrastructure and resources to deal with this calamity are extremely limited or are lacking in some countries. The community dynamics in various African localities also pose a great challenge to mitigate the threat of the virus to the 1.2 billion population of the continent. As of April 2020, greater than 140,000 confirmed SARS-CoV-2 cases had been reported on the African continent. It has been reported that the confirmed cases in Africa are much lower than in the United States. The available data suggest that most African countries have inadequate health care systems and access to them, with challenges such as lack of equipment, funding, insufficient training of healthcare workers and inefficient data transmission. Even personal protective equipment (PPE) and basic hygienic supplies like soap and water are subject to shortages in some parts of the continent. Despite all these challenges, it is noteworthy that some progress is being made by some African countries. For example, scientists in Nigeria and Ghana have sequenced the SARS-CoV-2 genome, while Senegal has developed rapid and affordable test kits. These efforts are expected to lead to understanding the spread and environmental impact of the virus on the continent. The potential genetic and environmental factors modulating disease spread and containment are subject of investigations and this calls for action in developing regional/global research strategies and collaborations. The session speakers will present and discuss the spread and toxicological, environmental, and public health impacts of the COVID-19 pandemic outbreak in Africa, focusing on lessons learned, identifying research needs, and proposing research strategies for collaborative work and coordination of ongoing interventions to adequately address this global pandemic.

Abstract #
#1062 2:45 PM  Understanding the Spread and Toxicological, Environmental, and Public Health Impact of the COVID-19 Pandemic on the African Continent.


2:50 PM Genomic Epidemiology of SARS-CoV-2 in Africa.  C. Happi. Redeemer’s University, Ede, Nigeria. Sponsor: A. Adeogun

3:05 PM The Role of Toxicology and Toxicologists in Combating the COVID-19 Pandemic.  M. Dourson. Toxicology Excellence for Risk Assessment, Cincinnati, OH.


3:50 PM Panel Discussion/Q&A.
Tuesday, March 16, 11:15 AM to 2:00 PM

Symposium Session: Developmental Toxicity Hazard Assessment without Animals: Pathways and Prospects

Chair(s): John Rogers, US EPA; and Nicole Kleinstreuer, NIEHS/NICEATM.
Primary Endorser: Reproductive and Developmental Toxicology Specialty Section
Other Endorser(s): In Vitro and Alternative Methods Specialty Section; Regulatory and Safety Evaluation Specialty Section

Global efforts are underway to transition toxicological risk assessment away from vertebrate animal models, as exemplified by the announcement from the US Environmental Protection Agency (US EPA) administrator announcing the Agency’s intent to virtually eliminate use or funding of vertebrate animal research within 15 years. The Lautenberg Chemical Safety for the 21st Century Act requires that new approach methodologies (NAMs) be developed and that NAMs should replace animal models only when they are deemed to provide information of equivalent or better scientific quality. This goal is perhaps most aspirational for developmental toxicity hazard assessment given the complex and dynamic nature of human pregnancy and embryofetal development. "Teratogen screens” have been developed and used for prioritization and mechanistic studies for decades. Now, new discoveries and technologies, along with the urgency to reduce animal usage, have emboldened the belief that replacement of animals for developmental toxicity hazard assessment and dose-response is within sight. NAMs that are based largely on in vitro data and in silico models provide a path forward to animal-free testing for developmental toxicity. This session will present the latest in NAMs, including cheminformatics and connectivity mapping, utility of transcriptomics for hazard assessment, advances in stem cell models, and data driven in silico models. Current examples will be provided. Establishing scientific confidence in the reliability and relevance of NAMs requires comparisons to our current human and animal knowledge base, and automated tools to enhance literature searching and reference data curation/annotation will be discussed. The unifying theme of the session and the panel discussion to follow will be to discuss breakthroughs, opportunities, and challenges in NAMs for developmental toxicology, and how they can ultimately contribute to an animal-free system for developmental hazard identification and dose-response that is equivalent to or better than existing animal-based regulatory tests.

Abstract #

#1063 11:15 AM Developmental Toxicity Hazard Assessment without Animals: Pathways and Prospects.
#1064 11:15 AM Introduction: Evolution of Approaches to Animal-Free Predictive Developmental Toxicology: Can We Get There from Here? J. Rogers. US EPA, Research Triangle Park, NC.
#1065 11:25 AM Biotechnology Plus 60 Years of Data Support Predictive Toxicology. G. Daston. Procter & Gamble, Cincinnati, OH.
#1066 11:50 AM Automated Approaches to Anchoring Alternatives. N. Kleinstreuer. NIH/NICEATM, Research Triangle Park, NC.
#1067 12:15 PM Stem Cell–Based In Vitro Morphogenesis Models to Investigate Developmental Toxicity of Chemical Exposures. Y. Marikawa. University of Hawaii, Honolulu, Hi. Sponsor: J. Rogers
#1069 1:05 PM Synthetic Microsystems, Computational Intelligence, and Artificial Life. T. Knudsen. US EPA, Research Triangle Park, NC.
1:30 PM Panel Discussion/Q&A.
A rich body of literature exists that has demonstrated adverse human health effects on the brain following exposure to ambient air particulate matter, and there is strong support for an important role of ultrafine (nanosized) particles, mainly from combustion processes. With global production having increased exponentially over the past decades, and a significant proportion not being disposed of properly, engineered and plastic particle pollution also is now a serious concern for brain health. Plastic debris spans orders of magnitudes in size, including nanoplastics, originating from products within which they were intentionally added, such as cosmetics or generated during use or by the degradation of larger plastic items, such as textiles, tire wear, or artificial turf. Nanomaterials are specifically designed being very small, also with a wide range of applications, including in food and medicines. A key feature of such ultrafine/nanosized particles is their ability to cross biological barriers and thereby reach other organs than the lung, as well as the ability to be taken up via olfactory and trigeminal nerves, thereby bypassing the blood-brain barrier, leading to neurotoxic effects following inhalation exposures. This Symposium will highlight our current understanding of nanoparticle-induced neurotoxicity from various sources of emissions.

Abstract #


#1071  11:15 AM  From Ambient Particulate Matter, to Nanomaterials, to Microplastics—Similarities and Differences with Respect to Dosimetry and Toxicity: Introduction.  F. Cassee. Rijksinstituut voor Volksgezondheid en Milieu (RIVM), Bilthoven, Netherlands.

#1072  11:30 AM  Developmental Neurotoxicity of Traffic-Related Air Pollution.  T. Cole. University of Washington, Seattle, WA.

#1073  12:00 Noon  Brain Metal Dyshomeostasis and Ultrafine Particulate Matter and Neurodevelopmental Disorders.  D. Cory-Slechta. University of Rochester Medical Center, Rochester, NY.

#1074  12:30 PM  Traffic-Related Air Pollution Particles: A Risk Factor for Alzheimer’s Disease?  R. Schins. IUF—Leibniz Research Institute for Environmental Medicine, Düsseldorf, Germany. Sponsor: F. Cassee

#1075  1:00 PM  Exposure to Inhaled Incidental Nanosized Particles Activates Markers of Neurotoxicity and Alters Dopaminergic Transmission.  A. De Vizcaya-Ruiz. Cinvestav, Mexico City, Mexico.

Acetaminophen (paracetamol, N-acetyl-p-aminophenol; APAP) is the most common drug taken in overdose in the US and United Kingdom (UK). In the US, APAP overdose accounts for more than 56,000 hospital visits and around 450 deaths due to acute liver failure each year. Annually, overdose directly leads to around 100,000 hospital visits in the UK, with around half of these patients admitted to hospital for emergency antidote treatment. APAP also is directly responsible for the deaths of 100–150 people per year in the UK. The mechanism of APAP hepatotoxicity has been extensively investigated in mouse models that faithfully represent the human disease and in human hepatocytes. At therapeutic doses, APAP is mostly glucuronidated and sulphated, then excreted. A small percentage is converted to the reactive intermediate N-acetyl-p-benzoquinoneimine (NAPQI), which is detoxified by reaction with glutathione. However, after overdose, excess NAPQI binds to intracellular proteins, causing increased oxidative stress, mitochondrial injury, and cell death. N-acetylcysteine (NAC) is the current treatment for APAP overdose. It acts by replenishing hepatocellular glutathione to increase the detoxification of NAPQI. Although highly effective at preventing hepatotoxicity when used within 8 h of overdose, it is associated with the following challenges: (1) reduced efficacy when administered later than around 8 h after overdose ingestion; (2) adverse drug reactions (ADRs): nausea/vomiting occurs in more than half of recipients and anaphylactoid reactions in about a third; and (3) prolonged duration: the regime is time-consuming, taking at least 21 h, leading to significant hospital bed occupancy. Recently, much-needed new treatments for APAP overdose have emerged, guided by increased understanding of the underlying pathophysiology and galvanized by new high sensitivity/specificity biomarkers of liver injury. In this session, we will review the landscape of new treatments with presentations from world-leading preclinical and clinical experts who are leading these efforts.

**Abstract #**

#1077 11:15 AM  **Novel Emerging Treatments for Acetaminophen Toxicity.**

11:15 AM  **Introduction.**  *J. Dear.* University of Edinburgh, Edinburgh, United Kingdom.

#1078 11:20 AM  **What Does a New Treatment for Acetaminophen Overdose Have to Be Able to Do?**  *R. Dart.* Rocky Mountain Poison and Drug Center, Denver, CO. Sponsor: *J. Dear*

#1079 11:50 AM  **Novel Regimens for Acetylcysteine Treatment.**  *S. Thomas.* Newcastle University, Newcastle, United Kingdom. Sponsor: *J. Dear*

#1080 12:20 PM  **Preclinical Evidence for New Treatment Targets in Acetaminophen Hepatotoxicity.**  *H. Jaeschke.* University of Kansas Medical Center, Kansas City, KS.

#1081 12:50 PM  **Clinical Studies with Fomepizole in Acetaminophen Overdose.**  *S. Curry.* University of Arizona, Phoenix, AZ. Sponsor: *J. Dear*

#1082 1:20 PM  **Clinical Studies with Calmangafodipir in Acetaminophen Overdose.**  *J. Dear.* University of Edinburgh, Edinburgh, United Kingdom.

1:50 PM  **Panel Discussion/Q&A.**
While gene-editing technologies such as RNAi, transcription activator-like effector nucleases, and zinc finger nucleases have been in use for years, none offer the ease of use and specificity of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-Cas9 approaches to advance our understanding of both fundamental biology and the adverse effects of chemical exposure. Forward and reverse genetic approaches can be applied across *in vitro* and multiple *in vivo* model systems for an unprecedented understanding of conserved modes of toxicity, potential susceptibility, and impacts on human and environmental health. This presentation will provide cutting-edge examples of how researchers are applying CRISPR/Cas-9 to characterize effects of gene edits and ultimately causally reveal key molecular events resulting from chemical exposure across multiple disciplines of toxicology. Presentations will focus on environmental toxicants and combine ‘omics-based pathway discovery with gene editing in cell and zebrafish model systems. In addition, innovative applications relevant to toxicity testing will be explored, including CRISPR-mediated genome-wide cell knockouts for rapid chemical toxicity screening and novel mode-of-action discovery to hypothesis driven loss-of-function edits in the zebrafish model to validate the essentiality of key molecular targets in diverse adverse outcome pathways or disease states. Overall, attendees will encounter novel case studies in the domains of neurotoxicity, carcinogenicity and occupational safety, and endocrine toxicity that collectively demonstrate unparalleled advances in adverse outcome pathway/network discovery facilitated by gene-editing technologies.

Abstract #

#1083 11:15 AM  Pairing Adverse Outcome Pathway Discovery with Advances in Gene Editing to Solve Toxicity Mechanisms.


#1087 12:10 PM  Using CRISPR-Cas to Identify How Endocrine Disruptors Cause Malformations and Functional Defects in the Zebrafish Heart. D. Gorelick. Baylor College of Medicine, Houston, TX.

#1088 12:30 PM  Gene Editing Reveals Microbiome-Host Signaling Mechanisms That Are Perturbed by Chemical Exposure. T. Tal. Helmholtz Centre for Environmental Research, Leipzig, Germany.

12:50 PM Panel Discussion/Q&A.
The relationship between exposure to environmental chemicals/pharmaceuticals, tissue dose, and toxic mechanism cannot be properly understood without a thorough understanding of compound metabolism, whether it is bioactivation or detoxification, or somewhere in between. Specifically, a thorough understanding of the role that the major metabolic enzyme family, the cytochrome P450s (CYPs), play in metabolism is needed, as these enzymes are of critical importance in the detoxification of harmful environmental chemicals and drugs. CYP enzymes are particularly challenging to study because they may vary in their metabolism of chemicals, they exhibit significant overlap in substrate specificity between isoforms, and they have large differences in complement and function across species. To add to these challenges, toxicology is moving toward high-throughput assays in toxicity testing due to the expanding number of chemicals found in commerce and the environment. In this session, we will examine the state-of-the-science of CYP in metabolism, novel \textit{in vitro} and \textit{in vivo} high-throughput assays, the challenges to implementation of these assays, and the development of various novel knockout and humanized models to support extrapolation of data from these systems. This session also will highlight future directions for the application of these systems in intervention and prevention of exposure to harmful environmental chemicals and to accelerate the prediction of toxicity of novel pharmaceuticals.

\textbf{Abstract #}

| #1089 | 11:15 AM | Improving Our Understanding of Toxicant Metabolism and Cytochrome P450s Using Novel Knockout Models and High-Throughput Methods. |
|       | 11:15 AM | Opening Remarks: Highlights from NIEHS Xenobiotic Metabolism Portfolio. \textit{D. Carlin}. NIEHS, Research Triangle Park, NC. |
| #1090 | 11:35 AM | The Future of P450 Research: Basic Questions and Practical Applications. \textit{P. Guengerich}. Vanderbilt University School of Medicine, Nashville, TN. |
| #1091 | 12:00 Noon | High-Throughput Screening for Zebrafish Cytochrome P450 Substrates Provides Insight into Enzyme Function. \textit{J. Wilson}. McMaster University, Hamilton, ON, Canada. |
| #1092 | 12:25 PM  | Cytochrome P450 Knockout Zebrafish in Toxicology. \textit{J. Goldstone}. Woods Hole Oceanographic Institution, Woods Hole, MA. |
|       | 1:40 PM | Panel Discussion/Q&A. |
Tuesday, March 16, 11:15 AM to 2:00 PM

**Workshop Session: New Approach Methodologies for Exposure: Advancing Chemical Risk Assessment**

**Chair(s):** John Wambaugh, US EPA; and Angelika Zidek, Health Canada.

**Primary Endorser:** Exposure Specialty Section

**Other Endorser(s):** Biological Modeling Specialty Section; Occupational and Public Health Specialty Section

This Workshop will review new approach methodologies (NAMs) for exposure science that have been developed to address the thousands of chemicals in commerce and the environment with little or no data. Public health chemical risk is the product of both inherent chemical toxicity and the potential for human exposure. The tools to characterize both toxicity and exposure have evolved significantly in the past decade. NAMs for exposure science are being developed to enable risk assessors to more rapidly address public health challenges and chemical regulation. These chemicals include those present in the home (such as flame retardants, plasticizers, fragrances), occupational settings (such as pesticides, solvents, cleaners), and the environment (such as persistent organic pollutants and “down the drain” pharmaceuticals and consumer product ingredients). NAMs for exposure science include (1) new methods that can be broadly applied for biomonitoring and biostatistics, (2) the application of machine learning to data-poor situations, (3) high-throughput exposure models for making predictions from limited chemical and scenario descriptors, (4) high-throughput toxicokinetic data and models enabling in vitro to in vivo extrapolation (IVIVE) of high-throughput toxicity data, and (5) chemical risk prioritization strategies that can be broadly applied across large numbers of chemicals. This Workshop will review new technological developments advancing exposure science as well as provide case studies of how NAMs are now being used. All the NAMs presented can inform assessment of the chemical effects on public health. In this session, each speaker will present a NAM for exposure, with an emphasis on the most recent developments; describe the key challenges in understanding that NAM; describe publicly available data and tools that are available to toxicologists; demonstrate application of the exposure NAM to toxicology and chemical risk assessment; clearly identify the chemical “domain of applicability” and any underrepresented chemical classes, and identify obstacles to regulatory acceptance of the exposure NAM. The Workshop will conclude with a moderated panel discussion where speakers will address audience questions on how to apply the presented methods in chemical risk assessment.

**Abstract #**

1. **New Approach Methodologies for Exposure: Advancing Chemical Risk Assessment.**
   


5. **High-Throughput Toxicokinetics Enables Risk-Based Prioritization.** J. Wambaugh. US EPA, Research Triangle Park, NC.


1:20 PM **Panel Discussion/Q&A.**
Pulmonary toxicology research is facing the challenge of correlating in vitro mechanistic investigations and in vivo pathophysiological responses. *Ex vivo* techniques like Precision-Cut Lung Slices (PCLS) are a useful approach for validation and translation of results. This versatile method allows analyses of various toxicological endpoints and direct translation of results between animal and human tissues. Many established methodologies from *in vitro* and *in vivo* pulmonary toxicology are applicable to PCLS, allowing for cross-model endpoint validation. Further, PCLS enable observation of live cellular and physiological responses to toxicants within the preserved structure of the lung. In addition to their scientific value, PCLS also contribute to the refinement, reduction, and replacement (3R) of animal experimentation in research. Overall, PCLS have a high potential for improving the validation of *in vitro* methods, the translation of experimental results to humans, and the fulfillment of 3R criteria for toxicity testing. In this Workshop Session, established researchers from academia, industry, and government will present applications for PCLS in pulmonary toxicology to promote the techniques’ value to the broader scientific audience. Importantly, PCLS are not only a valuable tool in research, but already an established asset to address toxicological testing requirements from industry and pharmaceutical manufacturers. This will be showcased in the Workshop’s opening presentation by Dr. Holger Behrsing, who is part of the Institute for In Vitro Sciences Inc., a nonprofit contract research organization in Maryland. Further, Dr. Behrsing will discuss the potential validation of PCLS as a standardized testing method. For industry needs as well as classic toxicology research, constant optimization of PCLS methodology is ongoing. In his talk, Lieutenant Colonel Dr. Timo Wille from the German Armed Forces will present PCLS use for military research as well as the latest results on improved PCLS storage conditions, which support long-term experimentation and enable investigation of chronic lung damage. A valuable feature of PCLS is preservation of essential pulmonary cell functions—most frequent, airway responsiveness in different disease models or after toxicological exposure have been investigated. As one of the leading experts in this PCLS-related field, Dr. Cynthia Koziol-White from Rutgers, The State University of New Jersey, will present the latest results from asthma and environmental exposure studies performed with PCLS derived from human lung tissue, also touching on underlying mechanisms of the cellular responses. Another field of application for PCLS is risk assessment studies, which compose a significant portion in the developmental process of pharmaceuticals and chemicals designated for human application. Currently, most of these studies are performed in animals, as required by law, but full translatability of results to humans is not guaranteed with this approach. PCLS, however, uniquely present the opportunity to use human source material. In her presentation, Dr. Katherina Sewald from the Fraunhofer Institute for Toxicology and Experimental Medicine in Germany will explain the workflow and challenges behind the preparation of PCLS from human lung tissue, as well as results from application of human PCLS for toxicity testing. Completing the Workshop Session, Dr. Melanie Koenigshoff from the University of Colorado will link on Dr. Wille’s presentation and elaborate on PCLS use for early-stage chronic disease modeling, with special focus on idiopathic pulmonary fibrosis. The session will conclude with a 15-minute panel discussion facilitated by the session Chairs, which will give participants and speakers the opportunity for additional exchange and in-depth discussions.

**Abstract #**

#1101 11:15 AM  
**Precision-Cut Lung Slices: A Versatile Tool for Pulmonary Toxicology.**

*Introduction.*  
J. Herbert. Rutgers Ernest Mario School of Pharmacy, Piscataway, NJ.

#1102 11:25 AM  
**Human Precision-Cut Lung Slices: Advancing Their Utility and an Argument for Standardization.**

H. Behrsing. Institute for In Vitro Sciences Inc., Gaithersburg, MD.

#1103 11:55 AM  
**Cold Storage of Rat Precision-Cut Lung Slices: A Model Upgrade to Expand Applicability.**

T. Wille. Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany.

#1104 12:15 PM  
**Assessment of Airway Responsiveness in Human Precision-Cut Lung Slices: New Applications of an Established Method.**

Scientific Sessions—Tuesday, March 16

| #1105 | 12:45 PM | Early Events of Pathogenesis of Respiratory Diseases Induced by Agents in Human Lung Tissue. K. Sewald. Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany. Sponsor: J. Herbert |
| 1:45 PM | Panel Discussion/Q&A. |

Tuesday, March 16, 2:45 PM to 4:15 PM

Symposium Session: Evolving Technologies for Determination of Biotherapeutic Specificity

Chair(s): Timothy MacLachlan, Novartis AG; and Shari Price, Charles River.

Primary Endorser: Biotechnology Specialty Section

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

Monoclonal antibody therapeutics evolved from low molecular weight drugs with the promise of substantially higher specificity than low molecular weight drugs, and thus with much lower potential for toxicity. Since safety of monoclonal antibodies is directly linked to the specificity of their binding to therapeutic targets, developers of monoclonal antibody therapeutics have evaluated specificity of their products using the “Tissue Cross Reactivity” assay, based on an immunohistochemical method where the drug candidate is panned across a large number of human tissues. Recently, several platforms for screening for potential cross reactivity have become available, from protein and cellular arrays to flow cytometry-based methods, and their utility as possible replacements of immunochemistry method has been considered. This session will address the growing options that sponsors have to evaluate specificity of monoclonal antibody pharmaceuticals in the preclinical safety package.

Abstract #

| #1107 | 2:45 PM | Evolving Technologies for Determination of Biotherapeutic Specificity. |
| #1108 | 2:50 PM | Introduction. T. MacLachlan. Novartis AG, Holliston, MA. |
| #1109 | 3:15 PM | “TCR 2.0”: Reviewing Experience with Methods to Detect Off-Target Binding of Monoclonal Antibodies. J. Cavagnaro. AccessBio L.C., Boyce, VA. |
| | | Protein and Cell-Based Arrays to Assess Specificity of Biotherapeutics. A. Vicart. Novartis AG, Basel, Switzerland. Sponsor: T. MacLachlan |
| 4:05 PM | Panel Discussion/Q&A. |
Tuesday, March 16, 2:45 PM to 4:15 PM

Workshop Session: The Methodological Road toward Single Cell High-Throughput Transcriptomics (scHTTr)

Chair(s): Brian Chorley, US EPA; and Oswaldo Lozoya, NIEHS.

Primary Endorser: Molecular and Systems Biology Specialty Section

Other Endorser(s): In Vitro and Alternative Methods Specialty Section

Measuring transcriptomic events at a single cell level has revolutionized our understanding of cellular biology and response to the environment. In a high-throughput transcriptomics (HTTr) screening setting, single cell measurements reduce background noise associated with bulk RNA-sequencing techniques, providing more accurate assessments of adverse cellular response. Single cell assessments also increase the fidelity of transcriptomic alterations in organotypic screening models or complex cellular makeups of in vivo samples of animal test models for later tiered chemical testing. Unfortunately, the hundreds of thousands of samples performed in a high-throughput screening setting are not conducive for most established single cell methods due to the high costs and bioinformatically intensive environment associated with this type of data. However, recently introduced methodology and informatic approaches are providing a clear path forward for single cell high-throughput transcriptomics (scHTTr). In this Workshop, the first two presenters will describe developing technologies that will reduce the read depth, increase the throughput, and significantly decrease the cost of single cell transcriptomic changes in toxicological screening batteries conducive for toxicological and drug-screening applications (Single Cell TempOSeq and sci-Plex). The final speaker will present a case study using a scHTTr method to assess the effects of Polycyclic Aromatic Compounds (PACs) mixtures on resident immune cells and progenitors in the adult mouse bone marrow as part of a comprehensive hazard assessment. With these recent advancements, scHTTr is now at the point of implementation into toxicological assessments to increase the measured resolution of transcriptomic responses and better assess the potential adverse health impacts of toxicant and drug exposures. This abstract does not necessarily reflect US Environmental Protection Agency (US EPA) policy. Mention of trade names is not an endorsement or recommendation for use.

Abstract #

#1111  2:45 PM  The Methodological Road toward Single Cell High-Throughput Transcriptomics (scHTTr).
       Introduction.  B. Chorley. US EPA, Research Triangle Park, NC.


#1114  3:40 PM  Exposure to Polycyclic Aromatic Compound Mixtures Impacts Resident Immune Cell Progenitors in the Bone Marrow of Adult Mice.  O. Lozoya. NIEHS, Research Triangle Park, NC. Sponsor: B. Chorley

4:05 PM  Panel Discussion/Q&A.
As more than 20 million US citizens either have served or are currently serving in the military, the Departments of Defense and Veterans Affairs are tasked with identifying the potential threats that these individuals may encounter and ensuring their safety while in service and quality of life after separation. Military service involves a vast and unique set of toxicological considerations when compared with most occupational settings, which can vary for each individual, depending upon the mission. While some of these hazards, such as many organic solvents, are not unique to military service, and parts of their toxicity profiles have been established, other threats to human health, such as materials developed to achieve certain mission-specific outcomes, have emerged that are not well understood. As these threats evolve, the need to characterize their associated toxicities requires novel, progressive approaches that transcend classic methodologies. As representative examples of the methods being used to understand the unique health consequences of military service, the speakers in this session will discuss: (1) surveillance of veterans who endured blast injuries during deployment; (2) designing a framework to elucidate intergenerational effects of military exposures; (3) evaluating the long-term health implications of occupational jet fuel exposure; and (4) employing tools to characterize chemical threats and provide guidance for treatment. These topics will highlight some hazards and exposure pathways specific to military personnel and the challenges involved in maintaining their health during and after their service.

Abstract #

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<th>Time</th>
<th>Title</th>
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<tbody>
<tr>
<td>#1115</td>
<td>11:30 AM</td>
<td>Challenges and New Approaches in Characterizing Toxicity within the Military.</td>
<td>M. Johnson. US Army Public Health Center, Aberdeen Proving Ground, MD.</td>
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<tr>
<td>#1116</td>
<td>11:35 AM</td>
<td>Biomarkers of Exposure and Early Effect in the Medical Surveillance of War-Injured Veterans with Retained Metal Fragments.</td>
<td>J. Gaitens, and M. McDiarmid. University of Maryland School of Medicine, Baltimore, MD.</td>
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<td>#1117</td>
<td>12:05 PM</td>
<td>A Retrospective Investigation of the Long-Term Health Implications of Occupational Jet Fuel Exposure in the Air Force.</td>
<td>T. Vincent¹, G. Wolff, J. Escobar², and W. Culpepper³. ¹US Department of Veterans Affairs, Washington, DC; ²US Air Force School of Aerospace Medicine, Wright-Patterson AFB, OH; and ³Department of Veterans Affairs, Washington, DC.</td>
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<td>#1118</td>
<td>12:35 PM</td>
<td>Generational Effects of Military Exposures to Chemical Toxicants of Interest.</td>
<td>M. Williams¹, V. Davey², and K. Block³. ¹US Army Public Health Center, Aberdeen Proving Ground, MD; and ³US Department of Veterans Affairs, Washington, DC.</td>
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<td>#1119</td>
<td>1:05 PM</td>
<td>Predictive Toxicology in Preparation for the Unknown Threat.</td>
<td>K. Glover. US Army Combat Capabilities Development Command Chemical Biological Center, Aberdeen Proving Ground, MD.</td>
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<td>2:05 PM</td>
<td>Panel Discussion/Q&amp;A.</td>
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Symposium Session: Identifying and Communicating Adverse Neurological Outcomes from Parental Cannabis Use

Chair(s): Kristen Ryan, NIEHS/NTP; and Edward Levin, Duke University.

Primary Endorser: Neurotoxicology Specialty Section

Other Endorser(s): Clinical and Translational Toxicology Specialty Section; Reproductive and Developmental Toxicology Specialty Section

The expansion of legal cannabis in the United States brings with it increased use and consequently increased risk of adverse effects. Cannabis use by pregnant women in the United States has also increased as much as 62% (2002–2014) with an overall prevalence of use between 3%–16%. One emerging area of concern has risen from epidemiological evidence highlighting a variety of neurological impairments in children associated with maternal cannabis use during pregnancy. In parallel, experimental animal studies have demonstrated that parental THC exposure causes neurodevelopmental and neurobehavioral impairments in offspring. Additional data from clinical and experimental animal studies have revealed that abnormal epigenetic imprinting on sperm is associated with parental cannabis use. These findings point to important risks of cannabis use on reproduction and could be a mechanism for adverse neurodevelopmental deficits in the next generation. However, our understanding is not nearly complete, which could contribute to some confusion among consumers or a lack of concern related to cannabis use prior to conception or during pregnancy. In this session, the first speaker will begin by documenting the increasing use of cannabis for pain and nausea by women during pregnancy and while breastfeeding. Some misconceptions regarding cannabis use and risk among consumers also will be presented. As a result of increased use, longitudinal studies are demonstrating a link between fetal cannabis exposure and decreased growth, cognitive impairment, and behavior deficits in children. The second speaker will provide evidence in rodents corresponding to clinical findings that allows for in-depth assessments of neurobehavior and associated molecular phenotypes. Results from human and animal studies also will be discussed in the context of generating education strategies or interventions to improve the mental health outcomes of children with early neurodevelopmental outcomes of early-life cannabis exposure. In addition to maternal exposure, the third speaker in this session will highlight new evidence in preclinical rodent models showing that paternal exposure to cannabis prior to conception causes neurobehavioral impairment in the offspring, possibly through changes in DNA methylation. Paternal exposure impacts on offspring neurodevelopment is a largely understudied area. The next speaker strengthens the weight of evidence by linking parental cannabis exposure and adverse effects on neurodevelopment in a third species (i.e., zebrafish). Use of this complementary model system allows for the assessment of cannabis as a complex mixture on development, behavior, and reproduction across multiple generations, which is often a resource-intensive task in rodent models or human studies. The final speaker in this session provides insight from the public health perspective, focusing on the real-world application and utilization of preclinical and clinical research critical to the development of public health recommendations and risk communication. The session will end with an informal deliberation among panel speakers and the audience to (1) review the current weight of evidence for neurological deficits in children as a result of parental cannabis use during pregnancy, (2) propose strategies for research data gaps, and (3) discuss communication strategies to highlight risks for consumers. This session brings together experts across clinical and preclinical research settings, including several non-SOT members with expertise specifically identified to highlight the state of research regarding parental cannabis exposure and adverse consequences for consumers. This session brings together experts across clinical and preclinical research settings, including several non-SOT members with expertise specifically identified to highlight the state of research regarding parental cannabis exposure and adverse consequences for consumers. Importantly, adverse effects on neurobehavior are supported by results across multiple species, including humans, rodent models, and zebrafish, which emphasizes the need for more toxicological research during critical stages of development. Furthermore, the toxicological science of drugs of abuse has been greatly underrepresented at SOT relative to its societal importance and progress in the field. In 2019, SOT had one Workshop about the toxicology of drug abuse. That Workshop focused on how many types of drug abuse affect adolescence. In 2021, we have a chance to continue our efforts promoting research into the socially important areas of the toxicology of drug abuse, this time with a focused discussion of cannabis impacts on early development and its persisting neurotoxic effects.

Abstract #

#1121 11:30 AM  Identifying and Communicating Adverse Neurological Outcomes from Parental Cannabis Use. K. Ryan. NIEHS/NTP, Research Triangle Park, NC.


#1123 12:05 PM  Neurodevelopmental Outcomes of Early-Life Cannabis Exposure. A. Bara. Icahn School of Medicine at Mount Sinai, New York, NY. Sponsor: K. Ryan
Indoor air quality continues to be a concern for developed and developing nations because of the increasing amount of time people spend indoors (> 90%). Indoor air, whether in working environments or households, can contain both gaseous and particulate pollutants, including toxic chemicals and microorganisms. Household air pollution has been reported to cause ~4 million premature deaths annually. Overall, indoor air pollution is the leading cause of adverse health outcomes such as lung cancer, as well as cardiovascular and pulmonary diseases in children and adults. In the United States, approximately half a million households are exposed to indoor air pollutants, with the majority of the exposure coming from burning solid fuels like wood. Wood smoke contains a complex mixture of compounds such as polyaromatic hydrocarbons (PAHs), volatile organic compounds (VOCs), and particulate matter (PM). Exposure to fine PM (PM$_{2.5}$) has been studied extensively due to its potential to cause more hazardous outcomes especially in higher health risk groups, including pregnant women, children, elderly, and people with underlying health issues. The use of personal exposure monitors to improve the understanding of household air pollution and to help inform strategies for reducing the exposures has been utilized in several studies. The vast variety of indoor air pollutants, including VOCs, PAHs, PM, environmental tobacco smoke, and mold, can create complex indoor environments with mixed exposures that pose challenges for characterization of the pollutants and identifying the causation of the health outcomes. Therefore, monitoring the indoor air pollutants whether in households or occupational environments via routine and periodical measurements is extremely informative for regulating the indoor air quality. Personal exposure monitors also have been used in several studies to help inform strategies for reducing these exposures. This session will explore the complexity of indoor pollution case studies in both occupational and household environments and will include adverse health outcomes of some specific pollutants. A discussion will follow by presenting various tools for exposure assessments, including in vivo internal dose assessments and a novel aggregate modeling approach. This session aims to address the significance and challenges of assessing indoor air quality due to the diverse nature of indoor pollutants. It will illustrate how the exposure data are incorporated into assessment tools to identify data gaps and inform decisions for regulation, mitigation, and prevention of adverse health outcomes.

Abstract #

#1127 11:30 AM  **It Is Not Just Air: Exposure to Indoor Air Pollution, Diagnostic Tools, and Evaluation of Health Effects.**
**11:30 AM Introduction.** E. Mutlu. NIEHS/NTP, Research Triangle Park, NC.

#1128 11:40 AM  **Air Pollution Exposure and Health: Filling in the Blanks.** J. Thornburg, and R. Chartier. RTI International, Research Triangle Park, NC. Sponsor: E. Mutlu

#1129 12:05 PM  **Investigation of Systemic Exposure of Volatile Organic Compounds (VOCs) following Inhalation Exposure: A Case Study with Mixed Xylene Isomers.** E. Mutlu. NIEHS/NTP, Research Triangle Park, NC.

#1130 12:30 PM  **Exposure, Health Risks, and Control of Volatile Organic Compounds in Nail Salons.** L. Montoya. University of Colorado Boulder, Boulder, CO. Sponsor: E. Mutlu

#1131 12:55 PM  **Fungal Exposures within the Indoor Environment.** T. Croston. NIOSH, Morgantown, WV. Sponsor: E. Mutlu


1:45 PM  **Panel Discussion/Q&A.**
In recent years, the march toward an animal-free future for safety assessment has accelerated and now seems within reach. However, in the agricultural, chemical, and pharmaceutical sectors, animal studies are still quite heavily relied upon to characterize the hazard and risk profile of a new chemical or product. Where regulations currently demand the generation of animal data, performing parallel assessments using nonanimal methods will help to bridge the gap and fast-track the animal-free future of toxicology testing. This Symposium aims to be a practical session to provide guidance and shared examples that can bridge the current gap, culminating in a panel session where recommendations can be discussed and explored. For example, good-quality, integrated kinetic data and predictions could provide a wealth of information that could be used for IVIVE, setting up in vitro assays at relevant concentrations, and increasing confidence in the safety assessment. Integrated mode-of-action investigations could provide better information on the mechanism of effect seen in animals and their potential human relevance. This will require a concerted effort between different stakeholders and the adoption of modern and common practices to testing and assessment. This Symposium also will consider what the agricultural, chemical, and pharmaceutical sectors can learn from industries that are already operating in an animal-free environment, and how future technologies can help to usher in a truly animal-free toxicity testing future. In the first presentation, Dr. Lowit will present the perspective of a regulatory agency, the US Environmental Protection Agency (US EPA), who have set an ambitious target for reducing animal use and explain options open for waiving animal studies and using new approach methodologies (NAMs). In the second presentation, Dr. Terry will present an overview of a modern agricultural product’s mammalian toxicology program, where animal studies are still heavily relied upon but where avenues exist to fully embrace and implement the 3Rs (replacement, reduction, and Refinement) and NAM approaches wherever possible. Dr. Dent will then present experience and learnings from the cosmetic industry, which has been “animal-free” for many years and leads the field in application of NAMs. Finally, Dr. Boekelheide will summarize the learnings and present a vision for “bridging the gap” between a reliance on animal data and the animal-free future of toxicology testing. After these presentations, there will be a panel discussion that will be moderated by Dr. Sewell and will be a practical session to discuss examples of real use presented in the previous talks. Key examples will be identified by speakers ahead of time for the panel discussion and preagreed “charge questions” will be designed to draw out discussion from the audience and panel on the pros/cons/barriers to application of each example to different sectors. For example, perhaps methods in integrated toxicokinetics could be better or differently applied in different sectors. How could this help to speed the adoption of animal-free approaches, and what are the benefits, costs, and challenges associated with the different approaches outlined? An important feature of the discussion also will be to further explore what the different sectors can learn from each other in the application of nonanimal approaches. The output from this panel session will form a publication in the peer-reviewed literature to widen the audience and discussion even further.

Abstract #


#1135 12:10 PM  Advancing Safety Assessment in the Crop Protection Sector: Building the Bridge to an Animal-Free Future.  C. Terry. Corteva Agriscience, Indianapolis, IN.

#1136 12:45 PM  Evidence from Experience in an Animal-Free Sector/Exposure-Based Toxicity Testing and Translation into Global Requirements.  M. Dent. Unilever, Sharnbrook, United Kingdom. Sponsor: A. Lowit

#1137 1:20 PM  The Path Forward to a Near Future That Relies Primarily on Nonanimal Tests for Safety Assessment.  K. Boekelheide. Brown University, Providence, RI.

1:55 PM Panel Discussion/Q&A.
Understanding and quantifying dose-response relationships is a critical element in assessing and informing the safety of chemicals or drugs. Selecting appropriate doses in animal toxicity studies, especially top-dose levels, will enhance interpretability of study results used in human health risk assessments and minimize animal distress. Conventionally, top doses in repeated-dose toxicity studies are guided by the consideration of the Maximum Tolerated Dose (MTD). Recently, incorporating kinetic data to support the selection of top dose in repeated-dose toxicity studies for environmental chemicals, such as the Kinetically Derived Maximum Dose (KMD), has been a topic of intense international debate. KMD refers to the dose at, or slightly above, the deviation from linear kinetics based on blood levels of the parent compound or significant metabolites. There is little value in setting a top dose higher than the dose at which absorption is saturated, since systemic dose does not increase with increasing external doses beyond this point. On the other hand, when a detoxification process, such as biotransformation or excretion, is saturated, toxicity data generated by doses much higher than saturation may not be predictive of health risks resulting from much lower environmental exposures. In the pharmaceutical field, kinetic information is routinely considered in preclinical tests, and a common criterion for dose selection is limiting doses to those that do not saturate absorption. Kinetic information, however, is not as routinely collected or used in studies on environmental chemicals. While it is generally accepted that integrating knowledge of kinetics with toxicity information, such as mode of action, toxic moiety, toxicity endpoints, and site of action, can provide insights to dose selection, many argue against the use of KMD approach to select top dose in repeated-dose studies.

The objective of this Symposium is to provide an overview of the role of kinetics in dose-response toxicology studies and potential impact of nonlinear kinetics on dose-response relationships and define under what conditions KMD is appropriate to refine regulatory risk assessment. The session overview will highlight commonly raised challenges related to the KMD concept, such as determining an inflection point from sparse kinetic data or lacking exposure data to compare with doses used in repeated-dose toxicity studies. The first presentation will describe the significance of both toxicokinetic and toxicodynamic processes for observed dose-response relationships. In the second talk, the “how” and “when” to use kinetics in dose selection will be described throughout mammalian toxicology studies submitted for registration of agrochemicals. The third presentation offers the regulatory perspectives on the role nonlinear kinetics play in reviewing preclinical studies in drug application packages. The fourth presentation highlights examples from the chemical industry using kinetic data in study design and retrospective analysis of studies with emphasis on preventing the use of doses in animal studies that would not add value to predicting human safety. The final presentation will give a regulatory perspective on agrochemicals submitted for evaluation in Canada and case studies where kinetic data have been used to complement other data in dose selection and study interpretation. Using case studies on drugs and agrochemicals, this session will demonstrate how industries and regulatory agencies overcome some of the commonly raised challenges in incorporating kinetic data for regulatory needs. The overarching goal is to encourage more frequent use of kinetic data to provide a better perspective on the relevance of animal study results to human health risk assessment.

Abstract #

#1138  11:30 AM  Opportunities and Challenges in Utilization of Toxicokinetic Data in Dose-Level Selection for Repeated-Dose Toxicity Studies.

#1139  11:35 AM  The Role of Toxicokinetics and Toxicodynamics in Dose-Response Studies.  H. Barton. Independent Consultant, Mystic, CT.

#1140  12:05 PM  Informing Toxicity Study Design Using Kinetic Data: From Beginning to End.  J. Domoradzki. Corteva Agriscience, Indianapolis, IN.

#1141  12:35 PM  Perspectives of Kinetic Considerations in Drug Applications.  J. Hawes. US FDA, Silver Spring, MD.
The power of toxicological research relies on our ability to accurately assess the impact of toxicant and pharmacological exposures on an organism's development and determine if these chemical exposures contribute to organ dysfunction or disease states. To address this complex task, toxicologists have relied on and integrated a variety of in vitro, in vivo, and in silico models. In this Symposium, we highlight the power of the zebrafish, *Xenopus*, and medaka models for conducting predictive and mechanistic toxicology studies to prioritize the testing of existing compounds and aid in the development of safe, novel commercial products, as well as determine the appropriate usage of critical pharmacological agents during sensitive windows of development. The first speaker will describe how transgenic zebrafish lines have been leveraged to screen 300 Phase I ToxCast chemicals and, subsequently, identify chemical disruptors of skeletal, vascular, or neuromast morphogenesis. The researchers demonstrate how the data obtained from aquatic screens can be integrated with existing in vitro data to generate testable hypotheses regarding mechanisms of action and cellular targets. The second speaker will discuss how multiple aquatic models can be used in conjunction with in vitro assays to predict the endocrine-disrupting potential of novel compounds and, thus, establish a valuable platform for prioritizing the development of new chemical products for use in commercial applications. The third speaker will discuss the important variables and confounding factors that can affect the light/dark locomotor activity test, a well-established zebrafish neurotoxicity assay, and how accounting for these factors improves the reliability of this essential assay for detecting chemically induced changes in behavior. The fourth speaker will describe how different genetically encoded calcium indicators (GECIs) can be used to perform functional neuroimaging in zebrafish and how GECIs can be used to determine which brain regions and neuronal subtypes are impacted by toxicant exposures. Finally, the Symposium will end with an example of how zebrafish can be used to determine the developmental windows in which antiviral drugs can safely be used during pregnancy to prevent HIV transmission. Together, the talks in this Symposium demonstrate the diverse ways in which aquatic models are being used to further our understanding of chemical toxicity, predict adverse outcome prior to chemical exposure in humans, understand the impact of neurotoxicants on brain function, and optimize the safe use of pharmacological agents to treat devastating diseases.

**Abstract #**


#1145 11:30 AM  Introduction to Aquatic Toxicology Models and Session.  *J. Plavicki*. Brown University, Providence, RI.

#1146 11:35 AM  A Pipeline for Prediction of Developmental Toxicants; Screening in Zebrafish and Correlation to ToxCast Data.  *M. Bondesson*. Indiana University, Bloomington, IN.

#1147 12:05 PM  Combined Approach of In Vitro and Aquatic Models to Predict Developmental Toxicity and Endocrine Disruptors.  *E. Bianchi*. Corteva Agriscience, Indianapolis, IN.


#1149 1:05 PM  Using Genetically Encoded Calcium Indicators to Understand How Developmental Neurotoxicants Affect Neuronal Function.  *N. Martin*. Brown University, Providence, RI.
New alternative method development generally focuses on establishing in vitro fit-for-purpose assays providing mechanistic insight and on predictive in silico computational tools. The development of in vitro assays that are relevant and amenable to characterizing toxicity has become increasingly sophisticated and complex, requiring the integration of sophisticated computational approaches to aid with data analysis. For example, high-content, high-throughput, and multiplexed assays can yield multiparametric outputs, requiring additional development of custom analysis approaches. Addressing the challenge of integrating complex data and developing custom computational analysis approaches to ultimately deliver simple, articul, and informative endpoint readouts is the new frontier in assay development. Assay systems presented in this session will tackle not only in vitro assay development considerations but also how the integration of computational solutions can refine in vitro systems when applied upfront or enhance data analysis yielding powerful, mechanistically relevant, informative, and interpretable outputs from complex systems.

Abstract #

#1150 11:30 AM  The Power of Integrating Computational Toxicology with Multiparametric In Vitro Assay Systems.

#1151 11:30 AM  Introduction: Multiparametric Assays Driving Computational Modeling, and Vice Versa.  M. Martin. Pfizer Inc., Groton, CT.


#1153 12:20 PM  Can We Improve Clinical DILI Risk Prediction Using In Vitro Toxicokinetic Assays in Combination with Available Physical Chemical Properties and In Vitro Safety Assays?  J. Jackson. Pfizer Inc., Groton, CT.


#1155 1:30 PM  Modeling Steroidogenesis Disruption: Leveraging High-Throughput In Vitro Screening Data to Predict Mode-of-Action and Pathway-Level Perturbations.  A. Karmaus. Integrated Laboratory Systems Inc., Morrisville, NC.

2:05 PM  Panel Discussion/Q&A.
**Symposium Session: Across the Life Span: Emerging Mechanisms of Prenatal and Transgenerational Toxicity**

**Chair(s):** Joseph Jilek, University of Arizona; and Sumira Phatak, Utah State University.

**Primary Endorser:** Women in Toxicology Special Interest Group

**Other Endorser(s):** Postdoctoral Assembly; Reproductive and Developmental Toxicology Specialty Section

Toxic perturbations during early windows of susceptibility and the subsequent ontological impacts define broad theories of toxicity and are generally supported by epidemiological studies. However, mechanistic differences often fail to consider variability within affected populations, including sex, genetics, and epigenetics. Specifically, in recent years, the National Institutes of Health have escalated guidelines pertaining to the use of specific sexes in biomedical research involving animal models. As such, the goal of this Symposium Session is to expand upon existing understanding of developmental and transgenerational origins of disease, introducing additional variables that influence the trajectory of toxic effects. Every year, the Postdoctoral Assembly (PDA) and Graduate Student Leadership Committee (GSLC) propose a Scientific Session to highlight significant contributions of trainees, allowing them the opportunity to share cutting-edge research via an oral presentation to internationally recognized experts in toxicology. Three trainees will tackle this topic by presenting their research that centers around prenatal and early-life exposures to environmental contaminants—metals and phthalates—each evaluating a different factor that alters canonical ontological toxic effects. First, combined effects of pre- and postnatal cadmium exposure and postnatal high-fat diet will be explored. This work will introduce the audience to both adverse effects of prenatal metal exposure, as well as sexually dimorphic effects due to poor diet. Next, the effects of phthalates on female reproductive aging will be presented. This work demonstrates not only that environmental phthalate exposure elicits sex-specific effects, but also that these prenatal exposures elicit transgenerational effects. Finally, the influence of specific non-coding RNAs—an emerging paradigm in toxicoepigenetics—on neurodevelopment will be introduced, as well as how disruption of this system by lead may selectively interfere with neurodevelopment. Overall, in addition to providing a valuable platform for trainee oral presentations, this session will stimulate conversation around new variables that determine toxicological effects across the life span.

**Abstract #**

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<td>#1157</td>
<td>2:50 PM</td>
<td>Sexual Dimorphism of Cadmium-Exacerbated Diet-Induced Liver Disease.</td>
<td>J. Young. University of Louisville, Louisville, KY.</td>
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<td>#1158</td>
<td>3:15 PM</td>
<td>Perinatal Exposure to an Environmentally Relevant Phthalate Mixture Accelerates Biomarkers of Reproductive Aging in a Multigenerational and Transgenerational Manner in Female Mice.</td>
<td>E. Brehm, C. Zhou, L. Gao, and J. Flaws. University of Illinois at Urbana-Champaign, Urbana, IL.</td>
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<td>#1159</td>
<td>3:40 PM</td>
<td>Perinatal Exposures: Effects on piRNA Expression and Implications for Neurodevelopment.</td>
<td>R. Morgan, B. Perera, J. Goodrich, T. Jones, and D. Dolinoy. University of Michigan, Ann Arbor, MI.</td>
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<td>4:05 PM</td>
<td>Panel Discussion/Q&amp;A.</td>
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The advent of novel ocular biotherapeutics has revolutionized the treatment of ocular diseases and brought immense medical benefits to patients. While substantial experience was gained on the nonclinical safety toxicology study design, dose selection, endpoint evaluation, and data interpretation to enable clinical development, the nonclinical safety strategies for the development of novel ocular biotherapeutics are still evolving. The goal of this Symposium is to share the advanced sciences and new data involving the key nonclinical toxicology topics regarding the development of antibody and gene/cell therapies for ocular diseases. The industry and US Food and Drug Administration (US FDA) expert will share experience, case examples, and data from the recent years as well as provide thought-provoking strategies. The first speaker will discuss modeling and simulation-based PK-TK prediction and translation, and points to consider for dose selection for drugs administered via intravitreal injection. Ocular inflammation is a common finding in nonclinical intravitreal toxicology studies with biologics. The second speaker will focus on examining types, timing, and translatability of ocular inflammation in nonclinical intravitreal toxicity studies with biologics. Biodegradable polymer-based ocular biopharmaceuticals, a novel way to deliver drugs in the eye, has the potential to maintain effective drug concentrations in the eye for an extended period of time, reducing the need for frequent ocular injections. The third speaker will discuss the challenges and opportunities in the development of biodegradable polymer-based ocular biopharmaceutical delivery. Gene therapy has proven successful in restoring vision due to congenital mutations and holds great promise for treating a broad range of ocular diseases. The fourth speaker will share firsthand experience in the nonclinical and clinical development of the ocular gene therapy. The final speaker will provide US regulatory perspectives on the nonclinical consideration for cell and gene therapies for ocular products. In the end, a Q&A session will engage the audience on the presented topics for further discussion. Attendees of this session will have a better understanding of the current approaches and strategies in the nonclinical toxicological development of novel ocular therapies.
Establishing a pipeline for the next generation of scientists is critical for the advancement and expansion of toxicology. Only a limited number of students are exposed to toxicology through curricula in typical undergraduate science majors. As a result, immersion experiences including fellowships and internships provide intensive training of undergraduates in toxicology. Typically, summer programs include full-time mentored research in toxicology for up to three months. These experiences cover responsible conduct of research, experimental design, literature evaluation, data interpretation, and scientific communication. Cohort experiences that engage multiple undergraduate students provide the opportunity for networking and other career-directed activities. This session aims to provide five-minute talks by successful summer program directors and principal investigators from academia, government, and industry that highlight innovations in undergraduate student engagement in toxicology research. These programs range from small (two to five) to large (10–25) numbers of students per summer. A “blitz” of short talks will provide tangible examples that individual scientists and programs can apply to designing and developing their own summer research experiences. This interactive session will be particularly valuable to research advisors, program directors, and near-peer mentors (including graduate students and postdocs). Undergraduates who attend this session will gain insight into what features and initiatives they should be looking for in a robust summer training experience. Topics that will be highlighted include innovation in recruitment, resources, weekly programming, peer-peer networking, faculty training, diversity and inclusion, field trips, internships in pharmaceutical companies, and social enrichment. As programs have had to adapt to virtual training as a result of the COVID-19 pandemic, speakers will describe innovative approaches to deliver engaging and meaningful experiences online and how these initiatives may have long-term value in reaching students in remote locations across the globe. Additional attention will be placed on pipelines and partnerships between liberal arts colleges and research universities, as well as long-term sustainability of programs using sound financial models. Opportunities for funding summer internships from federal sources such as NIH and organizations including SOT will be reviewed. The second half of the session will include a moderated panel discussion of various approaches to recruitment, mentoring, team building, networking, presentation, assessment, matriculation into PhD programs, and long-term tracking. During the panel discussion, attendees are encouraged to ask questions of successful program directors with deep experience in developing and maintaining successful summer internships. Using interactive polling, the Chairs will survey the attendees for topics in which they are most interested and for future sessions on undergraduate toxicology research.

Abstract #

#1166 
2:45 PM Innovation in Toxicology Training during Summer Undergraduate Internships.
2:45 PM Welcome and Introduction. L. Aleksunes. Rutgers, The State University of New Jersey, Piscataway, NJ.
2:50 PM Recruiting Strategies for Place-Bound Undergraduates Interested in Environmental Health Science. K. Watanabe. Arizona State University, Phoenix, AZ.
2:55 PM “Lunch and Learn” Sessions to Explore Toxicology Research and Careers. L. Schnackenberg. US FDA/NCTR, Jefferson, AR.
3:00 PM Treat Them All the Same DIFFERENTLY! C. Curran. Northern Kentucky University, Highland Heights, KY.
3:15 PM Social and Scientific Enrichment: Keys to a Successful Summer Research Internship. K. McMartin. Louisiana State University Health Sciences Center Shreveport, Shreveport, LA.
3:20 PM They Don’t Know What They Don’t Know. C. Hayden. Novartis Institutes for BioMedical Research, East Hanover, NJ. Sponsor: M. Humble
3:25 PM Panel Discussion. M. Humble. NIEHS, Research Triangle Park, NC.
Despite extensive preclinical testing, new drug candidates still fail during clinical trials when safety adverse events not detected in preclinical studies occur in human subjects or when humans prove to be more susceptible to effects identified in preclinical studies. Although catastrophic outcomes are rare during clinical testing, high-profile clinical safety failures do occur, illustrating the need to understand translational safety to improve clinical safety. This Symposium highlights the use of quantitative systems toxicology (QST) modeling approaches to improve translational safety assessment. Transitional safety depends on predicting an outcome in one species based on testing in another and thus represents a fundamental problem in evolutionary biology. Systems biologists have developed models, including modular and network models, to assess the preservation of biology across scales of evolution. These studies create an opportunity to apply similar methods to modeling complex biological systems in a quantitative framework for safety predictions based on convergence (i.e., preservation) or divergence of biochemical and biological pathways relevant to drug action. To advance the application of QST modeling, these novel modeling approaches need to be merged with existing PBPK modeling methods to link drug exposure to pathogenesis in a multi-scale QST framework. An ideal QST framework will incorporate the exposure prediction and the concept of preservation across species, preclinical to human, for the underlying metabolic and stress response pathways that underpin a mechanism of action. Constructing multi-scale QST models across scales of complexity spanning cells to intact organisms represents both a significant opportunity and a significant challenge. For example, testing molecules in advanced human microphysiological systems provides data that can support models of compound exposure and cellular stress responses. Transcriptomic and metabolomic data can inform activation of stress response networks and global metabolic models, respectively, linked to metabolism and disposition of a novel drug candidate within an adverse outcome pathway that spans molecular responses to pathogenesis in vivo. However, data from these types of systems is most useful when the preservation of function, for example, between a human in vitro testing system and an intact human organ or tissue, is understood. Quantitative systems modeling provides methods to address the challenge of assessing preservation of mechanism across scales of biological complexity. The speakers in this session will tackle various aspects of the QST modeling and, in particular, the challenge of developing multi-scale and multidimensional quantitative systems models. The session will open with a summary of recent progress toward merging systems models with traditional PBPK models into complex multi-scale and multidimensional QST models. Following this introduction, the presenters will focus on case studies illustrating the potential for QST models to improve translation of nonclinical to clinical safety by focusing on common organ targets for drug-induced injury, liver, kidney, gastrointestinal systems, and heart. The speakers will summarize progress in the field, illustrate new concepts that are nearing application, and highlight the opportunities and challenges in achieving a more quantitative estimate of human safety.

Abstract #

#1167 11:15 AM **Challenges and Opportunities in Applying Quantitative and Translational Systems Toxicology Models to Drug Safety Testing.**


#1168 11:20 AM **Challenges and Opportunities in the Application of Integrated Multi-scale Systems Modeling.** C. Fisher.

Certara UK Limited, Sheffield, United Kingdom.

#1169 11:55 AM **Modeling Stress Responses across Scales of Complexity: From High Content Imaging in Cells to Modeling Co-expression Networks.** B. van de Water.

Universiteit Leiden, Leiden, Netherlands.

#1170 12:30 PM **Modeling Cardiovascular Safety Using a Quantitative Systems Pharmacology Approach.** D. Leishman.

Lilly Research Laboratories, Indianapolis, IN.
A goal of chemical toxicity assessment is to derive a “safe” human dose that is protective for the majority of the human population. Despite decades of knowledge highlighting the importance of genetic sequence variation on toxicity outcomes, conventional toxicity testing uses only a limited number of donor cell lines or animal strains, neither of which appropriately account for interindividual variability inherent in a diverse human population. To address this data gap, regulators apply a default uncertainty factor to account for potential interindividual differences in toxicokinetic (TK) and toxicodynamic (TD) parameters and to provide a margin of safety. However, as suggested by prior studies, this default factor may not be sufficiently protective of sensitive subpopulations, depending on the chemical x gene interaction underlying sensitivity. Therefore, it is critical to consider population variability in toxicity testing to more accurately and comprehensively evaluate risks of xenobiotic exposure and to derive adequately protective reference doses. Recent developments in in vitro and in silico models have greatly enhanced our ability to perform data-rich population-based toxicity testing. Such developments include cell-based population models composed of diverse individuals; advancements and increased throughput of molecular tools such as RNA-sequencing and high content imaging that can provide a great depth of information about population responses; and application of sophisticated statistical modeling to calculate the uncertainty around the population data and to provide more precise estimates of TK and TD variability. The goal of this session is to communicate the importance of assessing the population dynamics in hazard and risk assessment and to discuss emerging tools in toxicology that facilitate the advancement of population-based analysis. Four speakers from multiple disciplines and sectors will discuss the development and application of various population-based approaches in different areas of toxicology. The first two speakers will discuss statistical approaches and models to address population-based TK variability. The first speaker will talk about the development of population-based physiologically based TK modeling and its implementation in risk prioritization. The second speaker will introduce an open-source physiologically based pharmacokinetic modeling tool that addresses the population variability specific to the pregnant population, a key sensitive subpopulation for whom toxicity testing is challenging and safety data are sparse. He will discuss how this model can help assess the safety of xenobiotics during pregnancy and guide regulatory decisions to better protect perinatal health. The next two talks will demonstrate the utility of in vitro population-based assays for investigating TD variability. The third speaker will discuss the power of utilizing a human induced pluripotent stem cell-derived cardiomyocyte population model and how coupling it to Bayesian concentration response modeling can provide robust and accurate data on the population variability in cardiotoxicity risk from chemical exposure. The last speaker will introduce a high content imaging-based in vitro developmental neurotoxicity assay using neural progenitor cells derived from the genetically diverse Diversity Outbred mouse population and discuss how this model can complete the parallelogram of the population-based risk assessment by providing complementary values to the human cell data and serving as a direct bridge to the in vivo toxicity data. Altogether, the presentations will convey how population-based investigation can provide a data-driven estimate of the interindividual variability, allow more informed hazard and risk assessment, and improve the protection of human health. Attendees of this session will (1) gain a greater understanding of the critical need for appropriately addressing population variability to fill the critical knowledge gap in toxicology; and (2) learn about the applications, strengths and limitations, and future potential of cutting-edge tools and models used in population-based assessment.

Abstract #


#1175  12:30 PM  **A Bayesian Method for Population-Wide Cardiotoxicity Hazard and Risk Characterization Using an In Vitro Human Model.**  A. Blanchette, S. Burnett, F. Grimm, I. Rusyn, and W. Chiu. Texas A&M University, College Station, TX.


1:40 PM  **Panel Discussion and Concluding Remarks.**  A. Blanchette. Texas A&M University, College Station, TX.

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**Thursday, March 18, 11:15 AM to 2:00 PM**

**Symposium Session: Hereditary Disorders of Manganese Metabolism: Mechanisms, Clinical Presentation, and Neurotoxicity**  
**Chair(s):** Somshuvra Mukhopadhyay, University of Texas at Austin; and Tomas Guilarte, Florida International University.  
**Primary Endorser:** Neurotoxicology Specialty Section  
**Other Endorser(s):** Metals Specialty Section

The last decade has seen a revolution in Mn neurobiology due to the discoveries of three hereditary disorders of Mn metabolism—mutations in the transporters SLC30A10 or SLC39A14 cause Mn neurotoxicity while mutations in the transporter SLC39A8 cause Mn deficiency. Work on these transporters and genetic disorders is transforming our understanding of Mn homeostasis, detoxification, and neurotoxicity. This session brings together the leading experts in the field and integrates human clinical studies with epidemiological and cutting-edge basic science studies to present the very latest work in this area. Due to the timeliness of the topic, the Symposium will be of wide interest to neurotoxicologists, metal biologists, geneticists, epidemiologists, and clinicians.

**Abstract #**

#1177  11:15 AM  **Hereditary Disorders of Manganese Metabolism: Mechanisms, Clinical Presentation, and Neurotoxicity.**

11:15 AM  **Introduction.**  S. Mukhopadhyay. University of Texas at Austin, Austin, TX.

#1178  11:20 AM  **Understanding Manganese Excretion and Neurotoxicity by Studying Two Rare Genetic Diseases.**

S. Mukhopadhyay. University of Texas at Austin, Austin, TX.

#1179  11:50 AM  **Natural History, Genetics, and Treatment of Hereditary Disorders of Manganese Homeostasis.**  S. Gospe. University of Washington, Seattle, Seattle, WA. Sponsor: S. Mukhopadhyay

#1180  12:20 PM  **Role of Manganese Transporter Genetics in the Susceptibility of Children to Environmental Manganese Exposure.**  K. Broberg. Karolinska Institutet/Lunds Universitet, Lund, Sweden. Sponsor: S. Mukhopadhyay

#1181  12:50 PM  **Is SLC39A8 Required for Brain Manganese Accumulation? Evidence from Studies Using Knockout Mice.**


#1182  1:20 PM  **SLC39A14 Knockout Mice: A Genetic Model to Study Manganese Neurotoxicity.**  T. Guilarte. Florida International University, Miami, FL.

1:50 PM  **Panel Discussion/Q&A.**
Workshop Session: Are Aircraft Cabin Fume Releases a Cause for Toxicological Concern?

Chair(s): Allister Vale, University of Birmingham, United Kingdom; and Horst Thiermann, Bundeswehr Institute of Pharmacology and Toxicology, Germany.

Primary Endorser: Clinical and Translational Toxicology Specialty Section

Other Endorser(s): Neurotoxicology Specialty Section; Occupational and Public Health Specialty Section

Studies that have analyzed the air of civilian and military aircraft have detected not only compounds traceable to various aviation fluids (jet fuel, lubricants, hydraulic fluid, and coolants), but also other chemicals such as pyrethroids and ozone. On rare occasions, failure or over-filling of the oil reservoir may give rise to a “fume event” (visible smoke, haze, and/or odors), which has been estimated to occur on 0.05% of flights overall (1 in 2,000). This Workshop will describe the features reported following fume events, critique the toxicological mechanisms proposed, and evaluate the investigations currently available to assess cabin crew and passengers. The largest investigation of cabin crew ever conducted (some 3,750 individuals) will be reported for the first time. This study, based on medical reports, showed that the majority of crew complained of odors similar to the smell of oil, “used socks,” or burned material. The symptoms most frequently experienced were headache, dizziness, and nausea (>20% each). The toxicological importance of various chemicals that air sampling has detected in cabin air will then be addressed. Some studies have identified tri-cresyl phosphate, an organophosphate used as a high-pressure lubricant in engine oil, in cabin air. Although the six ortho-isomers account for only 0.2% of all isomers, there is particular concern that tri-ortho-cresyl phosphate may be responsible for neurological sequelae, as this metabolite can bind both to human acetylcholinesterase (producing acute organophosphorus poisoning) and to Neuropathic Target Esterase (NTE), thereby initiating organophosphate-induced delayed neuropathy. High ozone concentrations, which are well documented on long-haul flights, can produce eye, nose, throat, and respiratory features. Pyrethroid spraying on some flights, which helps ameliorate airborne diseases, leads to clinically significant pyrethroid concentrations. Pyrethrins can also result in eye, nose, throat, and respiratory features. Finally, a critical assessment will be made as to whether analytical investigations can assist in the diagnosis of cabin fume events. An adduct of CBD with butyrylcholinesterase was first reported to be present in the serum of a group of asymptomatic aircraft passengers in 2011. More recently, adducts of the cresyl-benzodioxa-phosphorin-oxide-derived phosphoryl group with tyrosine residues have been detected, as well as histidine- and lysine-adducts with ortho-cresyl. Such peptides have been used as biomarkers in diverse smaller studies and case reports. However, these analytical methods are extremely sensitive and a correlation between these biomarkers and development of signs and symptoms has not yet been established firmly.

Abstract #


#1185 11:45 AM Is There a Toxicological Explanation for the Clinical Features Reported following Cabin Fume Events? A. Vale. University of Birmingham, Birmingham, United Kingdom.

#1186 12:10 PM Can Analytical Investigations Assist in the Diagnosis of Cabin Fume Events? H. Thiermann. Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany.

12:35 PM Panel Discussion/Q&A.
Thursday, March 18, 11:15 AM to 2:00 PM

Workshop Session: Navigating Your Health and Wellness through Graduate School and Early Careers

Chair(s): Courtney Sulentic, Wright State University; and Judith Zelikoff, New York University.

Primary Endorser: Women in Toxicology Special Interest Group

Other Endorser(s): Education and Career Development Committee; Graduate Student Leadership Committee

This timely and interactive session will specifically address the issue of how to maintain health and wellness while navigating through the stress of graduate school and early careers. Over the last several years, mental stress has become an overwhelming situation, particularly for certain generations. Seventy-six percent of Millennials report that the biggest cause for stress is work related. In addition, 44% of both Millennials (1981–1996) and Gen Xers (1965–1980) report experiencing irritability or anger due to stress, compared with 36% of Baby Boomers (1946–1964) and 15% of the Silent Generation (1928–1945). While the common stressors throughout the generations remain fairly constant, this presentation will discuss certain factors that could contribute to these generational mental health differences, including whether younger generations are more open about expressing their stress and the role that 24-7 connectivity and social media play. This session, designed for all generations, will cover issues such as (1) what factors and determinants contribute to the current sense of being “overwhelmed”; (2) how we can adapt to achieve the wellness we all need to survive and be successful both in life and our career; (3) how the COVID pandemic has impacted research productivity and creativity; and (4) in a post-COVID world, how graduate education will change and how we can maintain our “cool.” Following the presentations, the session participants will form medium-sized groups and provide one to two points each regarding the following topics: (1) What contributes to our professional stress level, and what are some potential coping strategies we can use to deal with it? (2) How do we see education/career development changing, and how do we maintain our health and wellness in a post-COVID world? The speakers will help guide the breakout group discussions and collect discussion points to report back for a final panel discussion with audience participation. To ensure a diverse perspective, we will recruit approximately 10 SOT members representing our diverse membership (i.e., gender, ethnicity, LGBT+, career stage, and sector) to facilitate the breakout group discussions. Participants will benefit from the opportunity to engage in a constructive dialogue regarding such issues as coping tools for handling mental stress during these difficult years, how to be the mentor/supervisor your trainee needs, and the art of communication.

Abstract #

#1187 11:15 AM  Navigating Your Health and Wellness through Graduate School and Early Careers.


#1189 11:25 AM  Graduate School: What Am I Doing Here? Dealing with Imposter Syndrome from the Perspective of an Early Doctoral Student.  S. Goodman. Texas A&M University, College Station, TX.

#1190 11:45 PM  Mental Health Crisis: The Dark Matter of Graduate Programs Everywhere.  S. Phatak. Utah State University, Logan, UT.

#1191 12:05 PM  Working Together to Keep Mentor and Mentee Connected, Physically and Mentally Healthy, and Safe.  C. Curran. Northern Kentucky University, Highland Heights, KY.

#1192 12:25 PM  The Pressure to Exceed Expectations: A Postdoc Perspective.  S. Carratt. Oregon Health and Science University, Portland, OR.

#1193 12:45 PM  The Facets of Inequity, Social Media, and 24-7 Connectivity.  S. Page. Association for Women in Science, Durham, NC. Sponsor: C. Sulentic

#1194 1:05 PM  Tips for Managing Stress as an Early Career Scientist.  L. Lewis. Takeda Pharmaceutical Company Limited, Medford, MA.

1:25 PM  Overview and Introduction to the Panel-Facilitated Breakout and Panel Discussion.  C. Sulentic. Wright State University, Dayton, OH.
Workshop Session: New Approach Methods for Cancer Risk Assessment

Chair(s): Nicole Kleinstreuer, NIEHS/NICEATM; and Gina Hilton, PETA International Science Consortium Ltd., United Kingdom.

Primary Endorser: Carcinogenesis Specialty Section

Other Endorser(s): In Vitro and Alternative Methods Specialty Section; Risk Assessment Specialty Section

New approach methods (NAMs) are rapidly emerging as cutting-edge tools to modernize cancer risk assessment. Such tools offer the promise of mechanistic insight to support structured frameworks for regulatory decision-making. Traditional apical endpoints, such as those measured in the rodent cancer bioassay(s), are used to identify potential human carcinogens for agrochemicals, food additives, and pharmaceuticals; however, decades of research have underscored limitations in the rodent cancer bioassays. These limitations provide opportunities to develop and refine NAMs for targeted use to support cancer risk assessment. Experts are working to modernize carcinogenicity testing with mechanistic approaches that reduce testing on animals and may provide more human health-protective information. This session has been modified from a previously accepted 2020 SOT Annual Meeting proposal to focus regulatory, industry, and nongovernmental organizations (NGOs) expert discussion toward current opportunities and lessons learned in the development and utilization of NAMs for human-relevant cancer risk and safety assessment. Speakers will present timely research in NAMs, including the ongoing Health Effects Innovation Initiative, which is working toward modernizing its carcinogenicity testing program, as well as a presentation highlighting the use of gene expression endpoints in short-term animal studies as a NAM to replace the use of the two-year rodent bioassay. Additionally, method developers will discuss utility of NAMs for carcinogenicity assessment through expert-driven in silico systems, small model organisms providing mechanistic insights, and complex organotypic model tumor systems that recapitulate human cancer. Presentations from these cross-sector experts will provide thought-provoking discussion on paradigm-shifting opportunities to implement NAMs for regulatory cancer risk assessment. These topics will include lessons learned while developing NAMs for carcinogenicity assessment, as well as practical considerations for use of NAMs for regulatory decision-making. The discussion panel will be composed of Workshop speakers and session Chairs, representing experts from government, academic, industry, and NGOs. Overall, this Workshop will be of interest to a wide range of stakeholders, including regulators, cancer toxicologists, systems modelers, and industry scientists.

Abstract #


#1196 11:15 AM  Incorporating NAMs into the DNTP Carcinogenicity Testing Program.  W. Casey. NIEHS/NTP, Research Triangle Park, NC.


#1199 12:30 PM  Toward Replacing the Two-Year Bioassay with Short-Term NAMs: Genomic and Nongenomic Thresholds Can Identify Rat Liver Tumorigens.  C. Corton. US EPA/ORD, Research Triangle Park, NC.


1:20 PM  Panel Discussion/Q&A.
Over the past decade, there has been much advancement in the use of zebrafish as a powerful alternative model in drug and toxicity screening. However, harmonization among protocols and methods used in zebrafish research is currently lacking, thereby resulting in divergent outcomes while testing the same set of compounds. Although there has been global consensus on an urgent need for protocol harmonization, this is the first time that a concerted effort has been made globally to evaluate protocols in a systematic way to understand underlying differences in outcomes. This Workshop highlights advancements from two major global efforts: (1) an effort led by the Organisation for Economic Co-operation and Development (OECD) on harmonization of protocol parameters in the field of developmental neurotoxicity; and (2) a task force within the European Teratology Society (ETS) that was created for exploring the Zebrafish Embryo Developmental Toxicity Assay (ZEDTA) as an alternative for developmental toxicity testing. Following regulations in Europe with regard to use of nonmammalian models, and the recent directive issued by the US Environmental Protection Agency to reduce funding for mammalian testing by 30% by 2025 and to eliminate all mammal testing by 2035, the use of complementary models such as zebrafish are expected to be on the rise. Hence, it is critical to understand how underlying study parameters may influence results as we move zebrafish research forward for prioritization and prediction of toxicity outcomes. The Chair will provide a brief introduction on the need and timeliness of this Workshop to advance zebrafish research globally. The first speaker will shed light on recent advancements in the field with respect to toxicity screening and drug development, highlight needs and data gaps, and provide information on several global efforts to address these issues. The second speaker will provide an update on an OECD-initiated global harmonization project for developmental neurotoxicity (DNT) testing that is being conducted by an OECD Zebrafish DNT sub-group. This talk will highlight extensive discussion and protocol optimization from zebrafish experts globally. The third speaker will shed light on parallel efforts with respect to developmental toxicity harmonization that is being conducted as part of European (ETS) and US expert groups. The fourth speaker will discuss the state of the field with regard to uptake and metabolism in zebrafish and some caution that needs to be exerted during compound evaluation. Finally, the last speaker will provide case examples of how differences in protocols and analysis may impact outcomes and will shed light on a suggested path forward for protocol optimization as the zebrafish is being used more extensively as a complementary screening tool.

Abstract #

#1201 11:15 AM  The Need for Protocol Harmonization in the Advancement of Zebrafish as a Model for Toxicological Screening: Global Perspectives and Recent Advancements.  
Introduction.  M. Behl. NIEHS, Research Triangle Park, NC.

Oregon State University, Corvallis, OR.

#1203 11:50 AM  An Inter-laboratory Case Study to Determine the Added Value of the Zebrafish Light-Dark Transition Test to Predict Developmental Neurotoxicity: Report from OECD DNT Expert Group.  E. Hessel.
Rijksinstituut voor Volksgezondheid en Milieu (RIVM), Utrecht, Netherlands. Sponsor: M. Behl


#1205 12:50 PM  Evaluation of the Uptake and Metabolism of Novel Toxicants by Zebrafish Larvae.  L. Ellis. Health Canada, Ottawa, ON, Canada. Sponsor: M. Behl

#1206 1:20 PM  Understanding the Influence of Protocol Parameters in Zebrafish Embryonic Developmental and Neurotoxicity Screenings on Compound Toxicity Outcome Interpretation.  J. Hsieh. NIEHS/NTP, Research Triangle Park, NC. Sponsor: M. Behl

1:50 PM  Panel Discussion/Q&A.
Most eukaryotic genes consist of protein coding modules (exons) interspersed with stretches of non-coding modules (introns). During RNA maturation, the introns are excised out and the exons are joined by a precisely tuned mechanism called splicing. The modular nature of exons and introns makes it possible to generate several unique exon combinations from a single gene by a process called alternative splicing. Thus, alternative splicing is a tightly coordinated process by which several mRNA and, consequently, protein isoforms can be generated from a single gene, often with different and sometimes completely opposing biological functions. About 90% of all human genes undergo alternative splicing, making it a major driver of gene regulation and generation of proteomic diversity. Recent studies unequivocally demonstrate that dysregulated alternative splicing is a common event upon a diverse range of toxic exposures. Data suggest that such dysregulated alternative splicing plays key roles in the pathogenesis of several diseases upon toxic exposures, especially cancer and immune responses. The goal of this session is to examine how alternative splicing modulates key physiological and pharmacological processes leading to disease outcomes/susceptibility because of toxic exposures. It will bring together a panel of experts to discuss and dissect the mechanisms by which dysregulated altered splicing brings about disease outcomes as well as modulates the effects of therapeutic intervention. The session will address pressing issues such as (1) How can alternative splicing regulate metabolism/detoxification/biotransformation of endogenous and exogenous toxicants and therapeutic molecules? (2) What are the mechanisms by which alternative splicing can modulate carcinogenesis? (3) What is the role of metals in bringing about genome-wide differential alternative splicing events leading to cancer? and (4) What are the computational and experimental challenges associated with studying genome-wide alternative splicing? The first talk will address how alternative splicing in cytochrome P450 proteins can modulate toxicant metabolism upon environmental exposure leading to interindividual differences in health outcomes. The second talk will describe the role of splice switch in ARNT isoforms by exogenous and endogenous toxicants in autoimmune disorders and its potential as a putative therapeutic target. The third talk will explore the possible contributions of differential alternative splicing in the pathogenesis of chronic arsenic exposure-induced skin cancer. Following this session, the attendees will develop a clear understanding of the mechanistic role played by alternative splicing dysregulation as harbingers of a diseases with emphasis on carcinogenesis upon toxic exposure. They also will understand the importance of application of RNA-seq techniques along with bioinformatic pipelines to identify differential alternative splicing events upon toxic exposure. In addition, they also will have a clear perception of the challenges and the pitfalls they might face while interpreting the alternative splicing data. Overall, the session aims to underline the emerging importance of alternative splicing in bringing about nuanced regulation of gene and protein isoform expression, culminating in adverse health outcomes. As a rapidly emerging paradigm in the area of toxicology coupled to its potential as a therapeutic target, alternative splicing dysregulation is of wide interest to academia, industry, and regulatory authorities.

Abstract #
#1207  2:45 PM  Revising Biology: Alternative Splicing in Toxicology.
#1208  2:50 PM  Alternative Splicing in the Cytochrome P450 Superfamily as Biomarkers of Chemical Exposure and Environmental Disease.  A. Annalora. Oregon State University, Corvallis, OR.
#1209  3:15 PM  Proper T Cell Activation Requires Specific ARNT Alternative Splicing Patterns for Fine-Tuning AhR Signaling.  C. Wright. University of Texas Medical Branch at Galveston, Galveston, TX.
#1210  3:40 PM  Differential Alternative Splicing as a Mechanism for Chronic Arsenic Exposure-Induced Squamous Cell Carcinoma.  A. Cardoso. University of Louisville, Louisville, KY.
Safety or uncertainty factors (UFs) are used by regulatory agencies to account for perceived deficits in toxicology data using animals. Toxicology now has technology to directly test for human mechanistic responses with tools such as microphysiological systems. “New approach methodologies” (NAMs) is a reference to any non-animal technology, methodology, approach, or combination used to provide information on chemical hazard and risk assessment. NAMs, including in vitro toxicology methods using human cells, are available from simple cell cultures to 3D models of human skin, liver, and other organs to similar human organs-on-a-chip. Although the focus of this debate is on organs-on-chips technology, the principles and application can be applied to other types of NAMs. NAMs are challenging the traditional “norm” of regulatory risk assessment that has been in place for many years, including uncertainty or safety factors. Are these factors needed for testing when human cells are used? This important question will be debated in the Roundtable discussion, with the hope of bringing some guidance to the development of 21st-century risk assessment. The question proposed is, “Will safety or uncertainty factors still be needed when using human cells?” This debate brings together two outstanding scientists to discuss and debate the issue. Michael Dourson, PhD, who co-authored the original paper detailing uncertainty factors, and Lorna Ewart, PhD, who was a leader in adopting organ-chip technology within the pharmaceutical industry, are our two debaters. Following the debate, Drs. Dourson and Ewart will be joined by Drs. Suzanne C. Fitzpatrick, US FDA; Silvia Barros, Universidade de São Paulo, Brazil; and Brinda Mahadevan, Abbott, India, in a panel discussion. Dr. Hayes will moderate the panel discussion.

Abstract #

#1211  2:45 PM  The Future of Uncertainty Factors with In Vitro Studies Using Human Cells.  
2:45 PM  Introduction.  S. Fitzpatrick. US FDA, College Park, MD.  
3:00 PM  For the Question: Uncertainty Factors Will Be Needed in In Vitro Studies Using Human Cells.  M. Dourson. Toxicology Excellence for Risk Assessment, Cincinnati, OH.  
3:50 PM  Panel Discussion/Q&A.
Symposium Session: Applications of Novel High-Throughput Approaches for Mechanism-Based Chemical Safety Assessment

Chair(s): Marcel Leist, Universität Konstanz, Germany; and Joshua Harrill, US EPA.

Primary Endorser: Molecular and Systems Biology Specialty Section
Other Endorser(s): Computational Toxicology Specialty Section; In Vitro and Alternative Methods Specialty Section

There is a need for quantitative systems toxicology to take advantage of human-relevant in vitro test systems in providing mechanism-based solutions for chemical safety assessment. This is essential since classical animal-based testing approaches have shown a very limited ability to predict adverse human health outcomes under environmental exposure conditions. Moreover, there is an enormous number of poorly characterized chemicals in the environment or approaching the market that humans may be exposed to that lack thorough safety evaluation. Efficient high-throughput methods, integrating mechanistic information based on the bioactivity of chemicals, represent a valid alternative for cost- and time-effective assessments of the possible biological consequences of exposure to environmental chemicals. These methods involve both high-throughput phenotypic screening that generates quantitative information at the single cell level as well as high-throughput transcriptomics that yields concentration-response information on gene expression changes at the cell population level. This session will demonstrate the use of transcriptomics-, metabolomics-, and phenomics-based approaches for characterization and/or predictions of mechanisms of action for potential use in chemical safety assessment. First, the use of high-throughput transcriptomics for identifying molecular biomarkers from short-term in vivo studies that forecast pathological manifestations in longer-term studies will be discussed. Second, the variability in sensitivity toward the activation of toxicity pathways in the human population will be discussed. This approach is based on high throughput transcriptomics-based concentration-response statistical modeling of 50 different primary hepatocyte human donors. In this context, the relevance in the application of setting safety factors also will be debated. Further, an approach for metabolome-based read-across will be presented. Data extracted by a large (>1,000 compounds) metabolomics database (MetaMap®Tox) have been used to assess biological similarity among compounds. Additionally, the application of a refined in vitro teratology method that combines functional and morphological endpoints (e.g., neuronal rosettes formation) with mechanistic endpoints (e.g., transcriptome changes) for efficient screening of developmental toxicants will be discussed. Finally, the use of a high content imaging-based phenotypic profiling method known as “Cell Painting” for bioactivity screening of chemicals, potency estimation, and prediction of putative mechanisms of action will be presented. Participants in this session will gain a broader understanding of how high-throughput screening approaches for assessing chemical effects on the transcriptome, metabolome, and phenome can be used for mechanism-based chemical safety assessment.

Abstract #

#1212 11:15 AM  Applications of Novel High-Throughput Approaches for Mechanism-Based Chemical Safety Assessment.


#1213 11:20 AM  Early Prediction of Late Adverse Outcome Using Benchmark Dose Modelling of High-Throughput Transcriptomics Data. S. Auerbach. NIEHS, Research Triangle Park, NC.


#1215 12:10 PM  Metabolomics-Based Read-Across Approach to Detect Biological Similarity. S. Sperber. BASF SE, Ludwigshafen am Rhein, Germany. Sponsor: M. Leist

#1216 12:35 PM  Impaired Formation of Neural Rosettes from Stem Cells as Teratological Correlate of Toxicant-Induced Transcriptome Disturbances. N. Dreser. University of Konstanz, Konstanz, Germany. Sponsor: M. Leist
Scientific Sessions—Monday, March 22

#1217 1:00 PM  
Application of Cell Painting, an Imaging-Based High-Throughput Phenotypic Profiling Assay for Bioactivity Screening of Environmental Chemicals.  
J. Nyffeler. US EPA, Research Triangle Park, NC.

1:25 PM  
Panel Discussion/Q&A.

Monday, March 22, 11:15 AM to 2:00 PM

Workshop Session: New Approaches for the Identification and Evaluation of Chemical Respiratory Sensitizers

Chair(s): Shannon Krieger, Dow; and Kristie Sullivan, Physicians Committee for Responsible Medicine.

Primary Endorser: In Vitro and Alternative Methods Specialty Section

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

Sensitization of the respiratory tract has significant potential health implications; however, the prediction of chemical respiratory sensitizers presents a challenge due to the lack of validated test guidelines and formally recognized assays for this endpoint. This Workshop will bring together representatives from industry, government, and the public sector to (1) discuss the current state-of-the-science for the identification and characterization of chemicals with the potential to cause respiratory sensitization; (2) outline the regulatory and practical needs for hazard identification, risk assessment, and risk management; and (3) describe progress on the development of standard methods and frameworks. The first speaker will provide an overview of respiratory sensitization, what is known of the adverse outcome pathway, where gaps in mechanistic understanding remain, and how those gaps impact the evaluation of chemical respiratory sensitizers. The second speaker will outline recent developments in regulatory approaches for assessment and evaluation of potential respiratory sensitizers. The third speaker will present on recent progress in the development of in vitro methods to identify and discriminate respiratory sensitizers and the needs for further improvements to eventually gain regulatory acceptance. The fourth and fifth speakers will describe the methodology of an ongoing effort to develop a weighted and categorized database of positive and negative respiratory sensitizers that could be used to evaluate in silico and in vitro approaches, including use of human clinical and occupational data in a weight-of-evidence approach. Although recent Workshops have been held to present the state-of-the-science for assessing inhalation toxicity, this Workshop will specifically focus on the adverse outcome of respiratory sensitization and will include a discussion of new approaches for regulatory assessment and evaluation. Attendees will leave with an understanding of the state-of-the-science and currently available tools as well the usefulness and limitations of the presented approaches and where challenges remain. The Workshop will conclude with a roundtable discussion and Q&A between the presenters and attendees.

Abstract #

#1218 11:15 AM  
New Approaches for the Identification and Evaluation of Chemical Respiratory Sensitizers.  
S. Krieger. Dow, Midland, MI.

#1219 11:20 AM  
Chemical Respiratory Sensitizers: Current Understanding and Remaining Gaps.  
S. Krieger. Dow, Midland, MI.

#1220 11:45 AM  
Evaluations for Chemical Respiratory Sensitizers under Section 5 of the Amended Toxic Substances Control Act (TSCA).  

#1221 12:15 PM  
Current Status of In Vitro Models to Identify Respiratory Sensitizers.  
A. Gutleb. Luxembourg Institute of Science and Technology, Belvaux, Luxembourg.

#1222 12:45 PM  
Development of a Reference List of Chemical Respiratory Sensitizers to Facilitate Evaluation of Integrated Approaches to Testing and Assessment.  
K. Sullivan. Physicians Committee for Responsible Medicine, Washington, DC.

#1223 1:10 PM  
Utilization of Human Evidence for Testing and Assessment of Chemical Sensitizers.  
R. Rajagopal. Unilever Safety and Environmental Assurance Centre, Sharnbrook, United Kingdom. Sponsor: S. Krieger

1:40 PM  
Panel Discussion/Q&A.
Monday, March 22, 11:15 AM to 2:00 PM

**Workshop Session: Tackling the Potential Human Health Impacts of Microplastics and Nanoplastics: Challenges for Toxicologists in the Assessment of Real-World Complex Mixtures**

**Chair(s):** Nigel Walker, NIEHS/NTP; and Anil Patri, US FDA/NCTR.

**Primary Endorser:** Nanoscience and Advanced Materials Specialty Section

**Other Endorser(s):** Mixtures Specialty Section; Risk Assessment Specialty Section

Micro- and nanoplastics are particles that are formed from the breakdown of bulk plastic waste and, in some cases, intentionally synthesized for commercial use. The degradation process of bulk plastics produces visible particles to sub-visible particles and ultimately nanoparticles with mixed compositions, shapes, and sizes. There are no universal consensus standards for the definition of micro- and nanoplastics, but microplastics are generally considered to be in the range of 5 mm to 1 micron and nanoplastics are considered to be less than a micron in size. With the annual global accumulation of millions of tons of plastics in oceans, rivers, soils, plants, and sediments, the formation of these micro- and nanoplastics will only increase in the future. Less than 15% of plastics produced globally are recycled according to some estimates, since they are inexpensive to manufacture but expensive to segregate and recycle plastic waste products. Even though the concern about plastic waste has existed for many years, the recent awareness of the increased presence of micro- and nanoplastics in the air we breathe and their detection in food, seafood, and water, resulting in human exposure, is causing public concern. While microplastics can be observed with light microscopy and quantified, measurement methods for sub-micron-size nanoplastics mixtures are also not available to conduct a thorough analysis, to aid in human exposure assessment, due to the myriad challenges associated with their collection, separation, isolation, and characterization of real-world mixtures from environmental and complex organic matrices. Lessons learned from pitfalls in nanomaterial assessment and assessment of hazard of complex mixtures can be utilized to address these challenges with complex nanoplastics mixtures. While this global problem has been brewing for decades, there is no current definitive evidence of human toxicity. The questions one would pose are (1) whether this is a real problem, and (2) if so, how to address this through appropriate studies with real-world samples, rather than “model compounds” that cannot capture the potential toxicity resulting from the complex mixtures. What makes it challenging is that unlike engineered nanomaterials, these incidental nanoplastics are not uniform and contain sizes ranging from nano to micron, with various chemical compositions along with chemicals adsorbed to them. This Workshop will bring multiple sector (government, academia, industry, nonprofit) experts to present on specific issues to keep in mind when exploring toxicological research related to the complex, real-world sample micro- and nanoplastics mixtures. The topics that will be covered include (1) various compositions and risks of contamination of microplastics collected from different parts of the oceans and water bodies; (2) challenges one would face in isolation and characterizing various aspects of real-world samples, highlighting collaborative efforts from government agencies; (3) case study examples, lessons learned, and toxicological assessment approaches from tire-wear debris mixtures; (4) challenges in predicting exposure; and (5) potential human health impacts of both micro- and nanoplastics.

**Abstract #**

#1224 11:15 AM  **Tackling the Potential Human Health Impacts of Microplastics and Nanoplastics: Challenges for Toxicologists in the Assessment of Real-World Complex Mixtures.**

#1225 11:15 AM  **Overview.**  N. Walker. NIEHS/NTP, Research Triangle Park, NC.

#1226 11:30 AM  **What Are the Risks of Global Contamination by Microplastics?**  K. Lavender Law. Sea Education Association, Woods Hole, MA. Sponsor: N. Walker


#1228 12:10 PM  **Challenges in Characterizing Environmental Health Risk of Microplastics: Experiences from the Tire Industry Project Related to Tire and Road Wear Particles.**  J. Panko. ToxStrategies Inc., Asheville, NC. Sponsor: N. Walker

#1229 12:30 PM  **Assessing and Predicting Human Exposure to Nano- and Microplastics.**  T. Fennell. RTI International, Research Triangle Park, NC.
This session will provide an update on the state of the art of thresholds of toxicological concern (TTC) as a springboard for where this concept will go in the future. The TTC concept is an approach implementing de minimis thresholds to prioritize chemicals for hazard characterization and risk management. The origins of the TTC stem from the US Food and Drug Administration’s Threshold of Regulation (FDA, 1995), which was developed as a tool to facilitate the safety evaluation of food packaging materials, components of which (might) have the potential to migrate into food at very low levels. It has since been expanded from a single value (the FDA Threshold of Regulation) to encompass a range of exposure limits based on potency bins for chemicals. The approach has been endorsed by various global regulatory agencies for the assessment of flavors, food contact materials, drug impurities, cosmetic ingredients, and beyond. Large datasets of cancer and non-cancer potency information underpin the TTC concept. While the basic principles of hazard characterization based on animal studies have hardly changed, testing guidelines have been updated and new studies have become available. In addition, there are greater opportunities to apply cheminformatics approaches to derive new structure-toxicity relationships, as well as new approach methodologies, which allow for incorporation of mechanistic or toxicokinetic information. The overall TTC concept has, if anything, become even more relevant due to the ever-increasing sensitivity of analytical methods, the need to prioritize large numbers of substances, and the desire to avoid animal testing. Recent expansion and reassessment of the two key toxicity datasets underpinning TTC—the cancer potency and noncancer datasets—to include additional chemicals and studies will be described along with the evaluation of the points of departures. For cancer potency, the focus was to substantiate the TTC exposure limits for compounds considered to pose a possible DNA-reactivity hazard versus those that do not by investigating the influence of DNA-reactivity on potency as well as refining risk estimates comparing benchmark dose levels (BMDLs) with carcinogenic potencies expressed as TD50s. Projects to expand the chemical applicability domain of noncancer datasets (e.g., by the inclusion of antimicrobials) and to derive TTC thresholds based on blood concentrations rather than external oral dose (internal TTC [iTTC]) to enable applicability to systemic toxicity via additional routes of exposure will also be described. Beyond the toxicity databases, novel concepts on how to group chemicals into structural categories, linked to potency groups for the de minimis thresholds, will be presented. Traditionally, this is achieved for the noncancer dataset by application of the Cramer et al. decision tree from 1978, which has been judged by regulatory agencies to deliver fit-for-purpose classification for TTC threshold derivation. However, the outcomes from two complementary projects will be highlighted to show how the Cramer decision tree (CDT) has been updated by expert knowledge versus applying a cheminformatic approach to devise structural categories. The range of diverse TTC projects demonstrate the multiple facets of hazard characterization with novel and traditional approaches. The session will provide an overview of the current status of TTC application, including limitations of technologies, and highlight good practice for regulatory-relevant databases in interpreting the results from in vivo studies, selection of appropriate results, transparency, and assessment of DNA reactivity by expert judgment, SAR, or read-across, as well as grouping structures and deriving TTC, including a variety of sources of variability, bias, and uncertainty. Finally, the session will provide a vision of how TTC can be used within risk assessment and regulatory frameworks. Specifically, the uncertainties behind TTC will be characterized and methods to overcome high uncertainty, and thus improve confidence, will be presented. These, in combination with the new developments in TTC presented in the session, will demonstrate the increasing transparency in the concept, which can form a valuable part of Next Generation Risk Assessment.

Abstract #

#1231 11:15 AM Thresholds of Toxicological Concern: Reassessing the Basis and Expanding the Horizon.
Environmental justice communities, “poor and minority communities that bear a disproportionate burden of environmental health risk,” not only face societal and psychosocial stressors, but are also unjustly exposed to disproportionate levels of environmental contaminants. Environmental contamination and socioeconomic and racial disparities in disease burden have been a long-standing public health problem with historical roots. The current COVID-19 pandemic has brought this issue to the forefront and increased public awareness of these disparities. Adding to the pressure posed by these social inequities are environmental factors such as air and water quality that plague these marginalized communities and contribute extensively to their vulnerability and disproportionate disease burden. This Workshop will discuss how environmental contamination and exposure contributes to the health disparities associated with marginalized populations, including Native Americans and urban communities, using specific case studies. Existing state and federal policies and the regulations currently in place and needed to protect such vulnerable populations also will be presented, along with possible solutions and suggestions of how to move the field of environmental health equity forward in our post-COVID world. The presentations will be followed by a question-and-answer panel discussion with all the participants.

**Abstract #**

**Workshop Session: The Community Exposome: Effects of Environmental Contamination on Health Disparities and Marginalized Populations through the Lens of a Toxicologist.**

**Chair(s):** Judith Zelikoff, New York University; and Courtney Sulentic, Wright State University.

**Primary Endorser:** Women in Toxicology Special Interest Group

**Other Endorser(s):** Hispanic Organization of Toxicologists Special Interest Group; Toxicologists of African Origin Special Interest Group

#1237 2:45 PM **The Community Exposome: Effects of Environmental Contamination on Health Disparities and Marginalized Populations through the Lens of a Toxicologist.**

2:45 PM **Introduction.** J. Zelikoff. New York University, New York, NY.

#1238 2:50 PM **The Nature of the Problem.** C. Jackson. NIEHS, Research Triangle Park, NC. Sponsor: J. Zelikoff

#1240 3:20 PM  Case Studies from Columbus, Ohio: Place Matters with Regard to Health Care Disparities and Disparate Health Outcomes.  D. Hood. Ohio State University, Columbus, OH.

#1241 3:35 PM  Environmental Justice Problems of Concern to Disadvantaged Communities: A Regulatory Perspective and Future Directions for Environmental Health Equity.  M. King. USDA Agricultural Research Service, Washington, DC.

3:50 PM  Panel Discussion/Q&A.

Monday, March 22, 2:45 PM to 4:05 PM

Informational Session: Toxicology for Chemists: Preparing Chemists to Design Safer Products through Smarter Molecular Design

Chair(s): Amy Cannon, Beyond Benign; and Pamela Spencer, ANGUS Chemical Company.

Primary Endorser: Sustainable Chemicals through Contemporary Toxicology Specialty Section

Other Endorser(s): Education and Career Development Committee

We live in a time of converging trends where chemists and toxicologists need to work together to understand the toxic effects of chemicals. While significant progress has been made in studying how chemicals impact human health and the environment, there is still a lack of proper training among chemists to understand how toxicology can be incorporated into curriculum such that it prepares the next generation of chemists for this transdisciplinary career. There is a movement toward teaching toxicology concepts to chemistry students within chemistry courses and programs, but despite this movement, toxicology principles remain a key missing piece to a chemist’s education. If design of safer products is to be successfully integrated into new product development, chemists must have a mechanistic understanding of how chemicals impact human health and the environment. Through this mechanistic understanding, scientists can design molecules that have reduced hazards to human health and the environment and ecosystem, an approach that is the best method for pollution prevention and avoiding the use and generation of hazardous chemicals. Some academic institutions have begun efforts to create their own courses on toxicology, or weave concepts into existing chemistry courses. Many institutions have shown interest in this area but do not have the resources or knowledge base to implement toxicology within a chemistry course or program. As more and more chemistry departments seek to integrate toxicology concepts into their courses and programs, there is a growing demand for educational materials and models for adoption. Beyond Benign, a nonprofit organization dedicated to Green Chemistry education, has partnered with a team of professional toxicologists and chemistry college and university faculty members to design an open-access curriculum for use within college and professional chemistry education programs. This session will serve as a means for sharing the Toxicology for Chemists curriculum and program and identifying collaborative opportunities for SOT members and chemistry educators to address a growing need for toxicology training in the chemistry curriculum. The goal of the Toxicology for Chemists program is to provide chemists with proper training on foundational principles of toxicology and mechanistic understanding of how chemicals impact human health and the environment. The key audience for this Informational Session is SOT members who are interested in contributing to the education and training needs of chemists, along with chemists involved in designing sustainable chemicals. Dr. Amy Cannon will kick off the session with an overview of the Toxicology for Chemists program. Two members of the program advisory group and curriculum contributors, Dr. Margaret Whittaker and Dr. Bryan Brooks, will present on methods and tools for better educating chemists on toxicology topics. Dr. John Warner, a founder of the field of Green Chemistry and co-author of the defining 12 Principles of Green Chemistry, will close the session by highlighting the opportunities for toxicology to provide chemists with better, smarter design skills and outline specific examples of chemical products designed by using the tools of toxicology.

Abstract #

#1242 2:45 PM  Toxicology for Chemists: Preparing Chemists to Design Safer Products through Smarter Molecular Design.

2:45 PM  Introduction.  A. Cannon. Beyond Benign, Wilmington, MA.

2:50 PM  Toxicology for Chemists: Curriculum and Resources.  A. Cannon. Beyond Benign, Wilmington, MA.
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<tr>
<th>Time</th>
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<tr>
<td>3:00 PM</td>
<td><strong>Educating Tomorrow’s Green Chemists in 21st Century Toxicology</strong></td>
<td>M. Whittaker, ToxServices LLC, Washington, DC.</td>
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<td>3:15 PM</td>
<td><strong>Educational Tools for Designing Safer Chemicals and Predicting Toxicity.</strong></td>
<td>B. Brooks, Baylor University, Waco, TX.</td>
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<td>3:30 PM</td>
<td><strong>Understanding the Needs for Chemists to Gain Training in Toxicology and the Opportunity for Better Chemical Product Design.</strong></td>
<td>J. Warner, Zymergen Inc., Wilmington, MA.</td>
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<td>3:45 PM</td>
<td><strong>Panel Discussion/Q&amp;A.</strong></td>
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**Enroll in the New SOT Mentor Match!**

This relaunched program is a free benefit that allows members to become or find a mentor within the Society.

[www.toxicology.org/mentormatch](http://www.toxicology.org/mentormatch)
Human-induced pluripotent stem cell (hiPSC)–derived neuronal cultures provide an excellent opportunity to model the central nervous system in vitro. These cultures are perceived as a good alternative for ethically debated, labor-intensive, and expensive in vivo experiments that have questionable human relevance, potentially due to inter-species differences. Data obtained with hiPSC-derived neuronal cultures might be more predictive of the human response to chemical exposure because using these cells circumvents inter-species translation. Also, these neurons allow for patient-specific risk assessment and drug testing as they maintain the donor's unique genetic blueprint. Because they reflect genetics unique to each donor, they allow for modeling of specific diseases. For example, hiPSC-derived neuronal cell lines have been made from donors with neurodegenerative diseases such as Parkinson's or Huntington's disease. In light of the aforementioned advances, the use of hiPSC-derived neurons is rapidly increasing. More and more research groups create their own hiPSC-derived neuronal cell lines. Over the past years, an expanding palette of hiPSC-derived neurons (and astrocytes) has become commercially available, saving researchers the time of performing the differentiation themselves, allowing for rapid assay development and translation to drug and chemical screening. However, hiPSC-derived neurons, whether commercially available or lab derived, have not (yet) been able to replace older and more traditional models such as, rat primary cortical cultures, hippocampal slices, and in vivo studies, nor are they incorporated in test guidelines and accepted by regulatory authorities. This session aims to address the important question of, Where do we stand now when it comes to the possibilities and opportunities of these alternative in vitro models for neurotoxicity testing and safety screening? What are the challenges and hurdles that must be overcome before hiPSC-derived neurons will be incorporated in regulatory guidelines and test batteries? The session aims to provide attendees with insights into the current usability of these neurons for in vitro safety testing and drug development and analyze the requirements for establishing scientific confidence in such approaches to render them appropriate for risk assessment purposes. To achieve these goals, this session will bring experts together from different sectors. Following an introduction on the topic, the first speaker will look at this from an academic perspective and talk about commercially available cells and how they can be used for drug safety testing and neurotoxicity screening. She will then continue to explain how this safety assessment can be performed on a more individualized level using subject-derived hiPSC-derived neurons. This speaker will give attendees an academic perspective of the possibilities and future of these human cell-based models. The next talk will be from a multi-stakeholder perspective to bridge from fundamental academic research to diverse stakeholder needs. The speaker is experienced with deriving and culturing neurons, also in complex multi-cell-type 3D systems, and collaborates closely with companies. She therefore is familiar with needs of different sectors. This talk will present work being done on complex multicellular 3D systems made from hiPSC-derived neurons and supporting cells and investigating their susceptibility to pesticides. High-throughput testing opportunities will be discussed as well as how academia and industry can help each other in progressing towards more high-throughput systems. The third talk will look at these model systems from a governmental regulatory perspective. What requirements do these cells need to meet before they can be incorporated in a governmental regulatory framework used, for example, in food safety regulations, and how do these regulatory authorities see alternative approaches now? The final talk will describe the criteria that these models need to meet from a pharmaceutical perspective. In this presentation, the speaker will focus on what pharmaceutical companies want to see before they incorporate hiPSC-derived neuronal model systems in their drug developmental test battery. He will outline how hiPSC-based models fit in neurotoxicity safety assessment and how they compare with the existing animal models. Presentations are followed by a panel discussion on future activities to evolve alternatives to meet regulatory and research needs. At the end of the session, it will be clear where we stand and what steps must be taken before hiPSC-derived neurons are accepted in the regulatory framework and incorporated in the drug developmental pipeline. The ultimate goal is to give perspectives on whether these neurons can replace or reduce in vivo tests.
Drug-induced liver injury (DILI) and hepatobiliary diseases remain significant issues for both drug developers and clinicians seeking to improve and advance the health of patients safely. Bile acids (BA) have been recognized as both indicators and causative agents of various liver toxicities for many years, but only with recent technological advances has the true potential of BA as biomarkers become clear. However, many significant obstacles currently exist, including the sensitivity and specificity of a BA response in a disease state or to a therapeutic agent, marked species variability in bile acid profiles, and an incomplete understanding of the factors controlling BA homeostasis. Similarly, the sheer amount of data generated leads to technical and interpretative challenges that arise due to the complexity of the integrated analysis required for quantification of individual BAs. Despite these unknowns, the potential of BA to provide additional insight into hepatobiliary disease has generated significant excitement across the field. This Workshop features three speakers who will focus on developments in understanding the utilization of BA in clinical diagnosis and drug development. Included among the discussion topics are (1) the use of BA indices and a score model to simplify a complex dataset to predict mortality and progression of cholestatic liver disease; (2) a real-world case study of how perturbing bile acid homeostasis can impact drug development; and (3) how establishing reference ranges for individual bile acids can lead to improved clinical diagnoses of hepatobiliary disease. The session will conclude with an interactive panel discussion driven by attendee questions. Together, these talks will highlight the challenges, opportunities, and application of bile acid profiling to further both the mechanistic understanding and the diagnosis of hepatobiliary injury.

Abstract #

#1243 11:15 AM Opportunities for Human-Induced Pluripotent Stem Cell–Derived Neurons in In Vitro Neurotoxicity Safety Testing.


#1245 11:55 AM iPSC-Derived BrainSpheres as Versatile Research Tool for Developmental Neurotoxicity and Neurological Disorders. L. Smirnova. Johns Hopkins University Center for Alternatives to Animal Testing (CAAT), Baltimore, MD.


1:25 PM Panel Discussion/Q&A.
Large-scale molecular data, including transcriptomics and high content imaging, have been available to scientists for over 25 years but have yet to be integrated into regulatory toxicology beyond providing supportive evidence of health effects, such as mode-of-action analysis for relatively data-rich chemicals. Considering that the vast majority of chemicals in commerce or the environment are data poor, there are considerable opportunities to leverage molecular data in a more integral way, such as informing dose-response assessment and identifying points of departure (PODs) for use in human health and ecological risk assessment. In a traditional risk assessment, a POD is typically obtained from resource- and animal-intensive low-throughput studies examining apical endpoints (e.g., histopathology, organ weights). More recent efforts have been aimed at increasing throughput of chemical evaluation by integrating PODs derived from molecular-based dose- or concentration-responses obtained using in vitro models or in vivo studies of shorter exposure duration. The aim of this Workshop is to present and discuss recent examples that demonstrate how molecular-derived PODs can be used in the chemical sector for risk assessment applications. This Workshop will specifically review current regulatory needs; present timely case studies from industry, Health Canada, the US Environmental Protection Agency (US EPA), National Toxicology Program, and the University of Ottawa; and open the floor to discuss specific paths forward to effectively integrate molecular-derived PODs into the risk assessment process with increased confidence. The first presentation will set the stage for Workshop participants by describing the current state of regulatory toxicity assessments and data requirements in the industrial chemical and pesticide spaces. The second speaker will dive deeper into the methods used in deriving molecular-based PODs from transcriptomic data, and the dose-response and temporal concordance of such PODs to traditional apical effect-based PODs. The third speaker will describe the current status of the US EPA high-throughput in vitro modeling effort aimed at analyzing both transcriptome and imaging data to screen and prioritize industrial chemicals as part of a tiered testing framework for hazard characterization. The fourth presentation will review use case studies that illustrate how molecular-derived PODs from short-term exposures in rodents are being used in risk assessment, with a focus on comparing pathway-specific to pathway-agnostic PODs and describe relationships between in vitro and in vivo molecular PODs. The last speaker will provide perspective on fit-for-purpose application of molecular-based data to human health risk assessment, with a focus on deploying molecular PODs in the regulatory toxicology space, and describe current use and “on the horizon” uses. Following the presentations, Workshop Chairs and speakers will engage audience participants in a question-and-answer session. The goal of this discussion is to be provocative about both the limitations of a molecular POD (e.g., may not easily identify specific hazards) and the opportunities of a molecular POD to dramatically increase chemical toxicity testing throughput while informing safe human use of chemicals.

Abstract #
#1252 11:15 AM Molecular-Based Points of Departure as the New Basis for Chemical Risk Assessment: Are We Ready? T. Barton-Maclaren. Health Canada, Ottawa, ON, Canada. Sponsor: J. Rager
#1253 11:15 AM Advancing the Use of Molecular-Based Points of Departure to Address Multisectoral Needs for Priority Setting and Chemical Risk Assessment. K. Johnson. Corteva Agriscience, Indianapolis, IN.
#1255 12:05 PM In Vitro Molecular PODs from High-Throughput Profiling Assays. C. Yauk. University of Ottawa, Ottawa, ON, Canada. Sponsor: J. Rager
#1256 12:30 PM Case Studies on the Use of Transcriptomic Points of Departure. J. Lambert. US EPA, Cincinnati, OH.
1:20 PM Panel Discussion/Q&A.
Workshop Session: Paving the Way for Greater Data Sharing to Advance Biomarker and Drug Development: Industry, Academia, and Regulatory Insights

Chair(s): Deidre Dalmas, GlaxoSmithKline plc; and Stacey Fossey, AbbVie Inc.
Primary Endorser: Clinical and Translational Toxicology Specialty Section
Other Endorser(s): Regulatory and Safety Evaluation Specialty Section; Risk Assessment Specialty Section

Data is at the heart of scientific advancement and biomarker and translational model development. Combining complementary strategies and pooling scientific data through cross-industry, academia, and regulatory collaborations with increased data sharing would bring unprecedented power, insight, and game-changing solutions to biomarker and translational model development (e.g., predictive safety and efficacy models). Utilizing existing data is both more efficient and more ethical. Yet, data sharing is still challenging. Pre-competitive collaborations, crowdsourcing, and open science sourcing (i.e., diverse strategies that seek external input and public engagement) can harness the power of data sharing using newly developed tools that protect proprietary data. These efforts will foster new and improved drug discovery and development to enable more effective and safer therapies. This Workshop will highlight ideas, ongoing efforts, and future aspirations from industry, consortia, academia, and the US Environmental Protection Agency (US EPA) on data sharing and how increased collaborations and new ways of working together can have greater impact on novel biomarker development and the drug discovery and development process. Data will be shared from a cross-industry survey conducted by the IQ DruSafe Biomarker Working Group on the current and future state of emerging safety biomarkers and will include use case examples from data collected as part of the survey. An emphasis will be placed on what is needed to modernize the development of methods, materials, and measures that can streamline drug development. This will include new data sharing tools being developed by the Critical Path Institute’s Predictive Safety Testing Consortium and Translational Quantitative Safety Testing Consortium to protect proprietary data and bring new medicines to patients in a more efficient manner. Case studies and examples will be shared and will include collaborative efforts presented by the US FDA showcasing the power of data sharing on patients. The Workshop will finish with an interactive panel discussion to foster open communication and dialogue with Workshop participants.

Abstract #


#1260 11:25 AM  Emerging Safety Biomarkers: Current and Future State. L. Ramaiah1, T. Zabka2, J. Burkhardt3, and D. Dalmas4. 1Pfizer Inc., Pearl River, NY; 2Genentech Inc., South San Francisco, CA; 3Pfizer Inc., Groton, CT; and 4GlaxoSmithKline plc, Collegeville, PA.

#1261 11:55 AM  Academic and Industry Collaborations: Data Sharing to Advance Drug Development. R. Sherrif5, F. Hunter6, B. Fuzi7, N. George8, R. Brennan9, and H. Hermjakob6. 5European Bioinformatics Institute and Translational Quantitative Systems Toxicology Consortium, Cambridge, United Kingdom; 6European Bioinformatics Institute, Cambridge, United Kingdom; 7Universität Wien, Vienna, Austria; and 8Sanofi, Waltham, MA.

#1262 12:30 PM  Current and Emerging Opportunities to Enable Scientific Data Sharing: Leveraging the Power of Working Together to Advance Drug Development. J. Burkey. Critical Path Institute, Tucson, AZ.

#1263 1:05 PM  Regulatory Insight into Data Sharing: Challenges and Opportunities for Public Health Impact. A. Parekh. US FDA/CDER, Silver Spring, MD. Sponsor: D. Dalmas

1:40 PM  Panel Discussion/Q&A: Leader—Stacey Fossey. S. Fossey1, D. Dalmas2, L. Ramaiah1, J. Burkey4, R. Sherrif6, and A. Parekh1. 1AbbVie Inc, Chicago, IL; 2GlaxoSmithKline plc, Collegeville, PA; 3Pfizer Inc., Pearl River, NY; 4Critical Path Institute, Tucson, AZ; 5European Bioinformatics Institute, Cambridge, United Kingdom; and 6US FDA/CDER, Silver Spring, MD.
Due to the importance of toxicological sciences for public and environmental health, it is key to increase the awareness of toxicology globally. Currently, disparities related to the perception and implementation of this science are observed between developed and developing countries. International outreach programs and actions directed to promote the excellence of toxicology among countries are fundamental to enhance the scientific, professional, and academic careers of current and future generations of toxicologists. Young to senior toxicologists, including leaders in the field that are interested in developing international connections and are motivated to improve and/or create an environment to facilitate an international network, are invited to discuss and learn about successful models and strategies to promote global outreach of toxicology. Initiatives such as coordination of international outreach programs, collaboration with international institutions, or creation of international interactive platforms between students and professionals foster an excellent environment to increase networking and expand awareness of toxicology globally. This session will cover major challenges frequently faced by developing countries, which could benefit from internationalization, to develop the toxicological sciences. Some examples of such challenges include difficulties engaging students on toxicological education, limitations to performing high-quality science and increasing the visibility and impact of toxicological research, and impediments to improving public health. The goals of this session are to highlight the strengths and challenges of toxicological international outreach models in order to maximize the potential to benefit individuals and institutions, and to discuss new strategies to increase the perception and application of toxicology around the world.

Abstract #

#1264 11:15 AM Strategies to Increase Global Awareness of Toxicology: Focus on Developing Countries.
11:25 AM SOT and IUTOX Efforts to Promote Toxicology Global Outreach. J. Manautou. University of Connecticut, Mansfield, CT.
11:50 AM International Mentoring as a Tool to Promote Toxicology Higher Education and Global Outreach. Z. Corsino. Rubius Therapeutics Inc., Cambridge, MA. Sponsor: A. de Conti
12:15 PM Internationalization of Research to Improve Diversity and Quality of Science. S. Barros. Universidade de São Paulo, São Paulo, Brazil.
1:05 PM Challenges for Toxicological Sciences Internalization in Countries from Africa. D. Hood. Ohio State University, Columbus, OH.
1:30 PM Panel Discussion/Q&A. A. de Conti. US FDA/NCTR, Jefferson, AR.
### Symposium Session: SETAC-SOT Session: Environmental Risk Assessment of PFAS

**Chair(s):** Michael Carvan, University of Wisconsin-Milwaukee; and Tamar Schlekat, Society of Environmental Toxicology and Chemistry.

**Primary Endorser:** Molecular and Systems Biology Specialty Section

**Other Endorser(s):** Occupational and Public Health Specialty Section; Risk Assessment Specialty Section

Per- and polyfluorinated alkyl substances (PFAS) are a universe of diverse substances that contain carbon-fluorine (C-F) bonds and are of emerging concern. PFAS have been used in a wide array of industrial and consumer uses, from fire-fighting foams and anti-stain products for carpet and upholstery to nonstick cookware. Many PFAS substances can be persistent in the environment and are thus being found in biota and many compartments of the environment. Emerging concerns over exposure to and potential effects of PFAS as well as management of PFAS have been challenging the environmental and health professional communities from researchers and engineers to regulators and managers. Due to the large number of substances and their difference, a substance-by-substance approach to predicting risk from PFAS and for environmental management of PFAS is not practical. Experts in human health and ecological health have come together to advance this issue, and this session aims to present the latest science in environmental chemistry, ecotoxicity, and human health toxicity for PFAS. This session will commence with a synthesis of progress made on various classification and grouping schemes for PFAS based on their chemical composition and properties. Then, the session will segue to a discussion of new *in vitro* and *in silico* models that are being developed to predict the toxicity of PFAS using a multiple lines of evidence approach that increases confidence in these new approach methodologies. The session will end with a review of current literature on the effects of PFAS on ecological endpoints. The last talk also will address the challenges faced in assessing the ecological risks of PFAS and discuss state-of-the-science approaches to meet these challenges. Experts will distill the work in that area and will identify future needs toward sustainable solutions based on current understanding. At the conclusions of their words, the speakers will then be available for a facilitated panel discussion.

**Abstract #**

#1265 2:45 PM  SETAC-SOT Session: Environmental Risk Assessment of PFAS.

2:45 PM Introduction. M. Carvan. University of Wisconsin-Milwaukee, Milwaukee, WI.

#1266 2:50 PM  PFAS Chemistry. S. Korzeniowski. American Chemistry Council Inc., Point Pleasant Beach, NJ. Sponsor: M. Carvan

#1267 3:15 PM  PFAS Ecotoxicology. G. Anklehy. US EPA, Duluth, MN. Sponsor: M. Carvan

#1268 3:40 PM  PFAS Human Health. C. Ng. University of Pittsburgh, Pittsburgh, PA.

4:05 PM Panel Discussion/Q&A.

### Informational Session: Safety Assessment of Devices Used in Assisted Reproduction Technology: Mouse Embryo Assay

**Chair(s):** Niranjan Goud, Greenwood Toxicology Associates LLC; and Benjamin Fisher, US FDA/CDRH.

**Primary Endorser:** Medical Device and Combination Product Specialty Section

**Other Endorser(s):** Association of Scientists of Indian Origin Special Interest Group

Medical devices are being increasingly used in the diagnosis and treatment of various conditions. One such example is the devices used in assisted reproduction technology (ART) such as catheters, needles, and culture dishes and media. The success rate of *in vitro* fertilization (IVF) depends not only on the nature of sperm and eggs obtained from the couples but also on the quality of devices used in the process. Before such devices are marketed for clinical use, care should be taken to ensure that they meet regulatory requirements for patient safety (in this case, to the survival of embryo/fetus). Though there are existing standards by ISO 10993 series, ASTM, and USP on
the manufacturing and biocompatibility testing of different medical devices, unfortunately there were no such regulations until recently for the ART device category. Since ART devices contact (either directly/indirectly) the gametes (sperm/eggs) and/or embryo, testing them in the mouse embryo assay (MEA) is considered relevant. The first speaker, from the US Food and Drug Administration (US FDA), will tell the history of the development of the MEA guidance document introduced in June 2019. He will describe the salient features of embryo culture and how the devices are tested. Particular focus will be on parameters of mouse strains, number of embryos for test and control groups, sample size, extraction methods, culture conditions, and acceptance criteria, which are essential for successful premarket submission to US FDA. Currently, IVF is a method of choice in the treatment of infertility. As per the recent CDC report, approximately 1.9% of all infants born in the United States every year are conceived using ART. The second speaker will give his perspective on the MEA as a functional and toxicological bioassay in detecting embryo toxicity; the standard procedures of using F1 hybrid mice in the development of one-cell or two-cell embryos and the acceptance criteria of percent blastocyst development; and methods in assessing the morphology and viability of embryos and the role of oil and ingredients in media such as protein and volatile organic chemicals on fertilization. Some devices are tested directly in the MEA, but extracts can also be used. He also will explain how various ART devices that are evaluated get market approvals not only for US FDA but also for other global regulatory bodies. The last speaker will describe the effect of detergents and cleaning agents used during the manufacturing of ART devices and the role of coatings/adhesives and endotoxins on the process of fertilization in some case studies. Perfumes and antiperspirants used by prospective parents, workers in device manufacturing plants, or health care staff in reproductive clinics also have an impact on embryo viability. In summary, the purpose of this Informational Session is to highlight the importance of testing the ART devices to the newly developed US FDA guidance on the MEA to minimize embryo lethality, which in turn could bring cheers to prospective parents and family.

Abstract #

#1269 2:45 PM Safety Assessment of Devices Used in Assisted Reproduction Technology: Mouse Embryo Assay.
2:45 PM Introduction. N. Goud. Greenwood Toxicology Associates LLC, Greenwood, IN.
3:35 PM Mouse Embryo Assay Test Failures: Prevention Strategies. N. Goud. Greenwood Toxicology Associates LLC, Greenwood, IN.
3:55 PM Panel Discussion/Q&A.
Symposium Session: Application of Computational Genomic Approaches to Address Toxicity Mechanisms and Prediction

Chair(s): Mark Gosink, Pfizer Inc.; and Minjun Chen, US FDA/NCTR.

Primary Endorser: Computational Toxicology Specialty Section

Other Endorser(s): Drug Discovery Toxicology Specialty Section; In Vitro and Alternative Methods Specialty Section

The physiochemical properties of compounds contribute to their safety and have been extensively used to predict toxicity. However, genomic context also plays a significant role in the development of compound-induced toxicity. Genomic information can provide critical insight into mechanisms and help improve the prediction of relevance of toxicities to humans and/or identify specific subpopulations that can avoid liability. This session will focus on the utilization of computational genomic approaches and information to elucidate toxicity through on- and off-target mechanisms and how genomic information can then be utilized to predict toxicity. The first two talks will focus on the utilization of coding and non-coding RNA expression data to understand toxicity mechanisms. The third talk also will utilize expression data but will delve into prediction of drug on- and off-targets. The fourth speaker will present on how individual genomic context can affect drug response and how this pharmacogenomic information is used by the US Food and Drug Administration (US FDA) in their evaluation of pharmaceuticals. Finally, the last presenter will discuss the work done by an academic/government/industry collaboration to develop a transcriptomic biomarker of genotoxicity and their efforts to get it accepted by the US FDA.

Abstract #

#1270 11:45 AM Application of Computational Genomic Approaches to Address Toxicity Mechanisms and Prediction.

11:45 AM Introduction. M. Gosink. Pfizer Inc., Groton, CT.


#1272 12:20 PM Computational Prediction and Wet-Lab Validation of Non-coding RNAs in the Regulation of Drug Metabolizing Enzymes Related to Drug Efficacy and Safety. B. Ning. US FDA/NCTR, Jefferson, AR.

#1273 12:50 PM Exploring the Use of Compound-Induced Transcriptomic Data Generated from Cell Lines to Predict Compound Activity toward Molecular Targets. D. Rouquié. Bayer SAS, Valbonne, France. Sponsor: M. Gosink


2:20 PM Panel Discussion/Q&A.
Botanical dietary supplements are widely used throughout the world. They have long had a place in preparing for or alleviating pain from pregnancy, easing nausea and vomiting, treating urinary tract infections, and facilitating labor. After birth, they have been used to initiate, maintain, and/or augment milk production during lactation. Reports from both Australia and the United States indicate that 36% and 45% of respondents, respectively, have used at least one herbal product during pregnancy. While women in particular use herbal products, there also is a wide array of botanicals available for men (e.g., to enhance sexual function) and children (e.g., to improve behavior and/or aid with sleep). Although there are varying levels of use reported, consumers are self-selecting or being advised by health care professionals to consume certain herbal products to improve health or to use during important life stages, including pregnancy. Thus, considerations of developmental and reproductive effects in the safety assessment are warranted, particularly when considering the possibility of exposure during pregnancy. The precautionary principle would state that herbal medicines and supplements should not be taken during pregnancy or breastfeeding unless the benefit to the mother outweighs any possible risk to the fetus/nursing infant. While this recognition may serve as general medical advice, there are clearly instances, as described, where pregnant/breastfeeding women are using botanical preparations under the direction or at the advice of health care professionals and/or without oversight. These issues are of concern, as some women may not even be aware that they are pregnant in the early stages of pregnancy. Labeling alone may not be the most appropriate or effective risk mitigation measure to warn women not to use herbal supplements during pregnancy. There is a clear need for evidence-based safety data that include evaluation of developmental and reproductive toxicity (DART) endpoints. Research on these botanical dietary supplements is complicated by the many diverse botanical products marketed for reproductive health, their chemical complexity due to the fact that many are mixtures, inherent variations in different extracts used in different products, and a lack of understanding of the biologically adverse effects or ability to identify long-term reproductive and/or developmental consequences. In this session, speakers will address the current procedures/methodologies for assessing botanicals in DART studies, the global regulatory guidelines, efforts to improve or design new methodologies, and successes/challenges associated with such approaches. The session will begin with an overview of botanical dietary supplements, highlighting the importance of evaluating DART for these complex mixtures and the unique challenges associated with studying them. Next, there will be a presentation of the regulatory landscape surrounding botanical dietary supplements in various regions around the world and the approaches being used and developed to inform risk assessment. Following speakers will present select examples of in silico and in vitro approaches for botanical ingredients and the successes and issues associated with these new testing paradigms. This session will highlight ongoing efforts to address challenges of generating safety data regarding botanical use during sensitive life stages and potential methodologies and challenges and will provide suggestions for paths forward for addressing botanical mixtures research.

Abstract #

| #1276 | 11:45 AM | Botanical Mixtures: Predictive Approaches to Evaluating Pregnancy, and Reproductive and Developmental Health. |
| #1277 | 11:45 AM | An Overview of Botanical Dietary Supplements: Key Research Needs and Unique Challenges of Botanicals Research. M. Huang. NIEHS/NTP, Research Triangle Park, NC. |
| #1278 | 12:10 PM | Global Regulations for Botanical Supplements and Their Role in Risk Mitigation of Phytochemicals in Breast Milk. R. Marles. Health Canada, Ottawa, ON, Canada. Sponsor: M. Huang |
| #1280 | 1:20 PM | Botanical Dietary Supplements and DART Screening Strategies for Decision Making. C. Mahony. Procter & Gamble, Egham, United Kingdom. Sponsor: M. Huang |
| #1281 | 1:55 PM | Challenges, Opportunities, and Solutions for In Silico Toxicology Applied to the Evaluation of DART Endpoints to Botanicals. M. Cronin. Liverpool John Moores University, Liverpool, United Kingdom. Sponsor: M. Huang |
Allergic contact dermatitis is an undesired side effect observed with many products, including cosmetics, natural extracts, drugs, chemicals, and medical devices. Over the last decades, a great deal of progress has been made in the development of alternative in vitro testing strategies to assess these issues, concurrent with the mechanistic understanding provided by the adverse outcome pathway framework. The use of animals in toxicology is under ever-increasing scrutiny, with mounting pressure to develop effective alternatives. Efforts should be devoted to developing reliable in vitro assays and integrated testing strategies capable of addressing toxicity concerns for a broad spectrum of products and chemicals. This will require a better understanding of the applicability domains of scientifically validated assays and methods that are currently being used so that chemicals can be tested appropriately in these assays to produce valid predictions. In addition, accurate definition of the applicability domains will facilitate modification and improvement of current and new assays to expand these domains, resulting in better coverage of the chemical space for prediction of sensitization potential. The purpose of this Workshop is to cover current knowledge on the applicability domains of these methods, to understand their limitations and the opportunities they offer. The session will open with a brief introduction by the session Chair followed by five presentations aimed at defining the current state of the applicability domains for in vitro approaches as well as recent progress to expand these domains. The first speaker will present the current status of an international collaboration charged with establishing international test guidelines for nonanimal testing strategies that would serve as full replacements to the animal tests for skin sensitization. The approach includes using the current nonanimal methods within their applicability domains to model skin sensitization. The second speaker will define the applicability domains and limitation for the individual OECD Test Guidelines 442c, 442d, and 442e, which address chemical peptide reactivity, keratinocyte activation, and dendritic cell activation, respectively. A complete understanding of the influence of chemistry on these factors is critical for accurate predictions and improvement of current approaches to expand the applicable chemical space that can be tested without the use of animals. The third speaker will focus on in chemico assessment of peptide reactivity, presenting a characterization of the currently validated Direct Peptide Reactivity Assay (DPRA) approach while providing insight into the novel Peroxidase Peptide Reactivity Assay (PPRA), which holds promise to expand the applicability domain of peptide reactivity assays to include pre- and pro-hapten requiring metabolism. The forth speaker will provide initial data for a novel dendritic cell activation assay, the THP-1 Activation Assay, which is being developed to expand the applicability domain of the current in vitro dendritic cell activation assays to include drugs that exhibit limited or no cytotoxicity. The final speaker will introduce the state of the art for novel in vitro approaches based on transcriptional profiling and machine learning to predict sensitization potential. These assays are showing promise for addressing issues of difficult-to-test substances including hydrophobicity, metabolism, solubility, and formulation, and the GARDskin assay will be used to illustrate the progress. Overall, this Workshop aims to better defined the applicability domains for nonanimal sensitization testing and identify progress and opportunities for expanding these domains. This Workshop represents an international collaboration between the Immunotoxicology Specialty Section of SOT and the Immunotoxicology and Chemical Allergy Specialty Section of EUROTOX in an effort to communicate and improve the science of alternative approaches for assessing potential for skin sensitization.

**Abstract #**

| #1282 | 11:45 AM | Applicability Domains and Future of Nonanimal Tests for Skin Sensitization.  
V. Johnson. Burleson Research Technologies, Morrisville, NC. |
| #1283 | 11:50 AM | International Regulatory Progress on Nonanimal Approaches for Skin Sensitization.  
N. Kleinstreuer. NIEHS/NICEATM, Research Triangle Park, NC. |
| #1284 | 12:20 PM | Chemistry behind Sensitization: Possible Limitation and Bottleneck of In Vitro Methods.  
R. Landsiedel. BASF SE, Ludwigshafen, Germany. |
| #1285 | 12:50 PM | The Use of Peptide Reactivity Assays for Skin Sensitization Hazard Identification and Risk Assessment.  
| #1286 | 1:20 PM | Drug-Induced Hypersensitivity: Opportunities to Expand NAMs for Skin Sensitization to Drugs.  
E. Corsini. Università degli Studi di Milano, Milan, Italy. |
The US Consumer Product Safety Commission (CPSC) received a petition in 2015 from a coalition of organizations and individuals representing physicians, patients, fire fighters, and consumers. The petition requested CPSC to ban non-polymeric, additive Organohalogen Flame Retardants (OFRs) as a class in four categories of consumer products. Due to the breadth of products and chemicals involved in the petition, CPSC sponsored a study through the National Academy of Sciences (NAS), and the report was released in 2019. NAS developed a class approach to hazard assessment and discussed the challenges with its application in the regulatory setting. The aim of this Workshop is to foster scientific discussion on approaches to evaluating OFRs. The Workshop will address issues such as (1) why OFRs are important for fire safety; (2) what level of data is needed to assess chemical classes; (3) what activities are being applied by other regulatory agencies for OFRs; and (4) whether new approach methodologies (NAMs) and read-across methods are ready for this regulatory application. This session will begin with an overall introduction by the Co-Chair, Linda Birnbaum, a Scientist Emeritus and former Director of NIEHS and NTP. The first speaker, who is leading the CPSC Toxicology and Risk Assessment group, will cover the CPSC perspective on the OFR project, including the petition, the 2019 NAS report, and past and current CPSC work related to OFRs. The second speaker, from Europe, will describe a broader overview of the global regulatory landscape. The EU issued bans on the production and use of polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCD), starting in 2002. Recent EU regulations related to OFRs include Registration, Evaluation, Authorization and Restriction of Chemicals (REACH); the Restriction of Hazardous Substances (RoHS); and the Waste Electrical and Electronic Equipment (WEEE). The current Community Rolling Action Plan (CoRap) of the European Chemicals Agency (ECHA), which prioritizes substances for risk evaluation, contains some OFRs that overlap with the CPSC activities. The third speaker, a toxicologist from industry, will discuss why OFRs are used in consumer products; how OFRs are incorporated into different materials; the mode of action by which OFRs retard fire; and how to balance the fire risk and health risk associated with OFRs. The fourth presentation, given by two speakers who are leading the US Environmental Protection Agency (US EPA) Toxic Substances Control Act (TSCA) effort on prioritization and risk evaluation of the high-priority substances, will focus on the US EPA perspective on OFRs, as well as the TSCA status of NAMs. The fifth presentation, from academia, will discuss what we know about human exposure for several types of OFRs, including results from biomonitoring studies and several epidemiology studies published over the past few years. The Workshop will conclude with an interactive discussion among the speakers, Co-Chairs, and audience. The session will cover multidisciplinary topics and will be of interest to regulators, risk assessors, toxicologists, chemists, exposure scientists, in vitro assay developers, computational toxicologists, and stakeholders. These comments are those of the panelists and do not necessarily represent the views of their respective institutions.

Abstract #
#1288 11:45 AM The Scientific Challenges in Regulating Organohalogen Flame Retardants (OFRs) as a Class in Consumer Products.
   11:45 AM Introduction. L. Birnbaum. NIEHS, Research Triangle Park, NC.
#1290 12:15 PM Organohalogen Flame Retardants: The European Situation and Legislation. J. de Boer. Vrije Universiteit Amsterdam, Amsterdam, Netherlands. Sponsor: X. Chen
#1292 1:05 PM  Organohalogen (OFR) and Other Flame Retardants: US EPA Toxic Substances Control Act (TSCA) Review Efforts. S. Barone. US EPA, Washington, DC.


#1293 1:35 PM  Human Exposure to Organohalogen Flame Retardants: Sources, Pathways, and Health Concerns. H. Stapleton. Duke University, Durham, NC.

2:00 PM  Panel Discussion/Q&A.
Oligonucleotide-based therapeutics that utilize nucleic acids to treat a variety of local and systemic diseases are very novel and relatively unknown to the public. This unique class of agents includes antisense oligonucleotides (ASOs), small interfering RNAs (siRNAs), aptamers, microRNA (miRNA) inhibitors and mimics, and modified messenger RNA (mRNA), which usually require special systems for delivery to patients and have specific safety considerations. In the last 20 years, several ASOs have been approved for the treatment of serious diseases, including fomivirsen for cytomegalovirus retinitis; mipomersen for homozygous familial hypercholesterolemia; nusinersen for spinal muscular atrophy; and inotersen for polynuropathy caused by hereditary transthyretin-mediated (hATTR) amyloidosis. In 2018, patisiran, the first RNAi therapeutic, was approved for the treatment of polyneuropathy of hATTR amyloidosis. Givosiran, another RNAi therapeutic, was approved in 2019 for the treatment of acute hepatic porphyria. A robust nonclinical and clinical pipeline features other ASOs, siRNAs, and modified mRNAs designed to treat systemic and local diseases in a variety of organ systems. This Symposium will provide current updates on the status of the ASO, siRNA, and modified mRNA platforms, their respective mechanisms of action, their chemistry, and some of the challenges each modality must overcome to enable effective systemic and localized delivery to target tissues, with an acceptable benefit-to-risk profile. Pharmaceutical development of these agents constitutes a prime example of bridging cutting-edge research with the established regulatory requirements allowing for clinical testing. Effective nonclinical safety assessment and the regulatory requirements for evaluating the risks and benefits of these molecules, including appropriate species selection and determination of safety margins, are of paramount importance in bringing these novel therapeutics to patients. Following this session, attendees will have a better understanding of the current thinking surrounding nonclinical safety evaluation and development strategies for this important emerging class of oligonucleotide-based therapeutics.

Abstract #

#1294 11:30 AM  Controlling the Message: Safely Navigating the Development of Novel Oligonucleotide Therapeutics.  
Introduction.  J. Sutherland. Alnylam Pharmaceuticals Inc., Cambridge, MA.

#1295 11:35 AM  Using a Toxicology Database to Better Understand the Species Relevance and Safety Attributes of 2’-MOE ASOs.  S. Henry. Ionis Pharmaceuticals, Carlsbad, CA.


#1297 12:45 PM  Delivering on the Promise of mRNA Therapeutics.  J. Senn. Moderna Inc., Cambridge, MA.  
Sponsor: J. Sutherland

#1298 1:20 PM  Oligonucleotide Therapeutics: Current Regulatory Considerations and What We Have Learned from the Submission Data to US FDA.  X. Chi. US FDA/CDER, Silver Spring, MD.  
Sponsor: J. Sutherland

1:55 PM  Panel Discussion/Q&A.
Thursday, March 25, 11:30 AM to 2:15 PM

Symposium Session: From Conception to Cane: Unique Life-Stage Considerations for Reproductive Toxicity

Chair(s): Michelle Kossack, Brown University; and Jodi Flaws, University of Illinois at Urbana-Champaign.

Primary Endorser: Reproductive and Developmental Toxicology Specialty Section

Other Endorser(s): Molecular and Systems Biology Specialty Section

The impact of toxicant exposures on the reproductive system is highly dependent on life stage. During the fetal period, germ cells migrate to the urogenital ridge, the indifferent gonad differentiates into the testis or ovary, and meiosis is initiated in the ovary. In rodent models, reproductive system development continues during the early postnatal period, making the developing gonad sensitive to toxicant exposures during the pregnancy and lactation periods. Once the gonad is fully developed, women and other female mammals have a finite number of oocyte-containing follicles. Throughout the fertile life span, these follicles grow and become capable of releasing oocytes for fertilization. Since the follicular reserve is not renewable, the original endowment is gradually depleted with age. Exposure to some toxicants can accelerate reproductive aging, shorten the reproductive life span, or lead to adverse reproductive outcomes in the children of aging parents. As the reproductive life cycle is started again with the next generation, epigenetic alteration incurred throughout a lifetime of environmental exposure may be passed on to subsequent generations. Each period of the reproductive life span is vulnerable to the perturbations from environmental chemicals resulting in reproductive toxicity. This Scientific Session will address the effects of life stage-specific reproductive toxicity. Beginning with pregnancy, through prenatal development, aging, and transgenerational effects, this session will explore how chemical exposure affects reproductive potential in both males and females. Further, the speakers will use case examples in human as well as mammalian and fish models to investigate the life stage–specific risk of exposure to environmental chemicals.

Abstract #

#1299  11:30 AM  From Conception to Cane: Unique Life-Stage Considerations for Reproductive Toxicity.
       11:30 AM  Welcome and Introduction to Speakers.  M. Kossack. Brown University, Providence, RI.
       11:35 AM  Introduction to Environmental Chemical Exposure during Reproductive Life Span and Sequelae.

#1300  11:55 AM  Endocrine-Disrupting Chemicals in Pregnant Women and Potential Modifying Factors.  R. Strakovsky.
              Michigan State University, East Lansing, MI.

#1301  12:25 PM  Disruption of Retinoic Acid Signaling: A Mechanism of Phthalate Toxicity in the Seminiferous Cord.
                   D. Spade. Brown University, Providence, RI.

                   US EPA/ORD, Research Triangle Park, NC.

#1303  1:25 PM  Epigenetic Inheritance of Exposure Effects in Medaka.  R. Bhandari. University of North Carolina at Greensboro, Greensboro, NC.
       1:55 PM  Panel Discussion/Q&A.
Workshop Session: Cannabidiol 2021: Science, Safety, and Societal Issues

Chair(s): Sol Bobst, ToxSci Advisors LLC; and George Corcoran, Wayne State University.

Primary Endorser: Ethical, Legal, Forensics, and Societal Issues Specialty Section

Other Endorser(s): Clinical and Translational Toxicology Specialty Section

The global cannabidiol (CBD) market was 7.1 billion in 2019, predicted to be 9.3 billion in 2020. The 2018 Farm Bill directed the US Department of Agriculture to update rules on hemp production. States have issued their own legislations as well. There are over 545 active compounds, 100 of which are cannabinoids that have limited safety or efficacy data. Challenges for researching cannabinoids remain due to the US Drug Enforcement Administration listing of cannabis with marijuana on Schedule I of the Controlled Substances Act. This Workshop will present current CBD basic and clinical research, describe challenges and opportunities for consumer product safety, as well as development of cannabis-derived medical treatments, and lay out the legal, regulatory, and social dilemmas created by the complex landscape of commercialization of cannabis-based products.

Abstract #
#1305 11:40 AM An Overview of the Pharmacology, Toxicology, and Popularity of CBD. H. Kamendi. Rx Remedies Inc., Baltimore, MD.
#1307 12:20 PM Interferon (IFN)-Gamma Is a Sensitive Target in CBD-Induced Immune Suppression In Vivo and In Vitro. B. Kaplan. Mississippi State University, Starkville, MS.
#1309 1:00 PM Cannabinoids: Treatment of Chronic Neuropathic Pain and Neuropsychiatric Disorders. D. Fox. Exigent, Austin, TX.
#1310 1:20 PM Cannabidiol Incorporation into Consumer Products in the US: Regulatory Challenges to Commercialization. L. Plunkett. Integrative Biostrategies LLC, Houston, TX.
1:40 PM Panel Discussion/Q&A.

Workshop Session: Regulatory Learnings from the EU Flagship Nonanimal Toxicology Project, EU-ToxRisk

Chair(s): Bob van de Water, Universiteit Leiden, Netherlands; and Maureen Gwinn, US EPA.

Primary Endorser: Regulatory and Safety Evaluation Specialty Section

Other Endorser(s): In Vitro and Alternative Methods Specialty Section; Risk Assessment Specialty Section

Within the EU, over 5,000 scientific projects in the field of health protection have been funded since 2007. Research funding programs start and end in cycles. Achieved scientific outcomes, highlights, and knowledge are passed on to new generations of scientists and consortia via protocols, publications, and conference sessions. Nevertheless, some of the basic or overarching learnings—i.e., beyond the mere scientific findings—are not equally well disseminated. Yet novel strategies, frameworks, and collaborative approaches often merit a more extensive discussion, with their development not only being a key factor for project success but also helping to push forward broader uptake and implementation. This session will present four key learnings derived from the EU-ToxRisk project, which has been
running since 2016 and is currently the largest collaborative toxicology effort in the EU, focusing on mechanism-based toxicity testing and risk assessment. Its mission is to develop the tools and strategies that will enable reliable animal-free risk assessment of chemicals. The session will discuss how close interaction among researchers and regulators can significantly improve targeting regulatory needs, thereby enhancing the societal impact of the project. Implementation is only possible with a mutual understanding of the developed methods and their areas of concrete application. Three approaches and tools that specifically address this issue will subsequently be introduced. Firstly, the use of practical case studies will be debated. The running of well-defined case studies, based on the use of new approach methods (NAMs) to solve a defined regulatory question, can increase confidence in non-validated approaches, as in the case of next-generation risk assessment. Secondly, the importance of implementing an efficient knowledge infrastructure—including high-quality data sharing, comprehensive test method descriptions, and integration of results and knowledge—will be described. And finally, the session will highlight the significance of establishing a good regulatory reporting practice for NAM-enhanced read-across (RAx). To this end, we published an advisory document structured along with the EU-ToxRisk RAx framework that also includes more common learnings obtained from confrontation with the regulatory community. Its application will improve the submission quality of RAx cases by registrants and, thereby, increase acceptance rates of nonanimal approaches. In this context, it is also crucial to foster close international cooperation, which is essential to drive and align testing requirements based on NAM approaches. The concluding talk of this session will, therefore, see international and harmonized efforts established within the EU-ToxRisk project and beyond, like, for instance, the Accelerating the Pace of Chemical Risk Assessment (APCRA) initiative and the OECD IATA Case Studies Project.

Abstract #
#1311 11:30 AM  Regulatory Learnings from the EU Flagship Nonanimal Toxicology Project, EU-ToxRisk.
#1312 11:35 AM  How Input from a Regulatory Advisory Board Can Enhance the Regulatory and Scientific Relevance of Your Project.  M. Herzler. Bundesinstitut für Risikobewertung (BfR), Berlin, Germany. Sponsor: B. van de Water
#1313 12:05 PM  Use of Case Studies for Increasing Confidence in Non-validated Approaches in Next-Generation Risk Assessment.  S. Escher. Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany. Sponsor: B. van de Water
#1315 1:05 PM  Components of a Good Regulatory Reporting Practice: The NAM-Enhanced Read-Across Advisory Document.  H. Kamp. BASF SE, Ludwigshafen am Rhein, Germany.
2:00 PM  Panel Discussion/Q&A.

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Poster Sessions

Poster presentations and sessions are a valued part of the Virtual 2021 Annual Meeting and ToxExpo. Poster presenters will be given easy-to-follow instructions and tools for uploading electronic files of their posters for display in the Virtual Poster Gallery. These instructions will include information on how to record an audio narrative for inclusion alongside your poster. The Virtual Meeting schedule also includes Poster Sessions during which attendees can chat with the poster authors.

Abstract Acceptances and Scheduling

Abstract acceptance notifications will be made by email in late December. Presenting authors also will receive information on session timing/instructions at that time. Please note that the complexity of the program planning process prevents any changes to the type, day, or time of the sessions.

Poster Session Schedule at a Glance

After each Poster Session has concluded, posters from that session will be available for on-demand viewing on the Virtual Meeting platform.

TUESDAY, MARCH 16

Author Attended: 11:15 AM to 1:00 PM (US EDT, UTC -4)  
- Carcinogenicity
- Epidemiology and Public Health
- Mixtures

Author Attended: 1:00 PM to 2:45 PM (US EDT, UTC -4)  
- Food Safety/Nutrition
- Metals

WEDNESDAY, MARCH 17

Author Attended: 11:15 AM to 1:00 PM (US EDT, UTC -4)  
- Biotransformation/Cytochrome P450
- Kidney
- Liver: In Vitro
- Liver: In Vivo

Author Attended: 1:00 PM to 2:45 PM (US EDT, UTC -4)  
- Nanotoxicology: In Vitro
- Nanotoxicology: In Vivo
- Nanotoxicology: Methodologies and Assessments
- Systems Biology

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<td><strong>THURSDAY, MARCH 18</strong></td>
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<tr>
<td>Author Attended: 11:15 AM to 1:00 PM (US EDT, UTC -4)</td>
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<tr>
<td>• Cardiovascular Toxicology/Hemodynamics</td>
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<td>• Chemical Threats and Bioterrorism</td>
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<td>• Ocular Toxicology</td>
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| **MONDAY, MARCH 22** |
| Author Attended: 11:15 AM to 1:00 PM (US EDT, UTC -4) | Author Attended: 1:00 PM to 2:45 PM (US EDT, UTC -4) |
| • Biological Modeling | • Bioinformatics |
| • Endocrine Toxicology | • Computational Toxicology I |
| • Immunotoxicity | • Risk Assessment |
| • Neurotoxicity: Developmental | • Tobacco and ENDS Toxicology |
| • Neurotoxicity: General | |
| • Reproductive and Developmental Toxicology | |

| **TUESDAY, MARCH 23** |
| Author Attended: 11:15 AM to 1:00 PM (US EDT, UTC -4) | Author Attended: 1:00 PM to 2:45 PM (US EDT, UTC -4) |
| • Exposure Assessment/Biomonitoring | • Alternatives to Mammalian Models I |
| • Neurodegenerative Disease | • Cell Death Mechanisms |
| • PFAS | • Computational Toxicology II |
| • POPs | • DNA Damage and Repair |
| • Reproductive and Developmental Toxicology II | • Respiratory Toxicology |
| • Safety Evaluation of Nonpharmaceutical Products | • Skin and Dermal Toxicity |

| **WEDNESDAY, MARCH 24** |
| Author Attended: 11:15 AM to 1:00 PM (US EDT, UTC -4) | Author Attended: 1:00 PM to 2:45 PM (US EDT, UTC -4) |
| • Alternatives to Mammalian Models II | • Disposition/Pharmacokinetics |
| • Biomarkers | • Education, Ethical, Legal, and Social Issues |
| • Clinical and Translational Toxicology | • Neurotoxicity: Metals |
| • Medical Devices | • Neurotoxicity: Pesticides |
| • Stem Cell Biology and Toxicology | • Pesticides |
| | • Safety Assessment: Pharmaceutical—Drug Discovery |

| **THURSDAY, MARCH 25** |
| Author Attended: 11:15 AM to 1:00 PM (US EDT, UTC -4) | Author Attended: 1:00 PM to 2:45 PM (US EDT, UTC -4) |
| • Animal Models | • Emerging Technologies |
| • Autoimmunity/Hypersensitivity | • Safety Assessment: Pharmaceutical—Drug Development |
| • Inflammation | |
| • Natural Products | |
| • Oxidative Injury and Redox Biology | |
| • Receptors | |
Virtual Exhibits

As an essential part of every SOT Annual Meeting, ToxExpo is going virtual in 2021. Exhibitors will present their products, services, and latest news through videos, links, photos, and more. In addition, exhibitors will be available for live chats, and attendees can submit a request to connect by using an inquiry feature. Essentially, attendees will be able to connect and interact with the Society’s valued and vetted exhibitor community.

The Exhibitors

Exhibiting organizations are experts in a variety of toxicology services and products, including:

» Contract research
» Preclinical research and testing
» Pharmaceutical product safety and toxicology
» Safety assessment
» In vitro research and testing

Discover the organizations exhibiting at ToxExpo in 2021 by visiting the ToxExpo website.

Exhibitor-Hosted Sessions

The Exhibitor-Hosted Sessions are commercially supported educational sessions hosted by ToxExpo exhibitors and Annual Meeting Supporters. These sessions are open to all Virtual Meeting attendees and will occur concurrently with other sessions and activities. Consult the 2021 SOT Online Planner to see the most up-to-date list of Exhibitor-Hosted Sessions.

View the up-to-date exhibitor list at www.toxexpo.com
Annual Meeting Support Opportunities

Annual Meeting Supporters make meeting attendance affordable for everyone, enabling the Society to facilitate the attendance of more scientists at a variety of career levels.

Annual Meeting Supporters will be recognized on the 2021 Virtual Meeting platform and as part of SOT Annual Meeting communications, depending on the support level, including digital publications, newsletters/emails, social media acknowledgments, and more.

If you are interested in supporting the SOT Annual Meeting, contact Laura Helm by email or by phone at 703.438.3115.

Become a Supporter

There are five categories of support available:

» Diamond ($10,000+)
» Platinum ($5,000–$9,999)
» Gold ($2,500–$4,999)
» Silver ($2,000–$2,499)
» Contributor ($1,000–$1,999)

www.toxicology.org/support

Thank You, Diamond Supporters

Thank you to the organizations that have expressed their Diamond-level support* of the Virtual 2021 SOT Annual Meeting and ToxExpo.

* As of December 11, 2020

Thank you to all the SOT 60th Annual Meeting and ToxExpo Supporters. View the current Supporter list at www.toxicology.org/support.