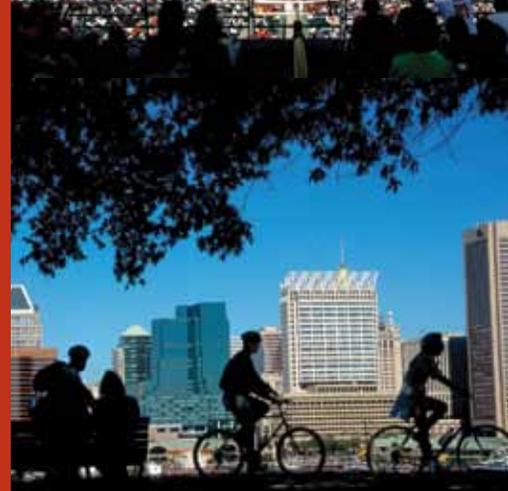
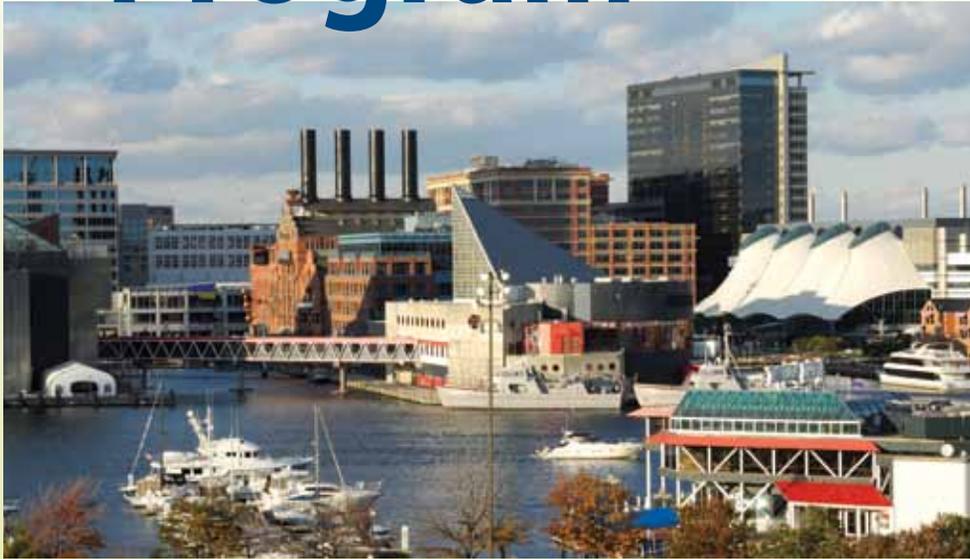


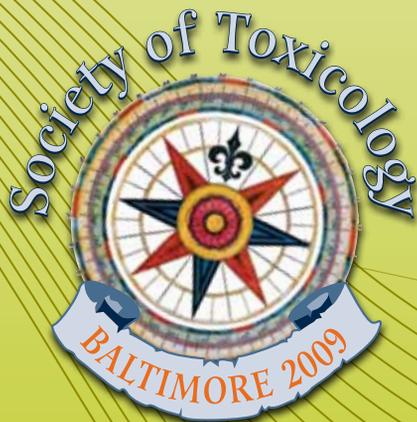


SOT | Society of Toxicology

Preliminary Program



48th Annual Meeting and ToxExpo™ Baltimore MARYLAND March 15-19, 2009

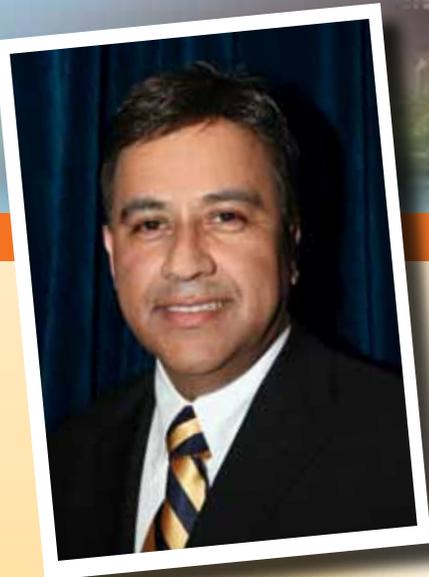


www.toxicology.org

Society of Toxicology

Baltimore, Maryland

2009



Dear Colleagues,

I cordially invite you to attend the 48th Annual Meeting of the Society of Toxicology, (SOT) which will be held March 15–19 at the Baltimore Convention Center in Baltimore, Maryland.

SOT's Annual Meeting is the forum to showcase toxicology's novel discoveries. For the science of toxicology, this 5-day event is the culmination of a year's worth of achievements in research and education.

The Annual Meeting also affords every member the opportunity to come together to learn about the latest scientific achievements from a myriad of experts in the field of toxicology. The thematic program that SOT instituted two years ago affords participants a unique opportunity to deepen their knowledge in topical areas and interact with leaders in the respective areas. Opportunities abound for members to meet other scientists they have never met and to network with friends and colleagues. The Annual Meeting also affords the chance to pause and pay tribute to those scientists who have distinguished themselves in their field of expertise and are the recipients of the Society's most prestigious awards. Finally, SOT members can take advantage of the ToxExpo™, which is the world's largest exposition of its kind. This exposition offers a comprehensive market place for product information and cutting-edge technology in one place.

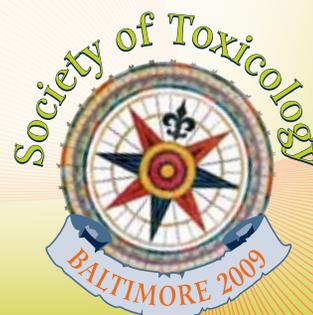
SOT's Annual Meeting is the premier event that the Society hosts every year to meet the needs of the entire toxicology community. More importantly, the Annual Meeting goes a long way toward fulfilling SOT's strategy of building the future of toxicology, highlighting the significant scientific achievements of members, and broadening the awareness of these accomplishments and their potential impact. One news publication that covered our Annual Meeting last year referred to SOT as the "world's foremost professional and scientific organization." Indeed, SOT's Annual Meeting brings together the foremost professionals in the field.

I urge you to join us for this event. Help us to make the 48th Annual Meeting an event to remember.

Sincerely,

Kenneth S. Ramos, B.S.Ph., Ph.D., ATS
2008–2009 SOT President

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48th Annual Meeting & ToxExpo™



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SOT | Society of Toxicology

Dear Colleagues,

On behalf of the Scientific Program Committee and the Society of Toxicology, I would like to invite you to join us at our 48th Annual Meeting to be held March 15–19, 2009, at the Baltimore Convention Center in Baltimore, Maryland.

The Scientific Program Committee has assembled an exciting program that provides an unparalleled venue for discussion of the latest scientific advances in the toxicological sciences. Your participation will allow you to be an active voice on important deliberations of the latest discoveries in toxicological sciences, the newest technologies to advance the pace of biomedical research and approaches to risk management decisions affecting our world today. The Annual Meeting will also facilitate meeting with your colleagues in a setting that readily lends itself to discussion of the science and practice of toxicology.

The program has been structured with significant input from our Specialty Sections and Special Interest Groups into 27 Symposia, 19 Workshops, 14 Roundtables, and 6 Keynote and named lectures to list a few. Recent developments will be featured at the meeting and complemented by thematic developments in five selected areas that include **Biomarkers, Epigenetics, Inflammation and Disease, Nanotechnology, and Neurodegenerative Disease**. Special platform and poster sessions will be organized around these and other topics to take advantage of outstanding abstract submissions from the general membership, as well as special invitations extended to prominent scientists in their respective fields.

In addition to the opportunity to be a part of cutting-edge scientific developments, you will be able to renew professional relationships, network with old and new colleagues, actively pursue job opportunities and interview on-site with potential employers, or simply catch up on recent events in the public, private and government sectors.

Our host city, Baltimore, known as “Charm City” for its hospitality, offers a world of unique attractions, entertainment, fine dining, and one-of-a-kind experiences. The crown jewel and an iconic landmark of Baltimore is the popular and scenic Inner Harbor, where you’ll find the world-famous National Aquarium. Surrounding the Inner Harbor, discover Baltimore’s rich history in the many charming and historic neighborhoods. Whether you are strolling past unique shops on the old cobblestone streets of Fell’s Point or experiencing the culture of Baltimore’s Mount Vernon Place, each neighborhood has something unique to offer. Baltimore is also home to many national historic landmarks, such as Fort McHenry and the Star-Spangled Banner Flag House. The city was also influential in the shipbuilding and transportation industries and is home to the first public railroad in the United States.

The success of the Annual Meeting depends on your active participation and contributions. Please register now on-line at www.toxicology.org or by completing and returning the Registration Form along with payment to:

SOT Registration
P.O. Box 91895
Washington, DC 20090-1895, U.S.A.

Come be part of the action! We look forward to seeing you in Baltimore.

Warmest Regards,

Cheryl Lyn Walker, Ph.D.
SOT Vice President and
Scientific Program Committee Chairperson

1821 MICHAEL FARADAY DRIVE, SUITE 300, RESTON, VIRGINIA 20190
Telephone: (703) 438-3115 Fax: (703) 438-3113 E-mail: sothq@toxicology.org
Web site: www.toxicology.org

Scientific Program Overview

Sunday, March 15

7:00 AM–7:45 AM

SUNRISE CONTINUING EDUCATION COURSE

1. Topics in Ethics: Conflict of Interest—Real or Imagined?—PBDEs As a Case Study

8:15 AM–12:00 NOON

MORNING CONTINUING EDUCATION COURSES

2. Free Radicals for Toxicologists—From the Basics to Inflammation and Disease
3. Characterizing Modes-of-Action and Their Relevance in Assessing Human Health Risks
4. Evaluation of Toxicity to Male and Female Reproductive Systems: Biology, Study Design, and Data Interpretation
5. Immunology for Toxicologists
6. Principles and Applications of Toxicokinetics
7. Translation of Safety Biomarkers in Drug Discovery and Development

1:15 PM–5:00 PM

AFTERNOON CONTINUING EDUCATION COURSES

8. Free Radicals for Toxicologists—From the Basics to Inflammation and Disease
9. Characterizing Variability and Uncertainty with Physiologically Based Pharmacokinetic Models
10. Current Approaches in Mixture Risk Assessment
11. How Similar Is Similar and How Relevant Is Relevant? Considerations in the Design of a Predictive Development Program for Biotherapeutics
12. New Frontier in Metal Toxicology: Genetic Susceptibility, Early Diagnosis, and Related Biological Indices
13. Stress As a Confounding Factor in Toxicology Studies

Monday, March 16

8:00 AM–9:00 AM

PLENARY OPENING LECTURE

Signal Transduction Pathway Used by Therapeutic Agents and Drugs of Abuse
Lecturer: Nobel Laureate Paul Greengard

9:15 AM–12:00 NOON

SYMPOSIA SESSIONS

- Eat Well, Breathe Well: Nutritional Determinants of Susceptibility to Airborne Pollutants
- MicroRNAs in Biology and Toxicology
- Superantigens, Cytokine Storm, and Toxic Reactions
- Zinc, Inflammation, and Diabetes

WORKSHOPS SESSIONS

- Dose Selection and Design Considerations in Safety Studies for Biotherapeutics
- From Genes to Organs: Advancements in Modeling Biological Systems
- Strategies to Integrate Systems Biology into *In Vitro* Screening in Early Nonclinical Safety Assessment

PLATFORM SESSIONS

- Applications in 'Omics Technologies to Problems in Toxicology
- Immunoregulation and Toxicity
- Mechanistic Insights for Reproductive Toxicology

9:30 AM–12:30 PM

POSTER SESSIONS

- Ah Receptor Mediated Signaling
- Apoptosis: Activators and Regulatory Pathways
- Cardiovascular Toxicity I
- Dermal Absorption and Skin Toxicity
- Information and Education
- Insights in Endocrine Action and Toxicology
- Nanotoxicology *In Vivo*
- Neurotoxicity—Developmental
- Receptors
- Redox-Cycling, Reactive Oxygen Species (ROS), and Damage
- Xenobiotic Biotransformation

12:10 PM–1:30 PM

ROUNDTABLE SESSIONS

- Devils Lie in the Details: Practices and Problems in Neuropathology—Significance for Neurotoxicology
- The Use of Engineered Nanomaterials in Food and Food-Related Products: Is This a Concern for Human and Environmental Safety?

HISTORICAL HIGHLIGHTS SESSION

- A Quarter of a Century (1984–2009) Since the Bhopal Disaster: Lessons Learned

INFORMATIONAL SESSION

- Peer Review of Toxicology, Exposure, and Risk Data: Ensuring the Best Science

12:30 PM–1:20 PM

LEADING EDGE IN BASIC SCIENCE AWARD LECTURE

The Structural Pervasiveness of Estrogen Activity—Benefits and Risks from the Eclectic Nature of Ligand Binding by the Estrogen Receptor
Lecturer: John Katzenellenbogen

1:00 PM–4:30 PM

POSTER SESSIONS

- Alternate Tests and Models I
- Assessment of Chemical Mixtures
- Biological Modeling
- Chemical and Biological Weapons
- Ecotoxicology
- *In Vitro* Methods, Models, and Mechanisms of Hepatotoxicity
- Neurotoxicity—Metals
- Safety Assessment for Non-Pharmaceuticals
- Toxicology of Kidney

1:40 PM–4:25 PM

SYMPOSIA SESSIONS

- Aromatase (CYP19) Gene Expression and Function: Current State of Knowledge As a Mode-of-Action for Toxicological Effects
- Genomic, Non-Genomic, and Epigenetic Mechanisms of Nuclear Hormone Receptor Action
- *In Vitro* Models of Human Toxicity Pathways
- Nitrate and Oxidative Stress in Toxicology and Disease
- Novel Signaling Mechanisms That Regulate Dopaminergic Neuronal Survival or Death: Implications in Parkinson's Disease
- Regulation of Drug Transporters in Different Disease States and Its Toxicological and Clinical Implications

WORKSHOP SESSIONS

- Agglomeration *Versus* Dispersion: How Nanoparticle Behavior Affects Exposure and Toxicity *In Vitro*, *In Vivo*, and in the Real World

PLATFORM SESSIONS

- Cellular Responses to Chemical Weapons
- Developmental Basis of Adult Disease
- Epigenetic Mechanisms of Xenobiotics
- Mechanisms of Hypersensitivity
- Mechanisms of PAH and Tobacco Carcinogenesis

4:30 PM–5:50 PM

SOT/EUROTOX DEBATE

Nanotoxicology—Much Ado About Nothing?

4:35 PM–5:55 PM

ROUNDTABLE SESSIONS

- Leveraging Non-Clinical Disease Models for Early Perspective on Safety and Risk during Drug Discovery
- Role of Regulatory Cooperative Efforts in Food Protection
- Weight of Evidence Advancements in Risk Assessment: Conceptual Frameworks and Case Studies Illustrating Fundamentals of Application

EDUCATION-CAREER DEVELOPMENT SESSION

- Grantsmanship Forum: Tools and Skills Needed to Navigate Toxicology Research Funding

Tuesday, March 17

7:30 AM–8:50 AM

ROUNDTABLE SESSIONS

- Biomarkers of Cardiac Hypertrophy and Skeletal Muscle Toxicity—Successes and Challenges Related to Their Implementation in Drug Development
- The Regulatory Frontier: Addressing Products of Nanotechnology

HISTORICAL HIGHLIGHTS SESSION

- Dioxin, Forty Years of Science: Are We Any Closer to Assessing Potential Risk?

INFORMATIONAL SESSION

- NIH Genes, Environment, and Health Initiative: Biomarkers and Biosensors for Detecting Response to Environmental Stress

8:00 AM–8:50 AM

TRANSLATIONAL IMPACT AWARD LECTURE:

Keap1 One Eye on the Target—Translating Molecular Toxicology into Cancer Prevention:
Lecturer: Thomas W. Kensler

9:00 AM–11:45 AM

SYMPOSIA SESSIONS

- Does Metal Toxicity Play a Role in the Etiology of Alzheimer's Disease?
- Epigenetic Implications for Toxicology
- Immunomodulation during Complementary and Alternative Medicine (CAM) Therapy: Risks and Benefits
- Nanotoxicology and Drug Delivery

WORKSHOP SESSIONS

- Low-Dose Non-Linearity: What Can Emerging Technologies Tell Us?
- Maternal Toxicity and Its Impact on Study Design and Data Interpretation
- Pesticide Mixtures: Experimental Evaluation and Computational Modeling

PLATFORM SESSIONS

- Advances in Animal and Alternative Models
- Advances in Biological Modeling
- Cellular and Biological Sources for Biomarkers
- Metal-Induced Carcinogenesis
- Xenobiotic Modulation of Signal Transduction Pathways and Gene Regulation

9:00 AM–12:30 PM

POSTER SESSIONS

- Biological Actions of Natural Products
- Cardiovascular Toxicity II
- Nanotoxicology *In Vitro*
- Reactive Oxygen Species (ROS) Stimulated Signaling
- Research in Disposition and Pharmacokinetics
- Risk Assessment Applications
- Role of PPAR and COX-2 in Chemical Carcinogenesis
- Safety Issues Concerning Food Products and Micronutrients

12:00 NOON–1:20 PM

ROUNDTABLE SESSIONS

- Is There a Future for Animal Models in the Investigation of Idiosyncratic DILI in Humans?
- National Children's Study: Opportunities and Challenges for Toxicologists
- Setting a Safe Starting Dose in Initial Clinical Trials with Biotherapeutics: Do I Use the NOAEL or the MABEL?

EDUCATION-CAREER DEVELOPMENT SESSION

- The Future of Environmental Health Science: Featuring NIEHS-Funded Early Career Investigators

12:30 PM–1:20 PM

DISTINGUISHED TOXICOLOGY SCHOLAR AWARD LECTURE

Role of Reactive Metabolites, Protein Adducts, Immune System, and Other Susceptibility Factors in Drug-Induced Liver Injury
Lecturer: Lance Pohl

1:00 PM–4:30 PM

POSTER SESSIONS

- Bioinformatics and Prediction of Toxicity
- Epidemiology and Exposure Assessment
- Functional Genomics in Toxicology
- Gene Regulation
- Genotoxicity I
- Hepatotoxicity of NSAIDs and Acetaminophen
- Hepatotoxicity: *In Vivo* Studies
- Pesticide—Toxicity

1:30 PM–4:15 PM

SYMPOSIA SESSIONS

- Aquatic Species As Sentinels for Human Health: Comparative Toxicology of Metals, Nanoparticles, and PCB's
- Mammalian Retrotranspositional Elements: Epigenetic Regulation, Species Differences, and Potential Roles As Mediators of Cellular Responses to Toxic Stress
- The Good, the Bad, and the Ugly of Toxicant-Induced Pulmonary Inflammation

WORKSHOP SESSIONS

- Improved Safety Biomarkers for Monitoring Kidney Injury
- Oxidative Stress As a Regulator of Normal Function and Mediator of Toxicant-Induced Damage with Impacts on Reproduction and Development
- Pesticides and Parkinson's Disease: Implications of New Epidemiology and Exposure Data to Risk Assessment
- Safety of High-Intensity Sweeteners: Bittersweet Controversy

PLATFORM SESSIONS

- Advances in Disposition and Pharmacokinetics
- Advances in Risk Assessment Science
- Effects of Inhaled Pollutants—Cardiopulmonary Toxicity
- Mechanisms in Immunotoxicology
- New Insights in Ecotoxicology

Wednesday, March 18

7:30 AM–8:50 AM

ROUNDTABLE SESSION

- Characterization and Application of PBPK Models in Risk Assessment

INFORMATIONAL SESSION

- Novel Translational Safety Biomarkers and Safety First at the FDA

EDUCATION-CAREER DEVELOPMENT SESSION

- Toxicologists: The Next Generation

SPECIAL SESSION

U.S. FDA Advisory Panel Appointments

8:00 AM–8:50 AM

KEYNOTE MEDICAL RESEARCH COUNCIL (MRC) LECTURE

The Ubiquitin Proteolytic System—From Basic Mechanisms through Human Disease and on to Drug Targeting
Lecturer: Nobel Laureate Aaron Ciechanover

9:00 AM–11:45 AM

SYMPOSIA SESSIONS

- From Mechanisms to Biomarkers: Basic and Applied Metabolomics in Toxicology
- Incorporating ‘Omics in the Study of Reproduction and Development
- Interactomes and Their Application in Toxicology
- Transcriptional Changes in Immunotoxicology: Transcription Factors, Signal Transduction, and Epigenetics

WORKSHOP SESSIONS

- Developing Brain: Safety Assessment for Pediatric Use of Pharmaceuticals
- Toxicology of Unintentional and Intentional Disasters

REGIONAL INTEREST SESSION

- Biofuels and the Bay: Characterizing Health and Ecosystem Impacts in the Chesapeake

PLATFORM SESSIONS

- Cardiopulmonary Toxicity of Inhaled Particles and Nanoparticles
- Endocrine-Toxicant Interactions
- Hot Topics in Metal-Induced Neurodegeneration
- Mechanisms of Persistent Organic Compound Toxicity
- Mechanisms of Pesticide-Induced Toxicity

9:00 AM–12:30 PM

POSTER SESSIONS

- Advances in Reproductive Toxicology
- Animal Models II
- Biomarker Discovery and Detection
- Biomonitoring and Exposure Assessment
- Cytoprotective Strategies Against Reactive Oxygen Species
- Genetic Polymorphisms
- Hypersensitivity and Autoimmunity
- Risk Assessment Research
- Metals—*In Vivo*
- Parkinson’s Disease

12:00 NOON–1:20 PM

SYMPOSIA SESSION

- Gene-Environment Interactions: Epigenetic Pathways in Chronic Disease Promotion and Progression

ROUNDTABLE SESSION

- Preclinical Evaluation of Cancer Hazard and Risk of Biopharmaceuticals

INFORMATIONAL SESSION

- Kinase Inhibitors As Targeted Therapeutics in Inflammation and Oncology—Approaches to Predict and Manage Clinical Toxicities

12:00 NOON–1:20 PM

SPECIAL SESSION

Meet the Director of NIEHS

12:30 PM–1:20 PM

MERIT AWARD LECTURE

Chemical Hepatocarcinogenesis—Mechanisms, Pathogenesis, and Thresholds
Lecturer: Gary M. Williams

1:00 PM–4:30 PM

POSTER SESSIONS

- Alternate Tests and Models II
- Chemical Carcinogenesis
- Developmental Basis of Disease
- Developmental Toxicology
- Genotoxicity II
- Inflammation
- Immunotoxicology
- Mechanisms of Chemoprevention in Chemical Carcinogenesis
- Metals—*In Vitro*
- Steatosis and Cholestasis in Hepatic Dysfunction
- Stem Cell Biology and Toxicology

1:30 PM–4:15 PM

SYMPOSIA SESSIONS

- Biomarkers: New Breakthroughs in the World of Air Pollution Studies
- New Insights into Skin Homeostasis and Carcinogenesis
- Pulmonary Effects of *In Utero* and Early Postnatal Exposure to Arsenic
- The Role of Inflammation during Metabolic Liver Disease and Drug-Induced Liver Toxicity: Novel Insights

WORKSHOP SESSIONS

- Food Allergy—Basic Mechanisms and Applications to Identifying Risks Associated with Plant Incorporated Pesticides and Other Genetically Modified Crops
- The Impact of Transcript Profiling in Drug Safety Assessment
- The Road to Personalized Medicine

PLATFORM SESSIONS

- Bioinformatics and Computational Toxicology
- Expression and Modulation of Cytochrome P450
- Mechanisms in Nanomaterial Toxicology
- Signal Transduction and Metal-Induced Toxicity

1:30 PM–2:30 PM

SPECIAL SESSION

Update from the NIH Center for Scientific Review
Speaker: Antonio Scarpa, NIEHS

4:30 PM–5:50 PM

ROUNDTABLE SESSION

- What Is an Adverse Effect in the Age of ‘Omics?

EDUCATION-CAREER DEVELOPMENT SESSION

- Career Opportunities and Transitions in Toxicology

Thursday, March 19

7:30 AM–8:50 AM

ROUNDTABLE SESSION

- Phototoxicology: A Passing Fancy or Enduring Concern?

INFORMATIONAL SESSION

- Lead: Children’s Exposures and Current Regulatory Standards

ISSUES SESSION

National Research Council (NRC) Vision

8:30 AM–12:00 NOON

POSTER SESSIONS

- Cardiopulmonary Toxicity
- Chemical-Induced Neurotoxicity
- Epigenetics
- Neurotoxicity—Pesticides
- New Applications in Animal Models
- Non-Clinical Safety Testing: Biological and Small Molecule Therapeutics
- Persistent Organic Compounds
- Regulations and Policy Implications in Toxicology
- Signal Transduction: Kinases
- Toxicology of Carbon Nanotubes

9:00 AM–11:45 AM

SYMPOSIA SESSION

- Heat Shock Proteins and the Toxicological Response

WORKSHOP SESSIONS

- Biomarkers for Assessing the Systemic Inflammatory Response Syndrome in Toxicology Studies
- Is Modulation of the Immune System by Perfluoroalkyl Acids a Human Health Concern?
- The Molecular Mechanism of Alpha, Beta-Unsaturated Carbonyl Toxicity: Getting in Touch with the Soft Side of Chemistry

Preliminary Program Content Reference

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

Preliminary Program Overview

Section	Description
Scientific Program Overview (pages ii and iv)	This reference guide lists the Annual Meeting sessions, including special lectures, Platform and Poster Presentations, Symposium, Workshops, Roundtables, and their scheduled dates and times. Please note that detailed information related to many of these sessions will not be available until the final <i>Program</i> is completed.
Thematic Session Index (pages vi–vii)	Each of the Annual Meeting sessions highlighted within the 5 themes are listed. The list of sessions is preceded by a brief description of each theme. Throughout the <i>Preliminary Program</i> , each scientific session tracked within a theme is identifiable by a ‘recurring’  symbol. This year, the Society will highlight 43 thematic sessions.
2009 SOT Award Winners (pages 24–25)	These pages list each of your fellow members who have been awarded a prestigious SOT award in recognition of their esteemed accomplishments in the field of toxicology. Several of these awards have special affiliated lectures. Those details can be found on page 35–38 in the Featured Sessions section.
Continuing Education Courses (page 27–34)	These pages list the 2009 CE course descriptions and presenter information. These courses have separate registration fees. Each participant in a CE course will receive a copy of the course syllabus. Course syllabi are available for sale on-site at the meeting while supplies last.
Featured Sessions (pages 35–38)	This section lists the Keynote and other special lectures and sessions for the 2009 Annual Meeting. Detailed information for these sessions will be available in the final <i>Program</i> .
Scientific Sessions (pages 39–87)	The <i>Preliminary Program</i> layout is similar to that of the final <i>Program</i> . Specifically, this section lists the scientific sessions in date, time, and alphabetical order beginning with Symposia, Workshop, Roundtable, Historical Highlight, Informational, and finally the Education/Career Development sessions.
Special Events (pages 88–94)	This section lists the student events including the Student Mixer, <i>In Vitro</i> Lecture, and committee meetings, etc. This section also highlights several scientific and career development sessions of interest to the SOT Student and Postdoctoral membership. A special highlight in this section includes the Educational Outreach initiatives undertaken each year at SOT including the Undergraduate Education Program and the <i>Paracelsus</i> Program.
Exhibits (pages 104–118)	ToxExpo™ is the profession’s largest trade show and best resource for the latest information in technology, equipment, and services. This section contains the current list of exhibiting companies and Exhibitor Hosted Sessions.

Scientific Session Types

Education-Career Development Sessions (80 minutes)—

Sessions that provide the tools and resources to toxicologists that will enhance their professional and scientific development (page 84)

Exhibitor Hosted Sessions (60 minutes)—Informative sessions developed by an exhibiting company (page 106)

Featured Sessions (50–60 minutes)—Keynote and other special lectures (page 35)

Historical Highlights (80 minutes)—Review of a historical body of science that has impacted toxicology (page 78)

Informational Sessions (80 minutes)—Scientific planning or membership development (page 80)

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

Poster Sessions (180–210 minutes)—Topic specific presentations that cover new areas, concepts, or data (see details in the final *Program*)

Regional Interest Session (165 minutes)—Central topics of relevance that describe public health and/or ecological problems of that region (page 87)

Roundtable (80 minutes)—Controversial subjects (page 69)

Symposia Sessions (80 or 165 minutes)—Cutting-edge science; new areas, concepts, or data (page 39)

Thematic Sessions (80–210 minutes)—Timely topics of relevance to toxicology (check the specific session type)

Workshop Sessions (165 minutes)—State-of-the-art knowledge in toxicology (page 56)

2009 Sessions: Thematic Approach

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

The 2009 scientific themes listed here illustrate the core contributions toxicology makes to these areas.

Biomarkers

Biomarkers are generating excitement as a means of dissecting and understanding normal biological processes, measuring environmental exposures, predicting disease outcomes, and assessing beneficial or adverse responses to pharmacologic and therapeutic agents. As such, biomarkers have been invaluable to toxicologists as tools for investigating and predicting toxic responses. In addition, a large body of research from the toxicological sciences has contributed to the identification and validation of biomarkers at the molecular, biochemical, and cellular level. Sessions highlighting the many contributions of toxicology to biomarker research will be featured along with sessions highlighting new discoveries related to the identification, validation, and utilization of biomarkers to interrogate health and disease.

- Translation of Safety Biomarkers in Drug Discovery and Development—*Continuing Education Course (AM07)*
- Biomarkers: New Breakthroughs in the World of Air Pollution Studies—*Symposia Session*
- From Mechanisms to Biomarkers: Basic and Applied Metabolomics in Toxicology—*Symposia Session*
- Improved Safety Biomarkers for Monitoring Kidney Injury—*Workshop Session*
- Biomarkers of Cardiac Hypertrophy and Skeletal Muscle Toxicity—Successes and Challenges Related to Their Implementation in Drug Development—*Roundtable Session*
- NIH Genes, Environment, and Health Initiative: Biomarkers and Biosensors for Detecting Response to Environmental Stress—*Informational Session*
- Novel Translational Safety Biomarkers and Safety First at the FDA—*Informational Session*
- Cellular and Biological Sources for Biomarkers—*Platform Session*
- Biomarker Discovery and Detection—*Poster Session*
- Biomonitoring and Exposure Assessment—*Poster Session*

Epigenetics

Heritable DNA and chromatin modifications determine gene expression patterns and underlie important biological processes including development, X chromosome inactivation, imprinting, and gene silencing and transcription. Alterations induced in key epigenetic determinants including DNA methylation and histone modifications contribute to the adverse health effect of many toxicants, including endocrine disruptors, carcinogens and teratogens. The “epigenome” is now receiving interest comparable to that formerly focused on elucidating the genome of humans and other organisms. Because of the importance of epigenetics in health and disease and the many new and emerging technologies coming into use for studying epigenetics, this theme has been selected to highlight recent advances in epigenetic research for the toxicological sciences.

- Epigenetic Implications for Toxicology—*Symposia Session*
- Gene-Environment Interactions: Epigenetic Pathways in Chronic Disease Promotion and Progression—*Symposia Session*
- Genomic, Non-Genomic, and Epigenetic Mechanisms of Nuclear Hormone Receptor Action—*Symposia Session*
- Mammalian Retrotranspositional Elements: Epigenetic Regulation, Species Differences, and Potential Roles as Mediators of Cellular Responses to Toxic Stress—*Symposia Session*
- Transcriptional Changes in Immunotoxicology: Transcription Factors, Signal Transduction, and Epigenetics—*Symposia Session*
- Epigenetic Mechanisms of Xenobiotics—*Platform Session*
- Epigenetics—*Poster Session*

Inflammation and Disease

While the inflammatory response plays an important role in the body's response to injury and infection, it also contributes to several acute and chronic diseases including nephritis, inflammatory bowel disease, autoimmune disease, arthritis, asthma, diabetes, Alzheimer's disease, and cancer. Inflammatory mediators such as reactive oxygen species (ROS), cytokines, and eicosanoids play key roles in these processes. Similarly, the acute-phase proteins such as glucocorticoids, C-reactive protein, and serum amyloids, have beneficial effects but can contribute to diseases such as heart disease and amyloidosis. These inflammatory responses also play a significant role in the adverse response of many organs following exposure to drugs and environmental agents. The important role of inflammation and inflammatory mediators as determinants of toxic responses and disease will be highlighted in sessions featured in this theme.

- Free Radicals for Toxicologists—From the Basics to Inflammation and Disease—*Continuing Education Course (AM02/PM08)*
- Nitrate and Oxidative Stress in Toxicology and Disease—*Symposia Session*
- The Good, the Bad, and the Ugly of Toxicant-Induced Pulmonary Inflammation—*Symposia Session*
- The Role of Inflammation during Metabolic Liver Disease and Drug-Induced Liver Toxicity: Novel Insights—*Symposia Session*
- Zinc, Inflammation, and Diabetes—*Symposia Session*
- Biomarkers for Assessing the Systemic Inflammatory Response Syndrome in Toxicology Studies—*Workshop Session*
- Is There a Future for Animal Models in the Investigation of Idiosyncratic DILI in Humans?—*Roundtable Session*
- Immunoregulation and Toxicity—*Platform Session*
- Inflammation—*Poster Session*

Nanotechnology

Nanomaterials are the building blocks for this promising new technology. These materials are currently being utilized in many diverse areas such as engineering, information technology, and diagnostics. Nanomaterials are now routinely produced and commercialized. Because little is known about their biology or the potential health impacts of these new products, these highlighted sessions will explore the potential implication(s) of their use.

- Aquatic Species as Sentinels for Human Health: Comparative Toxicology of Metals, Nanoparticles, and PCB's—*Symposia Session*
- Nanotoxicology and Drug Delivery—*Symposia Session*
- Agglomeration Versus Dispersion: How Nanoparticle Behavior Affects Exposure and Toxicity *In Vitro*, *In Vivo*, and in the Real World—*Workshop Session*
- The Regulatory Frontier: Addressing Products of Nanotechnology—*Roundtable Session*
- The Use of Engineered Nanomaterials in Food and Food-Related Products: Is This a Concern for Human and Environmental Safety?—*Roundtable Session*
- Cardiopulmonary Toxicity of Inhaled Particles and Nanoparticles—*Platform Session*
- Mechanisms of Nanomaterial Toxicology—*Platform Session*
- Nanotoxicology *In Vitro*—*Poster Session*
- Nanotoxicology *In Vivo*—*Poster Session*
- Toxicology of Carbon Nanotubes—*Poster Session*

Neurodegenerative Disease

Neurodegenerative diseases such as Huntington's, Parkinson's, and Alzheimer's are caused by loss of cells and/or cellular function in the brain. Dementias and movement disorders are becoming increasingly more common. These diseases often have a complex etiology and have been associated with genetic alterations, specific pathogens, alterations of normal physiological responses such as protein misfolding, and exposures to several environmental agents. The role of environmental agents, gene-environment interactions, early life exposures, and inflammatory mediators in the development of neurodegenerative disease, as well as elucidation of sequelae from acute toxic exposures to the onset of disease, will be highlighted in this theme as important areas of research for the toxicological sciences.

- Does Metal Toxicity Play a Role in the Etiology of Alzheimer's Disease?—*Symposia Session*
- Novel Signaling Mechanisms That Regulate Dopaminergic Neuronal Survival or Death: Implications in Parkinson's Disease—*Symposia Session*
- Pesticides and Parkinson's Disease: Implications of New Epidemiology and Exposure Data to Risk Assessment—*Workshop Session*
- Devils Lie in the Details: Practices and Problems in Neuropathology—Significance for Neurotoxicology—*Roundtable Session*
- Hot Topics in Metal-Induced Neurodegeneration—*Platform Session*
- Neurotoxicity—Developmental—*Poster Session*
- Parkinson's Disease—*Poster Session*

SOT Affiliates

**Abbott Laboratories**

Abbott Park, Illinois

Aegis Technologies Group, The

Orlando, Florida

Agilent Technologies, Inc.

Wilmington, Delaware

Alcon Research, Ltd.

Fort Worth, Texas

American Chemistry Council

Arlington, Virginia

American Petroleum Institute

Washington, D.C.

Ani Lytics, Inc.

Gaithersburg, Maryland

AstraZeneca R&D

Södertälje, Sweden

BASi Evansville

Mount Vernon, Indiana

Battelle

Columbus, Ohio

Bayer

Stilwell, Kansas

Bayer HealthCare Pharmaceuticals

Montville, New Jersey

Biogen Idec, Inc.

Cambridge, Massachusetts

**Boehringer Ingelheim
Pharmaceuticals, Inc.**

Ridgefield, Connecticut

Bristol-Myers Squibb Company

Princeton, New Jersey

CANTOX

Mississauga, Ontario, Canada

Celsis In Vitro Technologies

Baltimore, Maryland

Charles River

Wilmington, Massachusetts

Chevron Corporation

Richmond, California

Chlorine Chemistry Division

Arlington, Virginia

Colgate-Palmolive Company

Piscataway, New Jersey

Covance Laboratories Inc.

Madison, Wisconsin

Daiichi Sankyo Company Limited

Shizuoka, Japan

Dial Corporation,

A Henkel Company, The
Scottsdale, Arizona

Dow Chemical Company, The

Midland, Michigan

Dow Corning Corporation

Midland, Michigan

**DuPont Haskell Global Centers for
Health and Environmental Sciences, The**

Newark, Delaware

**ExxonMobil Biomedical
Sciences, Inc.**

Annandale, New Jersey

Genentech, Inc.

San Francisco, California

GlaxoSmithKline

King of Prussia, Pennsylvania

**Hamner Institutes
for Health Sciences, The**

Research Triangle Park, North Carolina

Harlan Laboratories, Inc.

Indianapolis, Indiana

Hoffmann-La Roche Inc.

Nutley, New Jersey

Honeywell International, Inc.

Morristown, New Jersey

**J&J Pharma R&D Companies
(Centocor, J&JPRD, Tibotec)**

Raritan, New Jersey

Lilly Research Laboratories

Indianapolis, Indiana

Merck & Co., Inc.

West Point, Pennsylvania

Millennium Pharmaceuticals, Inc.

Cambridge, Massachusetts

MPI Research

Mattawan, Michigan

Novartis Pharmaceuticals Corporation

East Hanover, New Jersey

Pfizer Inc

Groton, Connecticut

Procter & Gamble Company

Cincinnati, Ohio

**RTC Research Toxicology
Centre S.P.A.**

Pomezia, Italy

sanofi-aventis

Bridgewater, New Jersey

**Schering-Plough
Research Institute**

Kenilworth, New Jersey

Sequani, Ltd.

Ledbury, Herefordshire, United Kingdom

Suburban Surgical Company, Inc.

Wheeling, Illinois

WIL Research Laboratories, LLC

Ashland, Ohio

Wyeth Research

Collegeville, Pennsylvania

Preliminary Program

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March 15–19, 2009

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Registration Express

Register by February 20, 2009, with full payment and you'll receive your name badge and tickets in the mail before the meeting.



SOT Annual Meeting

Why Attend the Annual Meeting?

The Society of Toxicology (SOT) Annual Meeting is the largest toxicology meeting and exhibition in the world, attracting more than 6,500 scientists from industry, academia, and government from various countries around the globe. From the keynote address and special lectures, to a wide range of symposia sessions to continuing education courses that cover the basic and the advanced topics of the day, to the workshops, thematic sessions that complement the symposia, roundtables, poster sessions, and award presentations, SOT's Annual Meeting has something for every attendee. You will want to attend because:

Cutting-Edge Science and Innovative Perspectives

The SOT Annual Meeting provides the most complete and in-depth coverage of toxicology. The SOT Scientific Program Committee is charged with creating a thought provoking and dynamic program that captures all the latest scientific advances that have occurred during the past 12 months. The Committee reviews more than 2,400 abstracts to come up with a final program that is novel, multi-dimensional and comprehensive in scope.

Depth of Analysis

The five scientific themes—Biomarkers, Epigenetics, Inflammation and Disease, Nanotechnology, and Neurodegenerative Diseases—give the toxicologist a unique opportunity to delve into scientific sessions on these topics, which are both timely and highly informative.

Untold Networking Opportunities

During the five days that attendees participate in Annual Meeting, SOT offers a wide range of networking opportunities for everyone. In a congenial and welcoming atmosphere, Annual Meeting attendees can join in deliberations about the latest scientific research, meet old friends during the

ToxExpo™—A Great Opportunity for Exhibitors

We've Got the Numbers You Want

More than 6,500 scientists and researchers attend SOT's Annual Meeting and ToxExpo™. What better opportunity to—

- meet face-to-face.
- build relationships with new prospects.
- network with other exhibiting companies.

New Faces/New Leads

Research shows that 55% of the professional toxicologists who will attend the 2009 Annual Meeting and ToxExpo™ did not attend the 2008 Meeting in Seattle.

On-Line Marketplace at ToxExpo.com

ToxExpo™ exhibitors are listed on-line year around to increase your visibility and exposure to your target audience. It's a rich resource for all the services and products toxicologists need throughout the year.

For more information on exhibiting at the largest Toxicology trade show in the world, please visit www.toxexpo.com, or contact Liz Kasabian at SOT Headquarters: (703) 438-3115 ext. 1454 or e-mail: liz@toxicology.org.

A Global Audience

Nearly 20% of SOT's Annual Meeting and ToxExpo™ attendees represent scientists from countries outside the U.S. All are engaged in one or more of the following areas of research:

- Biological Modeling
- Biomarkers
- Carcinogenesis
- Comparative and Veterinary
- Dermal Toxicology
- Drug Discovery Toxicology
- Epigenetics
- Ethical, Legal, and Social Issues
- Food Safety
- Immunotoxicology
- *In Vitro* and Alternative Methods
- Inflammation and Disease
- Inhalation and Respiratory
- Mechanisms
- Metals
- Mixtures
- Molecular Biology
- Nanotoxicology
- Neurodegenerative Disease
- Ocular Toxicology
- Occupational and Public Health
- Regulatory and Safety Evaluation
- Reproductive and Developmental
- Risk Assessment
- Toxicologic and Exploratory Pathology

Baltimore Maryland

SOT Annual Meeting

receptions and luncheons, make new friends while you visit the ToxExpo™, or attend one of the many scientific sessions throughout the week.

A Global Audience

The Annual Meeting and ToxExpo™ attract not only a broad attendance from the U.S., but also from the global community with nearly 20 percent international attendees. Scientists from as far away as Australia, China, and Egypt come to the United States to participate in this event, exchanging lessons learned and sharing scientific findings and novel approaches with other toxicologists.

Value

The SOT Annual Meeting is cost-effective, with low registration fees, minimal travel to Baltimore for many, inexpensive high-quality Continuing Education courses, and exposure to the very latest advances in science. International attendees benefit from the good exchange rate.

Why Attend ToxExpo™ ?

An Exhibition Extraordinaire

ToxExpo™ is the profession's largest trade-show of its kind anywhere. Attendees and exhibitors from around the globe gather to exchange ideas and debut cutting-edge products, services, and technologies. Toxicologists and industry professionals have the unparalleled opportunity to gain first-hand knowledge on the latest advances from more than 350 exhibitors.

The following are the exhibit hours for the 2009 ToxExpo™ in Baltimore:

Monday	9:00 AM–4:30 PM
Tuesday	8:30 AM–4:30 PM
Wednesday	8:30 AM–4:30 PM

Daily Access All Year

ToxExpo™ continues throughout the year. Visit www.toxexpo.com for all your toxicology-related science information and data as well as information about current exhibitors. The site offers access 24/7, 365 days per year to resource for toxicologists worldwide. ToxExpo™ is a rich resource for the working scientist, the decision maker, the student—anyone looking for the best products and services that toxicology has to offer.

Baltimore, Maryland

Baltimore, Maryland, is the host city for the Society of Toxicology's 48th Annual Meeting. Scientific Sessions will be held at the Baltimore Convention Center during the week of March 15–19, 2009.

A city of surprises and unique experiences makes Baltimore the charm of the Mid-Atlantic. The crown jewel of Baltimore is the Inner Harbor, a scenic and popular waterfront area with dozens of retail stores, restaurants and attractions. But there's more to Baltimore than is seen at first glance. Charming historic neighborhoods surround the Inner Harbor, each offering its own character, history, and cuisine. Little Italy is a pasta lover's paradise. Fell's Point is the oldest section of Baltimore and still has the feel of an old English neighborhood with cobblestone streets, unique shops, and plentiful pubs and restaurants. And, there's Harbor East, a bustling waterfront stop with its own attractions, retail shops, and restaurants.

Baltimore is a dynamic city that continues to evolve while holding on to its maritime heritage. Since 1600, Baltimore waterways have been a passage for ships carrying commercial cargo and new citizens. It lies farther west than any other major Atlantic port, a point that endeared its harbors to shippers. More than 30 million tons of cargo pass through the Port of Baltimore every year.

Baltimore is now a major travel destination and welcomes 12 million business and leisure visitors each year. Even better, most sites and neighborhoods are within walking distance of each other, making Baltimore an ideal place for business as well as pleasure—the perfect city to host SOT's 2009 Annual Meeting! For more information about Baltimore, go to: www.baltimore.org.

Baltimore Convention Center

All scientific sessions will be held at the Baltimore Convention Center (BCC). SOT will be utilizing all the space within the Center for the various SOT activities and scientific sessions. With 300,000 square feet of exhibit space, 50 flexible meeting rooms and a 36,000-square-foot ballroom, the BCC is the premier location for conventions, tradeshows, and exhibitions in the Mid-Atlantic Region.

Located in downtown Baltimore between the Inner Harbor and Oriole Park at Camden Yards, the BCC is within walking distance from some of the city's best shops, sights, restaurants, and hotels. It is conveniently connected by skywalk to several major hotels and shopping facilities. The BCC offers its guests a variety of on-site services, including a business service center and eateries. Guests should also visit the two information kiosks run by the Baltimore Area Convention and Visitors Association (located at the Charles Street and Pratt Street lobbies) to buy attraction tickets, make restaurant reservations, or pick up brochures about all there is to see and do around the city. During the meeting, these desks will be open from 10:00 AM–5:00 PM, Sunday through Thursday. For more information about the BCC, visit their Web site at www.bccenter.org, or call (410) 649-7000.



SOT Annual Meeting

Questions?

Contact

Tel: (703) 438-3115

Career Resource and Development

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International Attendee Information

The Society of Toxicology invites scientists from around the world to attend its Annual Meeting, March 15–19, 2009. Individual invitations are not required for attendance at meetings of the Society of Toxicology. The meetings are open scientific events and SOT invites all interested persons to attend. However, you may request a formal invitation letter by sending your contact information to the SOT Registration Department at sothq@toxicology.org.

If you have been accepted to make a presentation at the meeting, please include the name and date of your presentation. You will need to make your own hotel reservations and register for the meeting.

We request that you contact the United States Consulate/Embassy and Currency Exchange in your own country regarding documentation and necessary information for your visit to the United States. If you need assistance, please contact the SOT Registration Department: tel: (703) 438-3115, fax: (703) 438-3113, or e-mail: sothq@toxicology.org.

It is critical that you submit your documentation as early as possible. The U.S. is advising visa applicants to apply **at least three to four months** in advance of their travel date. To increase security for citizens and visitors, the U.S. has updated its policies for visas. Here are some sources of information to help you through this procedure:

- www.UnitedStatesVisas.gov
A Web site that provides basic details about current visa policies and procedures.

- www.nationalacademies.org/visas
For additional visa information, contact International Visitors Office (IVO) of the National Academies of the Sciences at the above Web site. This should serve as a visa resource for all visiting scientists and scholars traveling to the United States. Additionally, a survey is available that can be used to assist future travelers with the visa process.

- **Make an Appointment**
Visit the U.S. Embassy or Consulate in your county regarding documentation, etc. Make sure you ask if there are any fees required. Most fees must be paid before your appointment.

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

- **Submit Your Application**
Send your application and passport along with supporting documents to the U.S. Embassy or Consulate.

- **Start Early**
As additional reviews may be required. This could add an additional 4–6 weeks to the processing time.

Sponsorship

The Society would like to invite your organization to be a sponsor of the 2009 Annual Meeting. SOT appreciates the generous contributions of sponsors that make the SOT Annual Meeting possible. Sponsor names are prominently displayed on the Annual Meeting Web site, as well as in print materials that are distributed before and during the Annual Meeting. Sponsorship is recognized through signage displayed around the Convention Center during the Annual Meeting.

There are four levels of sponsorship available: Diamond (\$10,000 or more), Platinum (\$5,000–\$9,999), Gold (\$2,500–\$4,999),

48th Annual Meeting and ToxExpo™



General Information

and Silver (\$1,000–\$2,499). You will find a complete menu of sponsorships designed to assist your organization in establishing a leadership position at the SOT 2009 Annual Meeting on the Web site at www.toxicology.org. Promotional opportunities can be reviewed at www.toxexpo.com.

For detailed information about SOT sponsor and promotional opportunities, please contact Marcia Lawson at SOT Headquarters: (703) 438-3115 or e-mail: marcia@toxicology.org.

For a listing of current sponsors, see the inside back cover.

Accessibility for Persons with Disabilities

The Baltimore Convention Center and most of the SOT hotels are accessible to persons with disabilities. If you require special services, please mark the appropriate box on the Registration Form. If you require more information about disabled access, please contact Heidi Prange at SOT Headquarters: (703) 438-3115 ext. 1424 or e-mail: heidi@toxicology.org.

Attire

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



Baltimore Activities

Baltimore is a destination that is ever-evolving with new and expanding attractions and one-of-a-kind offerings. With more than 130 attractions highlighting everything from education to history to entertainment, Baltimore truly offers something for everyone. Whether exploring the city's unique neighborhoods, arts and culture scene, family-friendly attractions, or historical treasures, Baltimore makes it easy to enjoy.



National Aquarium in Baltimore

501 E. Pratt Street, Pier 3
(410) 576-3800
www.aqua.org

The world-famous Baltimore Aquarium attracts over 1.6 million visitors per year and is the city's leading tourist attraction. See over 16,000 creatures in their natural habitat, including sharks, dolphins, sting-rays, sloths, and monkeys. View a life-size model of a humpback whale, visit a coral reef, or catch the live-action Dolphin Show. Be sure to also check out the Aquarium's new 4D Immersion Theater.

Maryland Science Center

601 Light Street
(410) 545-5927
www.mdsci.org

One of the oldest scientific institutions in the United States, the Maryland Science Center offers three full floors of hands-on exhibits, including a voyage through the human body and learning how microbes work for us. You'll also find a five-story IMAX Theater, Planetarium, Kids' Room, and a rooftop observatory.

Top of the World Observation Level

401 E. Pratt Street, 27th Floor
World Trade Center
(410) 837-VIEW
www.viewbaltimore.org

A spectacular and unforgettable 360-degree panoramic view of Baltimore awaits you from the top of the world's tallest pentagonal building. New exhibits about local landmarks, famous people and "firsts," and historic events will engage and inspire you to explore more of Charm City!

American Visionary Art Museum

800 Key Highway
(410) 244-1900
www.avam.org

This national museum and education center for outstanding original works of art created by intuitive, self-taught artists features seven art galleries, outdoor wild-flower sculpture gardens, museum store and gourmet restaurant.

The Baltimore Museum of Art

10 Art Museum Drive
(at N. Charles and 31st Streets)
(443) 573-1700
www.artbma.org

All year long, Maryland's largest art museum showcases a dazzling collection, ranging from ancient mosaics to contemporary



General Information

art, plus ever-changing exhibitions, sculpture gardens, an eclectic museum shop and a scenic restaurant. General admission is free.

Geppi's Entertainment Museum

301 W. Camden Street
(410) 625-7060

www.geppismuseum.com

Geppi's Entertainment Museum takes you on a memorable journey through the history of American pop culture. Visitors experience a timeline of nostalgic toys, comics and other collectibles highlighting familiar characters and icons, such as Superman, Batman, Howdy Doody, Betty Boop, Elvis, and many more.

Reginald F. Lewis Museum of Maryland African American History and Culture

830 E. Pratt Street
(443) 263-1800

www.africanamericanculture.org

A major Inner Harbor tourist destination with striking architecture, this museum highlights the history and accomplishments of Maryland's African American community, featuring exhibitions, a 200-seat theater, classrooms, and an oral history studio.



Baltimore Maritime Museum

802 S. Caroline Street
(410) 396-3453

www.baltomaritimemuseum.org

Tour USS Torsk, last victorious WWII submarine; USCGC Taney, last Pearl Harbor survivor afloat; Lightship Chesapeake, which marked the entrance of the Chesapeake Bay for 33 years; and the 7-foot Knoll Lighthouse, which guided mariners safely into Baltimore Harbor.

Port Discovery, the Children's Museum in Baltimore

35 Market Place
(410) 727-8120

www.portdiscovery.org

Port Discovery, the Children's Museum in Baltimore, offers three floors of educational and interactive exhibits, programs, and activities for children ages 2–10 years old. SOT is partnering with Port Discovery for a special event March 15 (see page 93).



Fort McHenry National Monument and Historic Shrine

2400 E. Fort Avenue
(410) 962-4290

www.nps.gov/fomc

This 18th-century brick fort defended Baltimore Harbor during the War of 1812 and is the birthplace of the American national anthem. The first official flags with 49 stars, and with 50 stars, were flown over Fort McHenry and remain there today. Park rangers offer visitor programs and special events that highlight the park's history.

Star-Spangled Banner Flag House

844 E. Pratt Street
(410) 837-1793

www.flaghouse.org

Visit the 1793 home of Mary Pickersgill, where she made the 30x42 Star-Spangled Banner that flew over Fort McHenry and inspired Francis Scott Key to write the words that would later become our national anthem.

Maryland Historical Society

201 W. Monument Street
(410) 685-3750

www.mdhs.org

Founded in 1844, the Maryland Historical Society is the state's oldest cultural institution and explores the heritage of the state through its museum, library, publications, and educational programs. It is also home of the original manuscript of Francis Scott Key's "Star Spangled Banner." The museum boasts of the East Coast's finest decorative art collection.

Baltimore Museum of Industry

1415 Key Highway, Inner Harbor South
(410) 727-4808

www.thebmi.org

The museum that works! Visit re-created workshops, explore industry from days past, and see the 1906 Steam Tug Baltimore—a national historic landmark. Enjoy hands-on activities for kids, tours for the whole family, outdoor pavilion and free parking.



General Information



Baltimore and Ohio Railroad Museum

901 W. Pratt Street
(410) 752-2490
www.borail.org

This fascinating and fun place for kids, families, and history lovers features the oldest, most historic and most comprehensive American railroading collections in the world. Participate in family activities and hands-on exhibits and explore thousands of artifacts, locomotives and rolling stock, and historic buildings. Recognized as the birthplace for American railroading, the museum site represents the creation of the first common carrier railroad in the Western Hemisphere.

National Museum of Dentistry

31 S. Greene Street
(410) 706-0600
www.dentalmuseum.org

See amazing teeth feats, marvel at George Washington's choppers (they're not made of wood after all!), sing along to vintage toothpaste commercials, and discover fascinating hands-on exhibitions about the power of a healthy smile.

Centerstage

700 N. Calvert Street
(410) 332-0033
www.centerstage.org

Considered one of the top 10 regional theaters in the country and honored as the State Theater of Maryland, this professional theater presents a variety of home-produced plays, from Shakespeare to August Wilson, Sondheim to Shaw, in two state-of-the-art theaters.

Sports

Sports Legends Museum at Camden Yards

301 W. Camden Street
(410) 727-1539
www.baberuthmuseum.com

This 22,000-square-foot museum includes exhibits devoted to Johnny Unitas, the Baltimore Orioles and Colts, and Baltimore's Negro Leagues, as well as the Maryland Terrapins and college athletics. Part of the same foundation and located just a few blocks away at 216 Emory Street is the Babe Ruth Birthplace Museum. See rare artifacts, photos, videos, and more at this national historic site, presenting the life of Babe Ruth, a Baltimore native and America's first sports celebrity.

Oriole Park at Camden Yards

333 West Camden Street
(888) 848-BIRD
www.orioles.mlb.com

Take a tour of this beautiful, baseball-only facility, home to the Baltimore Orioles. Visit the dugout, Press Level, Scoreboard/JumboTron Control Room, the exclusive Suite Level, and a historical perspective of the Camden Yards Area.

Shopping

Whether you're looking for classic clothing, fine collectibles, antiques, or even silly souvenirs, the Baltimore area gives you an astounding array of choices in shopping. Discover fine boutiques, galleries and specialty stores in some of Baltimore's older neighborhoods like Fell's Point and Mount Vernon.

Another popular shopping spot is the Harborplace & The Gallery at Harborplace. Located within two waterfront pavilions and a beautiful four-story glass atrium in the Inner Harbor, the Harborplace & The Gallery features a mix of 120 national retailers and unique shops, 12 restaurants, and 30 diverse eateries. For more information, call (410) 332-4191 or visit www.harborplace.com.



A shopping must for collectors is Baltimore's Antique Row, where numerous quality dealers feature furniture, bronze, silver, glass, pottery, porcelain, books, paintings, prints and more. Located at 831 N. Howard Street. Call (410) 462-1192 or visit www.imperialhalfbushel.com/baltimoreantiquerow.htm for more information and a listing of shops.

Pick up some tasty treats while you shop at Baltimore's public markets. Experience a true Baltimore tradition (since 1782!) at the famous Lexington Market, located at 400 W. Lexington St. The world's largest

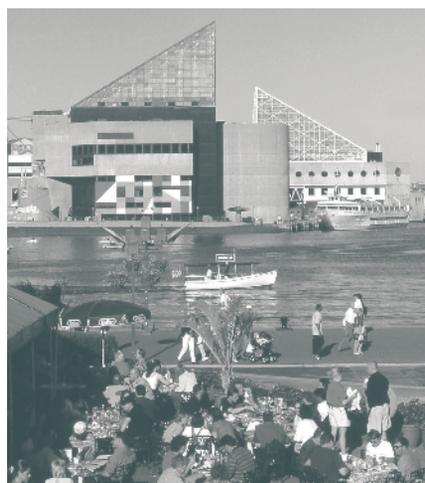


General Information

continuously running market for more than six generations, it features fresh produce, seafood, meat, candy, delicatessen and bakery vendors, and international cuisine, as well as various foods and general merchandise. The Market also plays live music every Friday and Saturday during lunch from Noon until 2:00 PM. Open Monday through Saturday, 8:30 AM–6:00 PM. Visit www.lexingtonmarket.com or call (410) 685-6169 for more information. Other popular markets include Broadway Market in Fell's Point and Cross Street Market in Federal Hill.

Food and Entertainment

Baltimore has restaurants to satisfy nearly every craving. Dining options include elegant gourmet cuisine, ethnic foods from around the world and plenty of fresh seafood from Maryland's Chesapeake Bay. Known for its famous Chesapeake Bay crabs, dining at one of the city's many seafood restaurants or crab houses is a must for all who visit. Visit www.chowbaby.com or www.yelp.com for restaurant reviews and search features.



For Italian lovers, be sure to visit the authentic Italian neighborhood of Little Italy, home to over two dozen cozy, family-owned Italian eateries located between the Inner Harbor and historic Fells Point. Whether your tastes tend

toward traditional, casual spaghetti and meatballs or innovative, upscale Italian cuisine, choices abound. For more information and a list of restaurants, visit www.littleitalymd.com.

If you're looking for a livelier scene to go along with your dining experience, Power Plant Live! boasts an eclectic collection of restaurants, bars, and clubs, including Baltimore's premiere music venue, Ramshead Live. Located one block from the Inner Harbor. Visit www.powerplantlive.com or call (410) 727-LIVE for a list of restaurants/clubs and a calendar of events.

Little Italy and the Inner Harbor are not the only neighborhoods with great food. Areas like Federal Hill, Canton, Fells Point, and Harbor East have experienced a surge of restaurant development. Each area is rich with culture and flair and brings a unique culinary scene to Baltimore.

Looking for More?

Come early or stay after the SOT Annual Meeting and explore the surrounding nearby cities of the East Coast. Baltimore is easily accessible to many major cities, such as Washington, DC, New York City, and Philadelphia. Only about 30 miles south of Baltimore is Maryland's quaint seaport town of Annapolis.

Believe it or not, we haven't even covered half of the many things to see and do in Baltimore. For a complete listing and other information about the city, call 877-BALTIMORE or visit www.baltimore.org, created by the Baltimore Area Convention and Visitors Association. They even have an interactive map that allows you to search and map out attractions, restaurants, historic sights and much more. The Baltimore Convention and Visitor Association will also be running two information desks at the Convention Center during the Annual Meeting from 10:00 AM–5:00 PM, Sunday–Thursday.



Baltimore Fun Facts

- The Baltimore's World Trade Center is the world's largest five-sided building.
- The first printing of the Star Spangled Banner took place in Baltimore in 1814. The original manuscript, written by Francis Key Scott, is on display at the Maryland Historical Society.
- Baltimore was home to the first ice cream factory in America in 1851.
- The first umbrella used in the United States was in Baltimore in 1772. Almost sixty years later, the city built the first American umbrella factory.
- Baltimore College of Dental Surgery was the first dental college in the world, which started in 1839.
- Built in 1827, the Baltimore and Ohio Railroad was the first public carrier railway in the U.S.
- In 1844, Samuel Morse operated the first telegraph line in the United States, which went between Washington, DC and Baltimore.
- Baltimore is home to the first formal monument to George Washington in the United States. Completed July 4, 1829, it still stands at Mount Vernon.
- Baltimore is the hometown and current residence of Olympic swimmer, Michael Phelps, who earned 8 Gold Medals at the 2008 Beijing Olympics and currently holds 7 world records.

48th Annual Meeting and ToxExpo™

General Information

Climate

Baltimore's climate is moderated by the nearby Chesapeake Bay, the Atlantic Ocean to the East, and the Appalachian Mountains to the West. Rarely reaching extreme cold or warm temperatures, Baltimore is a great city to visit at any time of the year. The average annual rainfall for March is 3.4 inches with about 40 inches of precipitation a year. Average temperatures for March are highs in the mid 50s °F and lows in the mid 30s °F. For an up-to-date, detailed weather forecast visit www.wbaltv.com/weather.

First Aid and Emergency Services at the Convention Center

If an emergency should occur while at the Baltimore Convention Center, proceed directly to the nearest white house phone, located throughout the facility, and dial 7055. You will be connected to the Security/Public Safety Office, open 24 hours. From any phone that is not a house phone, dial (410) 649-7055.

The First Aid room is located in the back of Exhibit Hall E. The first aid administrator will be on duty during SOT exhibit and show hours. During non-exhibit hours,

please dial 7055 for the Public Safety Office and a first aid administrator will meet you at your location. Please note that in accordance with the State of Maryland and the City of Baltimore regulations, the first aid administrator is not permitted to dispense any medication.

Guest Hospitality Center and Program

The SOT Guest Hospitality Center provides guest participants (non-scientists) with a place to meet and socialize with other guests. To visit the Hospitality Center, guests must register for the Annual Meeting with the person they are accompanying. Guests are welcome to attend the Welcoming Reception, but will not have access to the scientific sessions or the Exhibit Hall. Please remember to wear your badge to all SOT events. The Guest Hospitality Center will be located in the Hilton Hotel.

Housing Information

Make your hotel reservations through the Baltimore Housing Bureau on the SOT Annual Meeting Web site.

The Society of Toxicology has reserved and made arrangements for SOT Annual Meeting attendee discounted room rates

at various Baltimore hotels—known as the SOT hotel block. This block includes discounted room rates at many premier hotel chains and details can be found on the following page.

The Room Sharing program allows 2009 SOT Annual Meeting Registrants to identify others with whom a room might be shared. Access this option from the Annual Meeting section of the SOT Web site.

Did you know that your choice of hotel for the SOT Annual Meeting has direct impact on Society's strategic initiatives? Although we understand that making your reservations outside of the SOT hotel block can sometimes be more economical, it decreases the money available to the Society to carry out its strategic goals and may cause the Society to have to pay attrition fees for unutilized hotel rooms. In addition, the Society is unable to assist you if you have any difficulties with your room reservation, such as the hotel over-booking or misplacing your reservation.

SOT depends on the Annual Meeting revenue (hotel room commissions and rebates) to fund other programs throughout the year and to keep future registration fees low. Please assist the Society by making your hotel room reservation through the Baltimore Housing Bureau.

Take back souvenirs from the 2009 Annual Meeting!



SOT Memorabilia for Sale!

Shirts, hats, portfolios, and other items customized for SOT are available for purchase at the Annual Meeting in the registration area.

All items are reasonably priced and designed exclusively for SOT. Be sure to stop by the SOT Memorabilia Booth near the registration area to see items on display and to make purchases. These make great souvenirs for yourself, family, and friends. Cash, checks, and credit cards will be accepted. (Shipping is not available)





General Information

Hotel Accommodations

1) Days Inn Inner Harbor



\$139 Single/Double
100 Hopkins Place
Baltimore, MD 21201
Tel: (410) 576-1000
Fax: (410) 659-0257
Web site: www.daysinnerharbor.com



Club: Wyndham Rewards
Check in: 3:00 PM
Check out: 11:00 AM
1 block from Convention Center
\$18/day self parking
Complimentary wireless Internet available in guest room and throughout hotel

2) Hampton Inn at Camden Yards



\$155 Government Rate or
\$179 Single/Double
550 Washington Boulevard
Baltimore, MD 21230
Tel: (410) 685-5000
Fax: (410) 685-5002
Web site: www.baltimorecamdenyards.hamptoninn.com



Club: Hilton HHonors
Check in: 3:00 PM
Check out: 12:00 NOON
2 blocks from Convention Center
\$26/day valet parking
Complimentary wireless Internet available in guest room and throughout hotel.
Complimentary hot breakfast.

***Internet access and parking pricing are subject to change*

3) Hilton Baltimore



SOT Headquarters Hotel

\$192 Single/Double
401 West Pratt Street
Baltimore, MD 21201
Tel: (443) 573-8700
Fax: (443) 573-8799
Web site: www.baltimore.hilton.com

New hotel—Rating not yet determined

Club: Hilton HHonors
Check in: 3:00 PM
Check out: 12:00 NOON
1 block from Convention Center
\$26/day self and \$36/day valet parking
Internet access at \$9.95/day—wireless Internet available

4) Holiday Inn Inner Harbor



\$169 Single/Double
301 W Lombard Street
Baltimore, MD 21201
Tel: (410) 685-3500
Fax: (410) 727-6169
Web site: www.holiday-inn.com/bal-downtown



Club: Priority Club Rewards
Check in: 4:00 PM
Check out: 12:00 NOON
1 block from Convention Center
\$21/day self parking
Complimentary wireless Internet available in guest room and throughout hotel

5) Hyatt Regency Baltimore



\$205 Single/Double
300 Light Street
Baltimore, MD 21202
Tel: (410) 528-1234
Fax: (410) 685-3362
Web site: www.baltimore.hyatt.com



Club: Hyatt Gold Passport
Check in: 4:00 PM
Check out: 12:00 NOON
1 block from Convention Center
\$27/day self and \$36/day valet parking
Internet access at \$9.99/day—wireless Internet available

6) InterContinental Harbor Court Baltimore



\$199 Single/Double
550 Light Street
Baltimore, MD 21202
Tel: (410) 234-0550
Fax: (410) 385-6185
Web site: www.harborcourt.com



Club: Priority Club Rewards
Check in: 3:00 PM
Check out: 12:00 NOON
3 blocks from Convention Center
\$21/day self and \$32/day valet parking
Internet access at \$11.95/day—wireless Internet available

7) Marriott Inner Harbor at Camden Yards



\$189 Single/Double
110 South Eutaw Street
Baltimore, MD 21201
Tel: (410) 962-0202
Fax: (410) 625-7892
Web site: www.marriott.com/bwiih



Club: Marriott Rewards
Check in: 4:00 PM
Check out: 12:00 NOON
1 block from Convention Center
\$22/day self parking
Internet access at \$9.95/day—wireless Internet available

8) Radisson Plaza Lord Baltimore



\$180 Single/Double
20 West Baltimore Street
Baltimore, MD 21201
Tel: (410) 539-8400
Fax: (410) 625-1060
Web site: www.radisson.com/lordbaltimore



Club: Goldpoints Plus
Check in: 3:00 PM
Check out: 12:00 NOON
3 blocks from Convention Center
\$29/day valet parking
Complimentary wireless Internet available in guest room and throughout hotel

Baltimore, Maryland

General Information

9) Renaissance Harborplace



\$192 Single/Double
202 East Pratt Street
Baltimore, MD 21202
Tel: (410) 547-1200
Fax: (410) 539-5780
Web site: www.marriott.com/renaissanceharborplace



Club: Marriott Rewards
Check in: 4:00 PM
Check out: 12:00 NOON
2 blocks from Convention Center
\$26/day self and \$36/day valet parking
Internet access at \$9.95/day—complimentary wireless Internet in lobby

10) Sheraton Baltimore City Center



\$188 Single/Double
101 West Fayette Street
Baltimore, MD 21201
Tel: (410) 752-1100
Fax: (410) 385-6865
Web site: www.starwoodhotels.com/sheraton/baltimorecitycenter



Club: Starwood Preferred Guest
Check in: 3:00 PM
Check out: 12:00 NOON
3 blocks from Convention Center
\$23/day self and \$33/day valet parking
Internet available at \$9.95/day—wireless Internet available

11) Sheraton Inner Harbor



\$190 Single/Double
300 South Charles Street
Baltimore, MD 21201
Tel: (410) 962-8300
Fax: (410) 962-8211
Web site: www.starwoodhotels.com/sheraton/innerharbor



Club: Starwood Preferred Guest
Check in: 3:00 PM
Check out: 12:00 NOON
1 block from Convention Center
\$22/day self and \$30/day valet parking
Internet access at \$9.95/day—wireless Internet available

12) SpringHill Suites by Marriott



\$189 Single/Double
16 South Calvert Street
Baltimore, MD 21202
Tel: (410) 685-1095
Fax: (410) 685-1094
Web site: www.springhillsuitesbaltimoreinnerharbor.com



Club: Marriott Rewards
Check in: 3:00 PM
Check out: 12:00 NOON
4 blocks from Convention Center
\$28/day valet parking
Complimentary wireless Internet available in guest room and throughout hotel

13) Tremont Plaza



\$155 Government Rate or
\$159 Single/Double
222 St. Paul Place
Baltimore, MD 21202
Tel: (410) 727-2222
Fax: (410) 685-4215
Web site: www.tremontsuitehotels.com/the_plaza

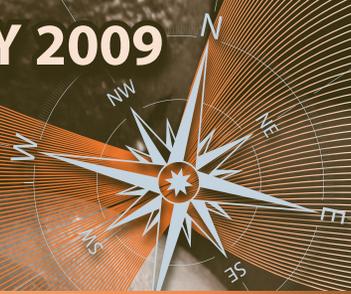


Club: N/A
Check in: 4:00 PM
Check out: 12:00 NOON
7 blocks from Convention Center
\$15/day self and \$25/day valet parking (adjacent, but not w/ hotel)
Complimentary Internet access in guest room—complimentary wireless Internet in lobby

Legend:

	Valet Parking
	Self Parking
	Fitness Center
	Swimming Pool
	Business Center
	In-Room Wireless
	In-Room Safe
	Gift Shop
	Concierge
	Complimentary Breakfast
	Restaurant

*All hotels have Internet access.
Hotel sales tax is currently 15.5%*



General Information

Hotel Map



48th Annual Meeting and ToxExpo™

General Information

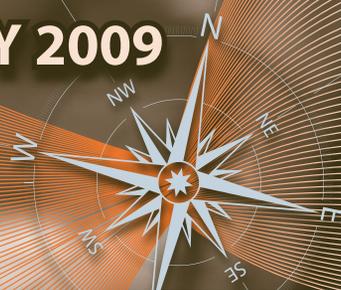
Hotel Services

Hotel	Rewards Program	Blocks to Convention Center	Single/Double Rate	Restaurant	Comp Breakfast	In-Room Safe	Fitness Center	In-Door Pool	Business Center	In-Room Wireless Internet	Room Service	Gift Shop	Concierge	Overnight Self Parking	AAA Rating
1) Days Inn Inner Harbor	Wyndham Rewards	1 Blocks	\$139	✓		✓	✓		✓	✓	✓		✓	✓	2-Diamond
2) Hampton Inn at Camden Yards	Hilton HHonors	2 Blocks	\$179 \$155 govt		✓		✓	✓	✓	✓					3-Diamond
3) Hilton Baltimore*	Hilton HHonors	1 Block	\$192	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A
4) Holiday Inn Inner Harbor	Priority Club Rewards	1 Block	\$169	✓			✓	✓	✓	✓	✓	✓	✓	✓	3-Diamond
5) Hyatt Regency Baltimore	Hyatt Gold Passport	1 Block	\$205	✓		✓	✓		✓	✓	✓	✓	✓	✓	4-Diamond
6) Inter-Continental Harbor Court Baltimore	Priority Club Rewards	3 Blocks	\$199	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	4-Diamond
7) Marriott Inner Harbor at Camden Yards	Marriott Rewards	1 Block	\$189	✓		✓	✓	✓	✓		✓	✓	✓	✓	3-Diamond
8) Radisson Plaza Lord Baltimore	Goldpoints Plus	3 Blocks	\$180	✓			✓		✓	✓	✓	✓	✓		3-Diamond
9) Renaissance Harborplace	Marriott Rewards	2 Blocks	\$192	✓		✓	✓	✓	✓		✓	✓	✓	✓	4-Diamond
10) Sheraton Baltimore City Center	Starwood Preferred Guest	3 Blocks	\$188	✓			✓		✓		✓	✓	✓	✓	3-Diamond
11) Sheraton Inner Harbor	Starwood Preferred Guest	1 Block	\$190	✓			✓	✓	✓	✓	✓	✓	✓	✓	3-Diamond
12) SpringHill Suites by Marriott	Marriott Rewards	4 Blocks	\$189		✓		✓		✓	✓			✓		3-Diamond
13) Tremont Plaza	N/A	7 Blocks	\$159 \$155 govt	✓			✓		✓		✓		✓	✓	3-Diamond

*SOT Headquarters Hotel

All hotel accommodations and rates may be subject to change.





General Information

Hotel Reservation Information

Deadline: February 6, 2009

On-Line: www.toxicology.org

Telephone:

Toll-Free (USA and Canada):
(800) 282-6632

International: (410) 837-4636

Hours of Operation: 8:30 AM–5:30 PM
(EST) Monday–Friday

Fax: (410) 659-8398

Mail:

Baltimore Housing Bureau
100 Light Street, 12th Floor
Baltimore, MD 21202
United States

E-Mail:

conventionhousing@baltimore.org

Note: Although not stated, triple and quadruple occupancy can cost between \$15–\$20 extra per night.

Reservations and Deposits

All reservations for housing must be made through the Baltimore Housing Bureau and NOT with the hotels directly. All housing forms must be received by Friday, February 6, 2009. The form can be found on the SOT Annual Meeting Web site. Deposits: A credit card is required to guarantee a room; checks are accepted and should be made payable to BACVA/SOT equal to one night's room and tax to hold the room reservation. Deposits are refundable minus a \$25 fee if accommodations are cancelled 72 hours prior to arrival. Forms received without a payment will not be processed. If paying by check, mail U.S. funds drawn on a U.S. bank, to BACVA/SOT Housing, 100 Light Street, 12th Floor; Baltimore, MD 21202. Full payment can be made through the Baltimore Housing Bureau. No wire transfers or purchase orders will be accepted for housing.

Confirmations

Confirmation will be e-mailed, faxed, or mailed to you from the Housing Bureau once your reservation has been booked. (You will not receive a confirmation from your hotel.) If you do not receive confirmation within 2 weeks, please call the Housing Bureau.

Changes and Cancellations

The deadline date for new reservations is Friday, February 6, 2009. Continue to make any requests through the Baltimore Housing Bureau through March 9. If you cancel your reservation after February 12, 2009, you will be charged a \$25 processing fee. Beginning March 10 and up to 72 hours prior to your arrival, changes and cancellations must be made with your assigned hotel. *Note: some hotels charge an early departure fee.*

Any cancellations made within 72 hours of arrival date will result in forfeiture of your first night's deposit and tax. For any new changes after March 10, please ask the hotel to send you a new e-mail or fax confirmation showing the new change.

For best availability and immediate confirmation, make your hotel reservation *via* Internet or by phone. Faxed and mailed housing requests will take longer to process and your hotel selections may not be available.



Internet Access

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

Computers Available at the Convention Center

SOT will provide computers you can use to access the Internet. These computers are available to attendees in the E-mail Center, located in the Pratt Street Lobby on Level 300 of the Convention Center.

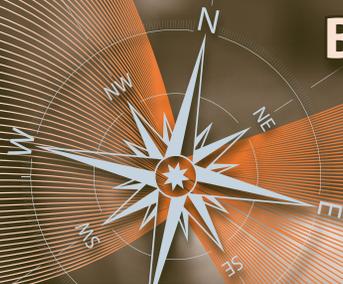
Wireless Access

“Hot Zone” designated areas in the Exhibit Hall will be clearly marked for laptop and handheld users to access the Internet *via* the Wi-Fi network at the Convention Center. Look for Wi-Fi network access instructions and locations in the *Program* and *ToxExpo™ Directory* or on the SOT Web site.

Internet E-mail Center

The SOT Annual Meeting E-mail Center is provided to help you stay connected to your colleagues during the Annual Meeting. SOT members, 2009 Annual Meeting attendees, including exhibitors and CRAD Job Bank registrants, can access the E-mail Center on the SOT Web site to send and receive e-mail messages during the 2009 Annual Meeting—just like a standard e-mail application. The difference? The 2009 SOT Annual Meeting E-mail Center gives you a unique mailbox without having to provide your personal e-mail address to correspondents.

The service will send an e-mail alert to you when you receive a message. Use the communication preference option to forward your incoming messages to your primary e-mail address or PDA.



General Information



Available 24/7, access to the E-mail Center is available any time of day and from any computer with an Internet connection, before, during, and after the 2009 Annual Meeting. Simply visit the SOT Web site and follow the E-mail Center link from the navigation.

To log into your mailbox, use your e-mail address and password or Annual Meeting badge number. If you don't know your login, you can use the SOT password retrieval request from the login on the SOT Web site or ask the Annual Meeting registration staff or E-mail Center attendant for assistance.

Job Bank users will have the option to send messages to the Annual Meeting E-mail Center mailboxes. E-mail Center users will have the option to send messages to Job Bank registrant mailboxes by name or Job Bank ID.

Additionally, the E-mail Center provides extended communication permitting members and Job Bank registrants who do not attend the meeting to communicate with attendees. Even colleagues and family members can e-mail messages into the Center.

Luggage/Coat Check

For your convenience, a luggage/coat check will be available in the Baltimore Convention Center near the Pratt Street Lobby on Level 300. The luggage/coat check will be open from Sunday, March 15 through Thursday, March 19. There will be a fee of \$2 per item checked and laptop computers will not be accepted.

Hours of operation:

Sunday.....	7:00 AM–8:30 PM
Monday	7:00 AM–8:30 PM
Tuesday	7:00 AM–8:00 PM
Wednesday	7:00 AM–8:00 PM
Thursday	7:00 AM–1:00 PM

Luggage/coat check hours are subject to change.

Media Support Services

The Society of Toxicology welcomes accredited representatives of media organizations. Journalists receive complimentary registration for all meeting sessions as well as media kits. Interviews can be arranged with guest speakers and a press room will be available for reporters. For more information about the program, please contact Martha Lindauer at SOT Headquarters: (703) 438-3115 or e-mail: martha@toxicology.org.

Meeting Requests: Hospitality Suites and Ancillary Meetings

All requests for hospitality suites and ancillary meetings must be approved by SOT Headquarters. To reserve a meeting room or hospitality suite, go to www.toxicology.org and complete the Ancillary Meeting Form on-line. Ancillary functions may only be hosted by SOT Associates, Exhibitors, or organizations affiliated with SOT. Hospitality suites and ancillary meeting space books fast. Submit your request now. Only meeting requests made by December 18, 2008, will be listed in the Annual Meeting Calendar and *Program*.

Meeting Pole

In order to facilitate attendees in locating friends and new acquaintances, a centralized meeting location has been designated on Level 300 between Rooms 324 and 327 in the Baltimore Convention Center. The lighthouse meeting pole makes it easy to locate colleagues and will also present a great photo opportunity.

Message Boards

Leave a quick note on the message boards. Note pads and push pins will be available to post messages on the message boards. SOT Message Boards will be located across from the Registration Desk near the E-mail Center located on Level 300 of the Baltimore Convention Center.



General Information

Parking Information

For those driving into Baltimore and staying overnight, please check hotel accommodations on page 10 for parking options or contact the hotel directly, as rates are subject to change.

If you plan on driving into Baltimore for the day, please see our suggested parking options below.

Please note that all parking prices are subject to change.

Sheraton Inner Harbor Parking Garage on Conway Street

Open 24 hours/day
 Current parking rate: \$22/day for guests of the hotel and \$26/day for all others
 In/Out privileges for guests only
 Sheraton Inner Harbor is connected to the Convention Center

Hyatt Regency Parking 300 Light Street

Open 24 hours/day
 Current parking rate for guests and public: \$27/day
 In/Out privileges for guests and public
 Hyatt Regency is connected to the Convention Center

Laz Parking 100 South Charles Street

(410) 625-2385
 Open from 6:00 AM to 12:00 Midnight
 Current parking rate: \$16/day
 From the parking garage: Head South on South Charles Street and the Convention Center will be on your right (across the street from the Hyatt Regency)

Laz Parking 100 East Pratt Street

(410) 244-8825
 Open 24 hours/day
 Current parking rate: \$21/day; \$12 if you enter between 6:00 AM and 9:00 AM and leave before 6:00 PM
 From the parking garage: Head West on East Pratt Street toward Light Street. Take a left on South Charles Street and the Convention Center will be on your right (across the street from the Hyatt Regency)

Oriole Park at Camden Yards Parking Lot C

Open 24 hours/day
 Open lot (not garage)
 Current parking rate: Monday–Friday is \$8/day if you enter before 2:00 PM and \$10/day after 2:00 PM; Weekend parking is \$10/day
 No In/Out privileges
 From the parking lot: Head North on West Camden Street. Take a left on South Howard Street. Take a right on West Pratt Street and the main entrance to the Convention Center will be on your right.

Photography Policy and Session Etiquette for Attendees

Out of courtesy for the scientific presenters, we appreciate your compliance with the following policies:

- Cell phones and other electronic devices should be set on mute.
- Electronic capture of scientific sessions by any method is prohibited.
- Children under the age of 15 are not allowed in scientific sessions unless consent is given by the session chair.

Session chairs are asked to strictly enforce these policies and individuals who do not comply will be asked to leave the session.

- Photography of poster presentations is prohibited without the specific consent of the presenter(s)/author(s).
- Children under the age of 15 are prohibited from accessing the Exhibit Hall at any time.

If you have any questions regarding these policies, please contact the SOT Headquarter staff at the Registration Desk.



48th Annual Meeting and ToxExpo™

General Information

Registration

On-line and early registration is strongly encouraged. The Annual Meeting Early Registration deadline is January 30, 2009. The registration fee for the SOT Annual Meeting includes admission to all scientific sessions, the Awards Presentation, and ToxExpo™, a copy of the *Program*, *The Toxicologist* on CD-ROM (abstracts), and the *ToxExpo™ Directory*. SOT will accept registrations by fax or mail until March 10. After March 10, you must register on-line or on-site at the Annual Meeting.

Registration Fees

ANNUAL MEETING REGISTRATION FEES:			
	Early Bird Registration (Received by Jan. 30)	Standard Registration (Jan. 31 to Feb. 20)	Final Registration (After Feb. 20*)
SOT Member	\$295	\$345	\$395
Non-Member**	\$590	\$640	\$690
SOT Retired Member	\$ 65	\$105	\$145
Postdoctoral SOT Member	\$ 80	\$120	\$160
Postdoctoral Non-Member**	\$160	\$200	\$240
Graduate Student Member	\$ 60	\$100	\$140
Graduate Student Non-Member**	\$120	\$160	\$200
Student Undergraduate	\$ 60	\$100	\$140
SOT Affiliate	\$ 0	\$ 0	\$ 0
Press	\$ 0	\$ 0	\$ 0
Guest (Non-Scientist)	\$ 70	\$ 85	\$100
CONTINUING EDUCATION SUNRISE MINI-COURSE FEES (includes continental breakfast):			
	Early Bird Registration (Received by Jan. 30)	Standard Registration (Jan. 31 to Feb. 20)	Final Registration (After Feb. 20*)
SOT Member/Corp Affiliate	\$ 55	\$ 80	\$105
Retired Member	\$ 55	\$ 80	\$105
Non-Member	\$ 75	\$100	\$125
Postdoctoral (SOT Member/Non-Member)	\$ 55	\$ 80	\$105
Graduate or Undergraduate Student (SOT Member/Non-Member)	\$ 25	\$ 50	\$ 75
Press	\$ 0	\$ 0	\$ 0
CONTINUING EDUCATION COURSE FEES:			
Courses run concurrently in AM and PM sessions.			
	Early Bird Registration (Received by Jan. 30)	Standard Registration (Jan. 31 to Feb. 20)	Final Registration (After Feb. 20*)
SOT Member/Corp Affiliate	\$150 each	\$175 each	\$200 each
Retired Member	\$110 each	\$135 each	\$160 each
Non-Member	\$300 each	\$325 each	\$350 each
Postdoctoral (SOT Member/Non-Member)	\$ 90 each	\$115 each	\$140 each
Graduate or Undergraduate Student (SOT Member/Non-Member)	\$ 45 each	\$ 70 each	\$ 95 each
Press	\$ 0 each	\$ 0 each	\$ 0 each

* After February 20, Final Registration rates apply. No substitutions after January 30, 2009. SOT will accept Registration Forms by fax or mail until March 10. On-line registration will be open until March 19. On-Site Registration Forms will be available at the Annual Meeting Registration Desk.

** Special offer to non-member 2009 Annual Meeting attendees: submit a complete application for membership between January 15, 2009 and the May 1, 2009 deadline, and if accepted, SOT will waive your 2009 dues.



General Information

On-Line Registration

SOT members and non-members are invited to register for the 2009 SOT Annual Meeting using the SOT On-Line Registration System. The system is designed for those who will be paying their registration fee by credit card and who have access to the Internet.

Registration information can be accessed via the SOT Web site at www.toxicology.org/register. After registration, you will receive an electronic confirmation. If you do not, please send an e-mail to jimd@toxicology.org.

Registrants may also fax or mail in their registration payments using the Registration Form located on pages 99 and 101.

Registration Materials

Badges and event tickets are mailed in advance if you register before February 20. When you arrive at the Baltimore Convention Center, please go to the registration area located in the Pratt Street Lobby on Level 300 to pick up your registration materials (i.e., *The Toxicologist* on CD-ROM, the *ToxExpo™ Directory* and other supplementary materials). You must present your 2009 Annual Meeting badge to obtain the registration materials. The materials will be available in bins near the registration area. If you have not already registered or have not received your badge, please go to the registration counters. NOTE: If you are registered and have your badge, you do not need to stand in the registration line.

Receipt of the Program and The Toxicologist

1. SOT Members in the U.S. and Canada will receive the printed *Program* and *The Toxicologist* on CD-ROM (with Itinerary Planner) prior to the meeting, as will U.S. and Canadian non-members who register by January 30, 2009.

Non U.S. SOT Members may pick up the printed *Program* and *The Toxicologist* on CD-ROM at the meeting or may request that these be mailed following the meeting. Send e-mail requests to jimd@toxicology.org.

2. Non-members in the U.S. who register after January 30 will receive the *Program* and *The Toxicologist* on CD-ROM (with Itinerary Planner) at the registration area on-site.
3. Registrants will receive the Annual Meeting abstracts in *The Toxicologist* on CD-ROM as part of the Annual Meeting registration fee. Annual Meeting attendees may purchase a printed version of *The Toxicologist* for \$20 per copy. You may preorder on the Registration Form and pick up a copy on-site or wait to purchase a copy on-site (available while supplies last). *The Toxicologist* will be available for download (February 2009) free-of-charge on the SOT Web site.
4. The Annual Meeting Itinerary Planner is available on the SOT Web site January–April.

NOTE: Please bring your copy of the *Program* with you to the meeting.

Satellite Meetings

Each year, SOT endorses several satellite meetings that are held in conjunction with the Annual Meeting. Satellite meetings are organized around scientific topics related to toxicology and are scheduled at the end of the Society's program. The 2009 satellite meetings will be held in and around the Baltimore area. Proposals for a Satellite Meeting should be sent by e-mail to heidi@toxicology.org to the attention of Cheryl Lyn Walker, SOT Vice President and Scientific Program Committee Chair. Requests approved by December 18, 2008, will be published in the final *Program*.

SOT Resource Pavilion

Do you know all the resources available through SOT and where to find them? Stop by the SOT Resource Pavilion to learn about SOT activities, membership benefits, strategic initiatives, and the endowment. Find materials to support the discipline of toxicology and educational tools for K–12 and public outreach. It is a one-stop shop for all your questions and member needs. Centrally located in the Charles Street Lobby and open the following hours:

Sunday.....	11:00 AM–2:00 PM
Monday	9:00 AM–4:30 PM
Tuesday	8:30 AM–4:30 PM
Wednesday	8:30 AM–4:30 PM
Thursday	8:30 AM–12:00 NOON

Tours

SOT is proud to offer all attendees and their guests a wide range of activities to make your visit to Baltimore more enjoyable. A tour desk will be located on Level 300 in the Pratt Street Lobby of the Baltimore Convention Center. Tour desk hours will be listed in the SOT *Program*, or you may visit the Annual Meeting section of the SOT Web site for details.

Discover Baltimore!

Sunday, March 15, 2009

10:00 AM–2:00 PM

\$36 per person

Minimum of 30 people

Uncover the history and heritage of one of the country's most unique cities! Your professional guide will share exciting stories and point out important landmarks as you make your way through "Charm City." You'll see Federal Hill on the shores of the Inner Harbor, Ft. McHenry, where brave Baltimoreans defended the city from British attack during the War of 1812, Oriole Park at Camden Yards, the first of many retro-style ballparks in the country, along with dozens of other significant locations.

General Information

Historic Homes of Baltimore

Monday, March 16, 2009

10:00 AM–4:00 PM

\$55 per person

Minimum of 30 people

Over the years many important historical figures have called Baltimore home. From the modest townhouse where Babe Ruth was born, to the opulent mansions of the Carroll family, you'll get a first hand look at these beautifully preserved homes. This tour includes interior visits to Mt. Clare Mansion, Evergreen House, and Homewood House.

Baltimore's Art and Culture

Tuesday, March 17, 2009

10:00 AM–3:00 PM

\$40 per person

Minimum of 30 people

This tour will take you to two world class art museums in Baltimore; the Baltimore Museum of Art and the Walters Art Museum. Both museums are home to priceless collections and works of art. You'll also see numerous examples of murals and public art around the city.

Discover Annapolis!

Wednesday, March 18, 2009

10:00 AM–4:00 PM

\$50 per person

Minimum of 30 people

You'll visit Maryland's charming capital city situated just 30 minutes south of Baltimore on the banks of the Severn River. While in Annapolis you'll visit the United States Naval Academy (photo ID required) and see the Maryland State House where George Washington resigned his military commission to become president of the United States.

Note: PHOTO ID REQUIRED

To register for these tours, please either fax, mail, or e-mail your Tour Registration Form, found on the SOT Web site, to Baltimore Rent-A-Tour. If you have any questions please call Baltimore Rent-A-Tour at (410) 464-7994 or (888) 842-6323.

The pre-registration deadline is Monday, February 16, 2009, for all tours. Baltimore Rent-A-Tour reserves the right to cancel tours if minimums are not met at that time.

Transportation

Air Transportation

Baltimore is serviced by three major airports: Baltimore/Washington International (BWI), Washington Dulles International (IAD), and Ronald Reagan Washington National (DCA).

Baltimore/Washington International Thurgood Marshall Airport (BWI) is located 10 miles south of the Baltimore Convention Center and downtown Baltimore. The airport provides almost 22 million passengers a year with non-stop service to an average of 70 domestic and international locations. With over 670 daily arrivals and departures, these flights are provided by 5 major domestic carriers as well as several regional and international airlines. For more information, call (410) 859-7992 or 1-800-I FLY BWI (435-9294), or visit www.bwiairport.com.

Both located in Northern Virginia, Washington Dulles International Airport is 61 miles from Baltimore, and Ronald Reagan Washington National Airport is 42 miles from Baltimore. For more information on these airports and modes of transportation to Baltimore, visit www.metwashairports.com.

Special Airfare Discounts

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

American Airlines

(800) 433-1790

www.aa.com

Discount Code: A6139AA

American Airlines is offering a 5% discount off the lowest applicable fare. The discount is valid March 8–25, 2009 for travel to BWI, Reagan, and Dulles airports. You may make reservations by calling the Meeting Services Desk at (800) 433-1790 from anywhere in the United States or Canada and refer to discount code A6139AA. A \$15 service fee per ticket will apply for each ticket booked over the phone. You may also book your ticket on-line at www.aa.com (no service fee applies) and under the promotion code section, type A6139AA to receive the SOT discount.

Northwest Airlines

(800) 328-1111

www.nwa.com

Discount Code: NYVVC

Northwest Airlines is offering a 5% discount off the lowest applicable fare. The discount is valid March 10–23, 2009 for travel to BWI, Reagan, and Dulles airports. You may make reservations by calling the reservation desk Mon-Fri (7:00 AM–7:30 PM CST) at (800) 328-1111 and refer to discount code NYVVC. A \$15 service fee per ticket will apply for each ticket booked over the phone. You may also book your ticket on-line at www.nwa.com (no service fee applies). Under the E-Cert section,



General Information

select Meeting Agreement (WorldFile Number) and type NYVVC to receive the SOT discount. Travel agents should go to www.worldagentdirect.com.

These rates do not apply to Delta flights even though they are one company.

Carlson Wagonlit

Carlson Wagonlit is the official travel management firm for SOT's 48th Annual Meeting. To take advantage of their services and savings, call toll-free (800) 525-6061, or direct (703) 276-2030 or (703) 276-2040 Monday through Friday, 9:00 AM–5:30 PM (Eastern Standard Time), ask to speak to Niki Markun or e-mail: NMarkun@carlsonwagonlit.com. To obtain the maximum discounted fares, call at least 60 days prior to departure. Lower fares are still obtainable up to 14 days in advance. Please note that Carlson Wagonlit charges a \$40 service fee per ticket.

Before calling Carlson Wagonlit, please gather the following information:

- The desired dates of arrival to and departure from Baltimore.
- Your home city or originating airport.
- Your approximate time of departure from the originating airport.
- The number of persons traveling (adults/children).
- Your method of payment, either credit card or check.
- Your airline frequent flyer number(s).

Identify yourself as a Society of Toxicology attendee. Carlson Wagonlit will find the best fare for you and e-mail an itinerary to you.

Ground Transportation

BWI Airport is served by shuttle bus, taxi, Light Rail, Amtrak train or limousine service. Ground transportation is located on the lower level of the airport terminal—the same level as baggage claim. For taxi and shuttle services, look for the service desks located on the same level. For more information on ground transportation from the airport, visit www.bwiairport.com or call (410) 859-7992.

Car Rental

Avis Rent A Car System is the official car rental company for the 48th Annual Meeting. SOT discounted rates, including unlimited mileage, begin at \$43.99 per day. These special group rates are good one week before and after the SOT Annual Meeting so you can take in the sights and explore the surroundings at your own pace. To reserve your car on-line, go to www.avis.com.

You may also call Avis directly at (800) 331-1600 to reserve your car. Be sure to mention the SOT Avis Worldwide Discount Number (AWD) T534999.

Light Rail

Light Rail stops at BWI Airport every half hour and takes you directly from BWI Airport to the Baltimore Convention Center for \$1.60 one way (prices subject to change). Board the Light Rail next to Pier E, the new international wing, located on the lower level.

Hours of operation:

Monday–Friday..... 6:00 AM–11:00 PM
 Saturday 7:00 AM–11:00 PM
 Sunday..... 11:00 AM–7:00 PM

SuperShuttle

The BWI SuperShuttle will transport you from BWI Airport to Baltimore's Inner Harbor Hotel District for approximately \$13 per person one way (prices subject to change). Upon arrival at the airport, proceed to one of the two ticket counters, located near baggage claims #1 and #10 on the lower level. Ticket counters are open between the hours of 6:00 AM and 2:00 AM. When counters are closed, please call (888) 826-2700 for information or to arrange service. For reservations and more information, call 1-800-BLUE VAN (258-3826) or visit www.supershuttle.com.

The Airport Shuttle

From the airport, your flight is tracked in real time, and you go directly to the vehicle from baggage claim. In other words, you are not put in a waiting area at the airport to be put on a multi line run through multiple hotels. From your hotel, you are given a pick-up time based on your flight departure time. Available from 4:00 AM to Midnight. The Airport Shuttle picks up and drops off at BWI, Dulles and Reagan Airports.

Discount rates are available each way for SOT attendees.

Discount Rates:

BWI Airport: \$17
 Dulles Airport: \$90

Note: Advanced reservations are required. Reserve your ride through the transportation section of the SOT Annual Meeting Web site, or call (800) 776-0323 and say "My SOT profile number is 141154." Visit www.theairportshuttle.com for more information.



Recognition and Social Events

Awards Ceremony

Sunday, March 15, 5:15 PM–6:30 PM
Room 321
Baltimore Convention Center

Open to all attendees

Join us as SOT honors our prestigious award winners at the SOT Awards Ceremony (pages 24–25). Please refer to the Awards and Fellowships section of the SOT Web site for complete details about the awards and submitting nominations for the next year.

Welcoming Reception

Sunday, March 15, 6:30 PM–7:30 PM
Ballroom
Baltimore Convention Center

Continue the celebration by attending the Welcoming Reception following the Awards Ceremony. The Welcoming Reception is a great opportunity to renew old friendships and to make new acquaintances. Please join the Society in this kick-off of the Annual Meeting.

25-Year (Or More) Member Reception

Sunday, March 15, 7:00 PM–8:00 PM
Room 324
Baltimore Convention Center

Have you been a member of the Society of Toxicology for 25 years (or more)? If so, please join your colleagues in celebration and recognition of the scientists who established the Society.

Student/Postdoctoral Fellow Mixer

Sunday, March 15, 7:30 PM–8:30 PM
Camden Lobby
Baltimore Convention Center

Ticket Required

All students and postdoctoral fellows are invited to attend this reception. Refreshments will be provided by SOT and sponsors. A cash bar will also be available. Ticket and Meeting Badge are required.

In Vitro Toxicology Lecture and Luncheon for Students

Monday, March 16, 12:15 PM–1:20 PM
Room 339
Baltimore Convention Center

Ticket Required

Lecturer: TBA
Title: TBA

Graduate students, undergraduates, post-doctoral scholars, and recipients of Colgate-Palmolive awards are among the guests at the *In Vitro* Lecture and Luncheon. The goal of the *In Vitro* Lecture series is to feature important research using *in vitro* and alternative techniques to study basic mechanisms and to illustrate how these test methods benefit animal welfare by refining and reducing animal use. Students and post-docs can reserve a ticket for the luncheon with a \$5 deposit when they register for the SOT Annual Meeting.

Postdoctoral Assembly Luncheon

Tuesday, March 17, 12:00 NOON–1:15 PM
Room 339
Baltimore Convention Center

Ticket Required

Amidst scrambling to attend all of the events at the meeting, this will be time for postdocs to kick back and relax! All postdoctoral fellows are invited to a casual luncheon organized by the Postdoctoral Assembly (PDA). We will announce the recipients of the Best Postdoctoral Publication Awards and acknowledge the postdocs who received awards this year from Specialty Sections and Regional Chapters. The PDA Board members will present an overview of accomplishments and future directions for the PDA and will introduce the new board members for 2009–2010. There will be a drawing for prizes. Postdocs can reserve a ticket when registering for the Annual Meeting.

Regional Chapter Receptions

Monday, March 16 through Wednesday, March 18, Various Times

(Refer to the Annual Meeting Program for more details.)

Many of the SOT Regional Chapters meet during the SOT Annual Meeting. A list of Regional Chapter receptions will be listed in the *Program Event Calendar*.

Special Interest Group Receptions

Monday, March 16 through Wednesday, March 18, Various Times

(Refer to the Annual Meeting Program for more details.)

Each of the 6 Special Interest Groups will hold a meeting/reception during the 2009 SOT Annual Meeting at the Hilton Hotel or at a local venue. All current and prospective SOT Special Interest Group members are encouraged to attend. The Event Calendar in the *Program* will have a listing of locations and function times.

Specialty Section Receptions

Monday, March 16 through Wednesday, March 18, Various Times

(Refer to the Annual Meeting Program for more up-to-date details.)

Each of the 22 SOT Specialty Sections will hold either a luncheon or early evening meeting/reception during the 2009 SOT Annual Meeting. All current and prospective SOT Specialty Section members are encouraged to attend. Dates for the Specialty Section Receptions are listed on the following page.

Recognition and Social Events

Specialty Section Receptions

Event	Date	Time
Biological Modeling Specialty Section Meeting Reception	Wednesday, March 19	6:00 PM–7:30 PM
Carcinogenesis Specialty Section Meeting Reception	Tuesday, March 18	6:00 PM–7:30 PM
Comparative and Veterinary Specialty Section Meeting Luncheon	Monday, March 17	12:00 NOON–1:30 PM
Dermal Toxicology Specialty Section Meeting Reception	Tuesday, March 18	6:00 PM–7:30 PM
Drug Discovery Toxicology Specialty Section Meeting Reception	Wednesday, March 19	6:00 PM–7:30 PM
Ethical, Legal, and Social Issues Specialty Section Meeting Reception	Tuesday, March 18	6:00 PM–7:30 PM
Food Safety Specialty Section Meeting Reception	Tuesday, March 18	6:00 PM–7:30 PM
Immunotoxicology Specialty Section Meeting Reception	Tuesday, March 18	6:00 PM–7:30 PM
<i>In Vitro</i> and Alternative Methods Specialty Section Meeting Luncheon	Tuesday, March 18	12:00 NOON–1:30 PM
Inhalation and Respiratory Specialty Section Meeting Reception	Wednesday, March 19	6:00 PM–7:30 PM
Mechanisms Specialty Section Meeting Reception	Tuesday, March 18	6:00 PM–7:30 PM
Metals Specialty Section Meeting Reception	Wednesday, March 19	6:00 PM–7:30 PM
Mixtures Specialty Section Meeting Reception	Monday, March 17	6:00 PM–7:30 PM
Molecular Biology Specialty Section Meeting Reception	Monday, March 17	6:00 PM–7:30 PM
Nanotoxicology Specialty Section Meeting Reception	Wednesday, March 19	6:00 PM–7:30 PM
Neurotoxicology Specialty Section Meeting Reception	Wednesday, March 19	6:00 PM–7:30 PM
Occupational and Public Health Specialty Section Meeting Luncheon	Wednesday, March 19	12:00 NOON–1:30 PM
Ocular Toxicology Specialty Section Meeting Reception	Tuesday, March 18	6:00 PM–7:30 PM
Regulatory and Safety Evaluation Specialty Section Meeting Reception	Monday, March 17	6:00 PM–7:30 PM
Reproductive and Developmental Toxicology Specialty Section Meeting Reception	Tuesday, March 18	6:00 PM–7:30 PM
Risk Assessment Specialty Section Meeting Reception	Monday, March 17	6:00 PM–7:30 PM
Toxicologic and Exploratory Pathology Specialty Section Meeting Luncheon	Tuesday, March 18	12:00 NOON–1:30 PM

Awards Ceremony

Sunday, March 15, 2009

The Society of Toxicology will present these Awards 5:15 PM–6:30 PM at the Baltimore Convention Center

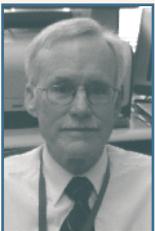
Society of Toxicology Awards



Achievement Award
Russell S. Thomas
*The Hamner Institutes for
Health Sciences*



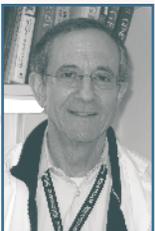
*Enhancement of Animal
Welfare Award*
Sally Robinson
AstraZeneca UK



Arnold J. Lehman Award
Michael Bolger
U.S. FDA NCTR



Founders Award
Roger O. McClellan
*Toxicology and Human Health
Risk Analysis*



*Distinguished Toxicology
Scholar Award*
Lance R. Pohl
NIH



*Leading Edge in Basic
Science Award*
John Katzenellenbogen
University of Illinois



Education Award
Janice E. Chambers
Mississippi State University



Merit Award
Gary M. Williams
New York Medical College



Education Award
Serrine S. Lau
University of Arizona



Translational Impact Award
Thomas W. Kensler
*Johns Hopkins Bloomberg School of
Public Health*



SOT Sponsored Awards

Congratulations!



Board of Publications Best Paper in Toxicological Sciences Award

The PPAR α -Humanized Mouse: A Model to Investigate Species Differences in Liver Toxicity Mediated by PPAR α

(ToxSci, January 2008, Vol. 101, No. 1: 132–139)

Qian Yang, Tomokazu Nagano, Yatrik Shah, Connie Cheung, Shinji Ito, and Frank J. Gonzalez

SOT/AstraZeneca IUTOX Fellowship for individuals from developing countries and Pfizer Undergraduate Student Travel Awards selected in December 2008 will be honored at the Awards Ceremony. Best Postdoctoral Publication Awards recipients will be recognized at the Postdoctoral Assembly Luncheon.

Sponsored Awards



AstraZeneca Traveling Lectureship Award

*Kim Boekelheide
Brown University*

Colgate-Palmolive Awards for Student Research Training in Alternative Methods

*Jennifer Cole
Texas Tech University*

*Colgate-Palmolive Grants for Alternative Research
(To be announced in the final Program)*

Regional Chapters, Special Interest Groups, and Specialty Sections offer awards throughout the year—Check the Web site for full details at www.toxicology.org.

The Colgate-Palmolive Postdoctoral Fellowship Award in In Vitro Toxicology and The Novartis Graduate Student Fellowship Award recipients selected in March 2009 will be honored at the Awards Ceremony.

Distinguished Toxicology Scholar Award Lecture: Role of Reactive Metabolites, Protein Adducts, Immune System, and Other Susceptibility Factors in Drug-Induced Liver Injury

Tuesday, March 17, 12:30 PM–1:20 PM

Lecturer: Lance R. Pohl, National Institutes of Health, Bethesda, MD

Leading Edge in Basic Science Award Lecture: The Structural Pervasiveness of Estrogen Activity—Benefits and Risks from the Eclectic Nature of Ligand Binding by the Estrogen Receptor

Monday, March 16, 12:30 PM–1:20 PM

Lecturer: John Katzenellenbogen, University of Illinois, Urbana, IL

Merit Award Lecture: Chemical Hepatocarcinogenesis—Mechanisms, Pathogenesis, and Thresholds

Wednesday, March 18, 12:30 PM–1:20 PM

Lecturer: Gary M. Williams, New York Medical College, Valhalla, NY

Translational Impact Award Lecture: Keap1 One Eye on the Target—Translating Molecular Toxicology into Cancer Prevention

Tuesday, March 17, 8:00 AM–8:50 AM

Lecturer: Thomas W. Kensler, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

SOT | Society of Toxicology

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Thank You

48th Annual Meeting and ToxExpo™

Continuing Education

Continuing Education Courses

The Continuing Education Program offers a wide range of courses that cover state-of-the-art knowledge in toxicology, as well as new developments in toxicology and related disciplines. Courses can be applied toward certifying and licensing board requirements and may also be used for recertification with the American Board of Toxicology (ABT). Both basic and advanced course topics are offered. The basic courses are intended to provide a broad overview of an area or to assist individuals in learning new techniques or approaches. The advanced courses are intended for individuals with previous knowledge of the subject or already working in the field.

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

Sunrise (7:00 AM–7:45 AM)

Morning (8:15 AM–12:00 NOON)

Afternoon (1:15 PM–5:00 PM)

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

Topics in Ethics: Conflict of Interest—Real or Imagined?—PBDEs As a Case Study

SR01

CE SUNRISE

Chairperson(s): Steven G. Gilbert, Institute of Neurotoxicology and Neurological Disorders, Seattle, WA and Philip Wexler, National Library of Medicine, Bethesda, MD

Sponsor:

Ethical, Legal, and Social Issues Specialty Section

Endorsed by:

Education Committee

Regulatory and Safety Evaluation Specialty Section

Throughout their professional lives, most toxicologists will confront an array of issues beyond the strictly scientific ones they have trained for. These may range across topics such as animals in research, human subject research, investigational and reporting bias, and conflict of interest concerns. The interdisciplinary nature of toxicology, its sometimes tangled regulatory framework, and implications for public safety and health, make policy considerations perhaps more relevant than they are for other sciences. Toxicologists, therefore, need to be braced for an array of ethical, legal, and social challenges, and to learn how to sensibly address allegations of conflict of interest or bias while practicing their science. This course will examine, through a case study related to polybrominated diphenyl ethers (PBDEs), the consequences of alleging conflict of interest or bias. In August, 2007 the U.S. EPA dismissed Deborah Rice from its PBDE review panel in

compliance with a request from the American Chemistry Council, and expunged her comments from the official record. Dr. Rice had previously expressed her views about PBDE's dangers as part of work with the Maine government. The U.S. EPA's rationale was "the perception of a potential conflict of interest." This incident highlights the challenge of a scientist holding a scientifically credible opinion about an issue prior to review by an expert panel (on which he/she is serving) assigned to assess the same issue. Under what circumstance does a position become a conflict of interest or bias? The practical and ethical issues raised in staffing scientific review panels affect scientists and policy makers. Course time will be provided for a discussion of conflict of interest and an examination of related incidents. Students will be provided with a selected list of Web resources related to the ethical issues under discussion.

- **The Relevance of Ethics to Science and Toxicology**, Steven G. Gilbert, Institute of Neurotoxicology and Neurological Disorders, Seattle, WA
- **Case Study of PBDE Review and Allegations of Conflict of Interest**, Deborah C. Rice, Maine Center for Disease Control and Prevention, Augusta, ME
- **Audience Discussion with Panel**, Deborah Rice, Steven Gilbert, and Philip Wexler

INFLAMMATION AND DISEASE

Free Radicals for Toxicologists—From the Basics to Inflammation and Disease

AM02 (REPEATS AS PM08)

CE BASIC

Chairperson(s): Lin L. Mantell, St. Johns University, College of Pharmacy, Queens, NY/The Feinstein Institute for Medical Research, North Shore-Long Island Jewish Health System, Manhasset, NY and Judith T. Zelikoff, New York University School of Medicine, Tuxedo Park, NY

Sponsor:

Immunotoxicology Specialty Section

Endorsed by:

Inhalation and Respiratory Specialty Section

Occupational and Public Health Specialty Section

The production of reactive oxygen species/reactive nitrogen species (ROS/RNS) has long been recognized to not only serve as a biomarker for oxidative stress, but also significantly contribute to the pathogenesis of various inflammatory tissue injuries and diseases. The emphasis of this course will be placed on an in-depth, state-of-the-art review of the relationship among free radicals, immunologi-

Continuing Education

CE

cally-related inflammatory responses and environmental exposures and diseases. At the conclusion of this session, the participants will be able to describe the basic concepts of free radicals as they relate to immune-mediated events, better understand the production of reactive oxygen/nitrogen species (ROS/RNS) from both inflammatory responses and exposure to environmental toxicants, and realize the impact of ROS/RNS on normal physiological responses and pathological processes.

- **Overview**, Judith T. Zelikoff, New York University School of Medicine, Tuxedo, NY
- **The Basics of Free Radicals**, Garry Buettner, University of Iowa, Iowa City, IA and Society for Free Radical Biology and Medicine
- **Reactive Metabolites of Oxygen and Nitrogen in Inflammation: The Good and the Bad**, Matthew Grisham, Louisiana State University Health Sciences Center, Shreveport, LA
- **Metal-Induced Oxidants and Anti-Oxidants: Agents That Regulate and Dysregulate Immune Cell Activities**, Michael A. Lynes, University of Connecticut, Storrs, CT
- **Free Radical Generation from Exposure to Particulate Air Pollutants and the Inflammatory Response**, Andy Ghio, U.S. EPA, Chapel Hill, NC
- **Summary**, Lin L. Mantell, St. Johns University, College of Pharmacy, Queens, NY/The Feinstein Institute for Medical Research, North Shore-Long Island Jewish Health System, Manhasset, NY

Characterizing Modes-of-Action and Their Relevance in Assessing Human Health Risks

AM03

CE BASIC

Chairperson(s): Stephen S. Olin, ILSI Research Foundation, Washington, DC and Samuel M. Cohen, University of Nebraska Medical Center, Omaha, NE

Sponsor:

Regulatory and Safety Evaluation Specialty Section

Endorsed by:

Carcinogenesis Specialty Section
Risk Assessment Specialty Section

Determining the mode(s)-of-action of a toxicant is the goal of many toxicology studies, and these data are often used in risk assessment. This course will present a systematic approach to characterizing the mode(s)-of-action (MOA) of toxicants and will lead participants through the application of a framework for evaluating the relevance of an animal mode-of-action in assessing human risk. A

brief introduction to the history and significance for risk assessment of MOA/human relevance analysis will lay the foundation for this course, with the first presentation providing the basic concepts involved in application of the MOA/human relevance framework. Subsequent presentations will demonstrate the application of the framework through selected case studies with both cancer and non-cancer endpoints. Case studies will examine issues such as multiple endpoints with shared or different MOAs, the extension of the framework to dose-response analysis, and the effect of lifestage on the analysis. The objective of the case studies is to show clearly how the framework analysis is done, to illustrate the importance of a systematic evaluation of the available data, and to provide course participants with the tools to begin applying the MOA/human relevance framework in their own work.

- **Introduction**, Stephen S. Olin, ILSI Research Foundation, Washington, DC
- **The Development and Significance of Mode-of-Action/Human Relevance Analysis**, Samuel M. Cohen, University of Nebraska Medical Center, Omaha, NE
- **Framework for Characterizing Modes-of-Action in Animals and Humans**, Alan Boobis, Imperial College, London, United Kingdom
- **A Mode-of-Action/Human Relevance Analysis for Thyroid Disruption and Its Relationship to Cancer and Neurodevelopmental Effects**, Kevin M. Crofton, U.S. EPA, Research Triangle Park, NC
- **Cytotoxicity, Carcinogenicity, and Dose-Response and the Mode-of-Action/Human Relevance Framework**, M. E. (Bette) Meek, University of Ottawa, Ottawa, Ontario, Canada

Evaluation of Toxicity to Male and Female Reproductive Systems: Biology, Study Design, and Data Interpretation

AM04

CE BASIC

Chairperson(s): Kok Wah Hew, Takeda Global Research & Development Center, Inc., Lake Forest, IL and Barry S. McIntyre, Schering-Plough Research Institute, Summit, NJ

Sponsor:

**Reproductive and Developmental Toxicology
Specialty Section**

Endorsed by:

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

The objectives of this course are to provide the basic tools for toxicologists who desire a better understanding of how to assess toxicant-related effects on animal reproduction and the subsequent potential risk(s) to human reproduction. The anticipated audience includes toxicologists who work in regulated product development (e.g., pharmaceutical, chemical, and pesticide industries), as well as scientists who may be responsible for monitoring contracted reproductive toxicity studies, so that they can understand the subject sufficiently to work with study directors (i.e., study design and interpretation of study results). Reproductive toxicity studies assess multiple interrelated endpoints in the male and female reproductive systems. In order to properly design, conduct, and interpret these studies, a broad knowledge of male and female reproductive organ development, anatomy, physiology, and endocrinology is required. Using this as a starting point, the overall designs of reproductive toxicity studies for regulatory submissions, and subsequent application of these data to assess potential risk in humans will be discussed. The first and second presentations will provide an overview of the anatomy and physiology of the male and female reproductive systems, respectively, as well as endocrine regulation of these systems. The third talk will discuss the study designs to evaluate toxicity to male and female reproductive systems based on current regulatory guidelines. The course will conclude with case studies of reproductive toxicity data, subsequent interpretation, and how these results are being used to assess potential risks to human reproduction. In summary, upon completion of this course, the attendee will have an appreciation for the key information required for the design of reproductive toxicity studies and interpretation of reproductive toxicity data and will be able to provide guidance for risk assessment in reproductive toxicity evaluation.

- **Introduction**, Kok Wah Hew, Takeda Global Research & Development Center, Inc., Lake Forest, IL

- **Male Reproductive System: Anatomy, Physiology, and Endocrine Regulation**, Kim Boekelheide, Brown University, Providence, RI
- **Female Reproductive System: Anatomy, Physiology, and Endocrine Regulation**, Anthony R. Scialli, Sciences International Inc., Alexandria, VA
- **Reproductive Toxicity Testing: Study Designs and Toxicity Endpoints**, Barry S. McIntyre, Schering-Plough Research Institute, Summit, NJ
- **Reproductive Toxicity Testing: Data Interpretation and Risk Assessment**, Donald G. Stump, WIL Research Laboratories, LLC, Ashland, OH

Immunology for Toxicologists

AM05

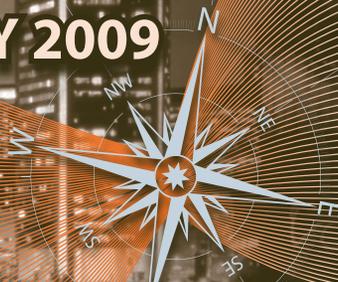
CE BASIC

Chairperson(s): Raymond Pieters, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, Netherlands and Ian Kimber, University of Manchester, Manchester, United Kingdom

Sponsor:

Immunotoxicology Specialty Section

The adaptive immune response that is found in mammals comprises a dedicated interacting system of tissues, cells and molecules that work in concert to provide specific immune responses and host resistance to pathogenic microorganisms and transformed cells. Specific immunity is supplemented by, and works in harmony with, the phylogenetically more ancient innate immune system. Immunotoxicology describes the study of adverse health effects that may result from the interaction of xenobiotics with one or more components of the immune system. Such health effects may take a variety of forms. These include frank immunotoxicity where there is a functional impairment of the immune system. The concern here is that compromised immune function may translate into an increased susceptibility to infectious and/or malignant disease. A second potential consequence of the interaction of chemicals or proteins with the immune system is allergy: defined as the adverse health effects that may arise from the stimulation of a specific immune response. Allergic disease may take one of several forms, those of greatest significance for toxicologists being skin sensitization and allergic contact dermatitis, allergic sensitization of the respiratory tract, food allergy, and idiosyncratic drug reactions. Finally, xenobiotics have also been implicated in the induction or exacerbation of autoimmune responses and autoimmune disease. This basic grade course will provide a firm grounding in fundamental and clinical aspects of immunology, and will describe the basic elements of immunotoxicity, allergy and autoimmunity in view of the interaction between innate and adaptive immunity.



Continuing Education

CE

The objective is to deliver an accessible guide to the immune system and immunotoxicology for general toxicologists.

- **An Introduction to Immunology: Fundamental and Clinical Aspects**, Ian Kimber, University of Manchester, Manchester, United Kingdom
- **Elementary Immunotoxicology**, Robert House, Dynport Vaccine Company-LLC, Frederick, MD
- **Allergy and Allergic Disease**, MaryJane Selgrade, U.S. EPA, Research Triangle Park, NC
- **Autoimmunity and Autoimmune Disease**, Raymond Pieters, IRAS, Utrecht University, Utrecht, Netherlands

Principles and Applications of Toxicokinetics

AM06

CE BASIC

Chairperson(s): Michael J. Bartels, Dow Chemical, Midland, MI and Charles Timchalk, Batelle Pacific Northwest Laboratories, Richland, WA

Sponsor:

Biological Modeling Specialty Section

Endorsed by:

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

Toxicokinetic (TK) data play an important role in chemical risk assessments. Chemical risk assessments are increasingly incorporating consideration of the mode of action (MOA) of the chemically-induced toxicity. Increasing reliance on MOA in such evaluations in turn requires increasingly detailed information regarding the active chemical moiety (parent compound or metabolite) and relevant target tissue dose metrics. This course will begin by providing background on the need for and role of toxicokinetic data in risk assessments. This presentation will include a discussion of the interaction between evaluation of MOA and toxicokinetic data and the role of such data in both interspecies and high to low dose extrapolations in risk assessment. We will go on to describe basic principles of pharmacokinetics from both the classical and physiologically-based approaches. The presentation will provide the conceptual and mathematical basis for developing a better understanding of pharmacokinetics and how pharmacokinetic analyses are conducted. In addition, we will address elements of the design of toxicokinetic experiments, conducted as part of subchronic/chronic toxicity studies. This presentation will include standardized approaches for TK sampling and data analysis. Finally, the presenters will provide examples of the integration of toxicokinetic data into current risk assessments, including the incorporation of

human biomonitoring data in the evaluation of chemical exposures and risks.

- **Introduction and Objectives**, Michael J. Bartels, Dow Chemical, Midland, MI
- **Why Is an Understanding of Toxicokinetics Important?** James S. Bus, Dow Chemical, Midland, MI
- **Basic PK Principles**, Sean M. Hays, Summit Toxicology, Lyons, CO
- **Toxicokinetic Study Design**, Shakil A. Saghir, Dow Chemical, Midland, MI
- **Application of Quantitative Toxicokinetic Data in Health Risk Assessment**, John C. Lipscomb, U.S. EPA, Cincinnati, OH

BIOMARKERS

Translation of Safety Biomarkers in Drug Discovery and Development

AM07

CE ADVANCED

Chairperson(s): Kay Criswell, Pfizer Global Research and Development, Groton, CT and Jennifer Colangelo, Pfizer, Inc., Groton, CT

Sponsor:

Regulatory and Safety Evaluation Specialty Section

Endorsed by:

**Comparative and Veterinary Specialty Section
Drug Discovery Toxicology Specialty Section**

Several major areas prove problematic in translating animal data/biomarkers to humans. This course focuses on translational issues in hematology, clinical chemistry, protein assays and peptide assays. It concludes with a risk assessment presentation summarizing the realities of implementing the overall process in defining human relevance of safety and efficacy from preclinical data. Preclinical data gathered in laboratory animals is required by regulatory agencies to determine safety in humans prior to marketing of new products. Species-specific differences in routine and esoteric serum biomarkers make the relevance of findings in animals difficult to interpret. Knowledge in this area is beneficial to the safe conduct of clinical trials and the inclusion of relevant biomarkers as effective safety and efficacy endpoints during new product development. Research scientists, industry scientists, laboratory personnel, and pathologists interested in biomarker development, translation, execution and applications from preclinical through clinical trials may be interested. The difference between data obtained in preclinical and clinical circumstances will be covered in this course.

Therefore, it may be of interest to anyone in a preclinical research setting through those engaged in clinical trials, as well as those evaluating the safety of industrial chemicals. Course objectives: identification of potential relevance or non-relevance of animal-based hematologic and clinical chemistry biomarkers to humans, identification of methods of overcoming species-specific problems in protein and peptides biomarkers, and understanding human relevance of animal data and the impact of biomarker utilization on speed and decision-making.

- **Translation of Safety Biomarkers: Introduction**, Kay A. Criswell, Pfizer Global Research & Development, Groton, CT
- **Does Preclinical Hematology Predict Human Safety?** Nancy Everds, Amgen Pharmaceutical, Seattle, WA
- **Translation of Clinical Chemistry Biomarkers: Pitfalls and Solutions**, Denise Bounous, Bristol-Myers Squibb, Princeton, NJ
- **Overcoming the Problems of Species: Specific Proteins and Peptides in Assay Development**, Jennifer Colangelo, Pfizer Global Research & Development, Groton, CT
- **Connecting the Dots to Define Human Relevance to Preclinical Data: Implementing Techniques to Enhance Speed of Delivery and Decision Making**, Michael R. Bleavins, Michigan Technology & Research Institute, Ann Arbor, MI

cally-related inflammatory responses and environmental exposures and diseases. At the conclusion of this session, the participants will be able to describe the basic concepts of free radicals as they relate to immune-mediated events, better understand the production of reactive oxygen/nitrogen species (ROS/RNS) from both inflammatory responses and exposure to environmental toxicants, and realize the impact of ROS/RNS on normal physiological responses and pathological processes.

- **Overview**, Judith T. Zelikoff, New York University School of Medicine, Tuxedo, NY
- **The Basics of Free Radicals**, Garry Buettner, University of Iowa, Iowa City, IA and Society for Free Radical Biology and Medicine
- **Reactive Metabolites of Oxygen and Nitrogen in Inflammation: The Good and the Bad**, Matthew Grisham, Louisiana State University Health Sciences Center, Shreveport, LA
- **Metal-Induced Oxidants and Anti-Oxidants: Agents That Regulate and Dysregulate Immune Cell Activities**, Michael A. Lynes, University of Connecticut, Storrs, CT
- **Free Radical Generation from Exposure to Particulate Air Pollutants and the Inflammatory Response**, Andy Ghio, U.S. EPA, Chapel Hill, NC
- **Summary**, Lin L. Mantell, St. Johns University, College of Pharmacy, Queens, NY/The Feinstein Institute for Medical Research, North Shore-Long Island Jewish Health System, Manhasset, NY

INFLAMMATION AND DISEASE

Free Radicals for Toxicologists—From the Basics to Inflammation and Disease

PM08 (REPEAT OF AM02)

CE BASIC

Chairperson(s): Lin L. Mantell, St. Johns University, College of Pharmacy, Queens, NY/The Feinstein Institute for Medical Research, North Shore-Long Island Jewish Health System, Manhasset, NY and Judith T. Zelikoff, New York University School of Medicine, Tuxedo Park, NY

Sponsor:

Immunotoxicology Specialty Section

Endorsed by:

Inhalation and Respiratory Specialty Section
Occupational and Public Health Specialty Section

The production of reactive oxygen species/reactive nitrogen species (ROS/RNS) has long been recognized to not only serve as a biomarker for oxidative stress, but also significantly contribute to the pathogenesis of various inflammatory tissue injuries and diseases. The emphasis of this course will be placed on an in-depth, state of the art review of the relationship among free radicals, immunologi-

Characterizing Variability and Uncertainty with Physiologically-Based Pharmacokinetic Models

PM09

CE BASIC

Chairperson(s): Hugh A. Barton, U.S. EPA, Research Triangle Park, NC and Gunnar Johanson, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden

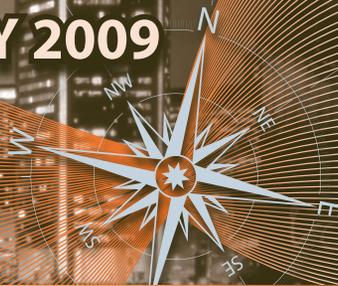
Sponsor:

Biological Modeling Specialty Section

Endorsed by:

Risk Assessment Specialty Section

As pharmacokinetic (PK) models are increasingly applied in risk and safety assessments, it is critical to improve the characterization of variability and uncertainty. Variability describes real differences among individuals arising from external exposure pathways, diet, health status, genetics, and other factors that contribute to differences in internal exposures or tissue dosimetry. Absent perfect knowledge, there are uncertainties arising from a range of sources



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including experimental error, that can impact confidence in model predictions. Physiologically-based pharmacokinetic (PBPK) models provide a biologically motivated description of processes influencing the absorption, distribution, metabolism, and excretion of endogenous compounds or xenobiotics. PBPK models rely on a wide range of *in vitro* and *in vivo* data to estimate parameter values and demonstrate the predictive capabilities of the models. This course will describe characterization of variability and uncertainty using PBPK models from a number of perspectives. The range of PBPK model structures and their applications in risk and safety assessment will be presented. How to approach characterizing uncertainty in the presence of variability will be described. Data from humans can be analyzed using PBPK models to characterize PK variability. Finally, linking variations in external exposure pathways with PK variability provides methods to characterize human dosimetry for use in risk assessments or interpretation of biomonitoring data.

- **Pharmacokinetic Models—What Are They and What Are They Used For?** Hugh A. Barton, U.S. EPA, Research Triangle Park, NC
- **Relating Data and Models to Characterize Parameter and Prediction Uncertainty**, R. Woodrow Setzer, U.S. EPA, Research Triangle Park, NC
- **Use of Human Experimental Data in PBPK Modeling of Population Variability**, Gunnar Johanson, Karolinska Institute, Stockholm, Sweden
- **Variability in Exposure and Internal Dosimetry Assessed with PBPK Models**, Cecilia Tan, The Hamner Institutes for Health Sciences, Research Triangle Park, NC

Current Approaches in Mixture Risk Assessment

PM10

CE BASIC

Chairperson(s): Moiz Mumtaz, CDC Agency for Toxic Substances & Disease Registry, Atlanta, GA and Christopher J. Borgert, Applied Pharmacology and Toxicology Inc., Gainesville, FL

Sponsor:

Mixtures Specialty Section

Endorsed by:

Inhalation and Respiratory Specialty Section

Occupational and Public Health Specialty Section

Risk Assessment Specialty Section

Human exposure to combinations of chemicals and drugs is an everyday reality of life. There is tremendous interest in scientific and regulatory tools for evaluating the joint toxic action of chemicals and drugs in mixtures. This course will provide an overview of the methods and tools reflective of the current state of knowledge in the area of mixture risk assessment, as well as illustrative, real-life examples of their application to risk assessment. We will begin with an introduction to the various approaches to mixture risk assessment and illustrate the use of these methods to assess risks associated with human exposure to contaminants in selected hazardous waste sites. The course will then describe the process of cumulative risk assessment of pesticides, highlighting the use of pharmacokinetic, pharmacodynamic and relative potency factors in the process. The development and application of relative potency factor approach to evaluate safety of mixtures of drugs will also be addressed. Finally, we will discuss the current approaches and tools for assessing the role of interactions in mixture risk assessment, with particular emphasis on the use of physiologically-based pharmacokinetic (PBPK) models. Course participants will be provided with data evaluation strategies, data sets from real world examples, exercise results, and discussion of uncertainty pertaining to the application of various mixtures procedures. The intended audience for this course will be experimentalists, modelers, epidemiologists and risk assessors interested in the assessment of health risks associated with human exposure to chemical and/or drug mixtures.

- **Assessing Risk from Chemical Mixtures at Hazardous Waste Sites**, Moiz Mumtaz, ATSDR, Atlanta, GA
- **Cumulative Risk Assessment of Pesticides**, Anna B. Lowit, U.S. EPA, Washington, DC
- **Relative Potency Factors in Drug Safety Assessment**, Christopher J. Borgert, Applied Pharmacology and Toxicology Inc., Gainesville, FL
- **Assessing the Role of Interactions in the Risk Assessment of Chemical Mixtures**, Kannan Krishnan, Université de Montréal, Montréal, Québec, Canada

How Similar Is Similar and How Relevant Is Relevant? Considerations in the Design of a Predictive Development Program for Biotherapeutics

PM11

CE BASIC

Chairperson(s): Laura Andrews, Genzyme, Framingham, MA and Leigh Ann Burns Naas, Pfizer Global Research and Development, San Diego, CA

Sponsor:

Comparative and Veterinary Specialty Section

Endorsed by:

Regulatory and Safety Evaluation Specialty Section
Toxicologic and Exploratory Pathology Specialty Section

Preclinical development programs that are designed to support the safe clinical use of biopharmaceuticals have considerations that are very different from programs designed to support the development of small molecule drugs. In particular, with more and more targeted therapeutics being developed a traditional development program is becoming more and more difficult. While the ICH S6 guidance continues to drive the program decisions more often than not a different approach is warranted due to species specificity and paucity of relevant animal models. To design a predictive non clinical program that will support not only first in human dosing but also eventual approval of the therapeutic is becoming more complex. Assuring safety in humans is the first and foremost task of a well designed program but assuring safety and application to specific patient populations is also essential to the targeted therapeutic products. Topics to be addressed in this course will include general pathology and physiology issues between species that might contribute to species selection/interpretation, utility of tissue cross reactivity to determine relevant species, considerations into the development of a homologous protein (from bench to beast), development and characterization of animal models as relevant species (including KO animals and models of disease), and additionally what to do if nothing is “relevant.” The course attendee will learn key concepts in the considerations for designing a predictive program for a biotherapeutic product.

- **Introduction to Course and Objectives**, Leigh Ann Burns Naas, Pfizer Global Research and Development, San Diego, CA
- **Understanding Comparative Physiology and Pharmacology**, Frank Geoly, Pfizer, Groton, CT
- **How Similar Is Similar: Understanding the Impact of Homologous or Surrogate Protein Development**, Jeanine Bussiere, Amgen, Thousand Oaks, CA

- **How Relevant Is Relevant: Understanding the Utility and Impact of Using Transgenic Models and Animal Models of Disease**, Joy Cavagnaro, Access BIO, Boyce, VA
- **Intergration of Concepts into Roadmaps for Development of Novel Biotherapeutics**, Laura Andrews, Genzyme, Framingham, MA

New Frontier in Metal Toxicology: Genetic Susceptibility, Early Diagnosis, and Related Biological Indices

PM12

CE ADVANCED

Chairperson(s): Wei Zheng, School of Health Sciences, Purdue University, West Lafayette, IN and Michael P. Waalkes, NCI at NIEHS, Research Triangle Park, NC

Sponsor:

Metals Specialty Section

Endorsed by:

Mechanisms Specialty Section
Neurotoxicology Specialty Section
Occupational and Public Health Specialty Section

Physical and chemical properties of many toxic metals are common in their tendency to donate electrons, their resistance to biotransformation and their similarity in physical sizes and electrical charges. Yet human responses to metal insults are not uniform such that metal-caused diseases may manifest in a particular population and spare in others. Thus, the inherited individual susceptibility must be taken into account when developing strategies for risk assessment or treatment becomes necessary. In many clinical cases, the signs and symptoms of metal intoxication are subtle and imperceptible. Because of these, clinically well defined metal diseases, such as lead-induced learning deficit or manganese-caused parkinsonism, are usually diagnosed too late for an effective therapeutic intervention. Thus, a reliable biomarker of a particular type of metal diseases, developed either based on injuries in biochemical and physiological functions or alterations in cellular signal pathways, bears a quintessential importance in metal toxicological research. This advanced course is intended to address the biological indices of metal toxicities from the angle of individual genetic susceptibility for early diagnosis. The course will provide an overview on metal-related biomarkers established from animal and human studies and the application of these biomarkers, such as lead, in risk assessment. Recent advancement in understanding the genetic susceptibility that contributes to metal-induced toxicities will then be discussed. Manganese will be used as an example to explore novel ideas to use integrated biomarkers combining exposure indices with biological outcomes. Finally, the course will illustrate an innovative way to



Continuing Education

CE

explore metal biomarkers by targeting at metal interaction with the cellular signal pathways. The course will survey these new frontiers in metal toxicological research by providing details specific to 'hot' metals, such as lead, manganese, arsenic and mercury. The intended audience for this course are those who desire an advanced introduction to mechanisms of metal toxicities, an advanced knowledge on metal-gene interaction and risk assessment, and an advanced technical approach in developing a useful biomarker for metal intoxication. The course will be of interest to others engaged in wider aspects of metal toxicology, neurotoxicology, carcinogenesis, risk assessment, and occupational health.

- **Introduction: Principles of Metal Toxicology**, Curtis D. Klaassen, University of Kansas, Kansas City, KS
- **Biomarkers of Metal Intoxication: How Predictive Are Exposures of Adverse Effects?** Deborah A. Cory-Slechta, University of Rochester, Rochester, NY
- **Genetic Susceptibility Underlying Metal-Induced Toxicities**, Jie Liu and Michael P. Waalkes, NCI at NIEHS, Research Triangle Park, NC
- **A Single Parameter Combining Multiple Bio-Indices As a New Approach to Discover Biomarkers of Metal Toxicities: A Case Study with Manganese**, Wei Zheng, Purdue University, West Lafayette, IN
- **Cell Signal Pathways Targeted by Toxic Metals**, Michael J. McCabe, University of Rochester, Rochester, NY

assessment of stress in the regulatory environment. Understanding the pathophysiology of major systems impacted by stress and the potential range of responses is key to assessing the contribution of stress to study findings. Effects of stress in animals and humans, including potential biomarkers, will be discussed. Key references for the understanding of stress-related findings will be provided.

- **Introduction**, Katie Sprugel, Amgen, Seattle, WA
- **Neurohormonal Aspects of Stress**, David Dorman, North Carolina State University, Raleigh, NC
- **Stress and Clinical Pathology**, Nancy Everds, Amgen, Seattle, WA
- **Stress and Endocrine Organs**, George Foley, Schering-Plough, Summit, NJ
- **Stress and the Immune System**, Paul Snyder, Purdue University, West Lafayette, IN

Stress As a Confounding Factor in Toxicology Studies

PM13

CE BASIC

Chairperson(s): Katie Sprugel, Amgen, Seattle, WA and Nancy Everds, Amgen, Seattle, WA

Sponsor:

Toxicologic and Exploratory Pathology Specialty Section

Endorsed by:

Immunotoxicology Specialty Section

Regulatory and Safety Evaluation Specialty Section

Women in Toxicology Special Interest Group

Stress can confound the interpretation of toxicity studies. The biology of stress includes complex interrelationships between neurologic and endocrine pathways. Stressors can have effects on in-life, clinical pathology, endocrine, and immune system parameters. Effects on any of these systems may be observed during a toxicity study. The challenge in toxicology is to differentiate between primary test article-related changes and secondary changes related to stress. This differentiation is fundamental to the

Plenary Opening Lecture: Signal Transduction Pathways Used by Therapeutic Agents and Drugs of Abuse



Monday, March 16, 8:00 AM–9:00 AM

Lecturer: *Nobel Laureate Paul Greengard, Vincent Astor Professor, The Rockefeller University, New York, NY*

Nerve cells communicate with each other through two distinct mechanisms referred to as fast and slow synaptic transmission. A number of components of the two signal transduction pathways have been identified. Fast synaptic transmission occurs *via* activation by a neurotransmitter of a ligand-gated ion channel. In contrast, slow synaptic transmission occurs *via* a signal transduction cascade that can be remarkably complex and that usually involves second messengers and/or protein phosphorylation/dephosphorylation reactions. A growing body of knowledge concerning slow signal transduction pathways has been utilized to elucidate the mechanism of action of therapeutic agents used for the treatment of schizophrenia, Parkinsonism, and depression, as well as of drugs of abuse, such as caffeine, cannabis, amphetamine, PCP, and LSD.

Dr. Paul Greengard is the Vincent Astor Professor of Molecular and Cellular Neuroscience at The Rockefeller University and Director of The Fisher Center for Alzheimer's Research. Greengard received his Ph.D. from Johns Hopkins in 1953. He spent five years in England receiving advanced training at the University of London, at Cambridge University and at the National Institute of Medical Research. Upon his return to the United States, Greengard worked as Director of the Department of Biochemistry at Geigy (now Novartis) Research Laboratories, in Ardsley, New York for eight years. In 1967, he left the pharmaceutical industry to return to academia. From 1968 to 1983 Greengard served as Professor of Pharmacology and Psychiatry at Yale University, at which time he moved to his current position at The Rockefeller University.

Over the years, Greengard's achievements have earned him many distinguished awards including the Metropolitan Life Foundation Award for Medical Research, The Charles A. Dana Award for Pioneering Achievements in Health, the Ralph W. Gerard Prize in Neuroscience from the Society for Neuroscience, The National Academy of Sciences Award in the Neurosciences, the 3M Life Sciences Award of the Federation of American Societies for Experimental Biology. In the year 2000, Greengard was awarded the Nobel Prize in Physiology or Medicine for his discoveries concerning signal transduction in the nervous system.

He is an Honorary Member of the National Academies of Science in Sweden, Norway, and Serbia and has been the recipient of many honorary degrees. He is a member of the National Academy of Sciences and of the Institute of Medicine of the National Academies.

Leading Edge in Basic Science Award Lecture: The Structural Pervasiveness of Estrogen Activity—Benefits and Risks from the Eclectic Nature of Ligand Binding by the Estrogen Receptor

Monday, March 16, 12:30 PM–1:20 PM

Lecturer: *John Katzenellenbogen, University of Illinois, Urbana, IL*

Estrogens have diverse actions in both reproductive and nonreproductive tissues, and compounds of remarkably diverse structure sources can display estrogenic activity. These structures can be either steroidal or nonsteroidal but are typically phenolic. Estrogens act through estrogen receptors (ERs), ligand-modulated transcription factors that regulate hundreds of genes. When estrogens bind to ERs, they stabilize specific conformations that reflect ligand size and shape, and the rigidified surface features of these complexes serve as docking sites for coregulators that alter the pattern of gene transcription in a cell- and gene-specific manner. Guided by X-ray crystallography, we developed modular, combinatorial approaches to prepare novel nonsteroidal estrogens having high selectivity for the ER subtypes, ER α or ER β , that are useful as pharmacological probes of receptor function. We have also diversified the three-dimensional structure of ER ligands, obtaining estrogens with unexpected biological selectivities of both fundamental and medical interest, and our estrogen-dendrimer conjugates can distinguish nuclear from extranuclear estrogen signaling. We have used estrogens labeled with fluorine-18 to image ER-positive breast tumors by positron emission tomography; this *in vivo* assessment of ER function is useful in predicting patient benefit from endocrine therapies. Our chemical, biochemical, and structural studies on the ERs and their ligands provide new insights into the broad functions of these receptors in biology and medicine. They also have assisted toxicologists by providing tools for distinguishing the specific receptors and mechanistic pathways through which some endocrine disruptor can act.



Featured Sessions

SOT/EUROTOX Debate

Monday, March 16, 4:30 PM–5:50 PM

Motion: Nanotoxicology—Much Ado About Nothing?

SOT Debater: Nigel Walker, NIEHS, Research Triangle Park, NC

EUROTOX Debater: Kai Savolainen, Finnish Institute of Occupational Health, Helsinki, Finland

Endorsed by:

Society of Toxicology (SOT)

European Societies of Toxicology (EUROTOX)

Translational Impact Award Lecture: Keap1 One Eye on the Target—Translating Molecular Toxicology into Cancer Prevention

Tuesday, March 17, 8:00 AM–8:50 AM

Lecturer: Thomas W. Kensler, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

The development of Nrf2 knockout mice provided the first key insights into the toxicological importance of this transcription factor's signaling pathway. As examples, Nrf2 knockout mice are more sensitive to acute hepatotoxic, pneumotoxic and neurotoxic challenges. In addition, chemical carcinogenesis is exacerbated in several target organs of knockout mice. Nrf2 regulates the expression of conjugating and antioxidative genes, as well as those affecting glutathione homeostasis, NADPH generation, solute transporters, and proteasome function. Collectively, these genes govern a broad-based adaptive response to environmental toxins and toxicants. Transcription of these genes is activated in response to oxidative and electrophilic stresses, leading to increased stability and nuclear accumulation of Nrf2. In some instances, cysteines on Keap1, a cytoplasmic tether for Nrf2, serve as sensors leading to pathway activation. Of great relevance to disease prevention, this pathway also can be induced by an expanding array of small molecule drugs and natural products including dithiolethiones, isothiocyanates and triterpenoids. These compounds are potent anticarcinogens in animal models and their efficacy is lost in Nrf2 knockout mice, highlighting the central importance of this pathway. Several of these inducers are currently being evaluated in clinical trials for cancer prevention in populations at high risk for environmental carcinogenesis.

Distinguished Toxicology Scholar Award Lecture: Role of Reactive Metabolites, Protein Adducts, Immune System, and Other Susceptibility Factors in Drug- Induced Liver Injury

Tuesday, March 17, 12:30 PM–1:20 PM

Lecturer: Lance R. Pohl, National Institutes of Health, Bethesda, MD

My research has been directed towards understanding the mechanisms of drug-induced liver injury (DILI). We developed chemical trapping, radiochemical, and stable isotope techniques for identifying reactive metabolites of chloroform, carbon tetrachloride, inhalation anesthetics, and other xenobiotics and provided evidence consistent with a mechanistic role in DILI for protein adducts of reactive metabolites. Then specific antibodies for detecting, purifying, identifying, and exploring the toxicologic consequences of specific protein adducts of hepatotoxic drugs were designed. This approach demonstrated that patients diagnosed with inhalation anesthetic-induced liver injury had serum antibodies that reacted with one or more purified endogenous liver proteins that had been the target of reactive trifluoroacetyl halide metabolites of inhalation anesthetics, thus the adaptive immune system may have a pathologic role in liver injury caused by inhalation anesthetics. Recently, we have uncovered risk factors unrelated to reactive metabolite formation that may have a role in determining the susceptibility of patients to DILI. Using a murine model of acetaminophen-induced liver injury (AILI) and several genetically deficient mouse strains, we discovered that endogenous interleukin (IL)-13, IL-10, and IL-4 were hepatoprotectants, whereas IL-6 was either a hepatoprotectant or a hepatoprototoxicant depending on its serum concentration. In contrast, endogenous macrophage-migration inhibitory factor, osteopontin, and NK and NKT cells enhanced AILI. In other studies, Kupffer cells protected against AILI, while endogenous glucocorticoids enhanced AILI. Both of these factors appeared to have a role in preventing drug-protein adducts released from injured hepatocytes from causing allergic reactions by inducing immunological tolerance. Comparisons of the proteomes and transcriptomes of mice that were susceptible or resistant to AILI led to the discovery of numerous other potential risk factors for DILI. Recent findings suggest that polymorphisms in genes encoding risk factors and/or their receptors may contribute to individual susceptibility. None of the research described here could have been done without the hard work and intellectual contributions made by my students, fellows, and colleagues and the continuous support of the Intramural Research Program of the NHLBI and NIH.

48th Annual Meeting and ToxExpo™

Featured Sessions

U.S. FDA Advisory Panel Appointments

Wednesday, March 18, 7:30 AM–8:50 AM

Chairperson(s): James A. Popp, Stratoxon, LLC., Lancaster, PA and Margaret A. Miller, U.S. FDA National Center for Toxicology Research, Rockville, MD

U.S. Food and Drug (FDA) Advisory Committees are panels of independent, outside experts who advise the agency on regulatory and research questions involving complex medical and scientific issues. FDA relies on Advisory Committees to ensure that FDA programs, products reviewed, and approvals are scientifically sound. A recent review of FDA Advisory Committee membership revealed that toxicologists are not routinely participating in these meetings. Toxicologists have a wealth of knowledge that could impact and improve agency decisions. Recognizing the need to include several disciplines in its decision-making, FDA is working to strengthen the Advisory Committee process by expanding participation of various scientific disciplines. This session will explain the role of FDA Advisory Committees and the rules governing participation on these Committees with a goal of encouraging participation by toxicologists. SOT members involved in FDA Advisory Committees will discuss their experience and provide insight on how to engage in the process.

- **Introduction for Advisory Committees at the Food and Drug Administration,** Michael Ortwerth, U.S. FDA, ACOMS, Rockville, MD
- **Advising the Food and Drug Administration: The Role of the Toxicologist,** Jim Riviere, North Carolina State University, Raleigh, NC
- **Participating in the Process: How and Why,** Margaret A. Miller, U.S. FDA, National Center for Toxicology Research, Rockville, MD

Keynote Medical Research Council (MRC) Lecture: The Ubiquitin Proteolytic System—From Basic Mechanisms through Human Diseases and on to Drug Targeting



Wednesday, March 18, 8:00 AM–8:50 AM

Lecturer: Nobel Laureate Aaron Ciechanover, The Rappaport Faculty of Medicine and Research Institute, Technion-Israel Institute of Technology, Bat Galim, Haifa, Israel

Dr. Aaron Ciechanover was born in Haifa, Israel in 1947. He received his M.Sc. (1970) and M.D. degrees (1975) from Hadassah and the Hebrew University School

of Medicine in Jerusalem and his D.Sc. in biochemistry from the Technion (1981). There, as a graduate student with Dr. Avram Hershko, they discovered the ubiquitin-proteasome system for regulated degradation of intracellular proteins. They demonstrated that covalent attachment of ubiquitin to the target substrate signals it for degradation by a downstream protease. They purified the conjugating enzymes, deciphered their mechanism of action, showed that the system degrades abnormal proteins in cells, and proposed a model according to which polyubiquitination functions as a recognition signal for a specific, downstream protease that degrades the substrate with the release of reusable ubiquitin. Through the years it has become clear that ubiquitin-mediated degradation of proteins is central to the regulation of basic cellular processes, including the cell cycle, transcriptional regulation, growth and development, differentiation, apoptosis, receptor modulation, DNA repair, and maintenance of the cell's quality control. With the multiple substrates targeted and processes involved, it is not surprising that the system has been implicated in the pathogenesis of many diseases, a broad array of malignancies and neurodegenerative disorders among them. This led pharma companies to initiate efforts to develop mechanism-based drugs. One of them to combat multiple myeloma, is already on the market with many more in the pipeline.

Following his graduate studies, Dr. Ciechanover obtained his postdoctoral training (1981–1984) with Dr. Harvey Lodish at the Massachusetts Institute of Technology (M.I.T.) and the Whitehead Institute in Cambridge, Massachusetts, U.S.A. There he studied receptor-mediated endocytosis and deciphered the mechanism of iron uptake by the transferrin receptor. In parallel and in collaboration with Drs. Alexander Varshavsky and Daniel Finley, he continued his work on the ubiquitin system. Following his return to Israel in 1984, he joined the Faculty of Medicine of the Technion in Haifa and established his own laboratory where he has continued to contribute significantly to the development of the field *via* studying, among other subjects, the mechanisms of ubiquitin-mediated regulation of transcription factors and growth promoting factors such as p53, Myc, MyoD, and NF- κ B. For his studies that led to the discovery of the ubiquitin system, Dr. Ciechanover, along with Drs. Avram Hershko and Irwin Rose, was awarded the Nobel Prize in Chemistry in 2004. Beforehand, in 2000, he shared the prestigious Albert Lasker Award for Basic Medical Research with Drs. Hershko and Varshavsky, and was awarded in 2003 the Israel Prize for Biological Research, the highest recognition bestowed by the State of Israel. Dr. Ciechanover is a member of the Israeli National Academy of Sciences and Humanities, the Pontifical Academy of Sciences of the Vatican, and the American Philosophical Society. He is a Foreign Fellow of the American Academy of Arts and Sciences, and a Foreign Associate of the National Academy of Sciences of the U.S.A. and its Institute of Medicine.

Featured Sessions

Meet the Director of NIEHS

Wednesday, March 18, 12:00 NOON–1:20 PM

Chairperson(s): Michael P. Holsapple, ILSI Health and Environmental Sciences Institute, Washington, DC

The Meet the Director program is a special 80 minute session that provides an opportunity for the leaders of major federal agencies to engage in a panel discussion of emerging trends in toxicology research and its funding. The session will be a particularly valuable opportunity to update our members on the future directions of the National Institute of Environmental Health Science. There will be a strong emphasis on change of direction and new initiatives that may impact the practice of toxicology in the near and long term.

This session will be immediately followed by an update from Antonio Scarpa from the NIH Center for Scientific Review.

Merit Award Lecture: Chemical Hepatocarcinogenesis—Mechanisms, Pathogenesis, and Thresholds

Wednesday, March 18, 12:30 PM–1:20 PM

Lecturer: Gary M. Williams, New York Medical College, Valhalla, NY

The distinction between DNA-reactive and epigenetic mechanisms of carcinogenicity was conceived in part from extensive findings with hepatocarcinogens in the hepatocyte DNA repair assay for DNA reactivity. These mechanisms were incorporated into understanding of the pathogenesis of liver neoplasia as a multistep process. In the first sequence, neoplastic conversion, hepatocytes are initiated through DNA alteration to form proliferative preneoplastic lesions. In the second sequence, neoplastic development, a variety of cellular and tissue epigenetic alterations facilitate the development of preneoplastic cells into neoplasms. DNA adduct formation is a form of toxicity involving electrophilic molecular alterations, in contrast to many epigenetic effects, which elicit adaptive responses resulting from modulation of basic metabolic processes mediated by receptor binding. Generally, epigenetic carcinogens are accepted as having carcinogenicity thresholds, whereas DNA-reactive carcinogens are assumed not to have thresholds. To investigate the possibility of thresholds for DNA-reactive hepatocarcinogens, the dose-response characteristics of two well studied representatives were investigated. By quantifying key bioindicators of effect, including DNA adduct formation, cytotoxicity, cell proliferation and induction of preneoplastic lesions, evidence was found for nonlinearities and no-effect levels at low doses, supporting the concept of thresholds.

Update from the NIH Center for Scientific Review

Wednesday, March 18, 1:30 PM–2:30 PM

Chairpersons: Kenneth S. Ramos, University of Louisville, Louisville, KY and Cheryl Lyn Walker, University of Texas MD Anderson Cancer Center, Smithville, TX

Speaker(s): Antonio Scarpa, National Institutes of Health, Center for Scientific Review, Bethesda, MD

Antonio Scarpa will provide Annual Meeting attendees with an update on important initiatives currently underway at NIH. Dr. Scarpa will also discuss the established Systemic Injury by Environmental Exposure (SIEE) Special Emphasis Panel (SEP) in the Digestive Health Integrative Review Group (IRG). This SIEE SEP will allow NIH grant proposals on toxicology to be reviewed by scientists familiar with the subject matter. This session also will provide an opportunity for a lively discussion of the importance of toxicology in advancing basic research and protecting public health and grants needed to support these efforts.

Issues Session: National Research Council (NRC) Vision

Thursday, March 19, 7:30 AM–8:50 AM

Chairperson(s): Michael P. Holsapple, ILSI Health and Environmental Sciences Institute, Washington, DC

This special session will continue the dialog begun at the highly successful 2008 NRC session in which Annual Meeting participants were provided an overview of the three National Academy reports addressing key issues impacting the Society and the profession of toxicology. Those reports included Toxicity Testing in the 21st Century: A Vision and Strategy, Application of Toxicogenomics Technologies to Predictive Toxicology and Risk Assessment, and Models in Environmental Regulatory Decision Making.

Monday

INNOVATIONS OF APPLIED TOXICOLOGY (IAT) SESSION

Eat Well, Breathe Well: Nutritional Determinants of Susceptibility to Airborne Pollutants

Monday, March 16, 9:15 AM–12:00 NOON

Chairperson(s): James G. Wagner, Michigan State University, East Lansing, MI and Ilona Jaspers, University of North Carolina Chapel Hill, Chapel Hill, NC

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Inhalation and Respiratory Specialty Section

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Susceptibility factors for adverse responses to air pollutant exposure include the host genome, exposure history, disease, age, and diet. In particular, the role of the underlying nutritional status has emerged as an important but understudied determinant of enhanced airway reactivity, inflammation, and immune responses that might be elicited or exacerbated by airborne toxicants. For example deficiencies in certain micronutrients are associated with enhanced inflammation to ozone, and dietary supplementation with antioxidants can protect from ozone-induced deficits in airway function. Both clinical and animal studies demonstrate that ozone-induced airway reactivity is related to increased body mass index. Similar relationships of nutritional factors and adverse airway responses exist for diesel exhaust, particulate matter, and cigarette smoke. Specific cellular and airway defenses include small molecular weight antioxidants (e.g., ascorbate, glutathione), and enzyme systems (e.g., catalase, SOD, Phase II enzymes) which are directly or transcriptionally affected by the diet. In addition, the type and amount of dietary lipids can predispose for either pro- or anti-inflammatory pathways. Based on our growing understanding of toxicological mechanisms that underlie the responses to many different types of inhaled pollutant exposure, it is now possible to test specific hypotheses for nutrient or lipid-based dietary interventions to protect from adverse airway inflammatory responses and their consequences in susceptible populations. To gain a clear understanding of these issues, it is important to address the current thinking and results

from preclinical and clinical translational studies, approaches that merge basic toxicological principles and biochemical nutritional science, and actively study the comparison of nutrient deficiency, supplementation and energy imbalance on toxicological outcomes from air pollutant exposure.

- **Food for the Lung: How Nutrition Affects Respiratory Toxicology**, Ilona Jaspers, University of North Carolina Chapel Hill, Chapel Hill, NC
- **Cigarette Smoke and Antioxidant Therapies in COPD**, Irfan Rahman, University of Rochester Medical Center, Rochester, NY
- **Protection from Ozone and Endotoxin-Induced Airway Inflammation by Gamma-Tocopherol**, James G. Wagner, Michigan State University, East Lansing, MI
- **Dietary Intervention with Sulforaphane, a Phase II Enzyme Inducer to Protect from Airway Inflammation**, David Diaz-Sanchez, U.S. EPA, Research Triangle Park, NC
- **Obesity Enhances Airway Inflammation and Reactivity to Ozone**, Stephanie Shore, Harvard School of Public Health, Boston, MA
- **Complementary and Alternative Medicine (CAM) in Protecting against Inhaled Toxicants**, David Peden, University of North Carolina Chapel Hill, Chapel Hill, NC

MicroRNAs in Biology and Toxicology

Monday, March 16, 9:15 AM–12:00 NOON

Chairperson(s): Mark E. Hahn, Woods Hole Oceanographic Institution, Woods Hole, MA and Raymond F. Novak, Wayne State University, Detroit, MI

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**Reproductive and Developmental Toxicology
Specialty Section**

Gene expression is highly regulated at many levels and altered gene expression is an important part of many toxicological mechanisms. Very recently, a fundamentally new mechanism of gene regulation, involving small RNAs known as microRNAs (miRNAs), has been discovered. MicroRNAs are single-stranded RNA molecules of ~22 nucleotides that function to regulate the synthesis of proteins by inhibiting the translation of mRNAs and promoting their degradation, or in some cases by stimulating their translation. MicroRNAs are abundant and evolutionarily conserved in eumetazoan animals.



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The human genome encodes hundreds of miRNAs, and a similar number of miRNAs occur in the genomes of other animals. Each miRNA can target hundreds of different messenger RNAs for degradation; up to 20% of the genes in a given genome may be regulated by miRNAs. The biological functions of miRNAs are not fully understood. However, recent studies have demonstrated important roles for miRNAs in the regulation of transcription factor expression and in pre-mRNA splicing. Studies in zebrafish and mammals have shown that miRNAs have important roles during embryonic development and that disruption of miRNA synthesis in embryos can have dramatic consequences. Altered miRNA expression is seen in a variety of cancers and in some cases is involved in the mechanism of tumorigenesis. Furthermore, miRNAs are involved in several human diseases and appear to regulate cellular responses to a variety of physiological and environmental stressors, including diabetes, high blood pressure, nutrient stress, hypoxia, and environmental chemicals. Thus, miRNAs have critical biological functions and there is an emerging understanding of the important role of miRNAs in toxicology, development, metabolic disease, and carcinogenesis. MicroRNAs have not yet been widely studied in a toxicological context; however, it seems likely that these small RNAs may have significant roles in regulating the genomic, proteomic, and functional response of cells and tissues to chemicals.

- **MicroRNA Regulation of Signaling Pathways during Development**, James G. Patton, Vanderbilt University, Nashville, TN
- **MicroRNAs in Human Cancers and Carcinogenesis**, Carlo M. Croce, Ohio State University School of Medicine, Columbus, OH
- **Aberrant MicroRNA Expression in Human Breast Oncogenesis**, Alan A. Dombkowski, Wayne State University, Detroit, MI
- **MicroRNA Expression in Hepatic and Non-Hepatic Tissues of Dioxin-Exposed Rodents**, Allan B. Okey, University of Toronto, Toronto, Ontario, Canada
- **The Role of Nuclear Receptors in miRNA Transcription**, Yatrik Shah, National Cancer Institute, Bethesda, MD

Superantigens, Cytokine Storm, and Toxic Reactions

Monday, March 16, 9:15 AM–12:00 NOON

Chairperson(s): G. Frank Gerberick, *The Procter and Gamble Company, Cincinnati, OH* and Ian Kimber, *University of Manchester, Manchester, United Kingdom*

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Immunotoxicology Specialty Section

The term superantigen (SAg) was coined by Marrack and Kapler in 1990 to describe a large family of exotoxins secreted primarily by *Staphylococcus aureus* and *Streptococcus pyogenes* that are associated with adverse health effects that can range from relatively mild and transient symptoms to catastrophic shock and death. These toxins have been implicated in a number of diseases including scarlet fever, staphylococcal food poisoning and cases of both streptococcal and staphylococcal toxic shock syndrome, as well as being suspected of playing roles in autoimmune diseases. A unique feature of SAGs is that, unlike conventional antigens, they do not require processing by antigen presenting cells (APC) and they can interact with a large proportion of T cells. SAGs have been well characterized and have very specific binding sites on the α or β chain of MHC class II molecules expressed on APC, and on the V β chain of the T cell receptor forming a tri-molecular complexes that bridge SAGs with T cells and APCs, thereby enhancing intracellular interactions. The polyclonal stimulation of T cells in juxtaposition with APC by SAGs leads to extensive cytokine production by both cell types including interleukin (IL)-2, interferon- γ and tumor necrosis factor- β by T cells, and IL-1 β and tumor necrosis factor- α by APC. The collective action of these cytokines, known as cytokine storm, is the trigger for the clinical manifestations of superantigen immunotoxicity. Moreover, adverse health effects precipitated by cytokine storm are relevant also for considerations of drug safety. One illustrative example of the clinical picture of the TeGenero TGN1412 therapeutic monoclonal antibody was observed in the London UK 2006 trial. Finally, the structure of superantigens, the mechanisms through which they interact with the immune system, and the nature and clinical consequences of cytokine storm will be described and reviewed.

- **Structure and Function of Superantigens**, Ian Kimber, University of Manchester, Manchester, United Kingdom
- **Clinical Manifestations of Superantigen Diseases**, Jeffrey Parsonnet, Dartmouth-Hitchcock Medical Center, Lebanon, NH
- **Immune Responses to Superantigens**, Malak Kotb, University of Cincinnati, Cincinnati, OH

- **Experimental Models for Evaluating Bioavailability of Superantigens**, Christopher Squier, University of Iowa, Iowa City, IA
- **Toxicological Considerations for Superantigen-Mediated Diseases**, G. Frank Gerberick, The Procter and Gamble Company, Cincinnati, OH

INFLAMMATION AND DISEASE

Zinc, Inflammation, and Diabetes

Monday, March 16, 9:15 AM–12:00 NOON

Chairperson(s): Lu Cai, University of Louisville, Louisville, KY and Wolfgang Maret, The University of Texas Medical Branch, Galveston, TX

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Metals Specialty Section

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Diabetes is a serious public issue due to its risk for chronic cardiovascular complications. However, mechanisms by which diabetes causes cardiovascular complications remain incompletely understood. Zinc (Zn) is one of the most abundant metals in the human body and therefore essential for the structure and activity of more than 300 enzymes and proteins. Zn deficiency was found to be associated with diabetes, but the direct role of Zn in diabetic etiology and its mechanisms are under-explored. Recent studies have shown that chronic inflammation is not only related to the onset of Type I and Type II diabetes, but also related to the development of diabetic complications. Zn deficiency may cause systemic inflammation that in turn becomes the initiate factor for the onset of diabetes and the development of diabetic complications. The current understanding of the roles of Zn homeostasis in the insulin signaling, systemic inflammation, diabetes and diabetic complications will be explored, as will the public awareness of proper intake of Zn-containing food in daily life. A brief overview highlighting the association of Zn with inflammation, diabetes and diabetic complications will begin this session. An important component of this exploration will cover how Zn sensitizes insulin function and the association of Zn with inflammation, insulin resistance and obesity. Researchers are aware that Metallothionein (MT) plays a critical role in Zn homeostasis, therefore, MT gene alterations and its association with Zn status, inflammation, diabetes and diabetic complications will be

discussed. Finally, the evidence of Zn to protect ischemic and the diabetic heart will be presented.

- **Introduction**, Lu Cai, University of Louisville, Louisville, KY
- **Pathophysiology of Cellular Zinc and Redox Buffering Mechanisms in Diabetes**, Wolfgang Maret, The University of Texas Medical Branch, Galveston, TX
- **Zn Regulation of Systemic Inflammation and Insulin Resistance in Obesity**, Jianping Ye, Louisiana State University, Baton Rouge, LA
- **Metallothionein Gene Polymorphisms and Zinc Homeostasis in the Susceptibility of Diabetes Mellitus and Cardiovascular Complications**, Robertina Giacconi, INRCA, Ancona, Italy
- **Protection of Metallothionein and Zinc against Diabetic Complications**, Lu Cai, University of Louisville, Louisville, KY
- **Signaling Mechanisms of Myocardial Protection by Zinc**, Irina Korichneva, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, New Brunswick, NJ

Aromatase (CYP19) Gene Expression and Function: Current State of Knowledge As a Mode-of-Action for Toxicological Effects

Monday, March 16, 1:40 PM–4:25 PM

Chairperson(s): Susan Laws, U.S. EPA, Research Triangle Park, NC and Thomas Sanderson, Institut National de la Recherche Scientifique, Laval, Québec, Canada

Sponsor:
Reproductive and Developmental Toxicology
Specialty Section

During the past five years, advancements have been made in our understanding of the regulation of aromatase (CYP19) gene expression and function in humans and wildlife. This cytochrome P450 microsomal enzyme is responsible for the conversion of androgens to estrogens, and is essential for maintaining estrogen homeostasis within multiple target tissues for both males and females. The expression of the human CYP19 gene is regulated through multiple promoters and co-factors that are target tissue specific. Thus, local regulation of estrogen concentrations within various target tissues may vary significantly from that observed in circulating serum. To date, the ability of environmental chemicals to inhibit the catalytic activity of aromatase, as well as resulting adverse effects on reproductive function, have been clearly demonstrated. However, specific effects on aromatase gene expression following exposure to environmental chemicals, and the physiological impact on local and systemic levels of estrogen, remain to be elucidated. In addition, the

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presence of elevated aromatase expression in hormone-dependent cancers underscores the need for determining if environmental chemicals can modulate the activity and expression of aromatase in humans and wildlife. To highlight these important findings, this session will provide an overview of the current state of knowledge regarding the regulation of aromatase (CYP19) gene expression, describe the toxicological consequences of altered aromatase gene expression and function in humans and wildlife, and present novel approaches for identifying environmental chemicals that disrupt the homeostasis of estrogen biosynthesis *via* this mode of action.

- **Overview: Biological Importance of Aromatase (CYP19) Expression and Function**, Susan Laws, U.S. EPA, Research Triangle Park, NC
- **Regulation of Aromatase and Other Steroidogenic Genes in Endometriosis**, Serdar E. Bulun, Northwestern University, Chicago, IL
- **Aromatase Regulation in Breast Cancer**, Colin Clyne, Prince Henry's Institute of Medical Research, Clayton, Australia
- **Understanding the Effects of Atrazine on Steroidogenesis in Wistar Rats**, Nicole Tinfo, North Carolina State University, Raleigh, NC
- **Differential Regulation of Aromatase Isoforms and Tissue Responses to Environmental Chemicals in Fish**, Lesley Mills, U.S. EPA, Narragansett, RI
- **Evaluation of (LPTA®) CD-1-Tg(Cyp19-Luc)-Xen Mice As a Bioluminescent Research Tool for the *In Vivo* Study of Endocrine Disruptors**, Thomas Sanderson, Université du Québec, Laval, Québec, Canada

EPIGENETICS

Genomic, Non-Genomic, and Epigenetic Mechanisms of Nuclear Hormone Receptor Action

Monday, March 16, 1:40 PM–4:25 PM

Chairperson(s): Cheryl Lyn Walker, University of Texas MD Anderson Cancer Center, Smithville, TX and Stephen H. Safe, Texas A&M University, College Station, TX

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Molecular Biology Specialty Section

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Carcinogenesis Specialty Section

Mechanisms Specialty Section

Reproductive and Developmental Toxicology Specialty Section

Our understanding of how nuclear hormone receptors respond to steroid hormones, endocrine disruptors and xenobiotics is rapidly evolving. Nuclear hormone receptors, which were once thought to act as simple transcription factors primarily through interaction with the DNA, are now appreciated to have equally important activities as activators of non-genomic signaling cascades within the cell and to interact with protein modifiers, such as arginine and lysine methyltransferases, to induce epigenetic modifications of chromatin in a ligand-, receptor-, co-activator and gene-specific fashion. Because of the importance of this class of receptors for many toxic responses, including those induced by xenoestrogens and xenobiotics, this session will highlight cutting-edge discoveries being made in this area that are having a major impact on the discipline of toxicology.

- **Introduction**, Cheryl Lyn Walker, University of Texas MD Anderson Cancer Center, Smithville, TX
- **Transcript Profiling of Estrogen-Responsive Genes**, George Daston, The Procter & Gamble Company, Cincinnati, OH
- **Non-Classical ER/Sp Activation of Estrogen Responsive Genes**, Stephen H. Safe, Texas A&M University, College Station, TX
- **Life, Death, and Transformation: Movements, Repeats, and ncRNAs?** M. Geoff Rosenfeld, University of California San Diego, San Diego, CA
- **Regulation of Transcription by Protein Arginine Methyltransferases**, Mark Bedford, University of Texas MD Anderson Cancer Center, Smithville, TX

In Vitro Models of Human Toxicity Pathways

Monday, March 16, 1:40 PM–4:25 PM

Chairperson(s): David Dix, U.S. EPA, Research Triangle Park, NC and Russell Thomas, The Hamner Institutes for Health Sciences, Research Triangle Park, NC

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In Vitro and Alternative Methods Specialty Section

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For toxicity testing programs to address the large numbers of substances of potential concern, a paradigm shift in the assessment of hazard and risk is needed that takes advantage of advances in molecular toxicology, computational sciences, and information technology. This shift represents an evolution of toxicology from an observational science, to a predictive science built upon mechanism-based, biological observations derived *in vitro*. Progress in developing robust, quantitative *in vitro* models of human toxicity pathways with the potential to replace the current reliance on *in vivo* animal data will be presented in this session. *In vitro* models are required that can identify cellular and molecular responses in critical biological pathways, and quantify these responses to allow extrapolation to determine whether adverse health effects might occur at anticipated exposure levels. A major challenge for this *in vitro* approach is the development of an appropriate battery of assays, cell types, and endpoints in order to model the response of all relevant toxicity pathways. Furthermore, the results from these high-throughput screening (HTS) assays will need to be linked to standard toxicity test results, facilitating an intelligent transition in testing paradigms. The five presentations will demonstrate examples where science, technology, and regulatory need have converged to produce initial successes in creating *in vitro* models of human toxicity pathways.

- **Evaluation of the ToxCast Suite of Cellular and Molecular Assays for Prediction of *In Vivo* Toxicity**, Keith Houck, U.S. EPA, Research Triangle Park, NC
- **Use of Nuclear Reporter Assays to Investigate Species Differences in Toxicity**, Richard Pepper, Syngenta Crop Protection, Inc., Greensboro, NC
- **Towards New *In Vitro* Toxicology Strategies for Decision Making: Acute Toxicity As a Case Study**, Gladys Ouedraogo, L'Oreal Advanced Research, Aulnay sous bois, France
- **Three-Dimensional Human Cellular and Metabolizing Enzyme Microarrays for High-Throughput Toxicity Screening**, Jonathan Dordick, Rensselaer Polytechnic Institute, Troy, NY

- **Microscale Liver Models for Drug Development and Toxicity Screening**, Sangeeta Bhatia, Massachusetts Institute of Technology, Cambridge, MA

INFLAMMATION AND DISEASE

Nitrative and Oxidative Stress in Toxicology and Disease

Monday, March 16, 1:40 PM–4:25 PM

Chairperson(s): Ruth A. Roberts, AstraZeneca UK, Macclesfield, United Kingdom and William Slikker, U.S. FDA, Jefferson, AR

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Carcinogenesis Specialty Section

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Neurotoxicology Specialty Section

Persistent inflammation and the formation and actions of reactive oxygen species play pivotal roles in tissue injury during disease pathogenesis and as a reaction to toxicant exposures. The associated oxidative and nitrative stresses promote diverse biological reactions including neurodegenerative disorders, cancer, atherosclerosis, and stillbirth. These effects occur *via* sustained cell proliferation and cell death and, in some cases, *via* induction of a pro-angiogenic environment. Exposure to ozone, a ubiquitous urban air pollutant, leads to the generation of reactive oxygen and nitrogen species in lung macrophages inducing inflammatory genes which play a key role in subsequent tissue damage. Similarly, the developing brain is susceptible to anesthetic-induced injury; recent studies have indicated that genes along the oxidative stress pathway are altered by this anesthetic treatment. In addition to a role in damage to the developing brain, inflammation, and oxidative stress are implicated in Parkinson's disease (PD), a neurodegenerative disease characterized by the loss of dopamine neurons. Recent data suggests a mechanistic link between oxidative stress and elevated levels of a neurotoxin endogenous to dopamine neurons. Such work has significant implications for the development of therapeutics and identification of novel biomarkers for PD pathogenesis. As well as a role in lung disease and neuronal injury, oxidative and nitrative stress is implicated in creating the pro-inflammatory microenvironment associated with the aggressive phenotype of inflammatory breast cancer. Targeting these pathways may help diminish the pro-inflammatory microenvironment that may contribute to the genetic instability and aggressive phenotype. This symposium begins with fundamental concepts in inflammation and progresses to how one



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might create a rational plan of treatment, based on understanding derived from basic principles. This session will appeal to both those with specialist knowledge in the field as well as to toxicologists looking to learn more about the role of nitrate and oxidative stress in toxicology.

- **Attenuation of Neurotoxicant-Induced Brain Injury Associated with Oxidative Stress and Mitochondrial Dysfunction**, William Slikker, U.S. FDA, Jefferson, AR
- **Regulation of Caveolin-1 Expression, Nitric Oxide Production and Tissue Injury by Tumor Necrosis Factor-Alpha**, Debra Laskin, Rutgers University, Piscataway, NJ
- **Oxidation/Reduction Responses and Toxic Shock**, Charles Smith, Seattle Children's Hospital Research Institute, Seattle, WA
- **Oxidative and Nitrosative Stress in Regulation of the Pro-Inflammatory Microenvironment and Aggressive Phenotype of Inflammatory Breast Cancer**, Fredika Robertson, University of Texas MD Anderson Cancer Center, Houston, TX
- **Generation of Reactive Intermediates during Dopamine Catabolism: Implications for Parkinson's Disease**, Jonathan Doorn, University of Iowa, Iowa City, IA

NEURODEGENERATIVE DISEASE

Novel Signaling Mechanisms That Regulate Dopaminergic Neuronal Survival or Death: Implications in Parkinson's Disease

Monday, March 16, 1:40 PM–4:25 PM

Chairperson(s): Zhengui Xia, University of Washington, Seattle, WA and Anumantha Kanthasamy, Iowa State University, IA

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Neurotoxicology Specialty Section

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In Vitro and Alternative Methods Specialty Section
Mechanisms Specialty Section
Occupational and Public Health Specialty Section

Parkinson's disease (PD) is the second most common aging-related neurodegenerative disorder characterized by loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc), resulting in irreversible motor symptoms including tremor, bradykinesia, and rigidity. Although the etiology of idiopathic PD, which accounts for at least 90% of all PD cases, has been elusive, epidemiological studies suggest a correlation between increased risk for PD and

occupational exposure to pesticides. Consequently, treatment of cultured neuronal and rodent models with pesticides has been useful in the investigation of PD pathogenesis. However, despite extensive research in the past, molecular mechanisms underlying dopaminergic neuronal death associated with PD remain incompletely defined. Recent studies using several pesticides including rotenone, paraquat, and dieldrin as models to investigate signal transduction mechanisms that regulate dopaminergic neuronal death will be presented. Furthermore, idiopathic PD is most likely caused by multiple factors, including a complex interaction between genes and the environment. Interestingly, mutations in LRRK2 found in dominant familial PD have also been found in idiopathic PD, and the penetrance of LRRK2 mutations is incomplete. Thus, LRRK2 may provide an example whereby the onset and progression of PD may depend on gene-environment interactions. Recent advances in the role of LRRK2 mutations, many of which increase its kinase activity, in dopaminergic neuronal death are also important to address. Data is available on signal transduction pathways that promote dopaminergic neuronal survival and should be of general interest to scientists studying neurodegeneration, neurotoxicology, pesticide toxicology, signal transduction, molecular mechanisms of toxicity, and occupational and public health. Presentation of this data is likely to accelerate understanding of cell signaling mechanisms underlying environmental neurotoxicant-induced nigral degenerative processes as well as to foster the identification of novel therapeutic targets for treatment of PD.

- **Synergistic Effects of Risk Factors that Converge on Dopamine Systems: Implications for Parkinson's Disease**, Deborah Cory-Slechta, University of Rochester School of Medicine and Dentistry, Rochester, NY
- **Mitochondrial Complex I Inhibition Is Not Required for Dopaminergic Neuron Death Induced by Rotenone, MPP+, or Paraquat**, Zhengui Xia, University of Washington, Seattle, WA
- **Novel Roles and Regulation of Survival Factor MEF2 in Dopaminergic Neurons**, Zixu Mao, Emory University, Atlanta, GA
- **LRRK2 Signaling and Neuronal Death**, Mark Cookson, National Institute on Aging, Bethesda, MD
- **Novel PKC Signaling in Oxidative Damage in Pesticide-Induced Dopaminergic Neurotoxicity Models**, Anumantha Kanthasamy, Iowa State University, Ames, IA

48th Annual Meeting and ToxExpo™

Symposia

Regulation of Drug Transporters in Different Disease States and Its Toxicological and Clinical Implications

Monday, March 16, 1:40 PM–4:25 PM

Chairperson(s): José E. Manautou, University of Connecticut, Storrs, CT and Nathan J. Cherrington, University of Arizona, Tucson, AZ

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Molecular Biology Specialty Section

Drug transporters play an important role in the uptake, distribution and elimination of pharmaceuticals, environmental contaminants and endogenous compounds. In the last decade, considerable interest has been centered on regulation of drug transporters and on how chemicals and disease states alter their expression. It is clearly important to understand the pharmacological and toxicological consequences of changes in drug transporter function. Both induction and repression of transporter expression have been documented with exposure to classical drug metabolizing enzyme inducers, treatment with target organ toxicants and under a variety of pathological conditions. Many of these changes are mediated by transcription factors, including CAR, PXR, Nrf2, as well as cytokines and related inflammatory mediators. Therefore, it is important to highlight the recent knowledge gained on how transporter expression changes during non-alcoholic steatohepatitis and drug-induced hepatotoxicity, as well as regulation of blood brain barrier transporters and its implications to the management and/or treatment of central nervous system disorders. Finally, this session will address the molecular regulatory mechanisms involved and the potential functional consequences, and understanding how changes in transporter expression or function may be involved in drug-drug interactions and the implications of these effects in drug development and the clinical setting.

- **Changes in the Expression of Drug Metabolizing Enzymes and Transporters during Fatty Liver Disease**, Nathan J. Cherrington, University of Arizona, Tucson, AZ
- **Acetaminophen-Induced Hepatotoxicity Alters the Expression of Multi-Drug Resistance Associated Transport Proteins**, José E. Manautou, University of Connecticut, Storrs, CT
- **Regulation of ABC Transporter Expression at the Blood-Brain Barrier**, David S. Miller, NIH/NIEHS, Research Triangle Park, NC
- **Applying Models of Altered Transporter Function to Mechanisms of Toxicity and Drug Interactions**, Lois D. Lehman-McKeeman, Bristol-Myers Squibb Company, Princeton, NJ

- **Clinical Drug and Toxicological Interactions Involving Drug Transporters**, Joseph W. Polli, GlaxoSmithKline, Inc., Research Triangle Park, NC

Tuesday

NEURODEGENERATIVE DISEASE

Does Metal Toxicity Play a Role in the Etiology of Alzheimer's Disease?

Tuesday, March 17, 9:00 AM–11:45 AM

Chairperson(s): Nasser H. Zawia, University of Rhode Island, Kingston, RI and Wei Zheng, Purdue University, West Lafayette, IN

Sponsor:
Neurotoxicology Specialty Section

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Metals Specialty Section
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Alzheimer's disease (AD) is a progressive neurodegenerative disorder whose clinical manifestations appear with advancing age. One of the pathological hallmarks found in brains of AD patients is a buildup of extracellular amyloid plaques that are rich in beta amyloid which is derived from the amyloid precursor protein (APP). Studies have shown that beta amyloid is a metalloprotein which binds zinc (Zn), copper (Cu) and iron (Fe). Exposure to low levels of lead (Pb) in early life has been linked to abnormal regulation and expression of APP, possibly by the reprogramming of APP expression. An epigenetic study of Pb-exposed subjects and work on beta-amyloid clearance from the brain following Pb exposure also provides evidence for a possible role for Pb in the etiology of AD. Manganese (Mn) exposure in primates has been recently shown to result in diffuse beta-amyloid plaques in the frontal cortex of young non-human primates. Experts in metal toxicology, neurotoxicology, and environmental epidemiology, who have performed pioneering work to address this newly emerging research area in metal neurotoxicology will address these issues.

- **Evidence for Lead As an Environmental Stressor of Alzheimer's Disease and the Role of Epigenetics**, Howard Hu, University of Michigan, Ann Arbor, MI
- **Promotion of Alzheimer's Disease Due to Exposure to Lead (Pb) Early in Life**, Nasser H. Zawia, University of Rhode Island, Kingston, RI

Symposia

- **Clearance of Brain Beta-Amyloid from the Cerebrospinal Fluid: Role of the Choroid Plexus and Effect of Pb Poisoning**, Wei Zheng, Purdue University, West Lafayette, IN
- **Amyloid-B Aggregation and Neurodegeneration in the Frontal Cortex of Manganese-Exposed Non-Human Primates**, Tomas R. Guilarte, Johns Hopkins University, Baltimore, MD
- **Early-Life Events May Trigger Biochemical Pathways for Alzheimer's Disease: The LEARN Model**, Debomoy Lahiri, Indiana University School of Medicine, Indianapolis, IN

EPIGENETICS

Epigenetic Implications for Toxicology

Tuesday, March 17, 9:00 AM–11:45 AM

Chairperson(s): Reza J. Rasoulpour, Dow Chemical Company, Midland, MI and Kathleen Gabrielson, Johns Hopkins Medical Institutions, Baltimore, MD

Sponsor:
Carcinogenesis Specialty Section

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Risk Assessment Specialty Section
Molecular Biology Specialty Section

The emerging field of epigenetics may profoundly impact the future of toxicology. Epigenetics can be defined as heritable changes in gene expression that do not involve genetic mutations and are propagated without continued stimulus. Discrete chemical modifications of the chromatin can regulate gene expression or repression and can be transmitted to daughter cells or future generations due to epigenetic memory. Although potentially reversible, these heritable changes may be classified as transgenerational, mitotic, or meiotic, implicating the wide-ranging impact of epigenetic control in cellular function. These epigenetic processes play fundamental roles in cell proliferation, differentiation, cancer development and toxicities. Epigenetic processes that occur in the cell include DNA methylation/demethylation at CpG islands, small nuclear RNA processes and protein acetylation/deacetylation. Understanding how these modifications are inherited from mother cells to daughter cells or from an organism to its progeny remains a major scientific challenge. Recently, there has been a growing concern that epigenetic events may play a role in chemically and/or nutritionally driven adverse health effects, with particular focus toward reproductive toxicity and non-genotoxic carcinogenesis. For example, changes in DNA methylation which target tumor suppressor and DNA repair genes for silencing is a well established and valid step

in cancer etiology. Overall, although the current literature consists of relatively few studies, there has been considerable interest by the popular press, government agencies, and the scientific community. Therefore, it is important to provide an introduction to epigenetic mechanisms and to highlight the current state-of-the-science in epigenetic toxicology.

- **Epigenetic Mechanisms of Nickel Ion Carcinogenesis**, Max Costa, New York University School of Medicine, New York, NY
- **Epigenetics: The New Genetics of Toxicology**, Randy Jirtle, Duke University, Durham, NC
- **Epigenetic Regulation in Development: Implications in Stem Cell Biology and Toxicities**, James Herman, Johns Hopkins University, Baltimore, MD
- **Is There a Common E-epigenome?** Shuk-Mei Ho, University of Cincinnati, Cincinnati, OH
- **MicroRNA Epigenetic Regulation**, Curtis Harris, National Cancer Institute, Bethesda, MD

Immunomodulation during Complementary and Alternative Medicine (CAM) Therapy: Risks and Benefits

Tuesday, March 17, 9:00 AM–11:45 AM

Chairperson(s): Barbara L.F. Kaplan, Michigan State University, East Lansing, MI and Prakash Nagarkatti, University of South Carolina School of Medicine, Columbia, SC

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Immunotoxicology Specialty Section

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Special Interest Group
Food Safety Specialty Section

There are over 40 million Americans who suffer from some form of degenerative disease and it is estimated that approximately one third of them will attempt using complementary and alternative medicine (CAM) to alleviate pain and suffering. Of the various CAM therapies, the use of plant products remains popular. However, there is lack of sufficient experimental and clinical proof that they are safe and effective. In 1998, the National Center for Complementary and Alternative Medicine (NCCAM) was established by the U.S. Congress as one of the NIH Institutes to provide funds to investigate if the popular CAM modalities are truly beneficial. In the United States, while drugs must be approved by the FDA as being safe and effective before they can be sold, the FDA is not authorized to evaluate the safety or efficacy of dietary supplements.

However, the FDA can ban the sale of supplements that are shown to be unsafe. On the other hand, the immunosuppressive properties of plant products, if found safe, can also be used to develop new therapeutic modality against inflammatory and autoimmune diseases. Herbal and plant-derived compounds are widely available in the market that claim to sustain, restore or enhance immunity. To begin addressing this issue an overview of CAM therapy with an emphasis on herbal and plant-derived compounds and their potential risks/benefits will be highlighted for their immunomodulatory properties. Benefits *versus* the risks of using certain plant-derived products that constitute CAM will be discussed including Cat's Claw, Echinacea, Ginseng, Thunder God Vine, Aristolochia, Kava, Ephedra, and St. John's Wart.

- **Immune Modulation by Plant-Derived Cannabinoid Compounds**, Barbara L.F. Kaplan, Michigan State University, East Lansing, MI
- **Mechanisms of Resveratrol-Induced Immunomodulation and Its Potential Use in the Treatment of Inflammatory and Autoimmune Diseases**, Prakash Nagarkatti, University of South Carolina School of Medicine, Columbia, SC
- **Immunomodulation by n-3 Polyunsaturated Fatty Acids**, James Pestka, Michigan State University, East Lansing, MI
- **Immunomodulation by 3,3'-diindolylmethane**, Leonard Bjeldanes, University of California Berkeley, Berkeley, CA
- **Eotaxin-1 Inhibition by 7, 4-dihydroxy Flavone Isolated from Glycyrrhiza Uralensis**, Xiu-Min Li, Mount Sinai School of Medicine, New York, NY

NANOTECHNOLOGY

Nanotoxicology and Drug Delivery

Tuesday, March 17, 9:00 AM–11:45 AM

Chairperson(s): Chris Somps, Pfizer, Inc., Groton, CT and Bob Chapin, Pfizer Global Research and Development, Groton, CT

Sponsor:

Nanotoxicology Specialty Section

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Drug Discovery Toxicology Specialty Section

Immunotoxicology Specialty Section

Regulatory and Safety Evaluation Specialty Section

The biopharmaceutical industry is looking at the rapidly developing, multifaceted field of nanotechnology as an opportunity for improved approaches to drug development. A good example is the

ongoing effort to exploit the unique physical and chemical properties of nanoscale materials for the purpose of improved drug delivery. Using nanoparticles with targeting ligands to precisely deliver a drug payload to a specific diseased tissue, while by-passing all other parts of the body, would clearly represent a game changing approach to drug development. However, before that future vision can be realized, significant unknowns and gaps in our understanding of the toxicology of nanoscale drug delivery platforms will need to be addressed. Academic and industry researchers, as well as government regulators, interested in the unique safety issues confronting drug developers will explore the use of nanomaterials for improved drug delivery. The program will consider the design and development of nanomaterials compatible with the unique requirements for drug delivery and therapy, focusing on material distribution and safety when intentionally delivered into physiologic systems. Special emphasis will be placed on properties that influence absorption, distribution, metabolism and excretion of nanomaterials, including immune system interactions, and properties that influence the toxicity of nanomaterials and their degradation products. Finally, we will explore the FDA's current activities toward developing a regulatory framework to support the development and safe use of nanomedicine products, including nanoscale drug delivery platforms.

- **Designing Favorable Elimination Features into Nanoscale Drug Delivery Systems**, Patrick Sinko, Rutgers, The State University of New Jersey, Piscataway, NJ
- **Evaluation of Cancer Nanotherapeutics' Stability and Disposition**, Stephan Stern, SAIC-Frederick, Inc., National Cancer Institute at Frederick, Frederick, MD
- **Safe Design of Nanoparticles for Therapy and Imaging: Physical and Chemical Characteristics**, Martin Philbert, University of Michigan, Ann Arbor, MI
- **Nanoparticle Interactions with Immune System**, Marina Dobrovolskaia, SAIC-Frederick, Inc., National Cancer Institute at Frederick, Frederick, MD
- **Safety Considerations for the Regulation of Nanomaterial-Containing Therapeutics**, Nakissa Sadrieh, U.S. FDA, Rockville, MD



Symposia

NANOTECHNOLOGY

Aquatic Species As Sentinels for Human Health: Comparative Toxicology of Metals, Nanoparticles, and PCB's

Tuesday, March 17, 1:30 PM–4:15 PM

Chairperson(s): John Pierce Wise, University of Southern Maine, Portland, ME and The Ocean Alliance, Lincoln, MA and Sylvain DeGuise, University of Connecticut, Storrs, CT

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Metals Specialty Section

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Aquatic toxicology has important implications for human health including using animals in aquatic environments as sentinels for both human health and the health of the aquatic environment and as models for human disease. Metals, nanoparticles, and organic compounds pose emerging and persistent concerns for public and aquatic health, but their full impacts are poorly understood. Given the current understanding of contaminants in the aquatic environment and the lessons that can be learned for human health it is important to address these issues. The panel of experts will highlight the emerging data that chromium may be a major pollutant in the marine environment with consideration that marine mammals are a sentinel species for human health, and also discuss potential novel adaptations in these whales to these exposures that may have implications for human health. The potential impact of metal nanoparticles using a fish model for development will be utilized to inform on how to rapidly determine which types of nanoparticles are more potent than others. The toxicity of nanoparticles will be compared and considered in human cells compared to cells from aquatic species to show how the response to these agents can be very different for various species. The impact of mercury will also be considered and its effects on development using a zebrafish model. It will consider how organochlorines impact the immune system of whales and humans and how whales may be sentinels for human health. Insight will be offered to researchers and risk assessors on the potential impacts of these chemicals, but even more importantly it reveals theories underlying these effects and thus suggests future directions in research for aquatic toxicology and aquatic models and how they relate to human health. For those currently engaged in nanotoxicology, metal toxicology, aquatic toxicology, risk assessment, regulatory management, occupational health, ecotoxicology, immunotoxicology, developmental toxicology, and toxicology education, this should be a particularly informative session.

- **Whales As Sentinels for Human Health: A Global Assessment of Chromium Pollution**, John Pierce Wise, University of Southern Maine, Portland, ME and The Ocean Alliance, Lincoln, MA
- **Relative Toxicity of Metal Nanoparticles to Developing Zebrafish**, Robert L. Tanguay, Oregon State University, Corvallis, OR
- **Comparative Toxicity of Silver Nanoparticles in Human, Marine Mammal and Fish Cells**, Sandra S. Wise, University of Southern Maine, Portland, ME and The Ocean Alliance, Lincoln, MA
- **Zebrafish Model for Understanding Methylmercury Developmental Neurotoxicity**, Michael J. Carvan, University of Wisconsin-Milwaukee, Milwaukee, WI
- **Immunotoxicity of PCBs, an Example of Marine Mammals As Sentinels for Human Health?** Sylvain DeGuise, University of Connecticut, Storrs, CT

EPIGENETICS

Mammalian Retrotranspositional Elements: Epigenetic Regulation, Species Differences, and Potential Roles As Mediators of Cellular Responses to Toxic Stress

Tuesday, March 17, 1:30 PM–4:15 PM

Chairperson(s): Richard D. Storer, Merck & Co. Inc, West Point, PA and Chunhua Qin, Merck & Co. Inc., West Point, PA

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Regulatory and Safety Evaluation Specialty Section

Epigenetic regulation of gene expression is being extensively investigated. However, approximately 38 to 47% of the mouse and human genomes respectively are composed of mobile elements (DNA transposons and retrotransposons) whose potential roles in susceptibility to toxicity and disease upon epigenetic dysregulation have not been fully explored. The retrotranspositional elements are the most numerous and complex, having promoter/enhancer activity, protein coding ability, and mutagenic potential and are subject to epigenetic control. Due to their structure and locations, often within, or proximate to genes and their regulation by DNA methylation,

these elements can modify gene expression and serve as epigenetic mediators of phenotypic variation in a species and strain-specific manner. In addition, some classes of retrotransposons remain active as mobile elements with the potential to create new somatic mutations involved in cancer and germline mutations with the potential to drive genome evolution and modulate disease susceptibility. In humans, long interspersed nuclear elements (LINE-1) and Alu elements are the two classes of retrotransposons that remain active (mobile) while the less numerous endogenous retrovirus (ERV) LTR retrotransposons have mostly lost this capacity. In contrast, in mice, members of the class of retroviral LTR retrotransposons, in particular intracisternal A particles (IAPs), have retained retrotransposon activity. Germline IAP transpositions in certain mouse strains such as in the Agouti and Axin genes have provided fascinating examples of phenotypic variation mediated by epigenetic mechanisms, namely diet- and/or chemically-induced changes in DNA methylation. Given the large number of these genetic elements, and the species differences in their sequences, activity, and distribution in the genomes, further investigation of their potential role(s) in mediating disease processes and cellular responses to endogenous chemicals and xenobiotics is warranted.

- **Mammalian L1 Retrotransposons are Potential Mutagens in Humans**, Haig H. Kazazian, University of Pennsylvania School of Medicine, Philadelphia, PA
- **Mechanisms of Epigenetic Regulation of L1 Elements in Human and Murine Cells**, Kenneth S. Ramos, University of Louisville School of Medicine, Louisville, KY
- **Genetics and Epigenetics of Endogenous Retroviruses**, Dixie L. Mager, British Columbia Cancer Agency and University of British Columbia, Vancouver, British Columbia, Canada
- **Intracisternal A-Particle (IAP) Genes: Distribution in the Mouse Genome and Potential Roles As Species-Specific Mediators of Cellular Responses to Toxic Stress**, Chunhua Qin, Merck Research Laboratories, West Point, PA

INFLAMMATION AND DISEASE

The Good, the Bad, and the Ugly of Toxicant-Induced Pulmonary Inflammation

Tuesday, March 17, 1:30 PM–4:15 PM

Chairperson(s): Lin L. Mantell, St. Johns University, College of Pharmacy, Queens, NY/The Feinstein Institute for Medical Research, North Shore-Long Island Jewish Health System, Manhasset, NY and Judith T. Zelikoff, New York University School of Medicine, Tuxedo Park, NY

Sponsor:

Immunotoxicology Specialty Section

Endorsed by:

Inhalation and Respiratory Specialty Section

A well-orchestrated lung inflammation induced by cytokines is critical to optimizing host defense capabilities, while avoiding or minimizing potential damage to lung tissues. Normally, pulmonary inflammation plays a pivotal role during positive immune responses against microbial and small particle pathogens. Unfortunately, certain inhaled toxicants, such as cigarette smoke and prolonged hyperoxia, can non-specifically induce dysregulated chronic and acute inflammation within the respiratory tract. Therefore it is important to examine the types of immunomodulatory events that occur in the lungs in response to environmental agents and to pathogens, and to demonstrate how similar effects induced by those disparate challenges can lead to distinctly different (i.e., helpful vs. harmful) outcomes. Our panel of experts will present cutting edge studies on the regulation of inflammatory responses by the inflammasome, the nervous system and carbon monoxide. An important outcome of this session is to have attendees be able to recognize the major putative mediators involved in induction of pulmonary inflammation, describe signaling pathways that mediate inflammatory responses to inhaled toxicants and pathogens, better understand the regulation of inflammatory response and identify potential targets and therapeutic strategies for further development for the amelioration of acute lung inflammatory injury and chronic diseases.

- **Introduction of Proinflammatory and Immunosuppressive Immune Responses by Cigarette Smoke Aldehydes**, Brian Freed, University of Colorado Denver School of Medicine, Aurora, CO
- **Exacerbated Pulmonary Toxicity by Proinflammatory Cytokine HMGB1 in Hyperoxia-Induced Lung Injury**, Lin L. Mantell, Johns University College of Pharmacy, Queens, NY/The Feinstein Institute for Medical Research, North Shore-Long Island Jewish Health System, Manhasset, NY

Symposia

- **Inflammasome Activation in Pulmonary Disease**, Matthew Poynter, University of Vermont, Burlington, VT
- **Inhaled Carbon Monoxide As Therapeutic Modality in Inflammatory Lung Diseases**, Augustine M. K. Choi, Brigham and Women's Hospital, Harvard University, Boston, MA
- **Physiology and Immunology of Cholinergic Anti-Inflammatory Pathway**, Kevin J. Tracey, The Feinstein Institute for Medical Research, North Shore-Long Island Health System, Manhasset, NY

- **Metabonomics in Pharmaceutical Discovery and Development**, Donald G. Robertson, Bristol-Myers Squibb, Princeton, NJ
- **Metabonomics and Transcriptomics: A Synergistic Approach to Biomarkers and Mechanisms of Toxicity**, Lois D. Lehman-McKeeman, Bristol-Myers Squibb, Princeton, NJ

Incorporating 'Omics in the Study of Reproduction and Development

Wednesday, March 18, 9:00 AM–11:45 AM

Chairperson(s): Susan Sumner, RTI International, Research Triangle Park, NC and Thomas Knudsen, U.S. EPA, Research Triangle Park, NC

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Reproductive and Developmental Toxicology Specialty Section

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In recent years, ground breaking research in genomic applications in the area of reproductive and developmental toxicology have been successful in linking changes in the expression of specific genes and their higher-level biological processes to effects induced by drugs or chemicals in developing tissues. While gene expression profiling has demonstrated the ability to provide mechanistic insight into the cellular mechanisms of drug and chemical-induced effects, proteomics provides advantages in areas beyond the genome. For example, post-translation modifications of proteins that are known to be involved in cell-cell signaling cascades for developmental pathways, the flux-balance in signaling molecules themselves, or the metabolic intermediates connecting to these pathways are important parts of our ability to understand the pathogenesis of fetal malformations. These higher-level operations can be inferred, but not directly evaluated through measurement of mRNA or DNA sequencing. In recent years, the application of proteomics in the study of reproduction and development has rapidly increased, while such studies that incorporate metabolomics approaches are at their infancy. A summary of the recent advances in genomic, proteomic, and metabolomic methodologies that demonstrate the successful use of these technologies in the study of reproduction and development will be provided. Finally, an illustration of how these data may be integrated by multi-scale models of dynamical systems will be highlighted that can serve to improve our understanding of reproductive and developmental toxicities.

- **Metabonomics in the Study of Reproduction and Development**, Susan Sumner, RTI International, Research Triangle Park, NC

Wednesday

BIOMARKERS

From Mechanisms to Biomarkers: Basic and Applied Metabolomics in Toxicology

Wednesday, March 18, 9:00 AM–11:45 AM

Chairperson(s): Donald G. Robinson, Bristol-Myers Squibb, Princeton, NJ, and Frank J. Gonzalez, National Cancer Institute, Bethesda, MD

Sponsor:

Molecular Biology Specialty Section

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**Drug Discovery Toxicology Specialty Section
Mixtures Specialty Section
Risk Assessment Specialty Section**

The use of metabolomics in the discovery of biomarkers and elucidating mechanisms of human disease is a rapidly expanding field. While nuclear magnetic resonance (NMR) has historically been used in mammalian metabolomics studies, LC/MS and GC/MS, with new and powerful chemometric software, makes this technology more widely available to individual academic laboratories. Metabolomics can also be used to study the metabolism of drugs, toxins and carcinogens and to find biomarkers for drug efficacy and toxicities. Preview studies from both academic and industrial laboratories will be highlighted to show the value of this burgeoning technology.

- **Introduction to Metabolomics: Metabolite Profiling in Toxicology**, Oliver Fiehn, University of California Davis, Davis, CA
- **From Drug Metabolism to Drug Metabolomics**, Jeffrey R. Idle, Universität Bern, Bern, Switzerland

- **Application of Transcriptomics to Assess Chemicals with Estrogenic Activity**, Jorge Naciff, The Procter and Gamble Company, Cincinnati, OH
- **Identifying Molecular Mechanisms of Gene Expression in Mammalian Gametes and Embryos Using Functional Genomics Approaches**, Erdogan Memili, Mississippi State University, Starkville, MS
- **Virtual Tissue Models in Developmental Toxicity Research**, Thomas Knudsen, U.S. EPA, Research Triangle Park, NC
- **Identifying Molecular Pathways That Modulate Environmental and Genetic Components of Complex Diseases**, Julia Gohlke, National Institute of Environmental Health Sciences, Research Triangle Park, NC
- **Iron Toxicity in the Mitochondria: Understanding Network Responses in Friedreich's Ataxia**, Bennett Van Houten, University of Pittsburgh, Pittsburgh, PA

Interactomes and Their Application in Toxicology

Wednesday, March 18, 9:00 AM–11:45 AM

Chairperson(s): Joel N. Meyer, Duke University, Durham, NC and Thomas Begley, GeNYsis Center, Rensselaer, NY

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Molecular Biology Specialty Section

A major challenge in the analysis of microarray data in toxicology and other fields is taking full advantage of the large and often very complex datasets that are obtained. A variety of tools are available for such analysis. The use of interactomes as an especially powerful systems biology tool applicable to the analysis of the transcriptomic response to toxicant exposure will be highlighted. Interactomes are networks of protein-protein, protein-DNA, and other interactions that occur in organisms. They are derived both from careful curation of decades of biological research on such interactions, and *via* higher-throughput assays designed to detect such interactions (e.g., yeast two-hybrid screens). By overlaying gene expression data on these interactomes, it is possible to analyze large, complex microarray datasets in a statistically robust and biologically meaningful fashion. Our panel of experts, who are foremost researchers in toxicological research utilizing interactomes, will discuss both the important toxicological findings and applications of this cutting-edge technology.

- **Systems Based Approaches for the Identification of Cellular Responses to Toxicants**, Thomas Begley, State University of New York at Albany, Albany, NY
- **Pathway Mapping of Chemical-Perturbed Regulatory Networks**, Ivan Rusyn, University of North Carolina at Chapel Hill, Chapel Hill, NC
- **Identification of New Biological Pathways Affected by Transition Metals**, Jonathan Freedman, National Institute of Environmental Health Sciences, Research Triangle Park, NC

EPIGENETICS

Transcriptional Changes in Immunotoxicology: Transcription Factors, Signal Transduction, and Epigenetics

Wednesday, March 18, 9:00 AM–11:45 AM

Chairperson(s): Keiko Nohara, National Institute for Environmental Studies, Tsukuba, Japan and Nancy I. Kerkvliet, Oregon State University, Corvallis, OR

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Numerous pioneering studies have taken advantage of innovative genomics technologies to demonstrate that various chemicals cause toxic effects by inducing transcriptional changes. These changes are induced by the activation or inactivation of various transcription factors by the direct binding of chemicals or indirectly through modulation of signal transduction pathways. Epigenetics has been recognized as another pivotal mechanism to regulate transcription particularly in development and cellular differentiation that has been found in response to environmental factors. The latest studies are shedding light on the relationship between transcription factor functions and epigenetic alterations. Particular focus will be given to several transcription factors or signal transduction pathways which are highly expressed in immune cells and/or closely related to immune suppression, such as the NF- κ B family, E2F, AhR and p53-activating ATM and ATR kinases, and also on the epigenetic regulation of immune reactions. Taking a broad as well as an up-close view of these up-to-date studies on how chemicals induce transcriptional changes and cause adverse effects in immune cells will advance our understanding of the characteristics of immunotoxicity and give insights into the mechanisms of transcription-mediated toxicity in general.



Symposia

Scientific

- **The E2F Family Is a Sensitive Target of Arsenite in the Thymus: A Characteristic Down-Regulation of E2F-Related Genes Revealed by Immunotoxicogenomics**, Keiko Nohara, National Institute for Environmental Studies, Tsukuba, Japan
- **Role of p53 and ATM/ATR in DMBA-Induced Immunotoxicity**, Scott W. Burchiel, The University of New Mexico College of Pharmacy Toxicology Program, Albuquerque, NM
- **NF- κ B Plays a Major Role in the Maturation of Dendritic Cells Induced by Chemical Sensitizers**, Marc Pallardy, University of Paris, Chatenay Malabry, Paris, France
- **Immune Programming by the Aryl Hydrocarbon Receptor**, B. Paige Lawrence, University of Rochester, Rochester, NY
- **Epigenetic Changes in T Helper Genes Affecting IgE Production *In Vivo* Following Combined Inhaled Diesel Exhaust Particles and Allergen Exposure**, Rachel Miller, Columbia University College of Physicians and Surgeons, New York City, NY

EPIGENETICS

Gene-Environment Interactions: Epigenetic Pathways in Chronic Disease Promotion and Progression

Wednesday, March 18, 12:00 NOON–1:20 PM

Chairperson(s): Heather S. Floyd, U.S. EPA, Research Triangle Park, NC and Sheppard A. Martin, University of Georgia, Athens, GA

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Occupational and Public Health Specialty Section
Student Advisory Council

The study of gene-environment interactions has become increasingly more common as it relates to disease susceptibility and chronic disease development. These studies aid in the characterization of environmental exposures and development of targeted prevention/treatment regimens. Traditional genetic endpoints can be expanded to include epigenetic modifications related to altered DNA methylation patterns, histone modifications, and germ-line reprogramming. Heritable alterations in the expression of particular genes or gene clusters and transgenerational effects that are linked to environmental exposures, such as gonadal sex determination and tumor development, are of particular interest. Alterations that result in chronic conditions present in early to mid-life stress the importance

of ongoing research efforts to characterize molecular mechanisms associated with these conditions. Gene-environment interactions resulting in the promotion of autoimmune or neurodegenerative diseases serve to highlight current public health issues with an epigenetic basis. This is an important platform that will highlight toxicologically relevant epigenetic alterations with accompanying disease states and showcase trainee achievements. This session is brought to you through the collaborative efforts of the Postdoctoral Assembly and the Student Advisory Council.

- **Lead-Induced Epigenetic Alterations in Alzheimer's Disease: Associations between Methylation Profiles and Amyloidogenesis**, Adermi Dosunmu, University of Rhode Island, Kingston, RI
- **Epigenetic Transgenerational Actions of Endocrine Disruptors**, Carlos Guerrero-Bosagna, Washington State University, Pullman, WA
- **Early Developmental Exposures to Estrogens/Bisphenol-A Impact a Specific Prostate Epigenome**, Wan-Yee Tang, University of Cincinnati College of Medicine, Cincinnati, OH
- **Abnormal T-Cell DNA Methylation and the Development or Promotion of Autoimmune Diseases Such As Lupus**, Donna Ray, University of Michigan Medical School, Ann Arbor, MI

BIOMARKERS

Biomarkers: New Breakthroughs in the World of Air Pollution Studies

Wednesday, March 18, 1:30 PM–4:15 PM

Chairperson(s): Michael Madden, U.S. EPA, Chapel Hill, NC and Stephen Edwards, U.S. EPA, Research Triangle Park, NC

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Inhalation and Respiratory Specialty Section
Mixtures Specialty Section

Biomarker measurement allows better understanding of the factors that influence the health outcomes from air pollutant exposures. In this session, new biomarker strategies will be highlighted to show the use of biomarkers to study health effects derived from air pollution and to provide updates on the utility of new biomarker techniques including 'omics-type of analyses. Our panel of experts will focus on improved use of biomarkers of exposure, effects, and susceptibility. Session highlights will include the use of select urinary PAHs to reflect exposure to petroleum-derived emissions that show similar body burdens across occupational and controlled exposure studies

and use of susceptibility factors such as obesity and employment status to demonstrate increased biological responses (e.g., heart rate variability) and health effects (e.g., mortality). Finally, our experts will cover the use of genomics to improve the understanding of the likelihood of the development of asthma as well as proteomics to identify unique exposure biomarkers and potentially the cell types producing the markers.

- **Use of Cardiac Markers and Susceptibility Factors for Examination of Particulate Matter Induced Toxicity in Humans**, David Christiani, Harvard University, Boston, MA
- **Coarse Particulate Matter Air Pollution and Hospital Admissions for Cardiovascular and Respiratory Diseases Among Medicare Patients**, Francesca Dominici, Johns Hopkins University, Baltimore, MD
- **Use of Gene Expression Changes in Blood to Elucidate Mechanistic Indicators of Childhood Asthma (MICA)**, Stephen Edwards, U.S. EPA, Research Triangle Park, NC
- **Comparing Urinary Biomarkers of Exposure to Polycyclic Aromatic Hydrocarbons**, Jon Sobus, University of North Carolina Chapel Hill, Chapel Hill, NC
- **Identification of Oxidatively-Modified Proteins As Biomarkers of Chronic Inflammatory Stress**, Joel Pounds, Pacific Northwest National Laboratory, Richland, WA

New Insights into Skin Homeostasis and Carcinogenesis

Wednesday, March 18, 1:30 PM–4:15 PM

Chairperson(s): Hollie Swanson, University of Kentucky, Lexington, KY and Robert Smart, North Carolina State University, Raleigh, NC

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Molecular Biology Specialty Section

It is important to note the following as it relates to the significance of the studies focused on understanding skin homeostasis and carcinogenesis. Researchers know that skin cancer is currently the most common type of human cancer and the skin cancer model is a well-studied model of multistage carcinogenesis that can provide mechanistic insights. Also, the common mechanisms elucidated from these studies are highly relevant to those involved in a number of chronic human diseases. Like other epithelial cancers, skin carcinogenesis involves initiation, promotion and progression that requires activation of oncogenes and inactivation of tumor suppressor genes. Activation of oncogenes, in particular Ras, often occurs following exposure to a number of chemicals and other agents. Signaling pathways upregulated following exposure to UV light, for example,

include that of the ErbB receptors. Keratinocytes that are thus initiated acquire the capabilities to bypass normal cell death pathways, such as apoptosis and proliferate and ultimately form pre-malignant lesions. Recent studies have shown redox signaling plays a key role in modulating oncogenic and tumor suppressive (i.e., p53) signals during skin carcinogenesis. In addition to p53, other proteins also thought to play important roles in suppressing epithelial tumorigenesis is C/EBP alpha that is involved in G1 checkpoint. Xenobiotics that can impinge on the regulation of skin homeostasis include dioxin, which likely exerts its tumor promoting activities, in part, via its ability to inhibit apoptosis and senescence. Thus, it is important to focus on the molecular and cellular mechanisms involved in maintaining proper skin homeostasis and how environmental factors may impinge on these mechanisms and contribute to the development of not only skin cancer, but also to the progression of chronic disease states of tissues such as the heart, esophagus, and nervous system.

- **Activation of the AHR Alters Cell Fate Decisions and Skin Homeostasis**, Hollie Swanson, University of Kentucky, Lexington, KY
- **ErbB2: A Regulator of the Skin's Response to Ultraviolet Irradiation**, Laura Hansen, Creighton University, Omaha, NE
- **Multifaceted Roles for C/EBPS in the DNA Damage Response Network and Skin Tumorigenesis**, Robert Smart, North Carolina State University, Raleigh, NC
- **Mitochondria and Skin Cancer: New Facet in an Old Partnership**, Daret St. Clair, University of Kentucky, Lexington, KY

Pulmonary Effects of *In Utero* and Early Postnatal Exposure to Arsenic

Wednesday, March 18, 1:30 PM–4:15 PM

Chairperson(s): R. Clark Lantz, University of Arizona, Tucson, AZ and Jie Liu, NIH, Research Triangle Park, NC

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Risk Assessment Specialty Section

Arsenic has long been recognized as a human lung carcinogen. In addition, the health effects of arsenic ingestion in the drinking water have also been associated with significant non-cancerous chronic pulmonary disease. It has been postulated that a significant proportion of adult lung disease originates *in utero* or in early

Symposia

infancy. Growth and development requires the temporal and spatial coordinated expression of genes and gene products. During this critical time, *in utero* and early postnatal exposure to toxicants has the potential to affect gene expression, altering organ structure and physiological function which can lead to adult disease. The effect of *in utero* and early postnatal arsenic exposure on lung disease and the effects of arsenic exposure during lung development on human cancer and noncancerous lung disease in adults will be presented. The adverse health outcomes associated with *in utero* and postnatal exposures and will demonstrate the importance of understanding the mechanisms and targets of arsenic during these developmental time points will be provided as an overview. Further discussions will focus on gene-environment interactions in arsenic metabolism, metabolism and distribution of arsenic during fetal development and cancerous and noncancerous animal models of *in utero* and early postnatal exposures. In order to fully understand the issues presenters, researchers will provide attendees with excellent examples and information from both population and laboratory based research that will indicate the importance of exposures during these sensitive developmental times. This symposium will be of interest to those involved in metal toxicology, developmental toxicology, public health, risk assessment and regulatory management.

- **Impact of *In Utero* and Childhood Exposure to Arsenic in Drinking Water on Mortality in Young Adults**, Allan Smith, University of California Berkeley, Berkeley, CA
- **Genetics, Intrinsic Environment, and Extrinsic Environment Influence Human Variability of Arsenic Metabolism**, Walter Klimecki, University of Arizona, Tucson, AZ
- **Arsenic Metabolism and Distribution in Developing Organisms**, David Thomas, U.S. EPA, Research Triangle Park, NC
- **Fetal Arsenic Exposure and Adult Lung Cancer in Mice—Implications and Potential Mechanisms**, Jie Liu, NIEHS, Research Triangle Park, NC
- **Alteration in Pulmonary Structure and Function Following *In Utero* and Early Postnatal Arsenic Exposure**, R. Clark Lantz, University of Arizona, Tucson, AZ

INFLAMMATION AND DISEASE

The Role of Inflammation during Metabolic Liver Disease and Drug-Induced Liver Toxicity: Novel Insights

Wednesday, March 18, 1:30 PM–4:15 PM

Chairperson(s): Shashi Ramaiah, Pfizer Global Research and Development, St. Louis, MO and Hartmut Jaeschke, University of Kansas Medical Center, Kansas City, KS

Sponsor:
Toxicologic and Exploratory Pathology Specialty Section

Endorsed by:
Drug Discovery Toxicology Specialty Section
Immunotoxicology Specialty Section

Hepatic inflammation is a common finding during a variety of metabolic diseases and drug-induced liver toxicity. The inflammatory phenotype noted in the liver can be attributed to the innate immune response generated by Kupffer cells, monocytes, neutrophils and lymphocytes (T, NK and NKT cells). The adaptive immune system is also influenced by the innate immune system leading to liver damage. A major question that continues to be debated is the precise role of these immune cells to liver damage. Liver injury mediated by neutrophils has been reported in a number of animal models such as ischemia-reperfusion injury, endotoxemia, alcoholic hepatitis, obstructive cholestasis and drug-induced liver damage such as by ANIT and acetaminophen overdose. Similarly Kupffer cells and lymphocytes are also implicated for hepatic pathology. The role of autoimmunity (Th17 cell) in idiosyncratic liver toxicity is an area of intense investigation. The role of each component of both innate and adaptive immune responses during hepatic inflammation in specific metabolic diseases and idiosyncratic liver toxicity will be discussed. The issues presented will span from fundamental mechanistic studies to clinical investigations on the role of neutrophils, lymphocytes, Kupffer cells and immune responses in liver damage during metabolic diseases and drug-induced idiosyncratic liver toxicity.

- **Role of Autoimmunity (Th17 cells) in Drug-Induced Liver Injury**, Jack Uetrecht, University of Toronto, Toronto, Ontario, Canada
- **Immune Regulation in Liver Disease**, David Adams, University of Birmingham, Birmingham, West Midlands, United Kingdom
- **Role of Hepatic Macrophages in Drug-Induced Liver Injury**, Cynthia Ju, University of Colorado Health Sciences Center, Denver, CO

- **Role of Neutrophils in Mechanisms of Drug Hepatotoxicity**, Hartmut Jaeschke, University of Kansas Medical Center, Kansas City, KS
- **The Contribution of Osteopontin to Hepatic Inflammation and Liver Injury**, Shashi Ramaiah, Pfizer Global Research and Development, St. Louis, MO

Thursday

Heat Shock Proteins and the Toxicological Response

Thursday, March 19, 9:00 AM–11:45 AM

Chairperson(s): Kathleen Gabrielson, Johns Hopkins Medical Institutions, Baltimore, MD and James Kang, University of Louisville, Louisville, KY

Sponsor:

Comparative and Veterinary Specialty Section

Endorsed by:

Immunotoxicology Specialty Section
Metals Specialty Section
Neurotoxicology Specialty Section

Heat shock proteins (HSPs) are protein chaperones that facilitate protein folding and function. HSPs are induced by heat stress, oxidative stress and multiple classes of toxins. In order to fully understand HSP, it is important to review the latest research on HSP biology in inflammation, metal toxicity, cardiac physiology, neurodegeneration, and endoplasmic reticulum stress. During inflammation, HSP70 is important in antigen presentation. HSP70 interacts with lipids and proteins and binds to its own message to change the mRNA stability to modulate inflammatory response. During metal toxicity, signal transduction pathways induced by metals are tightly linked to protective heat shock protein pathways. HSP gene expression can be induced pharmacologically by novel agents currently being tested to induce protection against toxicities. For cancer therapy, HSP90 inhibitors are currently being tested in clinical trials. In cancer cells, inhibition of HSP90 is attractive since HSP90 chaperones multiple proteins including erbB2 and Akt, telomerase, endothelial nitric oxide synthase, channels, hormone receptors like glucocorticoid receptor, and transcription factors like HIF1 α and AhR. It is not yet known whether HSP90 inhibitors will induce sufficient cancer cell death without inducing toxic side effects. Conversely, HSP90 inhibitors are proposed to reduce neurodegeneration, yet inhibition of HSP90 function in cardiomyocytes or endothelial cells *in vitro* is detrimental to cellular function.

Finally, the unfolded protein response (UPR) is a common stress response in various toxicities (from insecticides to metals). This exquisite pathway links endoplasmic reticulum and nucleus to influence cellular fate. The latest findings of the role of HSPs in the response to toxicities, inflammation and cellular degeneration will be presented.

- **Heat Shock Protein Immunomodulatory Response**, Antonio DeMaio, University of California San Diego, La Jolla, CA
- **Heat Shock Protein 90 Expression and Function in Neurodegeneration and Cardiac Degeneration: Clinical Implications of HSP90 Inhibitors**, Kathleen Gabrielson, Hopkins Medical Institutes, Baltimore, MD
- **Unfolded Protein Response-Role of Endoplasmic Reticulum and Nuclear Signaling Pathways in Toxicities**, Linda Hendershot, St. Jude Children's Research Hospital, Memphis, TN
- **Cross Talk of Heat Shock and Heavy Metal Regulatory Pathways**, Y. James Kang, University of Louisville, Louisville, KY



Workshops

Monday

Dose Selection and Design Considerations in Safety Studies for Biotherapeutics

Monday, March 16, 9:15 AM–12:00 NOON

Chairperson(s): Laura Andrews, Genzyme Corporation, Framingham, MA and Timothy MacLachlan, Genzyme Corporation, Framingham, MA

Sponsor:
Regulatory and Safety Evaluation Specialty Section

Endorsed by:
Reproductive and Developmental Toxicology Specialty Section
Occupational and Public Health Specialty Section

With many biotherapeutics being evaluated on a case-by-case basis there is often significant consideration that goes into selection of the highest doses to be used in a study, use of recovery groups, and the impact of immunogenicity on the outcome and interpretation of the study. Traditional approaches that rely upon a maximum tolerated dose for high dose selection may not be relevant or even feasible when considering biotherapeutic products. Establishing a range of toxicology endpoints in a study using a classical approach is often not feasible or practical with biotherapeutic products due to challenges that might involve formulation, concentration, stability and volume issues. In addition, the use of recovery groups needs to be considered and the utility of the information gained from the use of additional animals added to a study. Aspects of full recovery evaluation and the impact of immunogenicity on the outcome and interpretation of the study design will be discussed. Challenges continue to exist in the appropriate study design for reproductive evaluation of biologics and the utility of such studies to the safety package. These considerations as well as challenges that may be encountered with reproductive study designs will be covered, in addition to addressing some of the challenges with respect to dose selection and study design considerations, including reproductive study designs for biotherapeutics. Emphasis will be placed on choosing a high dose for toxicology studies and how does that relate to clinical trial dosing strategies; the impact of immunogenicity on the dosing strategy and the potential to dose higher; the use and information to be gathered from recovery animals and the selection of dose and dosing regimen for developmental and reproductive studies for biotherapeutics.

- **How High is High Enough When Selecting Top Doses for General Toxicology Studies?** Christopher Horvath, Archemix, Cambridge, MA
- **Recovery Groups: A Necessary Evil? Preclinical Development Considerations for Determination of the Need for and Duration of Recovery Groups,** James Green, BiogenIdec, Cambridge, MA
- **Impact of Immunogenicity on High Dose Selection for Chronic Studies—Should You Dose Higher? Pros and Cons,** Daniel Wierda, Eli Lilly and Company, Indianapolis, IN
- **High Dose Selection for DART Studies,** Jessica Couch, Genzyme, Framingham, MA

From Genes to Organs: Advancements in Modeling Biological Systems

Monday, March 16, 9:15 AM–12:00 NOON

Chairperson(s): Stephen Edwards, U.S. EPA, Research Triangle Park, NC and Charles Timchalk, Pacific Northwest National Laboratory, Richland, WA

Sponsor:
Biological Modeling Specialty Section

Endorsed by:
Drug Discovery Toxicology Specialty Section
Risk Assessment Specialty Section

As we consider the future of toxicity testing, the importance of applying biological models to this problem is clear. Modeling efforts exist along a continuum with respect to the level of organization (e.g., cell, tissue, organism) linked to the resolution of the model. Generally, a tradeoff is made whereby higher levels of organization are models with lower resolution. Consideration will be given to modeling efforts across the full range of this spectrum. First, a model will be described for intracellular signaling including important information on how the choice of cell type for *in vitro* studies affect the signaling seen. Next, two systems approaches will be highlighted which model genome-wide molecular changes (i.e. ‘omics) within and between tissues and the application to pharmaceutical target discovery and toxicity testing. Finally, biologically-based dose-response models for risk assessment and data requirements associated with these models will be covered followed by a progress report on the development of detailed tissue models and integration of such models with molecular and cellular changes. If incorporated into future toxicity testing, these approaches should greatly facilitate the definition and quantitative modeling of mode of action for important environmental stressors. The systems approaches also have the potential to greatly improve interspecies extrapolation. In addition, the models described will facilitate the use of *in vitro* data

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Workshops

for risk assessment thereby increasing the number of chemicals that can be evaluated each year. In considering these different modeling approaches, we hope to gain a better understanding of the future opportunities and challenges we face as we strive for increasingly higher resolution models at greater levels of organization.

- **Quantitative Systems Analysis of Hepatocellular Responses to Inflammatory Cytokines and Pharmacological Agents**, Douglas Lauffenburger, Massachusetts Institute of Technology, Cambridge, MA
- **Informatic and Statistical Integration of ‘Omics Data to Model Cellular Response to Stress**, Katrina Waters, Pacific Northwest National Laboratory, Richland, WA
- **Gene Networks Reflecting Tissue-Tissue Interactions Highlight Novel Causal Patterns of Association with Human Disease**, Eric Schadt, Rosetta Inpharmatics, Merck & Company, Seattle, WA
- **Biologically Based Dose-Response Modeling: The Potential for Accurate Description of the Linkages in the Applied Dose—Tissue Dose—Health Effect Continuum**, Rory B. Conolly, U.S. EPA, Research Triangle Park, NC
- **Virtual Organ Models for Multi-Scale Integration of Dose-Response Relationships**, Richard A. Corley, Pacific Northwest National Laboratory, Richland, WA

Strategies to Integrate Systems Biology into *In Vitro* Screening in Early Nonclinical Safety Assessment

Monday, March 16, 9:15 AM–12:00 NOON

Chairperson(s): John W. Davis, Pfizer Global Research and Development, Chesterfield, MO and Donna Dambach, Genentech Inc., South San Francisco, CA

Sponsor:

In Vitro and Alternative Methods Specialty Section

Endorsed by:

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

The toxicity of pharmaceutical compounds can be due to their interactions with unanticipated molecules in the body (off-target) or the direct consequence of over-inhibiting or stimulating the intended molecular target in a desired or undesired location (target-based). Such complex processes of toxicity pose significant challenges to toxicologists who seek to either proactively minimize potential liabilities by devising screening strategies or to elucidate

mechanistic understanding of an identified toxicity. The precept of systems biology (SB) is the ability to obtain, integrate and analyze complex data from multiple experimental sources using interdisciplinary tools with an overall goal of examining the gestalt of a biological process, e.g. disease or toxicity. A fundamental aspect of the application of a SB approach is the need to verify the physiological relevance of the data generated. Although most investigative toxicology studies that employ SB techniques are initiated as the result of a clinical or histological finding, SB approaches can be utilized and integrated to proactively evaluate potential target toxicity and to aid in the screening of molecules for favorable profiles during lead optimization. A common approach is to generate datasets *in vivo* using SB approaches and apply those learnings to develop *in vitro* models. The key to successfully implementing this approach is to anchor the data to traditional endpoints of interest, thus enabling a benchmarked relationship. The understanding of the relevance of SB data to the traditional endpoints coupled with data integration strategies aims at deriving more robust, mechanism-based risk assessments. Thus, it is important to implement strategies to obtain information early in the drug development process on potential safety risks, the challenges to evaluating predictivity, including *in vitro/in vivo* correlations, the need for increasing assay throughput, and general approaches to correlation/validation.

- **Introduction**, Donna Dambach, Genentech Inc., South San Francisco, CA
- **Application of Systems Biology Visualization and Analysis Tools in Risk Assessment**, Hisham Hamadeh, Amgen, Inc., Thousand Oaks, CA
- **Data Integration Strategies Reveal Potential Liabilities in Early Lead Optimization**, Matthew T. Cooper, Roche Palo Alto, Palo Alto, CA
- **Organ Slices Provide Mechanistic Insight into Drug-Induced Organ Injury and Facilitate Comparisons of Animal and Human Tissue**, Allison Vickers, Allergan, Inc., Irvine, CA
- **Systems Biology Approaches to Optimizing a Screening Battery**, Jinghai James Xu, Pfizer, Cambridge, MA
- ***In Vitro* Microarray Analysis of Hepatocytes for Lead Compound Selection**, Craig Thomas, Lilly Research Laboratories, Greenfield, IN

Workshops

NANOTECHNOLOGY

Agglomeration Versus Dispersion: How Nanoparticle Behavior Affects Exposure and Toxicity *In Vitro*, *In Vivo*, and in the Real World

Monday, March 16, 1:40 PM–4:25 PM

Chairperson(s): Joyce Tsuji, Exponent Inc., Bellevue, WA and Christie M. Sayes, Texas A&M University, College Station, TX

Sponsor:
Nanotoxicology Specialty Section

Endorsed by:
Drug Discovery Toxicology Specialty Section
Inhalation and Respiratory Specialty Section
Risk Assessment Specialty Section

Many studies of nanoparticles have noted a tendency of these particles to agglomerate and form larger particles in air, solution, or suspension. Consequently, dispersion of nanoparticles has been a challenge for toxicity studies and pharmaceutical or medical applications, which have used various means, both chemical and physical to deliver nanoparticles to cells, tissues, or organisms. Such methods are important in evaluating free nanoparticles. However, clumping of nanoparticles, or particle agglomerates, is a real world phenomenon that is relevant to understanding risks posed by nanomaterials. In some systems, agglomeration of particles in air or solution/suspension appears to increase with particle concentration and decreasing size. The solution's ionic strength and electrolyte concentration can affect agglomeration and surface characteristics. Particle characteristics can in turn affect agglomeration. Other factors, such as dispersants used in sunscreens or dissolved organic matter in aquatic environments may prevent clumping. Consequences of agglomeration include exclusion by biological barriers. Agglomerated carbon nanotubes have also been shown to exhibit different effects in the lungs than their more dispersed counterparts. Studies with aquatic organisms indicate less toxicity with increasing size of particle agglomerates, although agglomerated nanoparticles are not necessarily similar in toxicity to micron-sized particles. Therefore, it is important to explore determinants of nano-sized particle-to-particle interactions, including particle properties and environmental conditions, consequences of change in size on fate in the environment and within organisms, effects on toxicity, and the real world consequences of such particle behavior on health and environmental risks. Increase in the understanding of nanoparticle exposure and toxicity in recent years is enabling inferences on certain aspects of nanoparticles that may help us

design and interpret toxicity studies to better assess the health risks of applications of nanomaterials.

- **Introduction**, Joyce S. Tsuji, Exponent, Bellevue, WA
- **Physical & Chemical Characteristics Affecting Nanoparticle Behavior in Toxicology and Eco-Toxicology Studies**, Christie M. Sayes, Texas A&M University, College Station, TX
- **Effects of Particle Agglomeration on Pulmonary Toxicity**, Vincent Castranova, CDC NIOSH, Morgantown, WV
- **Stability of Nanoparticles for Biomedical Applications**, Martin Philbert, University of Michigan, Ann Arbor, MI
- **Nanoparticle-Macromolecule Interactions and Their Impact on the Rate and Extent of Particle Agglomeration**, Greg Lowry, Carnegie Mellon University, Pittsburgh, PA
- **Application of Toxicology Studies for Risk Assessment in the Real World**, Fionna Mowat, Exponent, Menlo Park, CA

Tuesday

Low-Dose Non-Linearity: What Can Emerging Technologies Tell Us?

Tuesday, March 17, 9:00 AM–11:45 AM

Chairperson(s): James Bus, Dow Chemical Company, Midland, MI and William Slikker, U.S. FDA, Jefferson, AR

Sponsor:
Risk Assessment Specialty Section

Endorsed by:
Inhalation and Respiratory Specialty Section
Regulatory and Safety Evaluation Specialty Section

Characterization of dose-response, as captured in the *Paracelsus* phrase, "The dose makes the poison," is a central tenant to the field of toxicology and risk assessment. Until recently, methodological limitations have prevented comprehensive examination of many of the fundamental biological phenomena underlying both toxicological responses and risk assessment assumptions at or below the low end of traditionally-defined toxicity dose-response curves. Relatively recent and rapid advances in cellular, biochemical, toxicogenomic, and analytical technologies, however, are now presenting opportunities to more accurately and comprehensively characterize the nature of dose-response curves, including its shape in low-dose ranges that are more relevant to actual, real-world human exposures. To this end, and pursuant to the recent recommendations proposed by the National Academies/National Research Council Report and a joint

SETAC-SOT sponsored Pellston Conference (NAS, “Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment,” 2007; DiGiulio and Benson, “Genomic Approaches to Cross-Species Extrapolation in Toxicology,” 2007), the practice of applying emerging technologies to characterize toxicant-induced responses in the low-dose range and shape of the dose-response are now being realized. Importantly, application of these molecular-level technologies may allow a more complete and predictive analysis of responses and/or associated risk assessment assumptions that are key to understanding human relevance of responses observed at the low end of the dose-response curve, i.e., decisions of whether to apply linear *versus* non-linear risk assessment approaches. Low-end dose-response analysis using emerging technologies on a number of diverse-acting compounds such as direct genotoxicants, cytotoxicants, and receptor-mediated and undefined-acting toxicants, and will discuss the evidence for the existence, or lack thereof, of thresholds and non-linearity for genomic and other biological responses to xenobiotics will be addressed.

- **The Potential of Genomic Dose-Response Data to Define Mode of Action and Low-Dose Behavior of Chemical Toxicants**, Russell Thomas, The Hamner Institutes, Research Triangle Park, NC
- **Transcript Profiling to Elucidate Responses to Estrogens at Dose Levels Below the Traditional No Observed Adverse Effect Level**, George Daston, Procter & Gamble, Cincinnati, OH
- **Phenotypic Anchoring of Carcinogen-Induced Gene Expression to DNA Adduct Levels Reveals a Coincidence between the No Transcriptional Effect Level (NOTEL) and the No Detectable Adduct Level (NODAL)**, Helmut Zarbl, University of Medicine and Dentistry of New Jersey, Princeton, NJ
- **Low-Dose Genotoxicity Assessment Using Biomarkers of Internal Dose and Flow Cytometry-Based Micronucleus Assay: Low-Dose Acrylamide Study in Mice**, Leslie Recio, Integrated Laboratory Systems Inc., Research Triangle Park, NC
- **Biological Thresholds and Non-Linear Dose-Responses for Multiple Endpoints in Methyl Methanesulfonate (MMS)-Treated Rats**, Matthew LeBaron, The Dow Chemical Company, Midland, MI

Maternal Toxicity and Its Impact on Study Design and Data Interpretation

Tuesday, March 17, 9:00 AM–11:45 AM

Chairperson(s): Bruce K. Beyer, *sanofi-aventis, Malvern, PA* and James Kim, *ILSI Health and Environmental Sciences Institute, Washington, DC*

Sponsor:

**Reproductive and Developmental Toxicology
Specialty Section**

Endorsed by:

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

Assessing maternal toxicity in DART studies is important because it can potentially influence the study's outcome, thus impacting risk assessment and regulatory decisions. Some degree of maternal/parental toxicity is required in developmental and reproductive toxicity (DART) studies by regulatory agencies. However, excessive maternal/parental toxicity is a confounding factor in study design and data interpretation. There is no clear consensus on levels of toxicity that are high enough to meet regulatory requirements but low enough to avoid confounding data interpretation. In addition, there is a need to distinguish true toxicity from exaggerated pharmacology. It also appears that there may be some differences in species susceptibility to maternal toxicity, with the rabbit being more sensitive than the rat in certain cases. Finally, there are conflicting reports in the literature about the relationship between maternal toxicity and fetal abnormalities. Current views of these issues as they impact study design and interpretation and discussion of these areas in which more knowledge is needed will be addressed.

- **Overview and Background**, Ronald D. Hood, The University of Alabama and Ronald D. Hood & Associates, Tuscaloosa, AL
- **Exaggerated Pharmacology Versus True Toxicity**, Bengt R. Danielsson, Uppsala University, and Uppsala and Pharmanet Consulting, Stockholm, Sweden
- **Relationships of Maternal and Fetal Weight Changes in Developmental Toxicology Bioassays**, Neil Chernoff, U.S. EPA, Research Triangle Park, NC
- **Postnatal Consequences of Maternal Toxicity**, Anthony R. Scialli, Tetra Tech Sciences, Arlington, VA
- **Regulatory Perspectives and Case Studies**, Karen Davis-Bruno, U.S. FDA, Silver Spring, MD

Workshops

Pesticide Mixtures: Experimental Evaluation and Computational Modeling

Tuesday, March 17, 9:00 AM–11:45 AM

Chairperson(s): Janice E. Chambers, Mississippi State University, Mississippi State, MS and Virginia C. Moser, U.S. EPA, Research Triangle Park, NC

Sponsor:

Mixtures Specialty Section

Endorsed by:

Biological Modeling Specialty Section
Neurotoxicology Specialty Section
Risk Assessment Specialty Section

Pesticides are applied in the environment to kill insects, weeds, fungi or other pests. They may be applied in mixtures, or, because of overlapping pest pressures, may result in environmental mixtures because of the proximity of times and spaces over which they are applied. Exposures of humans and other non-target organisms to currently registered pesticides and/or persistent legacy pesticides will, therefore, likely be to pesticide mixtures. Because of the vast number of potential mixtures, predicting the effects of pesticide mixtures for risk assessment purposes is ultimately best accomplished through the use of computational models that are based upon experimental results with defined mixtures. Recent research conducted on the neurotoxic or immunotoxic effects of pesticide mixtures and the mathematical approaches to predictive modeling of the resultant data will be reviewed. Modeling approaches include the use of biomarker data produced for some of these pesticides. We will address exposures to the anticholinesterase insecticides, i.e., the organophosphorus and N-methyl carbamate classes of insecticides and the results in serine esterase inhibition. The levels of inhibition of some of these serine esterases, such as blood cholinesterase, is routinely used, in laboratory animal experiments and in worker exposure monitoring, to assess the level of exposure and potential toxicity. To fully understand these experimental results, biomarker data in terms of experimental results and the use of biomarker data in constructing the computational models will be highlighted.

- **Cellular Signaling Pathways As a Target of a Pesticide Mixture**, Stephen B. Pruetz, Mississippi State University, Mississippi State, MS
- **Evaluation of Cholinesterase-Inhibiting Pesticide Mixtures Using a Dose-Additive Model**, Virginia C. Moser, U.S. EPA, Research Triangle Park, NC
- **In Vitro and In Vivo Effects of Several Low-Dose Binary Mixtures of Organophosphorus Insecticides**, Janice E. Chambers, Mississippi State University, Mississippi State, MS

- **OP Insecticide Mixture Exposure: Integrating Computational Approaches and Biomarkers to Reconstruct Dose**, Brad Reisfeld, Colorado State University, Fort Collins, CO

BIOMARKERS

Improved Safety Biomarkers for Monitoring Kidney Injury

Tuesday, March 17, 1:30 PM–4:15 PM

Chairperson(s): Frank D. Sistare, Merck and Co., Inc., West Point, PA and Frank Dieterle, Novartis Pharma AG, Basel, Switzerland

Sponsor:

Regulatory and Safety Evaluation Specialty Section

Endorsed by:

Comparative and Veterinary Specialty Section
Drug Discovery Toxicology Specialty Section
Toxicologic and Exploratory Pathology Specialty Section

A number of accessible biomarkers are becoming available to toxicologists and to clinicians as qualified tools that have demonstrated their ability to out-perform BUN and serum creatinine for monitoring the early onset of certain drug induced kidney pathologies. These tools are beginning to positively impact the development of drug candidates that may present with low grade kidney toxicities in first-in-human enabling GLP animal toxicology studies, especially when observed in a single species, and human irrelevance cannot otherwise be adequately assured. The biomarkers are showing utility not only for monitoring drug safety, but also for interrogating kidney disease progression and regression. Animal toxicology studies designed to assess the biological performance of these new safety biomarkers are providing new insights into fundamental aspects of kidney function, and are supporting potential opportunities to establish a positive response to intervention where kidney disease is a target for new therapies. With the positive response received recently from the U.S. FDA and EMEA regarding the acceptability and utility of certain qualified renal safety biomarkers for targeted regulatory applications, the challenge now is to expand the tool box and to define broader uses. Therefore, we should begin by understanding the performance strengths and limitations of the more robust kidney safety biomarkers established across numerous animal toxicology studies, understanding the molecular, cellular, and anatomical bases for kidney biomarker responses observed to chemical toxicities, and describing the research progress to fill the critical research and regulatory gaps and questions that remain. By fully grasping this information we should be able to present the strategy and progress made to bridge from animal studies to human

clinical trials where establishing the performance attributes of these biomarkers is far more challenging and finally present clinical data of biomarker responses to disease and drug-induced kidney injury matching the pre-clinical data and supporting the clinical qualification and utility of these and additional promising clinical biomarkers.

- **One-Year after the First Regulatory Qualification of Renal Biomarkers: Limitations, Opportunities, Advances, and Impact on Toxicology and Translational Medicine**, Frank Dieterle, Novartis Pharma AG, Basel, Switzerland
- **Preclinical Qualification of Novel Urinary Markers of Renal Injury**, Daniela Ennulat, GlaxoSmithKline, King of Prussia, PA
- **Integrating Animal with Clinical Data to Best Understand KIM-1 As a Kidney Safety Biomarker**, Joseph Bonventre, Harvard Medical School, Boston, MA
- **Acute Kidney Injury Network (AKIN): Advancing Clinical Applications of Promising Renal Biomarkers**, Ravindra Mehta, University of California San Diego, San Diego, CA
- **Improved Safety Biomarkers for Monitoring Clinical Renal Injury**, William Baer, ClinXus, Grand Rapids, MI

Oxidative Stress As a Regulator of Normal Function and Mediator of Toxicant-Induced Damage with Impacts on Reproduction and Development

Tuesday, March 17, 1:30 PM–4:15 PM

Chairperson(s): Sally Perreault Darney, U.S. EPA, Research Triangle Park, NC and Ulrike Luderer, University of California Irvine, Irvine, CA

Sponsor:
Reproductive and Developmental Toxicology
Specialty Section

Endorsed by:
Mechanisms Specialty Section

Exposures to certain chemicals and environmental factors are known to induce oxidative stress, either directly or indirectly, resulting in complex responses at the molecular level in cells and tissues. With respect to reproduction, high levels of endogenous antioxidants such as glutathione (GSH) as are normally present in gonads and embryos are suggestive of both regulatory and protective roles. Interestingly, endogenous reactive oxygen species may be beneficial by stimulating the signaling pathways necessary for gamete development and function and embryonic development. On the other hand, excess reactive oxygen species, including those

resulting from exposure to certain pharmaceuticals or environmental contaminants may impair reproductive cells by depleting endogenous antioxidants and inducing membrane lipid peroxidation and DNA damage. In turn, such damage may induce untimely apoptosis resulting in reduced numbers of healthy gametes and embryos. Indeed, environmental exposures that induce oxidative stress have been postulated to be a contributing factor in human infertility and abnormal pregnancy outcomes. Furthermore, recent evidence indicates that long term, low level oxidative stress may impair Leydig cell function with consequent decreases in testosterone secretion, thus contributing to declines in reproductive function with aging. To convey this message recent research findings on the relationship between oxidative stress and reproductive function with emphasis on specific reproductive and developmental toxicants that act in this manner, and whether polymorphisms in genes involved in the oxidative stress pathway that contribute to differential susceptibility will be addressed.

- **Shifting Concepts of Oxidative Stress: From a Global Imbalance to Disruption of Specific Redox Pathways—From Free Radical to Non-Radical Mechanisms**, Dean P. Jones, Emory University, Atlanta, GA
- **Oxidative Stress and Ovarian Follicular Atresia**, Patrick J. Devine, Institut Armand-Frappier, Laval, Québec, Canada and Ulrike Luderer, University of California, Irvine, CA
- **Oxidative Stress and Testicular Function**, Bernard Robaire, McGill University, Montréal, Québec, Canada and Barry R. Zirkin, Johns Hopkins School of Public Health, Baltimore, MD
- **Oxidative Stress in the Male Gamete: The Ying-Yang of Sperm Function**, Robert Aitken, University of New Castle, New Castle, New South Wales, Australia
- **Redox Regulation during Development and Early Embryonic Organogenesis**, Jason M. Hansen, Emory University, Atlanta, GA

Workshops

NEURODEGENERATIVE DISEASE

Pesticides and Parkinson's Disease: Implications of New Epidemiology and Exposure Data to Risk Assessment

Tuesday, March 17, 1:30 PM–4:15 PM

Chairperson(s): Tina Levine, U.S. EPA, Arlington, VA and Abby A. Li, Exponent Health Sciences, San Francisco, CA

Sponsor:

Neurotoxicology Specialty Section

Endorsed by:

Occupational and Public Health Specialty Section
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

Numerous animal and epidemiological studies have suggested a relationship between pesticide exposure and the development of Parkinson's Disease (PD). Frequently, scientists and the media question whether regulatory processes are sufficiently protective of this potential risk factor. However, there has been relatively little attention paid to the exposure side of the risk equation in the research to date. Furthermore, there is a tremendous need for an improved interface between toxicology and epidemiology. Thus, it is important that we focus our attention on new epidemiology and animal research with an emphasis on the exposure question and the implications of the findings for human health risk assessment. This session brings together speakers from government, academia and industry with knowledge of different aspects of pesticide risk assessment: toxicology, epidemiology, neurology, pharmacokinetics, and exposure assessment. The session will present new results of two important epidemiological studies on Parkinson's Disease that evaluate exposure of humans to pesticides, and an animal study that uses PBPK modeling to relate animal models of PD to estimated human exposure levels. The two epidemiological studies that will be presented are the Honolulu-Asia Aging study (HAAS) and the Farm and Movement Evaluation (FAME) Study of the Agricultural Health Study (AHS). In addition, the results of the Farm Family Exposure Study, which focused on exposure assessment to pesticides, will be discussed in relation to the practice of exposure assessment in agricultural worker epidemiologic studies. This session will end in a panel discussion that will be stimulated by two discussants representing industry and government who have specialized expertise in pesticide exposure assessment and have an understanding of the risk assessment process.

- **Introduction**, Tina Levine, U.S. EPA, Arlington, VA

- **A Neurologist's Bird's Eye View of Key Risk Factors of Parkinson's Disease**, J. William Langston, Parkinson's Institute and Clinical Center, Sunnyvale, CA
- **Honolulu-Asia Aging Study (HAAS): Relationship of Organochlorine Levels with Parkinson's Disease Risk**, Webster Ross, Veterans Affairs Pacific Islands Health Care System, Honolulu, HI
- **Farming and Movement Evaluation Study (FAME): Parkinson's Disease in Pesticide Applicators and Their Spouses**, Freya Kamel, National Institute of Environmental Health Sciences, Research Triangle Park, NC
- **Farm Family Exposure Study: Biomonitoring and Exposure Assessment in Agricultural Populations**, Bruce Alexander, University of Minnesota, School of Public Health, Minneapolis, MN
- **Pesticide Risk Assessment and Animal Models of PD**, Abby Li, Exponent Health Sciences, San Francisco, CA
- **Pesticide Exposure Assessment**, Kent W. Thomas, U.S. EPA, Research Triangle Park, NC and Carol Burns, The Dow Chemical Company, Midland, MI

Safety of High-Intensity Sweeteners: Bittersweet Controversy

Tuesday, March 17, 1:30 PM–4:15 PM

Chairperson(s): Madhusudan Soni, Soni & Associates, Vero Beach, FL and D. Charles Thompson, U.S. FDA/CDER, Rockville, Maryland

Sponsor:

Food Safety Specialty Section

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Association of Scientists of Indian Origin
Special Interest Group
Carcinogenesis Specialty Section
Regulatory and Safety Evaluation Specialty Section

The quest for the perfect high-intensity sweetener with a clean, sweet taste, no off-flavor, non-caloric, and no adverse health effects continues. To date, the U.S. Food and Drug Administration (FDA) has approved five artificial sweeteners: aspartame, acesulfame-K, neotame, and sucralose, in addition to saccharine. Currently, cyclamate is pending FDA approval/re-approval. The agency regulates high-intensity sweeteners as food additives, which must be approved as safe for their intended use before they can be marketed. Although these approved sweeteners have whetted the palates of millions of Americans over the years, the one problem common to all of them has been the controversies over their safety,

which have been anything but sweet. Saccharin has been marketed for more than 100 years and represents a good example of how the shifting requirements of the law and the progress of science can change a substance's status from "safe" to "unsafe." Both the products' manufacturers and the FDA maintain that the currently approved intense sweeteners are safe for their intended uses. Nevertheless, there are accusations in both the scientific literature and in the popular media about risks posed by these sweeteners. Is there really a cause for concern? To fully understand the issues, it is important to provide the current 'state of the science' as it relates to safety of the approved sweeteners; discuss the safety of certain sweeteners currently in development and/or approved outside the U.S., explore the evolving regulatory requirements for safety testing of sweeteners. The session will begin with a brief overview of the basic toxicological requirements for sweeteners in general, followed by presentations on specific controversial issues, lessons learned from previously approved sweeteners, concerns related to obesity, and a look at some possible future sweetener developments.

- **Why Is There Concern About Alternative Sweetener Safety?**
Ruth Kava, American Council on Science & Health, New York, NY
- **Toxicology and Pharmacology of Rebaudioside (Reb A),**
John Thomas, Indiana University School of Medicine, Fishers, IN
- **Controversies Surrounding Aspartame,** Bernadene Magnuson,
Cantox Health Sciences International, Toronto, Ontario, Canada
- **Taste and Behavioral Effects of High Potency Sweeteners,**
Eric D. Walters, Rosalind Franklin University of Medicine and
Science, Chicago, IL
- **FDA's Sweetener (Food Additive) Approval Process: Safety
Assurance Based on Scientific Assessment,** Alan M. Rulis,
Exponent, Washington, DC

Wednesday

Developing Brain: Safety Assessment for Pediatric Use of Pharmaceuticals

Wednesday, March 18, 9:00 AM–11:45 AM

Chairperson(s): Mary Jeanne Kallman, Covance, Inc., Greenfield, IN and LaRonda L. Morford, Eli Lilly & Company, Greenfield, IN

Sponsor:

Neurotoxicology Specialty Section

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Regulatory and Safety Evaluation Specialty Section
Reproductive and Developmental Toxicology
Specialty Section
Risk Assessment Specialty Section

With the recent enactment of the EU pediatric regulation as well as the reenactment of the Pediatric Research Equity Act and the Best Pharmaceuticals for Children Act in the US, increased expectations from a number of regulatory agencies for nonclinical support of pharmaceuticals for pediatric use have led to an increased need for testing in juvenile animals. One area of particular focus is on the developing central nervous system (CNS). Since development of the CNS continues through adolescence it is one organ system thought to be at high risk for drug toxicity. Safety assessment of the CNS is generally evaluated through functional assays including cognitive tests; however, histopathologic changes are also possible. Our panel of experts will discuss the relevant considerations when designing juvenile toxicity studies to evaluate potential effects on the developing CNS that will allow the most useful risk assessment for the intended clinical population.

- **Workshop Overview,** Mary J. Kallman, Eli Lilly & Company, Greenfield, IN
- **The Postnatal Developing Brain: A Target of Toxicity,** Gregg D. Cappon, Pfizer Global Research and Development, Groton, CT
- **Endocrine Endpoints: Interactions during Postnatal CNS Development,** David Mann, Morehouse School of Medicine, Atlanta, GA
- **Tests to Evaluate Cognitive and Emotional Function in Rodents,** Charles V. Vorhees, Children's Hospital Research Foundation, Cincinnati, OH
- **Industry Perspective: Start with the End in Mind,** LaRonda L. Morford, Eli Lilly & Company, Greenfield, IN
- **Histological Changes in Animals: Implications for Use in Pediatric Patient Populations,** Daniel D. Mellon, U.S. FDA, Silver Spring, MD



Workshops

Toxicology of Unintentional and Intentional Disasters

Wednesday, March 18, 9:00 AM–11:45 AM

Chairperson(s): Angela J. Harris, Center for Toxicology and Environmental Health LLC, North Little Rock, AR and Michael E. Ottlinger, U.S. EPA, Cincinnati, OH

Sponsor:

Occupational and Public Health Specialty Section

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Ethical, Legal, and Social Issues Specialty Section
Inhalation and Respiratory Specialty Section
Risk Assessment Specialty Section

There is no greater challenge in toxicology than making decisions concerning public health under extreme circumstances with limited data. Yet, with the ever increasing risk of terroristic activities, the occasional accidental release of chemicals during transport and manufacture, and the unpredictable occurrence of natural disasters such as volcanic activity, hurricanes and wild fires; toxicologists from a wide range of governmental agencies and companies are faced with making decisions that affect the health of impacted communities. Such responses to emergency situations is where the rubber meets the road in putting toxicological principles into public health practice. To address these issues topical disasters will be used to initiate discussion about the challenges faced during catastrophic events involving toxic agents in order to develop better strategies to address the toxicological impact on public health. We will consider the need for toxicological assessment and support during unintentional and intentional disasters with examples from recent events including Hurricanes Katrina and Rita, the California wild fires and the collapse of the World Trade Center. A brief roundtable discussion will follow to identify the idiosyncrasies and commonalities of dealing with unintentional and intentional disasters.

- **Introduction**, Michael E. Ottlinger, U.S. EPA, Cincinnati, OH
- **DHS Role and Responsibilities Under the New National Response Framework**, Mark Kirk, U.S. Department of Homeland Security, Washington, DC
- **Public Impact of Volcanic Activity**, Paul Nony, Center for Toxicology and Environmental Health, North Little Rock, AR
- **Risk Assessment and Public Health Implications of WTC Dust Contamination Topic**, Phil Goad, Center for Toxicology and Environmental Health, North Little Rock, AR
- **Monitoring and Surveillance of Disaster Responders: Tracking of the Health of WTC Clean Up and Recovery Worker**, Alison Geyh, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

- **Toxicological Risks of Urban Wildfires: Analysis of Fire Ash and Debris Following the Southern California Wildfires**, Shelley DuTeaux, California Environmental Protection Agency, Sacramento, CA

Food Allergy—Basic Mechanisms and Applications to Identifying Risks Associated with Plant Incorporated Pesticides and Other Genetically Modified Crops

Wednesday, March 18, 1:30 PM–4:15 PM

Chairperson(s): MaryJane Selgrade, U.S. EPA, Research Triangle Park, NC and Susan Laessig, U.S. EPA, Washington, DC

Sponsor:

Immunotoxicology Specialty Section

Endorsed by:

Food Safety Specialty Section
Occupational and Public Health Specialty Section

Food allergy is a relatively new concern for toxicologists as a result of the incorporation of novel proteins into food crops in order to promote resistance to pests and other stresses, improve nutrition, or otherwise modify the phenotype. Food allergy can manifest as inflammation of the skin (hives), gut, and/or lung and in the most extreme cases can result in anaphylactic shock and death. Thus, although the technology to modify crops genetically has many advantages over more conventional approaches, there is some concern that introduction of a novel protein into the food supply could result in unintentional introduction of a new food allergen and could pose a risk to susceptible individuals. A number of potential strategies have been proposed to assess this risk, but many questions regarding basic mechanisms underlying food allergy limit our ability to provide the public with information not only about potential allergenicity of transgenic proteins, but also about practices to limit the risks associated with conventional food allergens. The prevalence of food allergy is increasing, providing greater incentive to understand the process and need for additional safety assessment tools. It is important to note that current regulatory approaches and recent research that has improved our understanding of host responses such as sensitization and oral tolerance, developed unique animal models of allergy, and applied structural data bases, global gene arrays, and serum screening to both explore mechanisms and develop hazard identification methods.

- **Introduction: Food Allergy—A Toxicologists Point of View**, MaryJane Selgrade, U.S. EPA, Research Triangle Park, NC

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Workshops

- **An Animal Oral Exposure Model: Sensitization Versus Tolerance**, Christal Bowman, U.S. EPA, Research Triangle Park, NC
- **Mouse Strain Differences in the Response to Orally Administered Allergenic and Non-Allergenic Proteins**, Harm HogenEsch, Purdue University, West Lafayette, IN
- **Safety Assessment of Dietary Proteins for Allergenicity Using an Adjuvant-Free Mouse Model**, Venu Gangur, Michigan State University, East Lansing, MI
- **Prediction and Detection of Conformational Epitopes of IgE Antibodies**, Werner Braun, University of Texas Medical Center Galveston, Galveston, TX
- **Human Serum IgE Screening: Identification of Allergens and Potentially Cross-Reactive Proteins**, Richard Goodman, University of Nebraska, Lincoln, NE
- **On the Horizon—Exploratory Research Initiative in Food Allergy**, Susan Laessig, U.S. EPA, Washington, DC
- **opportunities and challenges for applying transcriptomics to drug safety assessment will be summarized.**
- **Impact of ILSI-HESI in Resolving Issues in Drug Safety Assessment Using Transcript Profiling: Case Review**, Cynthia Afshari, Amgen, Inc., Thousand Oaks, CA
- **Case Study: Applying Transcriptomics *In Vitro* and *In Vivo***, James Stevens, Lilly Research Laboratory, Greenfield, IN
- **Predicting Drug Safety Using Transcriptomics and System Biology Approaches**, Lois Lehman-McKeeman, Bristol-Myers Squibb, Princeton, NJ
- **Evaluating Safety Issues in Early Drug Development with Transcriptomics**, Eric A. G. Blomine, Abbott Laboratories, Abbott Park, IL
- **Summary: Opportunities and Challenges in Applying Transcriptomics to Drug Safety Assessment**, Frank Sistare, Merck & Company, Inc., West Point, PA

The Impact of Transcript Profiling in Drug Safety Assessment

Wednesday, March 18, 1:30 PM–4:15 PM

Chairperson(s): *Syril Pettit, Health and Environmental Science Institute, Washington, DC and Cynthia Afshari, Amgen, Inc., Thousand Oaks, CA*

Sponsor:

Drug Discovery Toxicology Specialty Section

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**Occupational and Public Health Specialty Section
Regulatory Safety Evaluation Specialty Section**

Transcript profiling technology has been around for a decade and is arguably the most developed systems biology approach that has been applied to drug safety assessment. Although there are examples where transcriptomics has been applied to safety assessment of drug candidates, much of the data remains unpublished and reports are anecdotal. In part, the lack of publication leads to the impression that transcriptomics has had little impact. Specific examples where transcriptomics are being applied to preclinical drug safety assessment will be highlighted as will the areas of success in addition to areas where transcriptomics has had less impact. The emphasis will be on case studies outlining applications that are being integrated into safety assessment and where the technology is being reduced to practice. The impact of the technology among scientists in industry and the regulatory community will be illustrated by sharing both positive and negative experiences. Industry scientists will present case studies that illustrate the use of transcriptomics to understand issues or risks that emerge in preclinical development. Finally, the

The Road to Personalized Medicine

Wednesday, March 18, 1:30 PM–4:15 PM

Chairperson(s): *Donna L. Mendrick, U.S. FDA, Jefferson, AR and Vishal S. Vaidya, Brigham and Women's Hospital and Harvard Medical School, Boston, MA*

Sponsor:

Molecular Biology Specialty Section

Endorsed by:

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

To improve the safety of marketed drugs and chemicals, new biomarkers are needed to identify unsafe compounds earlier, discover patients who are at risk of adverse events to specific drugs and chemicals prior to exposure, and provide tools for the management of patients that are or will undergo adverse events. Single nucleotide polymorphisms (SNPs) and gene expression alterations provide clues into a person's response to xenobiotics thus enabling personalized medicine. Our panel of experts will highlight new approaches being used in preclinical species to understand individuals' responses and improve preclinical detection of idiosyncratic drugs, the use of translational biomarkers to enable better correlation between animals and humans, and the status of monitoring SNPs in the clinic to avoid adverse events.

- **Modeling Chemical Toxicity in the Population: Mouse to the Rescue!** Ivan Rusyn, University of North Carolina at Chapel Hill, Chapel Hill, NC

Workshops

- **Towards Improvements in Toxicogenomics for Understanding Hepatotoxicity**, Weida Tong, U.S. FDA, Jefferson, AR
- **The Transition from Pre-Clinical to Clinical Safety Related Genomics**, Felix Frueh, Medco Health Solutions, Inc., Darnestown, MD
- **Translational Biomarkers for Kidney Toxicity**, Vishal S. Vaidya, Brigham and Women's Hospital and Harvard Medical School, Boston, MA
- **Predicting Toxicity in People**, Maryellen deMars, The Critical Path Institute, Rockville, MD

resulting from events such as ischemia, extensive tissue damage and necrosis, activation and release of stress hormones all can induce SIRS and MOD as a secondary toxic response. Whole body SIRS is considered an adverse finding in pre-clinical toxicology studies. Therefore, knowledge and use of the appropriate inflammatory biomarkers that reflects this pathological process is quite useful both preclinically and clinically. Additionally, pre-clinical and clinical monitoring of biomarkers that are early predictors or reporters of SIRS are valuable to the toxicologist in hazard identification and risk assessment of novel therapeutics with the potential to cause a pro-inflammatory response. To adequately explore these issues, we will highlight the progress and challenges of SIRS.

- **Current Concepts and an Overview of the Patho-Physiology of Cytokine Storm, SIRS, and MOD**, Steven Burdette, Wright State University, Dayton, OH
- **Diagnosis of Systemic Inflammatory Response in Preclinical Drug Development**, Weiping Shao, Merck & Company, West Point, PA
- **In Vitro Approaches to Investigating Cytokine Release Following Potential Agonist Immunostimulation**, Catherine Betts, AstraZeneca Safety Assessment, Macclesfield, United Kingdom
- **Monoclonal Antibody Induced Cytokine Release Syndrome: Preclinical Screening**, Peter J. Bugelski, Centocor Research and Development, Inc., Radnor, PA
- **Opportunities and Challenges for Safety Evaluation of Small and Large Molecule High Risk Targets**, Harsukh Parmar, AstraZeneca Pharmaceuticals, Loughborough, Leicestershire, United Kingdom

Thursday

INFLAMMATION AND DISEASE

Biomarkers for Assessing the Systemic Inflammatory Response Syndrome in Toxicology Studies

Thursday, March 19, 9:00 AM–11:45 AM

Chairperson(s): Calvert Loudon and Denise Bounous, Bristol-Myers Squibb Pharmaceuticals, Princeton, NJ

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Toxicologic and Exploratory Pathology Specialty Section

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Immunotoxicology Specialty Section

Systemic inflammatory response syndrome (SIRS) is a state of whole body inflammation that can result in multiple organ dysfunction (MOD), circulatory collapse and even death. SIRS is considered as a self-defense mechanism to non-specific insults that arise from chemical, necrotic (as a result of tissue damage), ischemic, or infectious stimuli that induce organ pathology. SIRS and MOD are complex processes that involve hemodynamic, humoral and cellular responses, complement activation and cytokine cascade. SIRS and MOD develops in stages that are mediated in part through acute phase proteins, cytokine dysregulation and hemodynamic events. In toxicology studies, safety evaluation of xenobiotics, pharmacologically active immune stimulants and immunosuppressants can induce SIRS and MOD in rats, dogs and non-human primates and therefore measurement of circulating mediators as biomarkers of SIRS and MOD will enable clinicians to avoid a potentially severe catastrophic event. Furthermore chemically-induced pathology

Is Modulation of the Immune System by Perfluoroalkyl Acids a Human Health Concern?

Thursday, March 19, 9:00 AM–11:45 AM

Chairperson(s): Jamie C. DeWitt, East Carolina University, Greenville, NC and Robert W. Luebke, U.S. EPA, Research Triangle Park, NC

Sponsor:
Immunotoxicology Specialty Section

Endorsed by:
Mechanisms Specialty Section
Risk Assessment Specialty Section

Perfluoroalkyl acids (PFAAs) used to manufacture myriad consumer products and are present in the environment, humans, and wildlife. PFAAs undergo degradation to a limited number of extremely stable products, including PFOA and PFOS; both are reported to alter immune function. Human immunologic and body burden data from a highly exposed population will provide context for the discussions of rodent data that follow. The animal data will address proposed modes-of-action for PFOA and PFOS, and body burdens associated with altered immune function. This workshop will appeal to a broad range of meeting attendees, including immunotoxicologists, risk assessors, and molecular, and regulatory toxicologists.

- **Workshop Introduction**, Jamie DeWitt, East Carolina University, Greenville, NC
- **Immune Status in a Community Exposed to PFOA: Findings from the C8 Science Panel Study**, Tony Fletcher, London School of Hygiene and Tropical Medicine, London, United Kingdom
- **PFOA-Induced Immunomodulation in Mice: An Overview**, Jamie DeWitt, East Carolina University, Greenville, NC
- **Adjuvancy and Immunosuppression: Mechanisms of Immunomodulation Following Dermal Exposure to PFOA in Mice**, Stacey Anderson, NIOSH, Morgantown, WV
- **Suppression of Immune Function in Mice after Developmental Exposure to PFOS**, Margie Peden-Adams, Medical University of South Carolina, Charleston, SC
- **Evaluation of the Immune System in Rats and Mice Administered Ammonium Perfluorooctanoate (APFO)**, Scott Loveless, DuPont Haskell Global Centers for Health and Environmental Sciences, Newark, DE

The Molecular Mechanism of Alpha, Beta-Unsaturated Carbonyl Toxicity—Getting in Touch with the Soft Side of Chemistry

Thursday, March 19, 9:00 AM–11:45 AM

Chairperson(s): Richard M. LoPachin, Montefiore Medical Center, Bronx, NY and Daniel J. Conklin, University of Louisville, Louisville, KY

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Mechanisms Specialty Section

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Neurotoxicology Specialty Section

Acrolein, acrylamide, 4-hydroxy-2-nonenal (HNE) and other α,β -unsaturated carbonyl compounds are members of a large class of chemicals known as the type-2 alkenes. These chemicals are characterized by a conjugated structure that is formed when an electron-withdrawing group is linked to an alkene. α,β -unsaturated carbonyl derivatives are used extensively in various industries and these chemicals are recognized as significant environmental pollutants and dietary contaminants. Consequently, human exposure to the conjugated alkenes is pervasive and has been associated with toxicity of most major organ systems. There is also substantial evidence that endogenous production of acrolein and HNE is an important component of diseases that involve cellular oxidative stress and lipid peroxidation; e.g., Alzheimer's disease and atherosclerosis. Clearly, type-2 alkene exposure has diverse pathogenic implications and therefore the potential role of these chemicals in human disease processes and environmentally acquired toxicities will be discussed. The conjugated α,β -unsaturated carbonyl structure of the type-2 alkenes is a soft electrophile that forms adducts with soft biological nucleophiles; i.e., cysteine sulfhydryl groups. In addition, amine groups on lysine and histidine residues are potential targets for adduct formation with these bifunctional chemicals. Accordingly, focus on the emerging recognition that type-2 alkenes produce toxicity through a common molecular mechanism involving the formation of adducts on functionally critical proteins will be a focal point of discussion. We will also consider how relative electrophilic reactivity and the route of intoxication determine the toxicological outcome of type-2 alkene exposure (e.g., hepatotoxicity, neurotoxicity). The leading researchers in the toxicity of α,β -unsaturated carbonyl compounds will provide unique information at the interface of chemistry and toxicology. Such information could offer insight into how the chemical environment impacts human health and might identify efficacious remediation strategies.

- **Session Overview**, Dennis R. Petersen, University of Colorado Health Sciences Center, Denver, CO



Workshops

- **Unsaturated Carbonyl Toxicity: Soft-Soft Interactions Described by Quantum Mechanical Parameters**, Terrence E. Gavin, Iona College, New Rochelle, NY
- **Atherogenic Effects of Enals**, Sanjay Srivastava, University of Louisville, Louisville, KY
- **Overview of Protein Targets Modified by the α,β -Unsaturated Aldehyde 4-Hydroxynonenal: Insights into Molecular Mechanisms Predisposing Proteins to Modification**, Dennis R. Petersen, University of Colorado Health Sciences Center, Denver, CO
- **Type-2 Alkenes Produce Nerve Terminal Damage: Relevance to Neurotoxicity and Neurodegenerative Diseases**, Richard M. LoPachin, Albert Einstein College of Medicine, Bronx, NY
- **Using Carbonyl Scavengers to Probe the Toxicological Significance of Acrolein-Mediated Protein Adduction in Lung Cells**, Philip Burcham, University of Western Australia, Nedlands, Australia

Monday

NEURODEGENERATIVE DISEASE

Devils Lie in the Details: Practices and Problems in Neuropathology—Significance for Neurotoxicology

Monday, March 16, 12:10 PM–1:30 PM

Chairperson(s): Bernard S. Jortner, Virginia Tech, Blacksburg, VA and Robert H. Garman, Consultants in Veterinary Pathology, Inc., Murrysville, PA

Sponsor:

Toxicologic and Exploratory Pathology Specialty Section

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Neurotoxicology Specialty Section

The pathologic examination of the nervous system is an important component of experimental and regulatory neurotoxicology and in studies of neurodegenerative disease. Given the significance of the scientific and public health assessments, the ease with which histologic artifacts can be introduced into the process, and the possibility that the latter may be interpreted as representing toxicant-induced changes it is important to highlight these issues. Recent publications so interpreting such artifacts underscore the need for a review of this subject within the toxicology community. Mark Butt will provide an overview of the proper practice of neuropathology as it relates to study design, tissue fixation and specimen preparation. Robert Garman will describe the artifacts found in histologic preparations of the central nervous system, including their genesis, morphology and potential interpretative problems while Bernard Joynter will review similar aspects of artifacts of the peripheral nervous system. This session will be of interest to pathologists, toxicologists, and neuroscientists involved in neurotoxicologic investigations.

- **Introduction**, Bernard S. Jortner, Virginia Tech, Blacksburg, VA
- **Contemporary Pathology Techniques for Evaluation of the Nervous System**, Mark T. Butt, Tox Path Specialists, LLC, Walkersville, MD
- **Artifacts in the Central Nervous System and Their Importance in Neurotoxicology**, Robert H. Garman, Consultants in Veterinary Pathology, Inc., Murrysville, PA
- **Histological Artifacts in the Peripheral Nervous System and Their Differentiation from Lesions**, Bernard S. Jortner, Virginia Tech, Blacksburg, VA

NANOTECHNOLOGY

The Use of Engineered Nanomaterials in Food and Food-Related Products: Is This a Concern for Human and Environmental Safety?

Monday, March 16, 12:10 PM–1:30 PM

Chairperson(s): T. Scott Thurmond, U.S. FDA, College Park, MD and Bernadene Magnuson, Cantox Health Sciences International, Mississauga, Ontario, Canada

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Nanotoxicology Specialty Section

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The advent of nanotechnology has brought with it questions related to human and environmental safety. The application of nanotechnology to food packaging and as food or color additives has generated questions on the safety of nanomaterials in biological systems. Thus, it is important that we consider concerns expressed in the literature, press, and general toxicology community for unforeseen human and environmental health effects that may potentially be associated with the use of engineered nanomaterials in food and food-related products. In order to understand these potential concerns we need to consider both general and specific questions. Does the current regulatory framework adapt well to engineered nanomaterials in food as it is designed to do for other new materials manufactured for use in foods? Are there knowledge gaps and/or research needs for regulators that when filled may better prepare us to assess human health and environmental risks of food-related engineered nanomaterials? Can toxicology data generated on nanomaterials *via* dermal or pulmonary exposure be of use in informing us in the assessment of risks from oral exposure to nanomaterials in food packaging or food additives? Does nanoencapsulation of a dietary or nutritional supplement as a means to alter bioavailability also increase its potential for toxicity? In exploring these issues, we will also take the opportunity to identify planned and ongoing research efforts in the area of food-related nanomaterials safety to facilitate discussion.

- **Introduction**, T. Scott Thurmond, U.S. FDA, College Park, MD
- **Overview of Risk Assessment for Oral Exposure to Nanoparticles**, Kathy Sarlo, The Procter and Gamble Company, Cincinnati, OH

Roundtables

- **Research and Educational Activities of the IFT/ILSI/NCL Food Nanotechnology Collaboration**, Bernadene Magnuson, Cantox Health Sciences International, Mississauga, Ontario, Canada
- **Environmental Risk Issues with Nanomaterials in Food**, Jo Anne Shatkin, CLF Ventures, Boston, MA
- **Assuring the Safety of Nanomaterials in Food Packaging: The Regulatory Process and Key Issues**, Nancy Rachman, Grocery Manufacturer's Association, Washington, DC
- **Science and the Regulatory Policy Landscape**, Richard Canady, U.S. FDA, Rockville, MD

Leveraging Non-Clinical Disease Models for Early Perspective on Safety and Risk during Drug Discovery

Monday, March 16, 4:35 PM–5:55 PM

Chairperson(s): *Monicah Otieno, Bristol-Myers Squibb Company, Princeton, NJ and Mark J. Graham, AstraZeneca Pharmaceutical LP, Loughborough, United Kingdom*

Sponsor:
Drug Discovery Toxicology Specialty Section

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Inhalation and Respiratory Specialty Section
Occupational and Public Health Specialty Section

Preclinical toxicity contributes to ~70% of compound failure during the drug discovery process, suggesting that approaches that reduce attrition due to pharmacology or chemistry can lead to successful selection of candidate drugs. The use of animal disease models to test for toxicity presents a unique opportunity for toxicologists to explore liabilities early in the drug discovery process. Rodent models, including tumor xenograft, metabolic, and inflammation models are especially attractive for combined efficacy/toxicology testing due to their repeat-dose testing paradigm and study duration. Thus, this forum will highlight the successes and challenges in the use of nonclinical disease models to evaluate safety endpoints. Thorough parallel testing in xenograft tumor models that includes acute and sub-chronic dosing paradigms, MTD determination, histological evaluation of tumor and normal tissue, and DMPK profiling can inform on both safety and efficacy of lead compounds. In addition, information obtained from such studies can often be applied toward a biomarker strategy or dose-scheduling plan for nonclinical and clinical development. Metabolic and chronic inflammatory disease models have altered physiology needs to be considered, as this may modulate the toxicological response. A robust analysis of the impact of disease phenotype on toxicity should be based on a reductive mechanistic model of an aspect of the human disease that

has common mechanisms with nonclinical models. Creative ways to generate early tolerability data for CNS molecules include an understanding of target pharmacology and interactions with other receptors, ion channels, and transporters. Behavioral or physiological changes (e.g., altered activity, stereotype, body temperature) can be evaluated in early pharmacokinetic studies. Combining receptor occupancy from pharmacology models, behavioral, and pharmacokinetic data can provide an integrated assessment for potential CNS side effects.

- **Introduction: The Pros and Cons of Using Non-Clinical Disease Models to Frontload Toxicology Studies**, Monicah Otieno, Bristol-Myers Squibb Company, Princeton, NJ
- **Preclinical Oncology Xenograft Tumor Models As Tools for Assessing Safety and Efficacy in the Development of Novel Cancer Therapies: An Integrated and Parallel Approach**, Michael Yakes, Exelixis, Inc., South San Francisco, CA
- **The Challenges Facing Discovery Toxicologists in Cancer Drug Discovery**, Alex Bell, AstraZeneca PLC, Alderley Park, United Kingdom
- **Creative Toxicology to Identify CNS-Related Side Effects**, Stephen Adams, Bristol-Myers Squibb Company, Wallingford, CT
- **The Influence of Disease on the Toxicological Response**, Mark J. Graham, AstraZeneca PLC, Alderley Park, United Kingdom
- **Rodent Models of Metabolic Disease: Discovery Toxicology in a Typical Pharmacology, but Atypical Toxicity Model**, Brian Gemzik, Bristol-Myers Squibb Company, Princeton, NJ

Role of Regulatory Cooperative Efforts in Food Protection

Monday, March 16, 4:35 PM–5:55 PM

Chairperson(s): *Jay Vodela, U.S. Department of Agriculture, Washington, DC and Kerry Dearfield, U.S. Department of Agriculture, Food Safety Inspection Services, Washington, DC*

Sponsor:
Food Safety Specialty Section

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Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

Chemical and microbial risk assessments are widely used in food safety decision making, in identifying data needs, and in implementing the Hazard Analysis and Critical Control Point (HACCP) Program. The HACCP Program is an excellent example of a collaborative effort between the U.S. Department of Agriculture and

the Food and Drug Administration. Collaboration among all food safety bodies, including state, federal and global partners provides a robust system for continued protection and preparedness of the food protection system. The chemical and microbial risk assessment communities benefit from this on-going collaboration and cooperation. Collaboration has led to advancements in the food safety information infrastructure, data mining, data sharing and the development of sophisticated risk assessment models (risk assessments, vulnerability assessments, etc.) to guide the creation of preventive measures as part of food protection efforts. Leaders from state, federal and international bodies will discuss cooperative and innovative approaches for chemical and microbiological risk assessments in order to provide the safest food supply to the consumer.

- **USDA/FSIS Perspective**, Kerry Dearfield, U.S. Department of Agriculture, Food Safety Inspection Services, Washington, DC
- **FDA Perspective and Experience**, Mike Bolger, U.S. FDA, College Park, MD
- **CDC Perspective**, Helen Schulz-Rogers, Center for Disease Control & Prevention, Atlanta, GA
- **EPA Perspective**, Tina Levine, U.S. EPA, Arlington, VA
- **CODEX Perspective**, Karen Hulebak, U.S. Department of Agriculture, Washington, DC
- **International Perspective**, Angelika Tritscher, World Health Organization, Geneva, Switzerland

Weight of Evidence Advancements in Risk Assessment: Conceptual Frameworks and Case Studies Illustrating Fundamentals of Application

Monday, March 16, 4:35 PM–5:55 PM

Chairperson(s): Pamela J. Spencer, Dow Chemical Company, Midland, MI and Jennifer G. Seed, U.S. EPA, Washington, DC

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Regulatory and Safety Evaluation Specialty Section

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Risk Assessment Specialty Section

Chemicals interact with biological targets ultimately at the molecular level producing key, necessary and causative events. Identification and quantification of these events leads to understanding of a toxicant's mode of action (MOA). Weight of evidence (WOE) approaches consider relevant scientific data, underlying assumptions and correlations to characterize the overall support for a hypothesized MOA. Frameworks for WOE analyses for MOA

in animals and their associated human relevance (HR) have been developed by the International Life Sciences Institute (ILSI) and International Programme on Chemical Safety (IPCS). Information reviewed as a basis for consideration of the WOE of MOA and its HR can be applied to refine the dose-response relationship and with sufficient data may be used in the derivation of Chemical Specific Adjustment Factors (CSAF), as outlined in the guidance developed by the IPCS. This includes using PBPK modeling to develop quantitative data to replace default assumptions for inter- and intra-species differences in tissue dosimetry. The principles for WOE considerations embodied in the HRF can potentially be extended to other areas to refine human health risk assessments. Characterizing the MOA and determining its relevance to the human system provides the foundation for developing non-default, CSAFs for application in health risk assessment. Therefore, it is important to provide a forum for discussion on how one might extend the framework into other areas with chemical specific case studies that use the MOA-HRF for analyzing cancer mode of action in animals, characterizing human dose-response and development of a CSAF.

- **Overview of the Human Relevance Framework**, M.E. (Bette) Meek, University of Ottawa, Ottawa, Ontario, Canada
- **Chemical Specific Adjustment Factors for Non-Cancer Endpoints**, John C. Lipscomb, U.S. EPA, Cincinnati, OH
- **Use of HRF for Analyzing Cancer Mode-of-Action for Propylene Oxide**, James A. Swenberg, University of North Carolina Chapel Hill, Chapel Hill, NC
- **Use of HRF and Development of CSAF for Ethylene Glycol**, Richard A. Corley, Pacific Northwest National Laboratory, Richland, WA



Roundtables

Tuesday

BIOMARKERS

Biomarkers of Cardiac Hypertrophy and Skeletal Muscle Toxicity—Successes and Challenges Related to Their Implementation in Drug Development

Tuesday, March 17, 7:30 AM–8:50 AM

Chairperson(s): David E. Watson, Eli Lilly & Company, Greenfield, IN and Warren Glaab, Merck Research Laboratories, West Point, PA

Sponsor:
Drug Discovery Toxicology Specialty Section

Endorsed by:
Regulatory and Safety Evaluation Specialty Section

Drug-related injury to cardiac and/or skeletal muscle is a common cause of safety-related attrition in drug development, and has resulted in the withdrawal of several efficacious pharmaceutical agents from the market. Improving our ability to detect muscle injuries should improve patient safety. Case studies are presented on successes and challenges related to the implementation in drug development of serological biomarkers of skeletal muscle necrosis, including differentiation of injury to Type I *versus* Type II muscle fibers; cardiac myocyte injury, including comparisons of the performance of cardiac troponins with other serological biomarkers and histopathology; and cardiac hypertrophy, including serological concentrations of natriuretic peptides, and their relationship to hemodynamic and structural changes in the heart. Scientific challenges that limit the broader application of these biomarkers are also addressed in a presentation on the changes in muscle structure and biochemistry that are driven by physiological and pathological processes, including those related to exercise, muscle atrophy, and drug toxicity in human muscle.

- **Introduction: Objectives of the PSTC Myopathy Working Group**, David E. Watson, Eli Lilly & Company, Greenfield, IN
- **Biomarkers of Cardiac Hypertrophy**, Heidi Colton, Merck Research Laboratories, West Point, PA
- **Mechanisms and Biomarkers of Skeletal Muscle Injury: Differentiating Muscle Fiber Type Injury**, Warren Glaab, Lilly Research Laboratories, Greenfield, IN

- **Implementation of Serological Biomarkers of Muscle Toxicity in Early Drug Discovery**, David E. Watson, Eli Lilly & Company, Greenfield, IN
- **Clinical Perspective on Drug-Induced Skeletal Muscle Pathogenesis—Mechanisms and Biomarkers**, Paul Thompson, Hartford Hospital, Hartford, CT

NANOTECHNOLOGY

The Regulatory Frontier: Addressing Products of Nanotechnology

Tuesday, March 17, 7:30 AM–8:50 AM

Chairperson(s): Tracey J. Woodruff, University of California San Francisco, San Francisco, CA and Edward Ohanian, U.S. EPA, Washington, DC

Sponsor:
Risk Assessment Specialty Section

Endorsed by:
Inhalation and Respiratory Specialty Section
Nanotoxicology Specialty Section
Occupational and Public Health Specialty Section

Nanomaterials, typically defined as manufactured materials that have at least 1 dimension <100 nanometers, are increasingly being produced worldwide. Nanomaterials have been used or proposed for use in a variety of products, ranging from computers, clothing, cosmetics, medical devices, coatings, and fuel cells, to new technologies for environmental clean-up. Use is expected to increase and it is estimated that by 2015 about 10% of output from the chemicals sector will have some influence from nanotechnology, greatly increasing opportunities for human exposures. There has been some evaluation of potential health risks from nanomaterials, but to date, these have not been pursued in a systematic way. Nanomaterials pose new challenges and opportunities to the regulatory and policy structure. There are an increasing number of regulatory and policy decisions being discussed or made at the state, federal, and international level. Given that this is still a new and emerging technology, there are opportunities to consider how to address potential health risks in the regulatory and policy framework prior to widespread use and adoption. The current discussion provides an overview of nanomaterials, the current state of regulations and policies for addressing nanomaterials, and consideration of how various entities propose that the government move forward to address nanomaterials.

- **What Are Nanomaterials, Where Do They Exist in Our Environment, and What are Human Risk from Nanomaterials?** Kevin Dreher, U.S. EPA, Research Triangle Park, NC
- **How are Nanomaterials Being Addressed in Regulatory Systems?** Jay Pendergrass, Environmental Law Institute, Washington, DC
- **Public Perception of Nanomaterials**, David Berube, North Carolina State University, Raleigh, NC
- **What Should We Do to Address Nanomaterials?** Jennifer Sass, Natural Resources Defense Council, Washington, DC and Terry L. Medley, DuPont deNumours, Wilmington, DE

INFLAMMATION AND DISEASE

Is There a Future for Animal Models in the Investigation of Idiosyncratic DILI in Humans?

Tuesday, March 17, 12:00 NOON–1:20 PM

Chairperson(s): Arie Regev, Eli Lilly & Company, Indianapolis, IN and Gerry Kenna, AstraZeneca, Cheshire, United Kingdom

Sponsor:

Regulatory and Safety Evaluation Specialty Section

Endorsed by:

Drug Discovery Toxicology Specialty Section

Idiosyncratic drug induced liver injury (DILI) remains a concern for drug development and patient safety, and continues to be the leading cause for regulatory action including withdrawal of drugs from the market, restrictions in indications, and warnings to health care providers and patients. Idiosyncratic DILI is typically unpredictable, and is largely undetectable, in preclinical animal studies. Accordingly, it is only in large scale clinical trials or, more often, post-marketing, that such toxicities are revealed. To date there is no universally accepted animal model for investigation or prediction of idiosyncratic DILI in humans. A lofty goal for preclinical scientists and physicians is to, not only develop animal models that detect idiosyncratic DILI, but to translate such knowledge into the clinic and allow identification of patients who would be susceptible or tolerant to a particular drug. Much effort has been expended in the study of improved/enhanced animal models that better predict untoward human idiosyncratic drug reactions. In some instances, the data imply that we can in fact identify drug candidates that may be predisposed to DILI. On the other hand, the multiple etiologies potentially underlying idiosyncratic DILI may render it difficult to routinely evaluate for, and predict, these events. A case example will be presented to illustrate this point. The complexities of using

non-standard animal models and endpoints in regulatory safety assessment studies also must be considered. These discussions are designed to highlight the current thinking on animal models for idiosyncratic DILI, and focus attention on the future direction of such research.

- **Is There a Future for Animal Models in the Investigation of Idiosyncratic DILI in Humans?** Gerry Kenna, AstraZeneca, Cheshire, United Kingdom
- **Idiosyncratic DILI: The Disease and Why It Is So Difficult to Predict**, Arie Regev, Eli Lilly & Company, Indianapolis, IN
- **Genetic Susceptibility in Man: The Case of Ximelagatran**, Ina Schuppe-Koistinen, AstraZeneca Research & Development, Södertälje, Sweden
- **The Future is Still Far Away**, Jack Uetrecht, University of Toronto, Toronto, Ontario, Canada
- **Animal Models of Idiosyncratic DILI: Right Around the Corner?** Robert A. Roth, Michigan State University, East Lansing, MI

National Children's Study: Opportunities and Challenges for Toxicologists

Tuesday, March 17, 12:00 NOON–1:20 PM

Chairperson(s): Sally Darney, U.S. EPA, Research Triangle Park, NC and Michael Dellarco, National Institutes of Health, Bethesda, MD

Sponsor:

Women in Toxicology Special Interest Group

Endorsed by:

Occupational and Public Health Specialty Section
Reproductive and Developmental Toxicology Specialty Section
Risk Assessment Specialty Section

The National Children's Study (NCS) is the first-of-its kind U.S. study tracking children's health from womb to adulthood. Involving 100,000 children across the country, the NCS will be the largest long-term study of children's health and development ever conducted in the U.S. Initiated in response to the Children's Health Act of 2000, the NCS is led by a consortium of agencies which include the U.S. Department of Health and Human Services, including the National Institute of Child Health and Human Development, the National Institute of Environmental Health Sciences at NIH, and the Centers for Disease Control and Prevention, and the U.S. EPA. The study seeks to address questions that can only be answered through a longitudinal study of this size and scope. The study's hypotheses

Roundtables

incorporate the following main outcomes—pregnancy outcomes, neurodevelopment and behavior, asthma, obesity and growth, injury, and reproductive development. NCS will ultimately reduce the public health burden of childhood chronic diseases and disorders, including not only pain and suffering, but also missed school days, health care expenses, and other costs to children, their families, and society at large. It will also be large enough to assess factors related to health disparities and differences in disease occurrence between groups of people. What does this study mean for toxicologists? The time is ideal to obtain input from toxicologists, as this landmark study is beginning to recruit families, to apply lessons learned from ongoing children's studies, including the application and interpretation of new biomarkers, and to develop exposure and dose models for pregnant women and infants. Its design and innovative approaches will provide unique opportunities to collect and relate early biomarkers of exposure and effect to disease outcomes later in development, and it will help the U.S. tease apart the complex interplay between environmental factors and genetic influences that impact health.

- **Introduction**, Sally Darney, U.S. EPA, Research Triangle Park, NC
- **The National Children's Study: Understanding the Developmental and Environmental Bases of Children's Health Risks**, Peter C. Scheidt, National Institutes of Health, Bethesda, MD
- **Assessing Exposures in the NCS Using a Combination of Tools and Models**, James Quackenboss, U.S. EPA, Las Vegas, NV
- **The Importance of the NCS for Toxicology and for Exploring Gene-Environment Interactions**, Elaine M. Faustman, Institute for Risk Analysis and Risk Communication, Seattle, WA
- **Putting Public Health into Children's Health Opportunities with the NCS**, Lynn R. Goldman, Johns Hopkins University, Baltimore, MD
- **Assessing Children's Cancer Risk Related to *In Utero* Exposure to Dietary Carcinogens**, Jos Kleinjans, Netherlands Toxicogenomics Centre, Zuid-Limburg, Netherlands

Setting a Safe Starting Dose in Initial Clinical Trials with Biotherapeutics: Do I Use the NOAEL or the MABEL?

Tuesday, March 17, 12:00 NOON–1:20 PM

Chairperson(s): Jeanine Bussiere, Amgen, Inc., Thousand Oaks, CA and Leigh Ann Burns Naas, Pfizer Global Research and Development, San Diego, CA

Sponsor:

Women in Toxicology Special Interest Group

Endorsed by:

Drug Discovery Toxicology Specialty Section
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

Years ago, establishment of safe exposures to new therapeutics utilized the determination of NOEL/NOAELs derived from routine toxicology studies followed by some form of dose adjustment prior to human exposure, an approach that evolved a few years later to include an interspecies scaling factor. In the past 15 years, however, approaches to clinical trial design have become more specific to the TA and questions being asked in these initial studies. During this same time, biotechnology-derived therapeutics have also evolved, becoming increasingly more diverse in nature and are much more specific to their targets. As a result of this evolution, an array of regulatory guidance has also arisen describing several approaches to establishing appropriate starting doses for clinical trials of a specific nature, for specific therapeutic areas, and high risk therapeutics. The most recent of these is pharmacology-based and involves the determination of the MABEL. This method is recommended for therapeutics that may present defined/perceived risk to those in FIH/FIP trials that is beyond what is generally accepted for new molecular entities. The choice to use the NOAEL or MABEL in selecting the starting dose falls to toxicologists and clinicians and may represent starting doses differing by orders of magnitude. A key starting point is determination of what constitutes elevated risk, an evaluation that depends on a combined assessment of the nature of the target, pharmacology, toxicology, and the intended patient population. Accurate estimation of the human efficacious dose is also critical and the complexity surrounding this prediction can have significant impact on the starting dose. Low and slow provides maximum safety but can also result in unnecessary time delays evaluating doses where little information may be gained, and in at least some instances may make it impossible to recruit patients who may have no benefit for weeks.

- **Introduction**, Jeanine Bussiere, Amgen, Inc., Thousand Oaks, CA
- **Points to Consider in Dose Selection for FIH Studies**, Christopher Horvath, Archemix, Cambridge, MA

- **Estimating the Human Efficacious Dose—It's Not As Simple As It Seems**, Mark Rogge, BiogenIdec, Cambridge, MA
- **U.S. Perspective**, Hanan Ghantous, U.S. FDA, Washington, DC
- **European Perspective**, Marc Pallardy, University of Paris, Chatenay Malabry, Paris, France
- **Balancing Patient Safety and Reasonable Expectation of Therapeutic Benefit**, Leigh Ann Burns Naas, Pfizer Global Research & Development, Inc., San Diego, CA

Wednesday

Characterization and Application of PBPK Models in Risk Assessment

Wednesday, March 18, 7:30 AM–8:50 AM

Chairperson(s): M.E. (Bette) Meek, University of Ottawa, Ottawa, Ontario, Canada and Harvey Clewell, The Hamner Institutes for Health Sciences, Research Triangle Park, NC

Sponsor:

Risk Assessment Specialty Section

Endorsed by:

Biological Modeling Specialty Section
Mixtures Specialty Section

Physiologically-based pharmacokinetic (PBPK) models are part of a broader continuum of increasingly data-informed approaches to dose response analysis ranging from default based on external dose to more biologically-realistic models. They facilitate the incorporation of dose measures of relevance to the mode of action of chemicals, and quantitative physiological scaling taking into account relevant chemical-specific physical chemical properties and biological constants. In this manner, PBPK models provide a representation of biologically effective dose as a basis for conducting more informed extrapolations across studies, species, routes, and dose levels. As a result, they increase precision and reduce uncertainty in risk estimates. Despite the availability of PBPK models for a number of chemicals incorporating significant additional biological data over default and the potential of such models to contribute more broadly to the development of additionally informative testing strategies, their adoption in regulatory risk assessment has been limited. This limited uptake is being addressed in a project undertaken as part of the World Health Organization/International Programme on Chemical Safety project on harmonization. The initiative includes preparation of guidance and case studies on the characterization, documentation, evaluation, and communication of PBPK models

for risk assessment. Aspects being addressed include the need for early and continuing communication between risk assessors and modelers, greater consistency in consideration of mode of action as a basis for relevant PBPK models and sufficiently transparent documentation of model development to support potential application. More consistent and transparent consideration of the basis for and output of PBPK models relative to default approaches in risk assessment is also being addressed.

- **Consideration of Mode of Action As a Basis for PBPK Modeling in Risk Assessment**, Ursula Gundert-Remy, Bundesinstitut fuer Risikobewertung, Berlin, Germany
- **Problem Formulation and Continuing Interaction of Modelers and Risk Assessors**, Harvey Clewell, The Hamner Institutes for Health Sciences, Research Triangle Park, NC
- **Model Development and Documentation for Risk Assessment: Communicating in a Familiar Context**, Hugh A. Barton, National Center for Computational Toxicology, Research Triangle Park, NC
- **Evaluation of PBPK Models in Risk Assessment**, Kannan Krishnan, Université de Montréal, Montréal, Québec, Canada

Preclinical Evaluation of Cancer Hazard and Risk of Biopharmaceuticals

Wednesday, March 18, 12:00 NOON–1:20 PM

Chairperson(s): Joy Cavagnaro, Access BIO, Boyce, VA and Laine Payton Myers, U.S. FDA, Silver Spring, MD

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Regulatory and Safety Evaluation Specialty Section

Endorsed by:

Carcinogenesis Specialty Section
Risk Assessment Specialty Section

The carcinogenicity testing of biopharmaceuticals may not always be possible by conventional means due to factors such as species specificity and immunogenicity. However, cause for concern for tumorigenicity of biopharmaceuticals is heightened based on knowledge and plausibility of particular mechanisms of action. Mitogenicity is a concern for exogenously administered biopharmaceuticals such as hormones and growth factors and may also be a concern for pharmaceuticals designed to stimulate their endogenous production. In an attempt to address the potential risks of these agents, investigators have explored the ability of growth factors to influence the growth of tumor cells expressing their receptors in *in vitro* and *in vivo* models. However, the value of these models to adequately address the clinical risk of enhanced tumor growth with therapeutically administered growth factors is not clear. Special



Roundtables

Scientific

issues of concern following chronic treatment of immunomodulatory pharmaceuticals and biopharmaceuticals include the potential for immune impairment leading to opportunistic infections and/or lymphoproliferative disorders. Experimental data will be presented from approaches that have been used in an attempt to answer the central question of the role of exogenous growth factors and immunomodulatory agents in tumor progression *in vivo*; these approaches include rodent tumor xenograft, and alternative short-term and traditional carcinogenicity models. This material will also provide an overview of the current practices in the assessment of carcinogenic risk of biopharmaceuticals including the challenges in assessing human derived proteins in animals and developing waivers of carcinogenicity assessments and labeling considerations.

- **Key Considerations in Assessing Carcinogenic Risk of Biopharmaceuticals—Overview**, Laine Peyton Myers, U.S. FDA, Silver Spring, MD
- **Assessment of Tumorigenic Risk of Growth Factors**, David Hovland, Amgen, Inc., Thousand Oaks, CA
- **Communicating Tumorigenic Risks of Immunomodulatory Biopharmaceuticals**, Peter J. Bugelski, Centocor Research and Development, Inc., Radnor, PA

What Is an Adverse Effect in the Age of 'Omics'?

Wednesday, March 18, 4:30 PM–5:50 PM

Chairperson(s): Rory B. Conolly, U.S. EPA, Research Triangle Park, NC and Barbara D. Beck, Gradient Corporation, Cambridge, MA

Sponsor:

Risk Assessment Specialty Section

Endorsed by:

Biological Modeling Specialty Section

Mechanisms Specialty Section

Regulatory and Safety Evaluation Specialty Section

Research in biology has recently been characterized by a switch in emphasis from reductionist studies that describe an organism based upon its biological components to more integrative ones that emphasize the processes through which these parts interact to produce the complex systems that form an organism. As it is applied to toxicology, this development has provided the opportunity to understand how perturbations of molecular-level signaling and regulatory pathways elicit apical toxic responses. In accord with these developments, the NRC (Toxicity Testing in the 21st Century: A Vision and a Strategy) has proposed a major paradigm shift. They believe that toxicity testing and risk assessment should involve

characterization, with an emphasis on relevant levels of exposure and dose-time response surfaces for *in vitro* perturbation of toxicity pathways. Before this approach can become a standard practice in risk assessment, and potentially, in biomonitoring, substantial research and development is needed in the development of enhanced capabilities for characterization and prediction of both exposure and tissue dosimetry. Thus, a comprehensive set of toxicity pathways and cell culture systems that embody these pathways, delineation of adaptive responses from frankly toxic responses, and correlation of the *in vitro* dose-time response surfaces for perturbation of toxicity pathways with apical responses measured *in vivo* (i.e. responses that are either adverse, or that represent critical steps on the route to adverse responses) should be specified. Finally, computational models of *in vivo* biology that will integrate toxicity pathway data obtained *in vitro* to predict *in vivo* dose-time response should, also be developed. The materials presented will enable us to consider a subset of these issues, highlighting some of the practical challenges posed by the NRC recommendation.

- **Overview**, Rory B. Conolly, U.S. EPA, Research Triangle Park, NC
- **Biological Perturbations and Adversity: A Perspective from the NAS Report—Toxicity Testing in the 21st Century**, Melvin E. Andersen, The Hamner Institutes for Health Sciences, Research Triangle Park, NC
- **Identification of Toxicity Pathways and Their Use in Evaluating HTS Data**, Christopher J. Portier, NIEHS, Research Triangle Park, NC
- **What Is an Adverse Effect from a Clinical Perspective?** Samuel M. Cohen, University of Nebraska Medical Center, Omaha, NE
- **Distinguishing Normal from Toxicologic Perturbations Using Metabolomics**, Dean P. Jones, Emory University, Atlanta, GA
- **Adaptive Physiology Versus Toxicity: Integrating 'Omics Technologies, Dynamics, and Mathematical Modeling into Your Experimental Design Process**, Kevin T. Morgan, sanofi-aventis, Carrboro, NC

Thursday

Phototoxicology: A Passing Fancy or Enduring Concern?

Thursday, March 19, 7:30 AM–8:50 AM

Chairperson(s): P. Donald Forbes, Toxarus Inc., Malvern, PA and Robert E. Osterberg, Aclairo Pharmaceutical Development Group, Inc., Vienna, VA

Sponsor:

Dermal Toxicology Specialty Section

Endorsed by:

Drug Discovery Toxicology Specialty Section
In Vitro and Alternative Methods Specialty Section
Regulatory and Safety Evaluation Specialty Section

Light is a necessary part of our existence as is air and water. Light is central to our interactions with both natural and artificial environments. Therefore we face a constant need to assess both risks and benefits, and to establish balanced guidelines for exposure in discussing this aspect of phototoxicology, which involves the influence of medications on biological responses to light (principally visible and ultraviolet radiation). Chronic phototoxicity is a proven precursor to skin cancer in human populations. Following up on earlier reports by R. Stern and others, a recent publication by Karagas and colleagues provides epidemiological evidence that reported use of photosensitizing medicine was associated with an increased risk of both basal cell carcinoma and squamous cell carcinoma. The widespread use of photosensitizing drugs and chemicals mandates adequate characterization of drug interactions and heightened counseling on sun exposure. In 2002 and 2003, the Committee for Proprietary Medicinal Products (CPMP) and the U.S. FDA published guidance documents describing their respective regulatory preferences for the testing of substances for phototoxicity and photo co-carcinogenicity. The EU has adopted an *in vitro* test method for photocarcinogenicity testing. Technical specialists generally, and the pharmaceutical industry in particular, have described problems with this regulatory guidance, particularly with regard to the over-prediction of *in vitro* tests and the duration of the *in vivo* tests. In the U.S. and other regions, the outcome of these tests may help to determine more appropriate wording that may be used in product labels to adequately characterize the risks of excess sun exposures. Thus, it is important that strategies for providing relevant safety information and novel testing approaches to provide useful shorter-term safety data to predict phototoxicities and photo co-carcinogenicity be explored.

- **What Are the Concerns Regarding Light and Drugs/Chemicals?** Robert E. Osterberg, Aclairo Pharmaceutical Development Group, Inc., Vienna, VA
- **Biomarkers Predictive of Skin Cancer Development in Photocarcinogenesis,** Paul C. Howard, U.S. FDA, Jefferson, AR
- **Clinical Phototoxicology: Relevance, Risk, and Regulation,** Warwick L. Morison, Johns Hopkins University at Green Spring Station, Lutherville, MD
- **European Experience with Phototoxicology and Recommendations for Modification of Photosafety Guidance,** Peter Kasper, BfARM Federal Institute for Drugs and Medical Devices, Bonn, Germany
- **How and Where Light Gets Toxic and Why It Matters,** David H. Sliney, Consulting Medical Physicist, Fallston, MD
- **Photo-Reactivity As a Tool in the Prediction of Phototoxic Potential,** Mark D. Smith, GlaxoSmithKline, King of Prussia, PA

Historical Highlights

Monday

A Quarter of a Century (1984–2009) Since the Bhopal Disaster: Lessons Learned

Monday, March 16, 12:10 PM–1:30 PM

Chairperson(s): Brinda Mahadevan, Schering-Plough Research Institute, Summit, NJ and Madhu Soni, Soni & Associates, Vero Beach, FL

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Association of Scientists of Indian Origin

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Ethical, Legal, and Social Issues Specialty Section
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

Bhopal was the site of one of the worst industrial disasters in history. During the night of December 2, 1984, nearly 30 metric tons of methyl isocyanate from the Union Carbide India Limited (UCIL), pesticide factory in Bhopal, India, leaked into the surrounding environment. On that fateful night over 2,000 individuals died immediately and more than 200,000 were directly affected. What followed this incident was the devastating impact of the chemical on the eyes, lungs and gastro-intestinal systems. Gynecological and obstetric complications soon became apparent, as did neurological disorders, immunological changes, emotional and mental stress. Twenty-five years later, the impact of the gas leak is evidenced by continuing medical and environmental issues. Besides safety challenges, the sheer scope of the Bhopal incident made it an extremely complex problem of public communication. The post-Bhopal era also witnessed a worldwide regulation on chemicals and toxicity and a demand by communities to the right to information. The story of the Bhopal gas disaster demonstrates the complexity of the interaction of science, public reaction and government in forming the regulatory policy. The historic, scientific, and global impact of the disaster will be explored to enable us to develop better public and environmental health and safety policies, to provide the current status of health effects from the disaster, and a review of the lessons learned from the disaster.

- **Introduction**, Brinda Mahadevan, Schering-Plough Research Institute, Summit, NJ
- **The Bhopal Gas Tragedy: Safety and Regulatory Lesson**, Rosalie Bertell, Grey Nuns of the Sacred Heart, Yardley, PA

- **The Bhopal Disaster and Pregnancy Outcome**, Daya Varma, McGill University, Toronto, British Columbia, Canada
- **The Bhopal Disaster: Lessons from Studying the Impact of a Disaster in a Developing Nation**, Ramana Dhara, Emory University, Atlanta, GA

Tuesday

Dioxin, Forty Years of Science: Are We Any Closer to Assessing Potential Risk?

Tuesday, March 17, 7:30 AM–8:50 AM

Chairperson(s): William J. Brock, Brock Scientific Consulting, LLC, Montgomery Village, MD and Ali Faqi, MPI Research, Mattawan, MI

Sponsor:

Regulatory and Safety Evaluation Specialty Section

Endorsed by:

Mechanisms Specialty Section
Mixtures Specialty Section
Risk Assessment Specialty Section

The word dioxin conjures up fears when another article appears in the media. Since the 1970s, there have been scientific publications reporting the potential environmental and human health hazards of exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD; dioxin) and possible mechanisms of toxicity. Numerous epidemiological studies have reported on Vietnam veterans, residents of towns in Italy and Missouri as well as workers in plants that produce the substances containing TCDD. Identification of possible health hazards has been the basis of toxicological research with an examination of possible reproductive effects, immunotoxicity, hepatic effects, cancer and a number of endpoints. Early mechanistic work identified the Ah receptor (AHR) and the role of this receptor in toxicity and changes in metabolic processes. AHR receptor research and the awareness that there is likely to be endogenous and naturally occurring AHR ligands that govern normal physiological processes has shed new light on the significance of the AHR. The EPA report of the 1980s examined the extent of environmental contamination leading to greater interest in environmental analysis of dioxin and the potential for accumulation into the food chain. However, because of regulatory and voluntary efforts subsequently introduced, the levels of dioxin in the environment and food chain have significantly declined. The margin of exposures should continue to increase as additional controls on dioxin emissions are enacted and

Baltimore, Maryland

Historical Highlights

environmental levels dissipate. The available scientific data have improved our understanding of the strengths and weaknesses of toxicity equivalency factors used in dioxin risk assessment. The NAS evaluation of EPA's draft dioxin reassessment identified a number of important uncertainties and errors of how dioxin risks were managed. This session will focus on the research that has been reported over the last 40+ years, the principles of mechanistic toxicology learned from this research and what the future of research into the human health and environmental effects of this particularly toxic compound.

- **Forty Years Later**, William J. Brock, Brock Scientific Consulting, LLC, Montgomery Village, MD
- **Prediction of Toxicity from Animal to Human: TCDD Case**, Ali Faqi, MPI Research, Mattawan, MI
- **Thirty-Plus Years of AH Receptor and Dioxin Toxicity: What Do We Still Need to Know?** Allan B. Okey, University of Toronto, Toronto, Ontario, Canada
- **Dioxin Toxicity in Humans: 30 Years of Experience at Seveso**, Paolo Mocarelli, University of Milano-Bicocca, Milan, Italy
- **Dioxin Risk Assessment and the Importance of the Recent NAS Recommendations**, Robert Budinsky, Dow Chemical Company, Midland, MI



Informational Sessions

Monday

Peer Review of Toxicology, Exposure, and Risk Data: Ensuring the Best Science

Monday, March 16, 12:10 PM–1:30 PM

Chairperson(s): Philip Wexler, National Library of Medicine, Bethesda, MD and Steve G. Gilbert, Institute of Neurotoxicology and Neurological Disorders, Seattle, WA

Sponsor:
Risk Assessment Specialty Section

Endorsed by:
Ethical, Legal, and Social Issues Specialty Section
Occupational and Public Health Specialty Section
Regulatory and Safety Evaluation Specialty Section

Toxicology data bases are increasingly important tools in the regulatory and risk assessment process. While most toxicologists are well-versed in the intricacies of peer review in relation to journal publications and grants, there is considerably less understanding of how this process works in the evaluation of chemical toxicities and risk values as reflected in certain databases and monographic series. Therefore it is important to present examples of the scientific peer review process within the context of online databases and publications focusing on the toxicity and risk assessment of chemicals. Issues such as panel selection, impartiality and conflicts of interest, funding, transparency in the conduct of meetings, procedure for reaching consensus, opposing views, and public involvement will be discussed for a number of high profile tools widely consulted in the toxicology community. Our panel of experts will reference many of these databases used including the National Library of Medicine's Hazardous Substances Data Bank, Toxicology Excellence for Risk Assessment International Toxicity Estimates for Risk, the International Agency for Research in Cancer's IARC Monographs and the European Centre of Ecotoxicology and Toxicology of Chemicals. Evaluating chemical toxicity when confronted with either a paucity of data or a bewildering array of sometimes conflicting data can be a particular challenge. High quality peer-reviewed databases can play a critical role in supporting the Globally Harmonized System (GHS) of Classification and Labeling of Chemicals and be relevant to ethical concerns such as the reduction of animal testing, by offering consolidated and vetted information. With an increasing insistence that the regulatory framework be supported by the best science, this session will delve into ways of reaching consensus and credible decisions on chemical toxicity and human health. It should appeal to a broad cross-section of toxicologists.

- **ECETOC Peer Review and Quality Control Process**, Neil Carmichael, European Centre of Ecotoxicology and Toxicology of Chemicals, Brussels, Belgium
- **Development of ATSDR Minimal Risk Levels (MRLs)**, Selene Chou, Agency for Toxic Substances and Disease Registry, Atlanta, GA
- **Scientific Peer Review: An Overview with Reference to the International Toxicity Estimates for Risk (ITER) Database**, Mike Dourson, Toxicology Excellence for Risk Assessment, Cincinnati, OH
- **IARC's Practice for Carcinogen Identification and Evaluation**, Ted Junghans, Technical Resources International, Bethesda, MD
- **The Peer Review Process for the Preparation of the Report on Carcinogens**, Mary Wolfe, National Toxicology Program, Research Triangle Park, NC
- **Science Review of the Hazardous Substances Data Bank (HSDB) of the National Library of Medicine**, Robert Menzer, Retired—Formerly U.S. EPA and University of Maryland, Gulf Breeze, FL
- **Peer Review Process for U.S. EPA's Integrated Risk Information System**, Peter Preuss, Abdel Kadry, Karen Hammerstrom, and John Vandenberg
- **RIVM Risk Limits—Peer Review in the Netherlands Government**, Marcel van Raaij, RIVM, Bilthoven, Netherlands

Tuesday

BIOMARKERS

NIH Genes, Environment, and Health Initiative: Biomarkers and Biosensors for Detecting Response to Environmental Stress

Tuesday, March 17, 7:30 AM–8:50 AM

Chairperson(s): Martyn Smith, University of California Berkeley, Berkeley, CA and David Lawrence, Wadsworth Center, Albany, NY

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Occupational and Public Health Specialty Section

48th Annual Meeting and ToxExpo™

Informational Sessions

Wednesday

The NIH established the Genes, Environment, and Health Initiative (GEI) in 2006 with a goal of establishing a foundation for large-scale gene environment interaction studies. A central component of this initiative is the Exposure Biology Program, led by the National Institute of Environmental Health Sciences in collaboration with the National Cancer Institute, National Heart, Lung, and Blood Institute, National Institute for Drug Abuse, and other NIH Institutes and Centers. The Exposure Biology Program aims to develop a new generation of tools for comprehensive exposure assessment. These tools stem from the efforts of four complementary program areas focused on improving detection of individual exposures to traditional environmental toxicants, assessing psychosocial stress and addictive substances, assessing diet and physical activity, and measuring biological responses to these factors. This activity is focused on the development and validation of new tools, approaches, and biomarkers that will enable fundamentally new directions in environmental epidemiology and the exploration of gene environment interactions. An overview of the GEI Exposure Biology Program will be presented by grantees from the Biological Response Indicators Program. The evolution of these new biomarkers and biosensors and how they may be used to assess early but persistent changes in key physiological pathways known to be involved in disease pathogenesis will be the primary focus. In addition, the application of new technologies and methodologies for improved detection of patterns of response to different chemical and lifestyle stressors in pathways that include oxidative stress, inflammation, and DNA damage will be highlighted. Presentations will cover transcriptomic and DNA adduct markers of tobacco smoke exposure, epigenetic alterations in breast stem/progenitor cells from endocrine disrupting chemicals, gene expression patterns from specific PCB congeners, and new biosensors for detecting protein adducts and genetic damage resulting from chemical exposures.

- **Overview of the Genes, Environment, and Health Initiative—Exposure Biology Program**, Daniel Shaughnessy, NIEHS, Research Triangle Park, NC and David Lawrence, Wadsworth Center, Albany, NY
- **Using ‘Omics and Lab-on-a-Chip Microdevices to Detect the Effects of Chemicals and Stressors**, Martyn Smith, University of California Berkeley, Berkeley, CA
- **PCB Congener Specific Oxidative Stress Response by Microarray Analysis**, Sisir Dutta, Howard University, Washington, DC
- **Environmental Epigenetics and Stem/Progenitor Cell Injury**, Tim H. M. Huang, The Ohio State University, Columbus, OH

BIOMARKERS

Novel Translational Safety Biomarkers and Safety First at the FDA

Wednesday, March 18, 7:30 AM–8:50 AM

Chairperson(s): William Slikker, Jr., U.S. FDA, Jefferson, AR and Federico Goodsaid, U.S. FDA, Rockville, MD

Sponsor:

Regulatory and Safety Evaluation Specialty Section

Endorsed by:

**Drug Discovery Toxicology Specialty Section
Risk Assessment Specialty Section**

The U.S. Food and Drug Administration has initiated a program called Safety First that increases focus on the safety evaluation of medical products throughout their life cycle. The safety of therapeutics is extensively evaluated prior to product approval; however, even the most extensive preapproval testing cannot ascertain a safety profile of a product that is used in all possible combinations of genetic backgrounds and health conditions in the population. Safety First is intended to bolster continued oversight of drugs already on the market as well as newly emerging products. The Office of Surveillance and Epidemiology at the Center for Drug Evaluation and Research (CDER) is developing the infrastructure and tools to achieve the goals of Safety First. They will utilize records of large healthcare organizations and electronic medical record databases, coupled with appropriate statistical techniques, to monitor safety signals. The agency also is accessing new databases listing possible side effects of drugs and their continuing dialog on safety questions. In addition, translational safety biomarkers are important tools both for the development of safer drugs as well as for effective surveillance of marketed drugs. These biomarkers provide a continuous metric with which to measure safety through nonclinical and clinical development. An outline will be provided on how Safety First will be implemented and how novel translational safety biomarkers are needed for its success.

- **The Safety First Initiative at the FDA**, Janet Woodcock, U.S. FDA, Rockville, MD
- **Safety First at the Office of Surveillance and Epidemiology**, Gerald Dal Pan, Center for Drug Evaluation and Research, Rockville, MD

Informational Sessions

- **Safer Phase-1 Trials with Novel Translational Safety Biomarkers**, Frank Sistare, Merck & Co., Inc., West Point, PA
- **Qualification of Exploratory Biomarkers into Drug and Regulatory Review**, Federico Goodsaid, U.S. FDA, Rockville, MD

Kinase Inhibitors As Targeted Therapeutics in Inflammation and Oncology—Approaches to Predict and Manage Clinical Toxicities

Wednesday, March 18, 12:00 NOON–1:20 PM

Chairperson(s): Michael A Breider, Ambit Biosciences Inc., San Diego, CA and Shem Patyna, Pfizer Global Research and Development, San Diego, CA

Sponsor:
Toxicologic and Exploratory Pathology Specialty Section

Endorsed by:
Drug Discovery Toxicology Specialty Section

Targeted therapy with either monoclonal antibodies or small molecules has been a major focus of recent pharmaceutical research efforts in the inflammation and oncology disease areas. In particular, cell surface and cytoplasmic kinases have been targeted with varying degrees of clinical success in human oncologic disease. Although targeted therapy does provide an opportunity for more predictable and manageable toxicity based on anticipated and characterized exaggerated pharmacology of kinase inhibition, there have been considerable safety surprises with the various kinase inhibitor therapies in man. Therefore, it is important to address the pharmacologic rationale of targeted therapeutics in inflammation/oncology and provide an overview of kinase inhibitor toxicity in preclinical and clinical settings to demonstrate the importance of kinase activity profiling. To highlight these various issues participants will be provided with an overview of kinase biology and the use of high-throughput kinase profiling as a drug development tool and the correlation of kinase-inhibitor cardiotoxicity to kinase specificity profiles using *in vitro* tools to predict toxicological liabilities of kinase inhibitors with an emphasis on cardiac injury. The on and off-target toxicity for currently marketed kinase inhibitors of observed toxicities of currently marketed kinase inhibitors will be provided to gain a broader understanding of the complexities of kinase inhibitor pharmacology and toxicology. Finally, the tools to be better prepared to assess the possible toxicity of kinase inhibitors through systematic kinase target analysis and will be addressed that will enable us to ultimately devise an early identification of safety and derisking strategies.

- **Human Kinome Overview and Current Research Tools to Profile Kinase-Inhibitor Specificity**, Patrick Zarrinkar, Ambit Biosciences, San Diego, CA
- **Correlation of Kinase-Inhibitor Cardiotoxicity to Kinase Specificity Profiles**, Kyle L. Kolaja, Roche Palo Alto, Palo Alto, CA
- **Overview of On and Off-Target Toxicity for Currently Marketed Kinase Inhibitors**, Michael A. Breider, Ambit Biosciences, San Diego, CA

Thursday

Lead: Children's Exposures and Current Regulatory Standards

Thursday, March 19, 7:30 AM–8:50 AM

Chairperson(s): Stacie L. Wild, Amgen, Inc., Thousand Oaks, CA and Kristina M. Hatlelid, U.S. Consumer Product Safety Commission, Bethesda, MD

Sponsor:
Women in Toxicology Special Interest Group

Endorsed by:
Metals Specialty Section
Occupational and Public Health Specialty Section
Reproductive and Developmental Toxicology Specialty Section

Recent news reports raise concerns about children's exposure to lead in toys, paint, candy, and other everyday materials. While the toxicity of lead has been well studied and the use of lead in many materials has been reduced or eliminated over the past 30 years, the possibility of lead exposure in children from both past and current uses of lead remains a public health priority. While a major contributor to lead exposure in children continues to be from the home, 30% or more of children aged <6 years with lead poisoning are exposed to lead through sources other than residential lead paint such as cosmetics, folk and traditional medications, painted and metallic toys and trinkets, and ceramic food ware. Examples regarding lead exposure and risk assessments from sources such as lead based ceramics in schools and bioassessability of lead exposure in children's products will be presented. Numerous agencies are involved in controlling lead exposure and enforcing regulations including the Centers for Disease Control and Prevention (CDC), U.S. Consumer Product Safety Commission (CPSC) and the U.S. FDA. CPSC regulates more than 15,000 types of consumer products

Informational Sessions

including the lead content of numerous products including paint and similar surface coatings on products and furniture intended for consumer use, including toys. The FDA is responsible for ensuring the safety of products as authorized in the Federal Food, Drug and Cosmetic Act. FDA has addressed lead issues for diverse products such as pesticides, metal food cans, lipstick and crystal baby bottles for infants. An overview of known mechanisms of lead toxicity as well as newer research on the long term effects of lead will be presented. Examples will be provided of children's exposures to lead and summarize efforts to reduce lead exposures. The session will conclude with those perspectives of regulatory agencies responsible for regulating lead-containing products, including discussion of pending legislation that could change how lead-containing consumer products are regulated and steps being taken to protect the public from excessive lead exposure.

- **Introduction**, Stacie L. Wild, Amgen, Inc., Thousand Oaks, CA
- **Childhood Lead Toxicity: Public Health Implications Past, Present, and Future**, Michael McCabe, University of Rochester School of Medicine, Rochester, NY
- **Recent Risk Evaluations and Lead Exposures from Children's Products**, Woodhall Stopford, Duke University, Durham, NC
- **CDC Perspective—Children's Lead Exposure**, Marissa Scalia, Centers for Disease Control and Prevention, Atlanta, GA
- **Current CPSC Regulations to Limit Children's Exposure to Lead**, Kristina M. Hatlelid, U.S. Consumer Product Safety Commission, Bethesda, MD
- **Current Lead Concerns/Regulations for FDA Regulated Products**, Michael Kashtock, Center for Food Safety and Applied Nutrition, College Park, MD



Education-Career Development Sessions

Monday

Grantsmanship Forum: Tools and Skills Needed to Navigate Toxicology Research Funding

Monday, March 16, 4:35 PM–5:55 PM

Chairperson(s): Srikanth S. Nadadur, NIEHS, Research Triangle Park, NC and Jerrold Heindel, NIEHS, Research Triangle Park, NC

Sponsor:
Career Resource and Development Committee

Endorsed by:
Education Committee
Postdoctoral Assembly
Research Funding Committee
Student Advisory Council

Toxicology research at academic institutions is supported by various extramural research funding mechanisms, of which the most common are research grants and fellowships. These research grants can be obtained either by investigator-initiated, generally unsolicited, or in response to research funding announcements by various funding agencies. Traditionally, the major research support for understanding the impact of toxic substances on public health is supported by the National Institute of Health (NIH) and its 26 different Institutes or Centers. While the National Institute of Environmental Health Sciences (NIEHS) supports toxicology research efforts to understand the impact of environmental pollutants, the National Institute of General Medical Sciences (NIGMS) supports research grants for a wide variety of agents including pharmaceuticals. Some of the federal agencies, such as the National Science Foundation, support research in the areas of environmental biology. Numerous non-profit organizations including the Pharmaceutical Research and Manufacturers of America (PhRMA) Foundation also provide research grant support, starting from predoctoral to sabbatical opportunities in pharmacology, toxicology and informatics. A representative Program Director from NIGMS, NIEHS, NSF and PhRMA Foundation will present the opportunities, tools, and skills needed for successful research funding. In highlighting this important funding opportunity available, one presentation will focus exclusively on successful grant writing noting specific requirements such as the correct mix of scientific knowledge and salesmanship to enable your to navigate NIH funding.

- **Introduction**, Srikanth S. Nadadur, NIEHS, Research Triangle Park, NC

- **Grant Programs at NIGMS to Support Toxicology Programs**, Richard T. Okita, National Institute of General Medical Sciences, Bethesda, MD
- **Grantsmanship at NIH: How to Swim with the Sharks and Survive**, Jerrold Heindel, NIEHS, Research Triangle Park, NC
- **Funding Opportunities at the National Science Foundation**, Sally O'Connor, National Science Foundation, Arlington, VA
- **Fellowship and Grant Opportunities for Clinical and Basic Toxicology at PhRMA Foundation**, Eileen M. Cannon, PhRMA Foundation, Washington, DC

Tuesday

The Future of Environmental Health Science: Featuring NIEHS-Funded Early Career Investigators

Tuesday, March 17, 12:00 NOON–1:20 PM

Chairperson(s): Vishal S. Vaidya, Harvard Institutes of Medicine, Boston, MA and Carol Shreffler, National Institute of Environmental Health Sciences, Research Triangle Park, NC

Sponsor:
Career Resource and Development Committee

Endorsed by:
Education Committee
Mechanisms Specialty Section
Postdoctoral Assembly
Research Funding Committee

An essential element of the mission of the NIEHS is the support and career promotion of the future generation of exceptionally talented and creative new scientists who will push forward research in understanding the impact of environmental exposures and human health. Support through critical transition stages has been identified as being particularly important in developing a cadre of talented early career scientists. In response, the NIH and the NIEHS has started the Outstanding New Environmental Scientist (ONES) Award which is one of many initiatives that it has taken to provide the funding for the research and career enhancement of scientists during the transition from postdoctoral to faculty positions, and to allow selected outstanding junior faculty to flourish. The ONES scientists are expected to make a long term career commitment to the environmental health sciences, and to bring innovative, ground breaking research thinking to bear on the problems of how environmental exposures affect human biology, human pathophysiology,

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Education-Career Development Sessions

and human disease. In the first three years, 21 awards have been made and the NIEHS ONES program has become an important showcase for the future leaders in environmental health sciences research. Three ONES awardees have been chosen to present who have had innovative publications in the first year of the award and who display a broad spectrum of research in the environmental health sciences. These exceptional scientists, who will present cutting edge science at the interface of molecular toxicology and environmental health sciences, are a model for junior faculty attendees who are considering applying for these competitive but highly rewarding grants.

- **Endocrine Disruption of the Hypothalamic Signaling That Regulates Puberty**, Heather B. Patisaul, North Carolina State University, Raleigh, NC
- **Cellular Responses to CrVI Induced DNA Damage: Role for the Werner Syndrome Protein**, Patricia Lynn Opresko, University of Pittsburgh, Pittsburgh, PA
- **Mechanisms of Pesticide-Induced Neurobehavioral Deficits: Relevance to ADHD**, Jason R. Richardson, University of Medicine and Dentistry of New Jersey, Piscataway, NJ

Wednesday

Toxicologists: The Next Generation

Wednesday, March 18, 7:30 AM–8:50 AM

Chairperson(s): Joan B. Tarloff, University of the Sciences in Philadelphia, Philadelphia, PA and Vanessa A. Fitsanakis, King College, Bristol, TN

Sponsor:

Education Committee

Endorsed by:

Postdoctoral Assembly
Student Advisory Council

An important component of the Society of Toxicology 2008–2011 Strategic Plan is the priority to build for the future of toxicology. In addition to ongoing K–12, graduate, and postdoctoral fellow educational activities, undergraduate educators have been meeting regularly to exchange ideas and teaching strategies. Principles and applications of toxicology can enter curricula through a variety of mechanisms, from dedicated programs that lead to baccalaureate degrees to single, stand-alone courses that satisfy intellectual curiosity. It is logical that college students who have positive experiences in toxicology courses will be more likely to enter graduate programs

and become our next generation of toxicologists. The Undergraduate Educators Forum hopes to establish a repository for course materials and to open the lines of communication for individuals involved in teaching undergraduate students. College-level education in toxicology demands different skills and approaches than those used for graduate or K–12 education. Developing critical thinking and analytical skills is particularly challenging for college students, who are more accustomed to accepting information without critique. In order to foster communication among educators it is important that we illustrate strategies that engage critical thinking and improve student learning and involvement. Several undergraduate college educators will present classroom-based exercises or assessments designed to stimulate student-based learning. Through this forum we will learn what has been developed for upper-level high school students and how these exercises and experiences may be modified for college students. This session will provide a venue for educators to discuss classroom experiences and educational philosophies.

- **Doing Toxicology Research in the Classroom**, Steven D. Mercurio, Minnesota State University, Mankato, MN
- **Brain-Based Learning: Explanations and Strategies**, Vanessa A. Fitsanakis and Donna Raines, King College, Bristol, TN
- **Strategies to Improve Students' Writing**, Peter J. Harvison and Joan B. Tarloff, University of the Sciences in Philadelphia, Philadelphia, PA
- **Teaching Toxicology: What's Available for Basic Labs?** Bruce Fuchs, National Institutes of Health, Bethesda, MD

Career Opportunities and Transitions in Toxicology

Wednesday, March 18, 4:30 PM–5:50 PM

Chairperson(s): Lauren Aleksunes, University of Kansas Medical Center, Kansas City, KS and Bernard Gadagbui, Toxicology Excellence for Risk Assessment (TERA), Cincinnati, OH

Sponsors:

Postdoctoral Assembly
Toxicologist of African Origin Special Interest Group

Endorsed by:

Career Resource and Development Committee
Student Advisory Council

It's never too early, or too late, to think about where your career in toxicology will lead you next. Whereas students and postdocs are typically familiar with the ins and outs of pursuing an academic research career, opportunities to investigate non-academic careers in toxicology can be few and far between. Early-career scientists

Education-Career Development Sessions

Scientific

often ask ‘What careers are available to toxicologists? What skills and experiences do I need to be competitive for these positions?’ Such questions are also relevant to established toxicologists looking to expand their work experiences or embark upon a new career path. Toxicologists that practice in various work sectors are faced with the difficult and sometimes painful task of transitioning from one sector to another as each sector often demands unique skills. Most often, guides on career transitions are not readily available for these toxicologists. The material to be presented provide participants with insight into toxicology careers in diverse settings, including industry, government, consulting groups, and nonprofit organizations, and provide information about career transitions across the various sectors. Our panel of experienced toxicologists will describe the paths that their careers have taken, intentional or otherwise. Both practical and applicable advice will be offered for those participants interested in pursuing similar avenues, or for those just wishing to step off the beaten path. The presenters will highlight their motivations, challenges, success stories, and lessons learned. Be sure to bring questions to ask our panel of seasoned toxicologists during the interactive question and answer period. Whether you are a graduate student ready to jump into a job search, or an established scientist looking to move your career in an unexpected direction, join us for an interactive and informative discussion designed to expand your awareness of unique and exciting scientific career opportunities for toxicologists and including how to successfully transition between sectors.

- **Toxicology Positions in Consulting**, James C. Lamb, IV, The Weinberg Group, Inc., Washington, DC
- **Looking Beyond Your Current Sector**, Myrtle A. Davis, National Cancer Institute, Bethesda, MD
- **Opportunities at a Contract Research Organization**, Nancy Gillett, Charles River Laboratories, Inc., Reno, NV
- **Making a Smooth Transition**, David Jacobson Kram, U.S. FDA, Silver Spring, MD
- **Toxicologists in Food Safety**, Jerry J. Hjelle, Monsanto Company, St. Louis, MO
- **Making a Successful Transition from Government to Non-Profit Sectors**, Michael L. Dourson, Toxicology Excellence for Risk Assessment (TERA), Cincinnati, OH

Regional Interest Session

Wednesday

Biofuels and the Bay: Characterizing Health and Ecosystem Impacts in the Chesapeake

Wednesday, March 18, 9:00 AM–11:45 AM

Chairperson(s): Michael Madden, U.S. EPA, Chapel Hill, NC and Annie M. Jarabek, U.S. EPA, Research Triangle Park, NC

Sponsor:

Risk Assessment Specialty Section

Endorsed by:

Mixtures Specialty Section

Occupational and Public Health Specialty Section

The Chesapeake Bay Commission has evaluated alternative fuel development efforts in the Chesapeake Region. Already under stress from anthropomorphic factors, the Chesapeake Bay Region could be adversely impacted by the wide spectrum of use of the region for biofuels production, transport, storage, and combustion. This Regional Interest session will characterize the potential adverse effects on public health and ecological degradation from the production and use of biofuels in the Bay, an uncertain and complex challenge. There are multiple types of biofuels that are derived from various feedstocks and production processes. The amount of land use devoted to biofuels in this region will vary tremendously in part by the biofuel stock in economic demand, the advances made in the growth rate and energy content of plant stocks, and whether it can be imported. Domestic corn planting in the Bay Region increased 11,000 acres from 2005 to 2006, primarily for use in ethanol production with consequences for decreased food availability, soil loss, and nutrient runoff. In contrast, a biodiesel production plant in Baltimore will import soybeans as the raw material due to economic incentives, thereby avoiding issues with domestic corn production. Potential human health effects will occur through exposure to the fuels, inhalation of combustion products, and fallout into water supplies. Algal blooms due to increased nitrogen deposition in the estuarine environment from biofuel production would impact public and environmental health. Air quality could be impacted from combustion, as could water quality through deposition of the fuel products into the Bay. Estuarine and marine organisms, some with commercial importance, could be adversely impacted. Ethical issues over the displacement of crops for food to energy for mobile sources have arisen and will be considered. Both the public health and ecological problems posed by the wide spectrum of biofuels being considered for use in the Bay will be addressed.

- **Introduction**, Annie Jarabek, U.S. EPA, Research Triangle Park, NC
- **Background on Biofuels and the Bay**, Michael Madden, U.S. EPA, Chapel Hill, NC
- **Overview: Biofuels and Potential Effects in the Bay**, Ann Pesiri Swanson, Chesapeake Bay Commission, Annapolis, MD
- **Health Effects of Exposure to Biofuels**, Mark Witten, University of Arizona, Tucson, AZ
- **Biofuels: Potential Impacts of Production, Storage, and Use on Estuarine Waters**, Joel Baker, University of Washington Tacoma, Tacoma, WA
- **Biofuels: Estuarine Ecotoxicological Impacts**, Charles Menzie, Exponent, Alexandria, VA
- **Ethics and Biofuels: Distributive and Intergenerational Justice**, Thomas Powers, University of Delaware, Newark, DE



Student and Postdoctoral Fellow Events

Student/Postdoctoral Fellow Mixer

Sunday, March 15, 7:30 PM–8:30 PM

Camden Lobby

Baltimore Convention Center

Ticket Required

The Student Advisory Council hosts this opportunity for students and postdoctoral fellows to gather, to meet new colleagues, and to reestablish relationships in an informal atmosphere at the beginning of the meeting. Tickets are obtained at no cost by registering for this event on the Annual Meeting Registration Form. Ticket and meeting badge are required. Complimentary refreshments and a cash bar will be available.

Regional Chapter/Special Interest Group Graduate Committee Meeting

Monday, March 16, 7:00 AM–8:30 AM

Room 302

Baltimore Convention Center

Representatives will conduct their business meeting.

In Vitro Toxicology Lecture and Luncheon for Students

Monday, March 16, 12:15 PM–1:20 PM

Room 339

Baltimore Convention Center

Ticket Required

Lecturer: TBA

Title: TBA

Sponsored by:

The Colgate-Palmolive Company

Graduate students, undergraduates, postdoctoral scholars, and recipients of Colgate-Palmolive awards are among the guests at the *In Vitro* Lecture and Luncheon. The goal of the *In Vitro* Lecture series is to feature important research using *in vitro* and alternative techniques to study basic mechanisms and to illustrate how these test methods benefit animal welfare by refining and reducing animal use. Students and postdocs can reserve a ticket for the luncheon with a \$5 deposit when they register for the SOT Annual Meeting.

Specialty Section Graduate Committee Meeting

Tuesday, March 17, 7:00 AM–8:30 AM

Room 306

Baltimore Convention Center

Representatives will conduct their business meeting.

Postdoctoral Assembly Luncheon

Tuesday, March 17, 12:00 NOON–1:15 PM

Room 339

Baltimore Convention Center

Ticket Required

Amidst scrambling to attend all of the events at the meeting, this will be time for postdocs to kick back and relax! All postdoctoral fellows are invited to a casual luncheon organized by the Postdoctoral Assembly (PDA). We will announce the recipients of the Best Postdoctoral Publication Awards and acknowledge the postdocs who received awards this year from Specialty Sections and Regional Chapters. The PDA Board members will present an overview of accomplishments and future directions for the PDA and will introduce the new board members for 2009–2010. There will be a drawing for prizes. Postdocs can reserve a ticket when registering for the Annual Meeting.

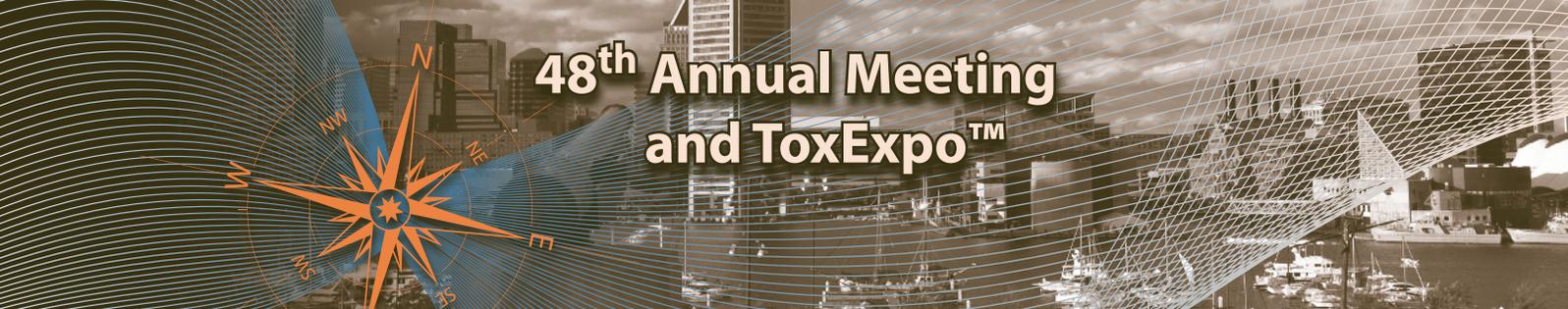
Student Advisory Council Meeting

Wednesday, March 18, 7:00 AM–8:00 AM

Room 302

Baltimore Convention Center

Current and incoming Student Advisory Council members will conduct their business meeting, then meet with SOT Council and the PDA Board.



48th Annual Meeting and ToxExpo™

Student and Postdoctoral Fellow Events

Lunch with an Expert

Date and time varies by group

This event is an informal gathering of a small group of students and a Toxicology Expert. Sign up *via* the Lunch with an Expert link in the Student Services section of the SOT Web site. The groups are matched by research interests and the Expert for each group identifies a time and place for the event. Groups meet at the Lunch with an Expert board located in the Pratt Street Lobby near the exit for the Hilton Skybridge to go together to the restaurant. Details for the group meeting will be sent in advance of meeting.

EDUCATION-CAREER DEVELOPMENT

Grantsmanship Forum: Tools and Skills Needed to Navigate Toxicology Research Funding

Monday, March 16, 4:35 PM–5:55 PM

Chairperson(s): Srikanth S. Nadadur, NIEHS, Research Triangle Park, NC and Jerrold Heindel, NIEHS, Research Triangle Park, NC

Sponsor:

Career Resource and Development Committee

Endorsed by:

Education Committee

Postdoctoral Assembly

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- **Introduction,** Srikanth S. Nadadur, NIEHS, Research Triangle Park, NC



Student and Postdoctoral Fellow Events

- **Grant Programs at NIGMS to Support Toxicology Programs**, Richard T. Okita, National Institute of General Medical Sciences, Bethesda, MD
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- **Funding Opportunities at the National Science Foundation**, Sally O'Connor, National Science Foundation, Arlington, VA
- **Fellowship and Grant Opportunities for Clinical and Basic Toxicology at PhRMA Foundation**, Eileen M. Cannon, PhRMA Foundation, Washington, DC

EDUCATION-CAREER DEVELOPMENT

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Tuesday, March 17, 12:00 NOON–1:20 PM

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Sponsor:
Career Resource and Development Committee

Endorsed by:
Education Committee
Mechanisms Specialty Section
Postdoctoral Assembly
Research Funding Committee

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EDUCATION-CAREER DEVELOPMENT

Toxicologists: The Next Generation

Wednesday, March 18, 7:30 AM–8:50 AM

Chairperson(s): Joan B. Tarloff, University of the Sciences in Philadelphia, Philadelphia, PA and Vanessa A. Fitsanakis, King College, Bristol, TN

Sponsor:
Education Committee

Endorsed by:
Postdoctoral Assembly
Student Advisory Council

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Student and Postdoctoral Fellow Events

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- **Doing Toxicology Research in the Classroom,** Steven D. Mercurio, Minnesota State University, Mankato, MN
- **Brain-Based Learning: Explanations and Strategies,** Vanessa A. Fitsanakis and Donna Raines, King College, Bristol, TN
- **Strategies to Improve Students' Writing,** Peter J. Harvison and Joan B. Tarloff, University of the Sciences in Philadelphia, Philadelphia, PA
- **Teaching Toxicology: What's Available for Basic Labs?** Bruce Fuchs, National Institutes of Health, Bethesda, MD

EDUCATION-CAREER DEVELOPMENT

Career Opportunities and Transitions in Toxicology

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Student Advisory Council

It's never too early, or too late, to think about where your career in toxicology will lead you next. Whereas students and postdocs are typically familiar with the ins and outs of pursuing an academic research career, opportunities to investigate non-academic careers in toxicology can be few and far between. Early-career scientists

often ask 'What careers are available to toxicologists? What skills and experiences do I need to be competitive for these positions?' Such questions are also relevant to established toxicologists looking to expand their work experiences or embark upon a new career path. Toxicologists that practice in various work sectors are faced with the difficult and sometimes painful task of transitioning from one sector to another as each sector often demands unique skills. Most often, guides on career transitions are not readily available for these toxicologists. The material to be presented provide participants with insight into toxicology careers in diverse settings, including industry, government, consulting groups, and nonprofit organizations, and provide information about career transitions across the various sectors. Our panel of experienced toxicologists will describe the paths that their careers have taken, intentional or otherwise. Both practical and applicable advice will be offered for those participants interested in pursuing similar avenues, or for those just wishing to step off the beaten path. The presenters will highlight their motivations, challenges, success stories, and lessons learned. Be sure to bring questions to ask our panel of seasoned toxicologists during the interactive question and answer period. Whether you are a graduate student ready to jump into a job search, or an established scientist looking to move your career in an unexpected direction, join us for an interactive and informative discussion designed to expand your awareness of unique and exciting scientific career opportunities for toxicologists and including how to successfully transition between sectors.

- **Toxicology Positions in Consulting,** James C. Lamb, IV, The Weinberg Group, Inc., Washington, DC
- **Looking Beyond Your Current Sector,** Myrtle A. Davis, National Cancer Institute, Bethesda, MD
- **Opportunities at a Contract Research Organization,** Nancy Gillett, Charles River Laboratories, Inc., Reno, NV
- **Making a Smooth Transition,** David Jacobson Kram, U.S. FDA, Silver Spring, MD
- **Toxicologists in Food Safety,** Jerry J. Hjelle, Monsanto Company, St. Louis, MO
- **Making a Successful Transition from Government to Non-Profit Sectors,** Michael L. Dourson, Toxicology Excellence for Risk Assessment (TERA), Cincinnati, OH



Educational Outreach Activities

Undergraduate Education Program

Saturday, March 14, 4:15 PM–9:00 PM

Sponsored by:
Committee for Diversity Initiatives

Chairperson(s): Mari Stavanja, Celanese International Corporation, Dallas, TX

This event is for undergraduate students and advisors receiving 2009 MARC and SOT travel funding and SOT program volunteers.

- 4:15 PM–5:45 PM** **Orientation for SOT Hosts, Peer Mentors, and Advisors**
- 5:45 PM–6:00 PM** **Opening Event**
- 6:15 PM–6:45 PM** **Dinner**
- 7:00 PM–8:00 PM** **Anniversary Celebration**

20th Anniversary Undergraduate Program Celebration

Saturday, March 14, 7:00 PM–9:00 PM

Sponsored by:
Committee for Diversity Initiatives

Chairperson(s): Claude McGowan, Johnson & Johnson, Skillman, NJ and Vicente Santa Cruz, Chevron Phillips Chemical Company, Belgium

The Anniversary Celebration honors previous program participants and organizers and is open to all who have been connected to the Undergraduate Program for Minority Students since 1989.

- 7:00 PM–8:00 PM** **Anniversary Celebration and Presentations**
- 8:00 PM– 9:00 PM** **Dessert and Networking**

Undergraduate Education Program

Sunday, March 15, 8:00 AM–7:30 PM

Sponsored by:
Committee for Diversity Initiatives

Chairperson(s): Mari Stavanja, Celanese International Corporation, Dallas, TX

The Sunday program is open to undergraduate students who are registered for this event on the Annual Meeting Registration Form, the undergraduate students receiving MARC, SOT, and Pfizer travel funding, and the SOT program volunteers.

8:00 AM–11:30 AM

Introductions and Special Toxicology Lectures

- 8:15 AM–8:50 AM** **Introduction to Toxicology, José Manautou, University of Connecticut, Storrs, CT**
- 9:00 AM–9:45 AM** **Nano-a-Nano: The Good, the Bad, and the Ugly, Martin Philbert, University of Michigan, Ann Arbor, MI**
- 9:45 AM–10:00 AM** **Break**
- 10:00 AM–10:45 AM** **Transcription Factors and Fetal Programming of Renal Disease, Adrian Nanez, University of Louisville, Louisville, KY—Program Alumnae**
- 10:45 AM–11:30 AM** **Research Presentation, TBA**
- 11:30 AM–11:45 AM** **Break**
- 11:45 AM–2:30 PM** **Lunch and Networking**

Breakout Sessions For Students

- 12:30 PM–1:05 PM** **What Is Graduate School and What Can I Expect?**
- 1:15 PM–1:55 PM** **How to Get into Graduate School: An Academic Advisor's Perspective**

For Advisors

- 12:30 PM–1:05 PM** **Tips for Advising Prospective Graduate Students or How to Get Your Students Accepted to Graduate School!!!**
- 1:15 PM–1:55 PM** **Best Practices: Idea Sharing About Keeping Students on a Science Path**

(continued to next page)

48th Annual Meeting and ToxExpo™

Educational Outreach Activities

All Participants

2:00 PM–2:40 PM

Career Opportunities in Toxicology—Panel Discussion,
Moderator: Vanessa Silva, Procter & Gamble, Cincinnati, OH—Program Alumnae
Academia: Alice Villalobos, Texas A&M University, College Station, TX
Industry: Robert P. Casillas, Battelle, Columbus, OH
Government: Marquee King, U.S. EPA, Washington, DC

2:40 PM–3:00 PM

Break

3:00 PM–3:30 PM

Host Mentor and Peer Mentor Meeting,
Adrian Nanez, University of Louisville, Louisville, KY

3:00 PM–5:00 PM

Student and Advisors: Open Time with Academic Toxicology Program Directors and Internship Sponsors,
Kim Daniel, Texas A&M University, College Station, TX

5:15 PM–6:30 PM

Awards Ceremony (including the recognition of the 20th Anniversary)

6:30 PM–7:30 PM

SOT Welcoming Reception

7:30 PM–8:30 PM

Student/Postdoctoral Fellow Mixer

Paracelsus Outside the Classroom

Sunday, March 15, 10:00 AM–12:30 PM, 1:00 PM–4:00 PM

Chairperson(s): Maureen Gwinn, U.S. EPA, Washington, DC

Sponsor:

Communications Committee

Partners:

Port Discovery Children's Museum
University of Maryland Biotechnology Institute

SOT invites meeting attendees and their families, as well as the larger community, to visit Port Discovery Children's Museum (www.portdiscovery.org) in Baltimore on Sunday, March 15. Port Discovery is near the Inner Harbor and is a top ranked children's museum. Toxicologists will enrich the museum exhibits with hands-on science activities to engage participants in the process of science and learn more about toxicology. Children can drop in and participate informally or those in Grades 1–5 can register for one of the groups scheduled to rotate among hands-on experiment stations. High school students will serve as group leaders for half

the day and will participate in their own special workshop at the University of Maryland Biotechnology Institute the other half of the day. Meeting participants may request complimentary tickets from Martha Lindauer at martha@toxicology.org. Request a morning or afternoon session if you wish to schedule your elementary children into one of the formal groups.

Undergraduate Education Program

Monday, March 16, 7:15 AM–2:00 PM

Sponsored by:

Committee for Diversity Initiatives

Chairperson(s): Mari Stavanja, Celanese International Corporation, Dallas, TX

7:15 AM–7:45 AM

Student, Advisor, Mentor Meeting

8:00 AM–9:00 AM

Plenary Lecture: Signal Transduction Pathways Used by Therapeutic Agents and Drugs of Abuse, Paul Greengard, The Rockefeller University, New York, NY—Nobel Laureate

9:15 AM–11:15 AM

Poster Session for Visiting Students

11:15 AM–12:00 NOON

Selected Scientific Sessions

12:00 NOON–1:15 PM

In Vitro Luncheon: TBA

1:30 PM–2:00 PM

Closing Session

Chairperson: Mari Stavanja, Celanese International Corporation, Dallas, TX

Undergraduate Toxicology Faculty Meeting

Tuesday, March 17, 3:30 PM–4:30 PM

The Education Committee is hosting the Undergraduate Toxicology Faculty Meeting for all faculty involved in the teaching of toxicology to undergraduates, or for those interested in including toxicology at the undergraduate level. Hear an update on initiatives for undergraduate faculty, provide your input, and network.



Educational Outreach Activities

SOT Resource Pavilion

Do you know all the resources available through SOT and where to find them? Stop by the SOT Resource Pavilion to learn about SOT activities, membership benefits, strategic initiatives, and the endowment. Find materials to support the discipline of toxicology and educational tools for K–12 and public outreach. It is a one-stop shop for all your questions and member needs. It is centrally located in the Charles Street Lobby and open the following hours:

Sunday, March 15	11:00 AM–2:00 PM
Monday, March 16	9:00 AM–4:30 PM
Tuesday, March 17	8:30 AM–4:30 PM
Wednesday, March 18.....	8:30 AM–4:30 PM
Thursday, March 19.....	8:30 AM–12:00 NOON

Toxicology History Room

For the first time ever, in 2009 the SOT Annual Meeting will feature a Toxicology History Room (THR). The exhibit will showcase documents and other printed matter, artifacts, memorabilia, and digital displays that highlight the historical importance and societal impact of toxicology, and the history of the SOT. The goal of the THR is to stimulate the interest of SOT members and other meeting attendees in the origins and evolution of the science of toxicology, and its societal component. The project is being spearheaded by members Steve Gilbert and Phil Wexler leading a Task Force consisting of Toni Hayes, Dori Germolec, Asish Mohapatra, Richard Lane, and Elizabeth Walker, with guidance from Ernie Hodgson, SOT Historian, and staff support provided by Martha Lindauer. Provided that the concept and implementation is well received, SOT plans to offer the THR as an ongoing and expanded Annual Meeting event. SOT membership involvement is welcomed. Please contact Martha Lindauer at martha@toxicology.org if you have historical items that you would like to loan or contribute, or would be interested in staffing the room.

The THR will be in the VIP Suite just off the Baltimore Convention Center Charles Street Lobby. Please stop by to learn about, and from, your past.

Notes



**With the 50th SOT ANNIVERSARY MATCH
Your Contribution has twice the IMPACT.**

**Contribution + Match = Twice
the Impact on the Endowment
Fund of your choice.**

**Help exhaust the SOT Council Approved \$500,000 50th Anniversary Match.
Every dollar you give is matched, so your contribution
has twice the IMPACT.**

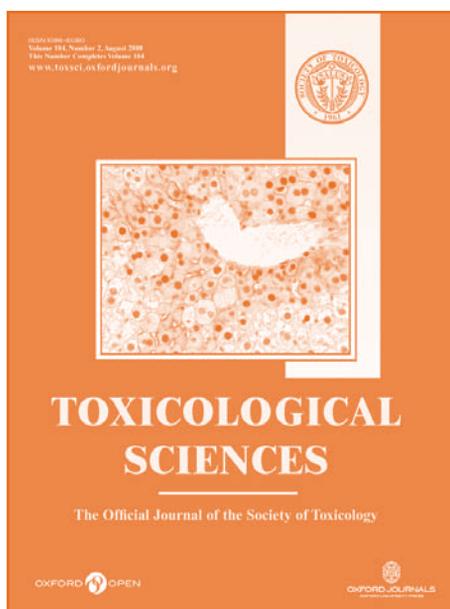
Recognition Level

<i>Paracelsus Circle</i>	\$500 or more	+	\$500 or more	=	\$1000 or more
Gold	\$250 or more	+	\$250 or more	=	\$500 or more
Silver	\$100 or more	+	\$100 or more	=	\$200 or more
Bronze	\$40 or more	+	\$40 or more	=	\$80 or more

**Make a contribution to the SOT Endowment Fund of your choice today.
Visit: www.toxicology.org/ai/csot/contribute.asp.**

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*ISI Journal Citation Reports 2007 Edition, published in 2008



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Registration Guidelines

Try SOT's On-Line Registration System

SOT members and non-members are invited to register for the 2009 SOT Annual Meeting using SOT's On-Line Registration System. The system provides a quick and easy method of registering *via* the Internet using a credit card. Registration information can be accessed *via* the SOT Web site at www.toxicology.org/register.

Mail or Fax Registration

Registrants may fax or mail their registration payments using the Registration Form located on pages 99 and 101.

Please type or print clearly.

REGISTRATION: No phone registrations will be accepted.

Please send Registration Forms to:

SOT Registration
P.O. Box 91895
Washington, DC 20090-1895

or

SOT Headquarters (Faxes only, with credit card)
Fax: (703) 438-3113

USPS Express packages must be mailed to:

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

Forms will be date-stamped as they arrive. This is your date of registration. Faxes will be accepted by SOT Headquarters only if a credit card number is clearly listed in the appropriate area.

NOTE: To prevent double-billing, if you are registering by fax, DO NOT mail your original registration form. SOT needs only one copy for processing. All mailed and faxed registration forms will be processed on-line by SOT staff.

Registration Guidelines:

PAYMENT: Registration Forms will be returned if not accompanied by one of the following methods of payment:

- Check (company or personal); U.S. Currency only. Please list all registrants on check memo or check stub.
- Government Purchase Order. (Check must be drawn from the U.S. Department of Treasury.)
- Money Order.
- Visa, MasterCard, Discover, Diner's Club, or American Express.

Registration Deadlines:

- Early Bird Registration until **January 30, 2009**
- Standard Registration until **February 20, 2009**
- Final Registration after **February 20, 2009**

DO NOT mail your Registration Form to SOT if it will arrive after March 10, 2009. SOT will accept Annual Meeting Registrations until March 10. After March 10, registrations not processed on-line will only be accepted on-site at the Annual Meeting. The on-line registration system will be open throughout the meeting and if you register on-line after March 10, 2009, you can easily pick up your badge at the "Badge Pick Only" registration counter.

GUEST REGISTRATION: The SOT Guest Hospitality Center provides guest participants (non-scientists) with a place to meet and socialize with other guests. The Center will be open Sunday through Thursday and information on local attractions, rental cars, and tours will be available there.

Guests must be registered for Annual Meeting to access the Hospitality Center. Guests must register with the person they are accompanying and are welcome to attend the Welcoming Reception. Reminder: Children under the age of 15 are not permitted in the Exhibit Hall at any time or in scientific sessions unless consent is given by the session chair.

ONE-DAY REGISTRATION: There is no reduced fee for one-day registration.

TICKETS: Tickets for Continuing Education courses and other events may be required. These tickets will be issued with your meeting badge. Annual Meeting registration is required to participate.

CONFIRMATION: You will be mailed a registration confirmation, name badge and Continuing Education and/or event ticket(s) before the meeting if your Registration Form is received by February 20, 2009. If your registration is received after February 20, you can pick up your badge and tickets at the registration counters on-site.

CANCELLATION REFUND POLICY: All requests for cancellations and/or refunds must be received in writing to SOT Headquarters by February 20, 2009. These refunds will be processed, less a \$50 cancellation fee, following the Annual Meeting. Refund requests received after February 20, 2009, will not be processed.

EXHIBITORS: Please go to the Exhibitor Service Center on-line to register. If your company would like more information on exhibit opportunities, go to www.toxexpo.com, select the ToxExpo™ option on the homepage, and follow the instructions from the invitation to exhibit selection, or please contact Liz Kasabian at SOT Headquarters: (703) 438-3115, fax: (703) 438-3113, or e-mail: liz@toxicology.org.

AMERICANS WITH DISABILITIES ACT (ADA): The Baltimore Convention Center is accessible to persons with special needs. If you have special needs, please check the special accessibility requirement box or contact Heidi Prange at SOT Headquarters: (703) 438-3115 ext. 1424 or e-mail: heidi@toxicology.org.



Registration Form (Part 1)

48th SOT Annual Meeting

March 15-19, 2009

R2009

FOR OFFICE USE ONLY

Date Received: _____
 Input: Initials: _____

(Required: Please check the appropriate box)

PLEASE PRINT CLEARLY OR TYPE

SOT Member Non-Member Badge Name: _____

First Name/Middle Initial: _____

Last Name: _____ Professional Degree(s): _____

Company Name: _____

(Is this a new employer and/or new address? Yes No)

Company (second line): _____

Department: _____

Street Address: _____

City: _____ Prov/State: _____ Zip: _____ Country: _____

Area Code/Phone Number: _____ Fax Number: _____

E-mail Address: _____

Special Accessibility Requirements: _____

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

Postdoc Graduate Student Undergraduate Student

Institution: _____ Advisor's Name: _____

Advisor's Phone Number: _____ Advisor's E-mail: _____

REGISTRATION FEES:

	Early Bird Registration (Received by Jan. 30)	Standard Registration (Jan. 31 to Feb. 20)	Final Registration (After Feb. 20*)	
SOT Member	\$295	\$345	\$395	\$ _____
Non-Member**	\$590	\$640	\$690	\$ _____
SOT Retired Member	\$ 65	\$105	\$145	\$ _____
Postdoctoral SOT Member	\$ 80	\$120	\$160	\$ _____
Postdoctoral Non-Member**	\$160	\$200	\$240	\$ _____
Graduate Student Member	\$ 60	\$100	\$140	\$ _____
Graduate Student Non-Member**	\$120	\$160	\$200	\$ _____
Student Undergraduate	\$ 60	\$100	\$140	\$ _____
SOT Affiliate	\$ 0	\$ 0	\$ 0	\$ _____
Press	\$ 0	\$ 0	\$ 0	\$ _____
Guest (Non-Scientist)	\$ 70	\$ 85	\$100	\$ _____

Guest Name: _____

METHOD OF PAYMENT:

All registrations submitted by hard copy or fax will be processed on-line by SOT staff.

Check or Money Order # _____

Government Purchase Order # _____

(U.S. GOVERNMENT P.O. FORM MUST BE ATTACHED)

American Express Diner's Club Discover MasterCard Visa

Credit Card #: _____ Expiration Date: _____

Signature: _____ Cardholder's Printed Name: _____

Registration Fee(s) (from part 1) \$ _____
 Continuing Education Courses (from part 2) \$ _____
 Student Functions (from part 2) \$ _____
 Optional Abstract Material (from part 2) \$ _____
TOTAL DUE \$ _____

* After February 20, Final Registration rates apply. SOT will accept faxed Registration Forms until March 10. On-line registration will be open until March 19. On-Site Registration Forms will be available at the Annual Meeting Registration Desk.

** Special offer to non-member 2009 Annual Meeting attendees: submit a complete application for membership between January 15, 2009 and the May 1, 2009 deadline, and if accepted, SOT will waive your 2009 dues.

RETURN THIS TWO-PAGE FORM WITH PAYMENT TO:
 Society of Toxicology • P.O. Box 91895 • Washington, DC 20090-1895
 Faxed forms are accepted only if using a credit card. Fax form to: (703) 438-3113.
U.S. GOVERNMENT PURCHASE ORDERS MAY BE FAXED OR MAILED WITH THE REGISTRATION FORM.
 Express packages may be mailed to:
 SOT Headquarters Registration Dept., 1821 Michael Faraday Drive, Suite 300, Reston, VA 20190-5332
 Questions? Contact SOT • Tel: (703) 438-3115 • E-mail: sothq@toxicology.org

Join SOT

Be a member of the premier group that is creating a safer and healthier world by advancing the science of toxicology

As an SOT member you can ...

Stay connected at www.toxicology.org
Access member-restricted information
Use the on-line Member Directory

Receive Reduced Registration Costs
for SOT meetings

Receive SOT Publications
The Toxicologist (CD-Rom)
Toxicological Sciences
Communiqué
Others

Join one of 22 Specialty Sections

Choose a Special Interest Group

Participate in Your Regional SOT Chapter

Communicate the Importance of your Discipline

Utilize Career Resources

Register for Mentor Match

Nominate for Awards

Volunteer and Demonstrate Your Leadership Skills

Find Products and Services Easily at Tox Expo™

Membership Fees:

Full Membership_____	\$135
Associate Membership_____	\$135
Postdoctoral Membership_____	\$35
Student Membership_____	\$20
Retired Membership_____	\$0

Easy on-line membership application takes approximately 15 minutes to complete.

Special Offer to Non-Member SOT 2009 Annual Meeting Attendees:

- Apply for SOT membership between January 15, 2009, and the May 1, 2009, deadline, and if accepted, SOT will waive your 2009 dues.
- Applications must be complete and sponsor letters received by the May 1 deadline.

Membership

www.toxicology.org

For complete information about membership in the Society of Toxicology, visit the SOT Web site at www.toxicology.org and select Member Information.



March 15-19, 2009



Registration Form

48th SOT Annual Meeting

(Part 2 continued from page 99)

March 15–19, 2009

CONTINUING EDUCATION COURSES:

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

	Early Bird Registration (Received by Jan. 30)	Standard Registration (Jan. 31 to Feb. 20)	Final Registration (After Feb. 20)	# of Courses	
SOT Member/Corp Affiliate	\$150 each	\$175 each	\$200 each	x _____	\$ _____
Retired Member	\$110 each	\$135 each	\$160 each	x _____	\$ _____
Non-Member	\$300 each	\$325 each	\$350 each	x _____	\$ _____
Postdoctoral (SOT Member/Non-Member)	\$ 90 each	\$115 each	\$140 each	x _____	\$ _____
Graduate or Undergraduate Student (SOT Member/Non-Member)	\$ 45 each	\$ 70 each	\$ 95 each	x _____	\$ _____
Press	\$ 0 each	\$ 0 each	\$ 0 each	x _____	\$ _____

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

	Early Bird Registration (Received by Jan. 30)	Standard Registration (Jan. 31 to Feb. 20)	Final Registration (After Feb. 20)	
SOT Member/Corp Affiliate	\$ 55 each	\$ 80 each	\$105 each	\$ _____
Retired Member	\$ 55 each	\$ 80 each	\$105 each	\$ _____
Non-Member	\$ 75 each	\$100 each	\$125 each	\$ _____
Postdoctoral (SOT Member/Non-Member)	\$ 55 each	\$ 80 each	\$105 each	\$ _____
Graduate or Undergraduate Student (SOT Member/Non-Member)	\$ 25 each	\$ 50 each	\$ 75 each	\$ _____
Press	\$ 0 each	\$ 0 each	\$ 0 each	\$ _____

STUDENT AND POSTDOCTORAL FUNCTIONS:

- Yes, I am an undergraduate student and would like to attend the Sunday Undergraduate Education Program. *Limited seating.* \$ Complimentary
- Yes, I am a student or postdoc registrant and would like to attend the complimentary Student/Postdoctoral Reception. \$ Complimentary
- Yes, I am a student or postdoc registrant and would like to attend the *In Vitro* Lecture and Luncheon. (A \$5 deposit is required and will be exchanged for the ticket at the luncheon. *Limited seating.*) \$ _____
- Yes, I am a postdoc registrant and would like to attend the Postdoc Luncheon on Wednesday. \$ Complimentary

OPTIONAL ABSTRACT MATERIAL:

2009 registrants will receive the abstracts, *The Toxicologist* on CD-ROM, as part of the Annual Meeting registration fee. A printed version of *The Toxicologist* will be available for purchase at \$20 per copy (available while supplies last).

Yes, I want to purchase the printed version of *The Toxicologist*. \$20 each x _____ \$ _____

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

A. Type of Organization: 1. Academia 2. Government 3. Military 4. Private Industry 5. Other _____ B. Job Function: 6. Analytical 7. Financial/Purch. 8. Health and Safety 9. Computer/Statistics 10. Mgmt-Corporate 11. Mgmt-Facilities 12. Mgmt-Personnel 13. Marketing/Sales	14. Quality Assurance 15. Regulatory 16. R&D-Admin. 17. R&D-Operations 18. R&D-Technical 19. Teaching 20. Other _____ C. Field of Work: 21. Biotechnology 22. Carcinogenesis 23. Epidemiology 24. Immunotoxicology 25. Infusion Tox. 26. Inhalation Tox. 27. Genetic Tox.	28. Mechanisms 29. Metals 30. Molecular Biology 31. Mutagenicity 32. Neurotoxicology 33. Pathology 34. Pharmacokinetics 35. Pharmacology 36. Occup. Health 37. Risk Assessment 38. Repro. & Dev. Tox. 39. General Tox. 40. Other _____ D. Product Interest: 41. Publications 42. Contract Services:	a. Analytical b. Aquatic Tox. c. Clinical Tox. d. Computer e. <i>In Vitro</i> Tox. f. Pathology g. Preclinical Tox. h. Quality Assurance i. Wildlife Tox. 43. Supplies/Equipment a. Analytical b. Clinical Chem. c. Hardware d. Software e. <i>In Vitro</i> f. <i>In Vivo</i>	g. Lab Animal h. Neurotoxicology i. Pathology 44. Other _____ E. Purchasing Responsibilities: 45. a. I make purchasing decisions b. I influence purchasing decisions c. I do not participate in purchasing decisions
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SOT Annual Meeting registrants grant SOT permission to reproduce, copy, and publish photographs taken at the Annual Meeting unless written notification by the registrant, stating otherwise, is submitted to SOT Headquarters prior to the Annual Meeting or while registering on-site.

There will be no refunds for cancellations received at SOT Headquarters after February 20, 2009.

SOT will accept faxed Registration Forms until March 10. On-line registration will be open until March 19. On-Site Registration Forms will be available at the Annual Meeting Registration Desk. There will be no refunds for Final Registrations.



SOT Job Bank

THE ULTIMATE RECRUITMENT AND EMPLOYMENT RESOURCE

Job Seekers—Your Dream Job Awaits You in the SOT Job Bank!!!

Employers are Looking for Candidates through this Service and You Don't Want to be Left Out

- All SOT Members can utilize the SOT Job Bank as a job seeker **Free-of-Charge**.
- Register and enter your candidate profile; it only takes 15 minutes to complete.
- Post your resume.
- Review the positions posted by major corporations, academic institutions, government agencies, and private research organizations; positions range from junior to senior level.
- Find potential matches to your skills and training appropriate to the stage of your career.
- Apply for positions.
- Gain access to information that will help you plan your near-term and long-term goals and objectives.
- See which sectors are hiring.
- Stay abreast of new and emerging areas.

Employers—Recruit Highly Qualified Candidates through the SOT Job Bank!!!

The SOT Job Bank is the Ideal Place to Streamline Your Recruitment Process and Provides your Organization with a Valuable Tool

- Search from a pool of distinguished candidates.
- Join the many employers who rely on this cost effective and efficient database to assist with their employment needs.
- Find the right candidate from among scientist trained in toxicology and the biological sciences with the expertise and right work experience for your position.
- Schedule interviews at the SOT Annual Meeting at the on-site Job Bank Center.
- SOT Affiliate Members receive a reduced registration rate in appreciation for supporting the Society in achieving its objectives.

*The On-Line SOT Job Bank Is Available 24/7 Any Time, from Any Place
at www.toxicology.org.*

SOT

Society of
Toxicology





48th Annual Meeting and ToxExpo™

Career Resource and Development Services

Streamline Your Job Search: Use SOT Job Bank Services

Free Job Search for SOT Members!

The Society is committed to providing SOT members with a unique and effective way to locate a position that matches your skills and training. To help you reach this objective, the Society provides the SOT on-line Job Bank and on-site Job Bank Center. These services are offered free of charge to all SOT members.

The on-line Job Bank includes more than 100 positions available at corporations, academic institutions, government agencies, and private research organizations. Employers rely on this on-line service to provide them with a robust database of candidates available for career opportunities, ranging from junior to senior level positions. **SOT Affiliates use this system at a reduced rate in appreciation of their commitment to helping further the objectives of the Society.** Candidates and employers alike can access this year-round service any time, any place at www.toxicology.org.

The SOT on-line Job Bank allows you to:

- Register as a candidate or employer
- Post employment positions or resumes
- Search the Job Bank database
- Contact employers or candidates

Once registered, candidates may search the listing of available jobs and employers may browse candidate profiles. Communication with a desired employer or candidate can even be made *via* e-mail messages created within the system.

Annual Meeting On-Site Job Bank Center

Located in the Baltimore Convention Center, the on-site Job Bank Center provides all the benefits mentioned as well as assistance in facilitating interviews at the SOT Annual Meeting.

All candidates and positions must be sought on-line. Employers recognize and appreciate that the Annual Meeting on-site Job Bank Center provides a cost-effective and efficient way to interview a distinguished pool of candidates. Therefore, interview rooms are available on a first-come, first-served basis. As with the on-line Job Bank, SOT Members have free access to the Center. For your convenience, printers will be available for producing hard copies of candidate profiles and position descriptions.

All users with current registration at the time of the Annual Meeting will be permitted to use this service. Although you are encouraged to preregister before entering the Job Bank Center, you can register on-site in Room 347. Employers and Candidates may take advantage of the multiple spaces available in Room 348 to hold interviews.

The Center is available during the following hours of operation:

Sunday	10:00 AM–4:30 PM
Monday	9:00 AM–4:30 PM
Tuesday	8:30 AM–4:30 PM
Wednesday	8:30 AM–4:30 PM

Job Bank access will be available—as always—through your personal computer and at the Annual Meeting E-mail Center. Access to the on-line Job Bank in the Center is limited to short searches for updates or new information. For additional information, contact Kristy Rand at SOT Headquarters: (703) 438-3115 ext. 1429 or e-mail: kristy@toxicology.org.

Mentor Match

On-Line Mentoring Program—NEW!!!!

The Society of Toxicology recognizes the importance of mentoring in the scientific and professional development of its members. The objective of the new on-line mentoring program Mentor Match is to provide a service that matches mentees with potential mentors from the SOT membership to provide advice on career path selection, professional development, and life/work balance issues. SOT members are encouraged to share their professional knowledge and experience by serving as mentors for colleagues and for the next generation of toxicologists. The SOT Annual Meeting provides a great opportunity for the mentor and mentee to meet in person. We strongly encourage members of the Society to visit the Mentor Match site and register on-line as mentors or mentees. The Mentor Match program will develop as individuals register, allowing the quantity of profiles to increase to a robust combination of both mentors and mentees. The Mentor Match program is accessible to all active SOT members by visiting www.toxicology.org/ai/newcrad/mentor-match.asp.

toxexpo.com



SOT | Society of Toxicology



You probably know ToxExpo™ as the exhibition associated with the Society of Toxicology's Annual Meeting—it's that—but it's also a great deal more. ToxExpo.com is:

- A unique environment to research products and services of exhibiting companies and keep you informed of new cutting-edge science and technology.
- A comprehensive approach to organizing the wealth of ideas and insights in cross-disciplinary areas of toxicology.
- The toxicology market place—your source for product information and resources to keep your lab competitive.
- The place where professionals will learn how to explore a rapidly changing science.
- A chance to think outside the box—find out how your work relates to research in other disciplines.
- Up-to-date information on state-of-the-art research equipment, technology, and the latest publications.
- A 24/7 comprehensive on-line resource, searchable by company name or by product or service. Available at www.toxexpo.com

Looking for a particular product or service? Check the category listing on www.toxexpo.com to see which companies offer the best product or service for your needs.

Exhibit Hours:

Monday, March 16, 9:00 AM–4:30 PM

Tuesday, March 17, 8:30 AM–4:30 PM

Wednesday, March 18, 8:30 AM–4:30 PM

Photography Policy and Protocols for Attendees

Out of courtesy for the scientific presenters, we appreciate your compliance with the following policies:

- Cell phones and other electronic devices should be set on mute.
- Electronic capture of scientific sessions by any method is prohibited.
- Children under the age of 15 are not allowed in scientific sessions unless consent is given by the session chair.

Session chairs are asked to strictly enforce these policies and individuals who do not comply will be asked to leave the session.

- Photography of poster presentations is prohibited without the specific consent of the presenter(s)/author(s).
- Children under the age of 15 are prohibited from accessing the Exhibit Hall at any time.

If you have any questions regarding these policies, please contact the SOT Headquarter staff at the Registration Desk.

Current 2009 ToxExpo™ Exhibitors

(as of 12/02/08):

2009 Annual Meeting sponsors are in orange

See complete listing of sponsors on page 120 and Inside Back Cover.

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2009 Exhibitor Listing

It all adds up to an uncommonly rich resource for the scientist, the toxicologist, the policy maker, the educator, the student—anyone looking for the best products and services that toxicology has to offer!

- Cellumen Inc.
CellzDirect
Celprogen Inc.
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Cerep
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CorDynamics
Cosmetic Ingredient Review (CIR)
Covance Inc.
Covance Research Products, Inc.
Critical Path Services
CXR Biosciences Limited
Data Integrated Scientific Systems (D.I.S.S.)
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Detroit R&D, Inc.
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Frontier BioSciences, Inc.
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HemoGenix Inc.
HistoTox Labs, Inc.
HSRL (Histo-Scientific Research Laboratories)
Huntingdon Life Sciences
IDEXX Preclinical Research Services
IIT Research Institute (IITRI)
Ina Research, Inc.
Informa Healthcare
Ingenuity Systems
Instech Solomon
Instem Life Science Systems
Institute for *In Vitro* Sciences, Inc. (IIVS)
IntelliCyt Corporation
In-Tox Products
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Midwest Research Institute (MRI)
Millbrook Breeding Labs
Millipore Corporation
MitoSciences Inc.
Molecular Toxicology, Inc (MOLTOX INC.)
MPI Research
MultiCASE, Inc.
National Biosafety & Biocontainment Training Program
National Library of Medicine—ORAU/ORISE
National Research Center for New Drug Safety Evaluation (Shenyang)
National Shanghai Center for New Drug Safety Evaluation & Research
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Research Diets, Inc.
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RTI International
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SkinEthic Laboratories
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Xybon Medical Systems
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Exhibitor Hosted Sessions

Monday

CANTEST Ltd.: Canada's Leading Analytical Laboratory, Providing Environmental, Nutraceutical, and Pharmaceutical Testing Services

Monday, March 16, 9:45 AM–10:45 AM

Presented by: CANTEST Ltd.

CANTEST provides GLP bioanalytical, Physical/Chemical, Environmental Fate and Ecotoxicology support to pharmaceutical and agro-chemical companies and government agencies worldwide. Its pharmaceutical laboratories are GMP and GLP compliant and have been inspected by the FDA. In this session, new techniques and instrumentation used in analytical labs, new regulations related to method development/R&D applications, and information about how industry can outsource and handle studies in CRO will be discussed.

Leveraging Bioanalysis to Compress Timelines in Regulatory Toxicology Studies

Monday, March 16, 9:45 AM–10:45 AM

Presented by: MDS Pharma Services

MDS Pharma Services will show you how to take a GLP approach to validated bioanalytical methods at the preclinical stage. Bioanalysis is now globally accepted by the pharmaceutical industry as a critical component in the journey of an NCE from the early discovery stage to the NDA filing.

Sysmex XT-V Hematology Workshop

Monday, March 16, 9:45 AM–10:45 AM

Presented by: Sysmex America, Inc.

This workshop provides an overview of the fluorescent flow cytometry technology and multi-species profile creation capability of the XT-V Hematology analyzer from Sysmex America. Applications specific to the toxicology market are highlighted *via* case examples of various animal species for whole blood, bone marrow and BALF specimens.

Cell-Based Assays for Predictive Toxicity

Monday, March 16, 11:00 AM–12:00 NOON

Presented by: Thermo Fisher Scientific

Panels of cell-based assays, measured using a quantitative imaging approach have been shown to be predictive of toxicity in humans. In this session we will review the cellular targets of toxicity, demonstrate the multi-parameter imaging approach and show cross-validation data with existing biochemical assays. The benefits of this approach for reducing potential toxicity risks in drug development will be outlined.

The Cardiovascular System and Drug Development

Monday, March 16, 11:00 AM–12:00 NOON

Presented by: Charles River

The cardiovascular system is an important therapeutic target for novel drug discovery and development. Development and utilization of appropriate models are essential to demonstrate the efficacy and safety of these drugs. Additionally, non-cardiac drugs can result in cardiovascular abnormalities which require further study and/or additional monitoring in clinical trials. Experiences from developing cardiac drugs and non-cardiac drugs with cardiac liabilities will be presented.



SOT Resource Pavilion

How can you advance the science of toxicology?

Stop by the SOT Resource Pavilion in the Charles Street Lobby of the Baltimore Convention Center to:

- **Access Information About SOT Membership**
- **Support the SOT Endowment**
- **Connect with SOT Volunteers**
- **Swap Communication Tips and Material for Topics Important to Toxicologists**

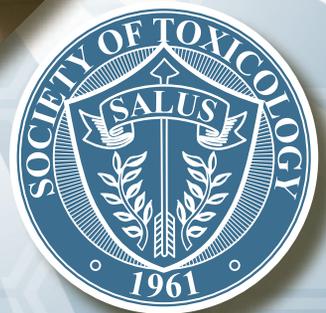
Animals in Research

K–12 Education

Public Outreach

Regulatory and Legislative Affairs

The Resource Pavilion is your connection to key resources and people in toxicology.





Exhibitor Hosted Sessions

Why You Should Conduct Your Next Preclinical Study in China

Monday, March 16, 11:00 AM–12:00 NOON

Presented by: Bridge Laboratories

Bridge Laboratories will share insights into the current status and trends of the China preclinical safety sector and how companies can leverage conducting work in Asia. Bridge is a preclinical CRO that provides US-level regulatory compliant drug development services globally and is among the leading and most established “western standard” CROs in China. The presentation will be based on an evaluation of preclinical CROs in China and Bridge’s experience in providing GLP toxicology services through their Beijing lab.

A Systems Toxicology Approach for Drug Discovery and Development

Monday, March 16, 12:15 PM–1:15 PM

Presented by: Ingenuity Systems

Within this session an overview of Ingenuity’s pathway and networks analysis software (IPA) will be presented with its specific molecular toxicity components specifically developed to understand drug toxicity and action. Following this overview, an industry relevant case study will demonstrate the functionality and richness of the toxicity module.

Cultures of Primary Hepatocytes As Predictive Models of the Liver

Monday, March 16, 12:15 PM–1:15 PM

Presented by: CellzDirect, Invitrogen

Liver function can be modeled *in vitro* using cultures of primary hepatocytes (high-throughput) monitoring metabolism, induction/cell-signaling, transport, and cytotoxicity endpoints. Correlation of gene expression data, metabolic activity, and cytotoxicity endpoints over concentration and time can provide an effective approach to explore mode of action pathways. We will discuss our research using these tools including the EPA’s ToxCast 320 chemical library (320 chemicals, ~350,000 data points).

Zebrafish: A Predictive Model for Assessing Safety and Toxicity

Monday, March 16, 12:15 PM–1:15 PM

Presented by: Phylonix

Zebrafish are increasingly used as an alternative model for assessing compound safety and toxicity. Numerous studies show >70% correlation with results in mammals. In this workshop, we will describe methods for assessing drug effects on major organs as well as several disease models for high throughput screening.

Embryology of Nonhuman Primates: Principles for Understanding Developmental Toxicology Study Designs Supporting Regulatory Submissions

Monday, March 16, 1:30 PM–2:30 PM

Presented by: SNBL USA

Preclinical toxicology professionals often oversee programs requiring reproductive toxicology assessments. Currently, many regulatory-mandated teratology studies are conducted using the nonhuman primate (NHP) model. Embryofetal developmental milestones dictate the types of parameters to monitor: mid-first trimester is the period of organogenesis; 2nd trimester involves organ/body remodeling; and 3rd trimester is the period of accelerated growth. Understanding classical NHP embryology will help professionals appreciate overall NHP reproductive biology and the precautions necessary to institute during study design and conduct.

Resourceful Direction in Drug Development

Partner with MPI Research in moving your
drug development projects forward.

We look forward to greeting you at SOT in **booth 2201**.

Ways to maximize clinical therapeutic investment will be addressed during our educational session on **Immunologic Considerations for the Support of Biologic Therapeutics and Other Innovative Immunomodulators**. Do not miss this informative session being held Monday, March 16, 2009, 1:30-2:30 pm, in room 337 of the Baltimore Convention Center.



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Exhibitor Hosted Sessions

Immunologic Considerations for the Support of Biologic Therapeutics and Other Innovative Immunomodulators—Preclinical and Development Commitments

Monday, March 16, 1:30 PM–2:30 PM

Presented by: MPI Research

This presentation will highlight immunologic characterizations required to enable successful IND registry of biologics including ligand binding assays for immunogenicity, PK/TK and other safety considerations to maximize clinical therapeutic investments.

Practical Approaches to Dosing Route Challenges in Non-Clinical Research

Monday, March 16, 1:30 PM–2:30 PM

Presented by: LAB Research Inc.

There are many biological molecules that are unsuitable for oral administration, and with the development of drugs that are targeted for delivery to specific sites in humans, there is an increasing need to develop animal models to facilitate pharmacological and non-clinical toxicological research. We present a selection of such models.

Characterizing On-Target and Potential Side Effects from Drug Targets Derived from Known Pathway and/or Protein Networks Using an Integrative Knowledge-Rich Approach

Monday, March 16, 2:45 PM–3:45 PM

Presented by: Ariadne

Find out how an integrative framework for organizing, analyzing and visualizing external and internal published findings can support research critical decision making and experimental designs throughout the drug development pipeline. The session will highlight how knowledge extracted from literature resources can be used to further elucidate knowledge on existing drugs/drug candidates and to find potentially novel biological relationships including potential side effects.

Dynamic Real-Time, Label-Free Cellular Analysis

Monday, March 16, 2:45 PM–3:45 PM

Presented by: Roche Applied Science

Join us to learn about a revolutionary impedance-based technology which enables dynamic real-time, label-free cell-based analysis. The presentation will show how dynamic real-time data facilitates discovery not possible with end-point analysis, focuses assay development, and can improve compound attrition rates.

HepaRG®: A Human Hepatic Cell Line with Unique Features

Monday, March 16, 2:45 PM–3:45 PM

Presented by: Biopredic International

HepaRG® is a bipotent cell line that gives rise simultaneously to hepatocytes and cholangiocytes. The hepatocytes are equipped with CYPs 1A, 2B, 2C, 2E, 3A, with drug transporters and with PXR and CAR in the same range of levels found in normal cultured hepatocytes. This cell line is now popular for CYP inductions studies, and begins to show its usefulness in the Comet and micronucleus assays, detection of reactive metabolites, cholestasis studies, and hepatotoxicity prediction.

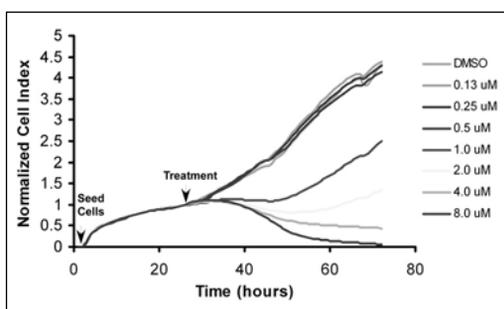


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Generate dynamic real-time data that:

- Enables discovery not possible with end-point analysis
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For more information and references please visit www.xcelligence.roche.com or call 800 262 4911.



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Exhibits



Exhibitor Hosted Sessions

Tuesday

Ion Channel Panels in Safety Assessment

Tuesday, March 17, 8:30 AM–9:30 AM

Presented by: ChanTest Corp.

Drug-induced ion channel dysfunction may result in diverse adverse reactions. ChanTest provides toxicity screening, secondary confirmatory screening, and selectivity profiling using Human Ion Channel Panels™ and automated patch clamp methods. ChanTest channel panels in combination with conventional methods facilitate decision-making in drug development.

Making Sense Out of Multiple Safety Attributes in Multiple Data Formats

Tuesday, March 17, 8:30 AM–9:30 AM

Presented by: Rosetta Biosoftware

As the ability to measure multiple safety attributes from preclinical, metabolomics, genetics, and transcriptomics data improves, the work to assimilate and interpret these data increases. This workshop describes how to use Rosetta Biosoftware technology in collaboration with the Predictive Safety Testing Consortium (PSTC) led by C-PATH to address these challenges.

Systems Toxicology Data Analysis Solutions from GeneGo

Tuesday, March 17, 8:30 AM–9:30 AM

Presented by: GeneGo Inc.

GeneGo's MetaDiscovery platform is a powerful suite of tools and molecular databases for the analysis of high content systems biology data. This session will demonstrate the power of the approach in predictive and mechanistic toxicology. Current capabilities of the system and upcoming enhancements for safety assessment will be presented.

All You Ever Wanted to Know About an IND—But Were Afraid to Ask

Tuesday, March 17, 9:45 AM–10:45 AM

Presented by: Ricerca Biosciences, LLC

Ricerca focuses on the integration of the IP to IND pathway by managing both chemistry and toxicology simultaneously. Some case studies will be presented to provide early-stage biotech with a high level overview of the challenges they can expect to meet as they progress their development.

Global Management of Rodent Colony Genetics

Tuesday, March 17, 9:45 AM–10:45 AM

Presented by: Charles River

Purposeful global management of rodent animal colonies is critical to minimize the effect of genetic variation on research results. Processes employed differ based on colony objectives, species/stock/strain characteristics and desired outcomes. As scientific discovery accelerates, effective management of these key research colonies takes on increased importance.

The Use of Metabolomics Data in Toxicology

Tuesday, March 17, 9:45 AM–10:45 AM

Presented by: BASF SE

BASF has developed a large metabolomics database (MetaMap™Tox) using data rich agro chemicals and drugs. Metabolite patterns established are indicative of different toxicological modes of action and can be used for early recognition of toxicity for new chemicals. Using blood samples, the information can be obtained from routine studies.

Elite NEN GMP-compliant Radiolabeling Services Position Compounds for ADME Success



PerkinElmer offers “elite” specialized expertise in NEN® GMP*-compliant radiosynthesis and radiolabeling of compounds for ADME research. With over five decades of experience, top-flight facilities and technology for performing radiolabeling, PerkinElmer provides unique, advanced services for meeting your testing and regulatory needs.

Improving the Odds of Screening with Radiolabeling

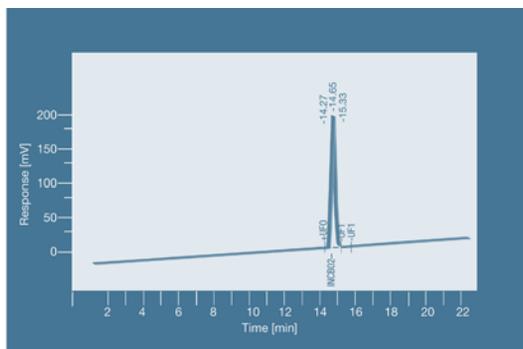
PerkinElmer provides extensive services to manufacture compounds tagged with radionuclides in order to help pharmaceutical companies and CROs accelerate drug development outcomes by discovering precisely what happens to a compound in the human body – studying its absorption, distribution, metabolism and excretion (ADME) activity.

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PerkinElmer offers clients an unparalleled combination of GMP facilities and services, radioactive manufacturing expertise and its vast product catalog of compounds for radioactive experimentation.

Purity of Compounds

All radiolabeled compounds are routinely 98%-plus pure – radiochemically and chemically.



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*Consistent with ICH Q7A, Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients, August 2001, Section 19, APIs for Use in Clinical Trials. PerkinElmer Life and Analytical Sciences has established a custom radiosynthesis process which provides acceptable GMP compliance and the assurance of quality for early drug studies.

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Exhibits



Exhibitor Hosted Sessions

Metabolomics: A Novel Tool for Understanding the Early-Stage Mechanistic Underpinnings of Drug Action and Safety

Tuesday, March 17, 11:00 AM–12:00 NOON

Presented by: Metabolon, Inc.

With increased regulatory scrutiny, understanding the mechanistic underpinnings of drug action and safety has become paramount. Earlier information on potential drug safety issues is required before deciding which compounds to take into the clinic. Global biochemical profiling provides unparalleled insight into the mechanistic action of drugs. The simultaneous analysis of hundreds of biochemicals enables the identification of both on-target and off-target effects. Many changes are seen within hours of dosing, providing early-stage indication of safety issues.

Neural, Mesenchymal, and Hematopoietic Toxicity Testing Using *In Vitro* Stem Cell Assays

Tuesday, March 17, 11:00 AM–12:00 NOON

Presented by: Stemcell Technologies Inc.

This session will highlight *in vitro* assay systems designed to quantify and assess neural, mesenchymal, and hematopoietic stem and progenitor cell populations from primary cell sources. The presentation will elaborate on how these assay systems can be used to evaluate compound toxicity.

Proposed Cardiac Safety Assessment: Overall Strategy from Non-Clinical to Clinical Phases

Tuesday, March 17, 11:00 AM–12:00 NOON

Presented by: Ina Research Inc.

INA will present its latest data from non-clinical (proarrhythmia model, atrioventricular block monkey) and clinical studies (thorough QT studies assessing ethnic and gender differences) in compliance with ICH-S7B/E14 guidelines for evaluating QT prolongation and TdP. An overall strategy for cardiac safety assessment from non-clinical to clinical will also be presented.

Non-Invasive Blood Pressure Measurements on Large Animals

Tuesday, March 17, 12:15 PM–1:15 PM

Presented by: emka TECHNOLOGIES

emka TECHNOLOGIES will present its recent developments in non-invasive blood pressure measurements on large animals.

Profiling Environmental Chemicals in the Cellular Stress Pathway Using Quantitative High-Throughput Screening

Tuesday, March 17, 12:15 PM–1:15 PM

Presented by: Promega Corporation

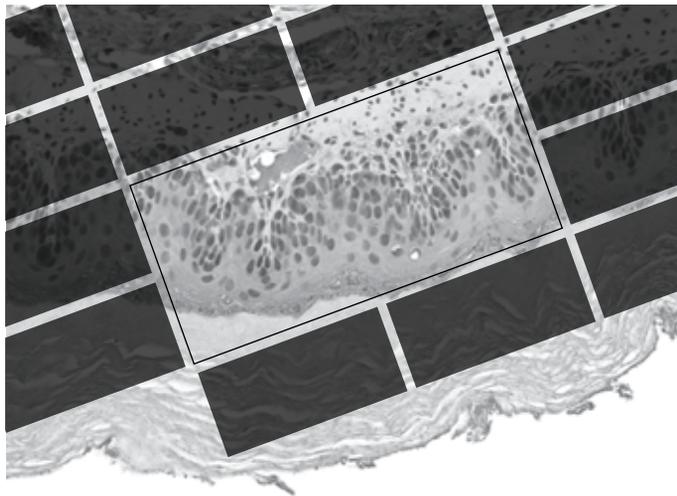
The NIH Chemical Genomics Center (NCGC) has developed *in vitro* assays utilizing quantitative high-throughput screening (qHTS), where concentration response curves for several thousand compounds are quickly and efficiently produced in cell-based 384- and 1536-well format. These assays identified compound-induced stimulation of the antioxidant response element (ArE) cellular stress pathways, glutathione levels, and cytotoxicity.

Using Genomic Approaches to Accelerating Toxicology Decisions

Tuesday, March 17, 12:15 PM–1:15 PM

Presented by: Affymetrix

Discover biomarkers, understand mechanisms of toxicity, and identify relationship between patient genetic diversity and response to treatment. Comprehensive pre-clinical portfolio spans rodents, canine, monkey, and human arrays. Complete solutions include ToxFX™ Analysis Suite, enabling you to rapidly understand compound safety through matching the toxicity of your compound against Iconix Toxicogenomics database.



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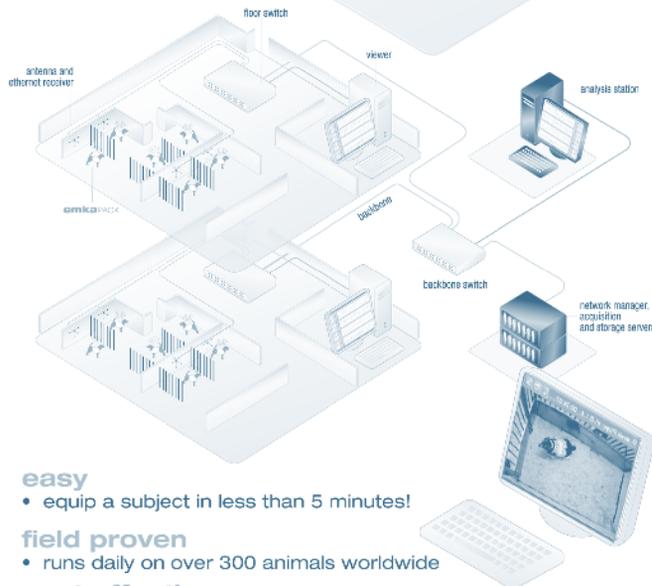
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Exhibits



Exhibitor Hosted Sessions

Environmental Health and Toxicology Program Resources

Tuesday, March 17, 1:30 PM–2:30 PM

Presented by: National Library of Medicine

The National Library of Medicine will present an overview of the Environmental Health and Toxicology Program resources. Resources include TOXNET, databases on toxicology, hazardous chemicals, environmental health, and toxic releases. Search techniques will be demonstrated highlighting the Dietary Supplements Labels Database and the Drug Information Portal.

NTP Criteria for Hazard Identification on Non-Cancer Studies

Tuesday, March 17, 1:30 PM–2:30 PM

Presented by: National Toxicology Program (NTP)

The National Toxicology Program (NTP) uses specific criteria to describe the strength of the evidence for conclusions for substances tested in its cancer bioassay. The program has now developed similar criteria for reaching conclusions from NTP immunotoxicology, reproductive toxicology, and developmental toxicology studies that will be presented at this session.

Regulatory and Scientific Issues that Impact the Development of Biotherapeutics

Tuesday, March 17, 1:30 PM–2:30 PM

Presented by: Covance

The preclinical development of a biotherapeutic requires the consideration of many factors that relate to the scientific and regulatory challenges faced. Of critical importance are the areas of manufacturing, characterization and purification, preclinical study design and selection of the relevant toxicology species, assay development and immunogenicity testing. Learn more about the critical considerations that will contribute to the success of your biotherapeutic development program.

A Novel *In Vitro* Method to Assess Skin Sensitization

Tuesday, March 17, 2:45 PM–3:45 PM

Presented by: CeeTox, Inc.

The session will describe a novel *in vitro* method that identifies test articles as skin sensitizers and predicts LLNA EC3 values as sensitizer classes. Details of the models and preliminary data sets will be presented. The alternative method may reduce animal testing and can support REACH and EU Amendment 7.

Integration of a Small Molecule R&D and Manufacturing Organization with Toxicology

Tuesday, March 17, 2:45 PM–3:45 PM

Presented by: WuXi AppTec

Integration of two separate organizations always presents challenges. Combining the assets of a Chinese based small molecule R&D and manufacturing company and a U.S. based medical device testing and biological manufacturing company has been not only a learning experience but has resulted in an organization with unmatched resources and potential.

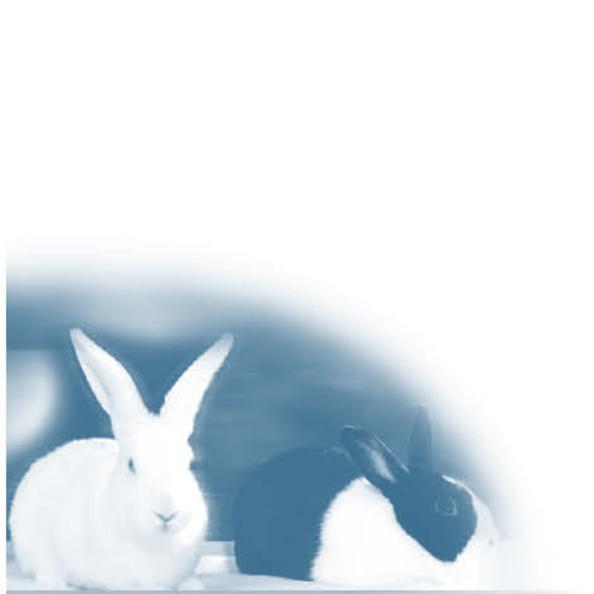
Software-As-a-Service in Preclinical: Remote Hosting of Data Systems—Are Laboratories Ready for This?

Tuesday, March 17, 2:45 PM–3:45 PM

Presented by: Instem

This presentation will explore issues around the growing demand for affordable alternatives to traditional on-site data collection and analysis software in preclinical laboratories. As appetites for Web-based systems increase, do vendors and laboratories really understand issues related to regulatory guideline impact, data security and access requirements, qualification and validation, and requirements for peak performance?

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Exhibitor Hosted Sessions

Wednesday

Cellular Systems Biology (CSB™) for Discovery Toxicology

Wednesday, March 18, 9:45 AM–10:45 AM

Presented by: Cellumen, Inc.

Cellular Systems Biology (CSB™) is a powerful new paradigm for both Discovery Toxicology and Predictive Toxicology. CSB Toxicity Profiling enables the simultaneous determination of dose-response relationships for multiple mechanisms of toxicity over several exposure times and produces a classifier with high precision (96.6%) for predicting the safety risk of unknown compounds.

Preclinical Studies in China: From Animal Supply to Regulatory Submission

Wednesday, March 18, 9:45 AM–10:45 AM

Presented by: Charles River

Pharmaceutical companies and CROs continue to make solid progress in their Asian R&D operations and relationships. Charles River will present its experience in the operation and regulation of its preclinical facility in Shanghai, together with the ongoing development of its Research Models and Services group in this region. In addition, the experience of two multinational pharmaceutical companies that are performing and managing R&D activities in China will be presented.

Strategic Study Design—Biopharmaceuticals and Beyond

Wednesday, March 18, 9:45 AM–10:45 AM

Presented by: Huntingdon Life Sciences

Safety assessment in clinical and preclinical studies is evolving in part due to the increased understanding of mechanism of action as seen with biopharmaceuticals. Evaluation of drug action (pharmacodynamics) is paramount for selection of an appropriate species and design of nonclinical studies. In addition to the traditional approach (i.e., pathology and clinical pathology) evaluation should include product-specific markers of activity and safety and be replicated throughout the entire drug development process so that Chemistry, Manufacturing, and Control (CMC), nonclinical and clinical, do not exist in isolation.

Drug Discovery: The Interface of Safety and Efficacy Evaluations in Lead Optimization

Wednesday, March 18, 12:15 PM–1:15 PM

Presented by: Covance

Lead optimization identifies lead candidates for further development. The challenges involve coordinating disciplines, such as receptor occupancy; imaging technology *in vivo* pharmacology models; and early evaluations of safety in toxicology studies. Applying this approach across all therapeutic areas of interest allows for the optimization of candidate molecules for safety and efficacy. The effective use of currently available tools should increase the probability of technical success and ultimately decrease the cost of drug development.



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The SOT Annual Meeting provides the most comprehensive coverage of toxicology. The scheduled scientific sessions and poster and platform presentations will present the latest “cutting-edge” research.

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Six scientific themes will allow attendees to gain depth of analysis on Cell Signaling, Gene-Environment Interactions, Metabolic Disease, Mitochondrial Basis of Disease, Toxicity Testing in the 21st Century, and Translational Toxicology.

Networking

The SOT Annual Meeting, toxicology’s largest meeting, allows you to network with colleagues and other leading scientists from around the world.

Value

The SOT Annual Meeting is cost-effective, with low registration fees, inexpensive high-quality continuing education courses, and exposure to the very latest advances in science. International attendees benefit from the good exchange rate.

ToxExpo™

The SOT Exhibition, ToxExpo™, is the profession’s largest tradeshow and a one-of-a kind event where attendees from around the globe gather to exchange ideas and debut cutting-edge research and technology in the field of toxicology. Attendees have the opportunity to gain first-hand knowledge about the latest products and services offered by more than 350 exhibitors. Visit www.ToxExpo.com for toxicology-related products and services.

DEADLINES

April 30, 2009

Session Proposals

October 3, 2009

Abstract Submissions

October 9, 2009

Award Nominations

January 22, 2010

Early Bird Registration

February 11, 2010

Housing Reservation

February 12, 2010

Standard Registration

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(as of December 10, 2008)

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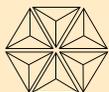
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