Mixtures Specialty Section Newsletter

Volume 3, Issue 1 August 2012

President's Message

Ken Wallace, PhD
MixSS President
University of Minnesota

Dear Colleagues,

How exciting it is to be a part of such a dynamic and rapidly growing SOT Specialty Section! The past two years have been filled with increasing numbers of scientific workshops and symposia offered throughout the US and Europe. Scientists from academia, industry and assorted regulatory agencies, many of whom are members of our own Specialty Section, have taken the lead in playing prominent roles in advancing the development of best practices for investigating and describing interactions amongst various and multiple stressors and how these can be translated for regulatory purposes. The increasing attendance at these meetings and growing membership of the Mixtures Specialty Section reflect the rapidly emerging importance of this field, making it an exciting time to be actively involved with this community of scientists.

The Specialty Section continues to be a catalyst for advancing mixture-related research and has provided numerous workshops, symposia and continuing education courses over the years at the Annual Meeting of SOT – this year is no different. The Specialty Section will be proudly sponsoring a workshop on cumulative risk in San Antonio. In addition, we have endorsed a second workshop on fine particle inhalation and cardiovascular disease. Besides these workshops, the Mixtures Specialty Section has endorsed symposia and roundtable discussions on an array of topics including tobacco regulation, air pollution, the complexities of dietary natural products and supplement toxicities, and a framework for air pollution criteria for inhaled mixtures. This year's scientific program offers a rich and diverse menu that should satisfy the most discriminating palate.

Because of the generosity of our members and select sponsors, the Mixtures Specialty Section offers an array of awards recognizing some of the best and most promising science presented at the Annual Meeting. This includes awards to recognize graduate student and postdoctoral trainees and for the most meritorious presentation across the entire scientific program. I encourage members to refer to the Awards Section

SOT 2012 Rewind San Francisco

Cynthia Rider, PhD
MixSS Secretary/Treasurer
NIEHS/DNTP

MixSS Officers

The 51st Annual Meeting (March 11-15, 2012 in San Francisco, CA) had many mixtures-related events and opportunities to interact with the mixtures research community.

The Advanced Continuing Education Course **"Specialized Techniques for Dose-Response Assessment and Risk Assessment of Chemical Mixtures (PM12)"** chaired by Jane Ellen Simmons (MixSS Past President; EPA/NHEERL) and Mike DeVito (NIEHS/DNTP) was well-attended and informative. *Let us know what you would like to see in future CE course offerings from the MixSS!*

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under Members/Scientists: SOT Services on the toxicology.org website.

We're all looking forward to another scientifically inspiring and socially enriching SOT Annual Meeting. I hope to see you all in San Antonio.

Ken Wallace

The **MixSS Officers** met on Monday morning to discuss business including: the current budget, the Newsletter, the website, membership, and awards. *Serving as a MixSS Officer is a great way to get involved. Contact past-president Michael Dourson (mdourson@tera.org) if you have an interest in running for office.*

The two MixSS-sponsored programs included:

The Workshop Session entitled **"Sufficient Similarity of Whole Representative Mixtures or a Relative Potency Factor Approach: Polycyclic Aromatic Hydrocarbons as a Case Study"** discussed the advantages and disadvantages of component-based and whole mixture risk assessment approaches as related to polycyclic aromatic hydrocarbons (PAHs). Speakers included: Julia Gohlke (University of Alabama at Birmingham), Glenn Rice (US EPA), John Incardona (NOAA), Erica Bruce (Baylor University), and Russell White (American Petroleum Institute).

And the Informational Session entitled **"Evolution and Implementation of Combined Chemical Exposure Methods: International Perspectives"**, which tapped leading international experts in cumulative risk for a discussion of the past and future of cumulative risk. Speakers included: Moiz Mumtaz (CDC/ATSDR), Bette Meek (University of Ottawa), Michael Faust (Faust & Backhaus Environmental Consulting GbR), and Alan Boobis (Imperial College)

Program sessions endorsed by MixSS included:

A Workshop Session entitled **"Novel Topics in Environmental Polycyclic Aromatic Hydrocarbon Metabolism Leading to Carcinogenesis"** with speakers: Frederick P. Guengerich (Vanderbilt University), Stephen Nesnow (US EPA), David E. Williams (Oregon State University), Lynn Flowers (US EPA), and Ruth A. Roberts (Astra Zenica)

A Symposium Session entitled **"The Toxicological Impact of Metals, Crude Oil and Chemical Dispersants from the Gulf of Mexico Oil Crisis on Human and Wildlife Health"** with speakers: Iain Kerr (University of Southern Maine), Samantha Joye (University of Georgia), Carys Mitchelmore (University of Maryland), Joe Griffitt (University of Southern Mississippi), Greg Mayer (Texas Tech University), and John P. Wise (University of Southern Maine)

The Workshop entitled: **"Advancing Food Safety in a Global Marketplace"** with speakers: Angelika Tritscher (WHO), Daniel Wilson (Dow Chemical Company), Alan Boobis (Imperial College, London), Bruce Chassy, (University of Illinois at Urbana-Champaign), and Clark Carrington (FDA)

Finally, the Workshop entitled **"Chemical Standardization of Botanical Medicines for Safe and Effective Use as Therapeutic Agents"** with speakers including: Cynthia Smith (NIEHS/NTP), Nandakumara Sarma (US Pharmacopeia), Ikhlas Khan (University of Mississippi School of Pharmacy), Craig Hopp (NIH/NCCAM), and Bala Manyam (Penn State University)

The **MixSS Reception** on Monday night provided a great opportunity to mingle with fellow members, congratulate awardees (see complete list on pages 3-4), and find out the latest about mixtures efforts around the world. In the scientific program, international mixtures experts provided their perspectives on current mixture-related activities.

Dave Mattie presents the Best Student Award to Paul Eden (University of Mississippi)

Ken Wallace congratulates outgoing MixSS President Michael Dourson on his outstanding leadership

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Mixtures in Pictures

Nigel Walker and Ken Wallace

Gian Paolo Rossini and Jane Ellen Simmons

Bette Meek and Sami Haddad

Julia Rager and Ken Sexton

And the Award Goes to...

Graduate Student Award

Paul R. Eden (Mississippi State University)
Association of Organochlorine Compound Body Burden and Adipokines with Prevalence of Type 2 Diabetes Mellitus

Post doctoral Award

Michelle C. DeSimone (North Carolina State University)
A Systems Approach to Investigating Cancer Susceptibility Due to Low Dose Co-Exposure to Environmental Carcinogens

Best Mixtures Abstract

(selected from the top 10 abstract pool)
Carl J. Johnston (University of Rochester)
Early Life Inhalation of Ambient Particles and Ozone Mixtures Sensitizes the Lung to Later Life Challenges

Top 10 abstracts (alphabetical order of first author):

Evaluation of Steroidogenic Pathway Disruption and Adrenal Steroid Hormone Secretion in the Human Adrenocortical H295R Cells by Lower Chlorinated PCBs, Their Metabolites and Commercial Mixtures S. Flor and G. Ludewig
OEH, University of Iowa, Iowa City, IA

Testing for Sufficient Similarity in Environmental Mixtures Using Exposure Data and Mixture Toxicology Data
C. Gennings[1] and L.G. Stork[2]
[1]Virginia Commonwealth University, Richmond, VA;
[2]The Monsanto Company, St. Louis, MO

Are *In Vitro* Effects of Metal Mixtures Predictable from the Responses to the Single Components?
F. Glahn[1], Q. D. Nguyen[2], J. Wiese[1], J. G. Hengstler[3], I. Grosse[2], and H. W. Foth[1]
[1]Institute of Environmental Toxicology, Martin Luther University, Halle/Saale, Saxony-Anhalt, Germany;
[2]Institute of Computer Science, Martin Luther University, Halle/Saale, Saxony-Anhalt, Germany;
[3]IfADo, Leibniz Research Centre for Working

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Environment and Human Factors, Technical University, Dortmund, North Rhine-Westphalia, Germany

Early Life Inhalation of Ambient Particles and Ozone Mixtures Sensitizes the Lung to Later Life Challenges
C. J. Johnston[1,2], R. Gelein[2], D. A. Cory-Slechta[2], J. N. Finkelstein[1,2], G. Oberdorster[2]
[1]Pediatrics, University of Rochester, Rochester, NY; [2]Environmental Medicine, University of Rochester, Rochester, NY

Developing a Fuzzy Neural Network Model for Predicting the Interactive Effects of Complex PAH Mixtures on the CYP1B1 Transcriptional Regulatory Network
A.J. Larkin[1,2,4], L. K. Siddens[1,4], S. K. Krueger[1,4], S. C. Tilton[3,4], K. M. Waters[3,4], W. M. Baird[1,4], D. E. Williams[1,4]
[1]Environmental and Molecular Toxicology, Oregon State University, Corvalis, OR; [2]Statistics, Oregon State University, Corvalis, OR; [3]Computational Biology and Bioinformatics, Pacific Northwest National Laboratory, Richmond, WA; [4]Superfund Research Center, Oregon State University, Corvalis, OR

Implementation of the Hazard Index Approach in Field Assessment of Chemical Mixtures
M. Mumtaz[1], P. Bourdillon[1], P. Ruiz[1], D. Mellard[2]
[1]Division of Toxicology and Environmental Medicine, CDC, ATSDR, Atlanta, GA; [2]Division of Health Assessment and Consultation, CDC, ATSDR, Atlanta, GA

Application of a Decision Tree Tool to the Evaluation of Cumulative Risks from Mixtures of Polar Compounds Measured in European Surface Waters
P. S. Price and X. Han
Toxicology & Environmental Research & Consulting, The Dow Chemical Company, Midland, MI

A Transcriptomics Approach Using HBCB to Prioritize Chemicals and Mixtures for Developmental Neurotoxicity Risk Assessment
D. T. Szabo[1], R. R. Shah[2], L. S. Birnbaum[3]
[1]US EPA/ORISE, Washington, D.C.; [2]SRA, Research Triangle Park, NC; [3]NIEHS, Research Triangle Park, NC

Distinct Cytochrome P450 Regulation by PAH Mixtures in Mouse Skin: Insights on Carcinogenic Mechanisms from Transcriptional Profiling of Tumor Initiation
S. C. Tilton[1], L. K. Siddens[2], S. K. Krueger[2], A. Larkin[2], K. M. Waters[1], D. E. Williams[2], W. M. Baird[2]
[1]Pacific Northwest National Laboratory, Richmond, WA; [2]Oregon State University, Corvalis, OR

Mixtures of Endocrine Disruptors: How Similar Must Mechanisms be for Concentration Addition to Apply?
T. Webster
Department of Environmental Health, Boston University School of Public Health, Boston, MA

See the MixSS website to find details on SOT 2013 Awards!

NOMINATE THE NEXT MIXSS OFFICERS

Nominations are open for the positions of vice president-elect, councilor, secretary/treasurer, post doctoral representative, and graduate student representative. Please consider nominating someone whom you think will help lead the area of combined exposures/chemical mixtures/multiple stressors research for SOT over the next 5 years. Self nominations are welcome. Please contact Michael Dourson (dourson@tera.org), with any nominations or questions.

MixSS MEMBER SURVEY Dose Additivity: Which Model Do You Use?

Jane Ellen Simmons (US EPA) and Cynthia Rider (NIEHS/NTP)

As mixtures experts, you are probably all familiar with the concepts of response additivity and dose additivity. These terms are used frequently in both toxicology and risk assessment discussions regarding mixtures. In our experience, response addition is pretty consistently described by the equation:

$$R_{mixture} = 1 - \prod_{i=1}^{n} (1 - R_i)$$

where $R_{mixture}$ is the response of the mixture and R_i is the response of mixture constituent *i* (note R is a number between 0 and 1).

Alternatively, the concept of dose addition is typically described by the equation:

$$\sum_{i=1}^{n} \frac{d_i}{EDx_i} = 1$$

where *n* is the number of constituents in the mixture that produces the same *x*% response as each individual dose at the EDx_i (dose of the constituent *i* that elicits *x*% effect when it is present alone), and d_i is the dose of that constituent in the mixture.

In contrast to the formula for response addition, which leads directly to predictions of the mixture response, there are many different equations used to make predictions of the mixture response based on the concept of dose addition.

When you (MixSS members) are calculating predictions based on dose addition, which equation do you use?

Please email responses (with references if possible) to Cynthia (cynthia.rider@niehs.gov) or Jane Ellen Simmons (Simmons.jane@Epa.gov).

Results will be posted in the next February 2013 Newsletter!

Upcoming Events

25th Annual Meeting of the Superfund Research Program (SRP): Celebrating 25 Years of Transdisciplinary Research & Training to Protect Human & Environmental Health

The University of North Carolina and Duke University will be co-hosting this event in Raleigh, NC (Marriot City Center) on **October 21-24, 2012**. Registration is required. See the website for details

http://eseconf.sph.unc.edu/2012/SRP/index.php

Many of the topics to be covered will be of interest to MixSS membership, including a focus on cross-disciplinary collaboration and cutting edge science.

The third day of the meeting will be a Special Symposium on **Exploring Novel Approaches to Complex Exposures**

Description from the website:

"SRP announces a special symposium to address the complexity of environmental exposures. Topics will focus on identifying and integrating emerging approaches and advanced technologies in the understanding of exposure and response to multiple stressors that are applicable to both human and environmental health. During this forum we will strategize on approaches to understand this exposure-disease paradigm."

Cumulative Risk Assessment (CRA) 2012 Webinar Series

The US EPA will be hosting a monthly webinar to discuss a broad range of topics that will inform the development of cumulative risk assessment guidelines. The first webinar presented by Ari Lewis (Gradient) entitled **"Nonchemical Stressors and Cumulative Risk Assessment: An Overview of Current Issues and Initiatives"** will take place **Wednesday, August 29, 2012, 3:00 p.m. - 4:00 p.m. EDT**. Find details and register for the webinars on the website:

http://www.scgcorp.com/crawebinars/index.htm

Updates on Past Events

A comprehensive report from the NIEHS Mixtures Workshop entitled "**Advancing Research on Mixtures: New Perspectives and Approaches for Predicting Adverse Human Health Effects"** (Sept. 26-27, 2011) will be available on the website (http://tools.niehs.nih.gov/conferences/dert/mixtures/) by the end of September, 2012.

Make the MixSS Work for You!

The MixSS is the only organized group dedicated to the science of mixtures. This offers a unique opportunity to bring together a diverse group of scientists interested in mixtures. *Help us to make MixSS a more useful resource for you!*

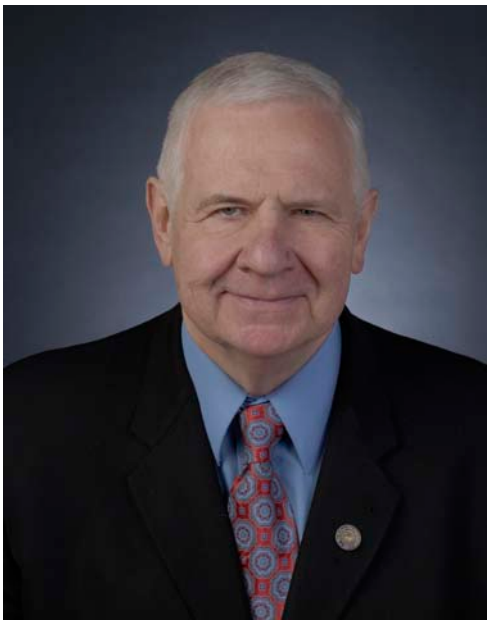
What are your suggestions for how to use the MixSS forum (website, Newsletter, etc.) to inform and engage the mixtures research community.

Here are some specific questions for motivation:

- How can we foster cross-disciplinary collaborations among researchers interested in complementary topics in mixtures?
- How would you like to see us highlight cutting-edge research in mixtures?
- Can we make better use of the ToXchange to increase communication among members?
- What can MixSS do to help you develop your ideas for annual meeting program submissions?

Please send any and all suggestions to the MixSS Secretary/Treasurer Cynthia Rider (cynthia.rider@nih.gov)

Meet the New MixSS Officer



Bruce Fowler (ICF) was elected as MixSS Vice President-Elect. In this position, Bruce will participate in MixSS planning activities and enter the presidential chain of succession.

Kembra Howdeshell (NIEHS/NTP) was elected as a MixSS Councilor. She will take over for Paul Price (Dow) and continue the tradition of being an excellent resource for MixSS. She will also participate in MixSS planning activities and serve as point person for MixSS website content.