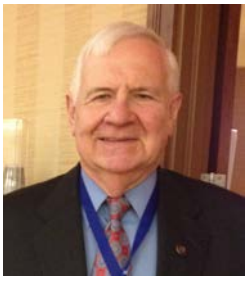
Mixtures Specialty Section Newsletter

Volume 5, Issue 1 September 2014

President's Message

Bruce Fowler, PhD, ATS
MixSS President



The issue of properly evaluating public health impacts from exposures to complex mixtures of chemicals and pharmaceuticals in air, food and water is of ever increasing importance. On the one hand, this problem area continues to rapidly expand with an influx of new chemical and physical agents, such as nanomaterials, being produced every day. In addition, there is the growing issue of concern for sensitive sub-populations on the basis of age, gender, genetic inheritance and nutrition raising the question of "dose makes the poison-to whom?" The overall situation is clearly complex in terms of providing useful scientific information to societal decision makers. I believe that the SOT Mixtures Specialty Section is in a unique position to provide leadership for the incorporation of sound modern science into risk assessments for both current and future mixture exposures on an acute and chronic basis. The technical tools available to us include state of the art scientific information such as exposure data generated by the CDC Biomonitoring Program, molecular pathway information from the EPA NexGen Initiative and the TOX21 Program coupled with ever more sophisticated computational modeling approaches capable of dealing with complex mixture exposures. The linking of solid analytical data with sophisticated analyses of molecular pathways coupled with rapid computer analysis is a potentially very powerful array of tools for understanding complex chemical interactions. In addition, these sophisticated methods may also be integrated with fundamental genotypic information to further refine the precision of risk assessment calculations. Computational toxicology methods also confer the flexibility to take into account age and gender which are formidable considerations but increasingly possible to manage. Given the above, I am optimistic that within the next decade, toxicologists engaged in mixtures research will be able to provide useful scientific information to address the issue of risks to sensitive sub-populations from multiple chemical exposures.
I would also note that the Mixtures Specialty Section is in a good position to facilitate collaborations with scientists in other SOT specialty sections such as risk assessment, nanotoxicology, food toxicology, epidemiology, metals and

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SOT 2014 In Review

Cynthia Rider, PhD
MixSS Secretary/Treasurer
NIEHS/DNTP

Another SOT meeting behind us, another opportunity to reflect on mixtures activities and accomplishments of our membership!

The officer's meeting took place on Tuesday, March 25th.

2013-2014 MixSS Officers

Topics discussed at the Officer's meeting included finances, awards, the RASS/MixSS webinar, membership, and the newsletter.

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mechanisms among others. These specialty sections each have interests in multiple chemical exposures and it is important for all of us to encourage collaborations. We could help each other leverage limited resources by co-sponsoring symposia and workshops not only within SOT but in other scientific societies such as the Society for Risk Analysis, American College of Toxicology and various epidemiology societies. The value of such collaborations rests not only with stimulating good interdisciplinary science but also in increasing the acceptance and value of mixtures research on a broader societal basis. There are clear challenges facing us based on what remains to be done but also good reason for optimism on the future of mixtures research in both the scientific and public health contexts. This future will be what we make of it and now is good time to begin.

Bruce Fowler

Later that day, the **MixSS sponsored** Workshop Session entitled **"Developmental Toxicity from Chemical Mixtures: Research to Application in Susceptible Populations"** and chaired by Danielle Carlin (NIEHS) and Moiz Mumtaz (CDC-ATSDR) highlighted a broad range of mixtures work. The first speaker, Dr. Robert Wright (Mount Sinai School of Medicine) discussed exposure to metal mixtures during critical developmental windows and epigenetic changes. Deborah Cory-Slechta (University of Rochester) described her work assessing the joint effects of lead and prenatal stress. Rogelio Tornero-Velez (US EPA) demonstrated use of methods from ecology to investigate patterns of exposure to mixtures. Chris Gennings (Virginia Commonwealth University) described her statistical approach for evaluating the similarity of multiple complex mixtures. Finally, Michael. Dourson (Toxicology Excellence for Risk Assessment) provided the risk assessment and regulatory perspective on mixtures and susceptible populations.

A notable event was the Wednesday night **MixSS Reception.** Jane Ellen Simmons (EPA and previous MixSS president) and Mike DeVito (NTP) engaged in a raucous debate over the future of mixtures risk assessment (moderated by Cynthia Rider [NTP]).

Rigorous arguments were put forth by Jane Ellen – laying out the case for continued focus on using component- based approaches for mixtures risk assessment and Mike DeVito - outlining the case for moving away from component-based approaches and toward whole mixture risk assessment.

With an audience vote, Mike walked away with the prize. However, both sides succeeded in entertaining and informing the audience!

Postscript: It was later pointed out that Cynthia actually has no idea how debates are supposed to work and that most of the audience was moderately to severely confused. However, she claims 1) she who runs the debate gets to make the rules and 2) that mixtures researchers are inherently drawn to complexity and should, therefore, be able to disentangle a debate that involves pro/con arguments for two different questions simultaneously.

Jane Ellen and Mike – still friends

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A big thank you to Dave Mattie

Incoming MixSS president Bruce Fowler (right) presented a plaque of appreciation to Dave Mattie (left) for his service as president 2013-2014.

Dave Mattie (Air Force Research Laboratory) has contributed so much to the MixSS. He served 2 terms as secretary/treasurer before entering the position of vice-president elect and serving as president. We know that he will continue to be a great resource as past president. Thank you, Dave!

And the award goes to...

Graduate Student Award

Axelle Marchand (Université de Montréal)
Studying the Impact of Volatile Organic Chemical Coexposures on the Urinary Excretion of Their Metabolites in Human Volunteers

MixSS vice president elect David Herr (right) presented the award to Axelle.

Post doctoral Award

Laura Datko-Williams (ORISE)
Assessment of In vivo Toxicological Interactions from Criteria Air Pollutant Mixtures

MixSS vice president-elect Dave Herr presented the award to Laura.

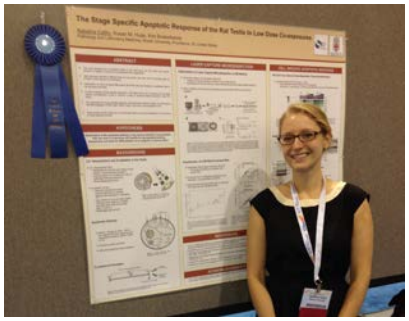
We are very grateful to Wiley for sponsoring the MixSS graduate student and post doc awards!

Best Mixtures Abstract

(selected from the top 5 abstract pool)
Kembra Howdeshell (NIEHS/NTP)
Dose Addition Predicts Effects of Phthalate Mixture on Male Reproductive Tract Development and Associated Fetal Testis Gene Expression in Rats

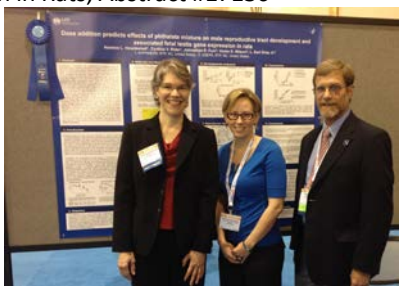
Top 5 Abstracts

(in alphabetical order by first author)
Authors: Natasha Catlin, Susan M. Huse, Kim Boekelheide; Title: The Stage-Specific Apoptotic Response of the Rat Testis to Low-Dose 2,5-Hexanedione and X-Irradiation Coexposure; Abstract #1710



Natasha Catlin

Authors: Kembra L. Howdeshell, Cynthia V. Rider, Johnathan R. Furr, Vickie S. Wilson, L. Earl Gray; Title: Dose Addition Predicts Effects of Phthalate Mixture on Male Reproductive Tract Development and Associated Fetal Testis Gene Expression in Rats; Abstract #1713c



Melanie Doyle-Eisele (center), MixSS Councilor, and Dave Mattie, MixSS President-Elect, presented the award to Kembra (left).

Authors: Alix Leblanc, Etienne Blanc, Ariane Ambolet-Camoit, Chantal Benelli, Sylvie Bortoli, Robert Barouki, Martine Aggerbeck; Title: Xenobiotic Mixtures Decrease Human Hepatic Gluconeogenesis and Glucose Oxidation; Abstract #1011

Authors: Axelle Marchand, Rocio Aranda-Rodriguez, Andy Nong, Sami Haddad; Title: Studying the Impact of Volatile Organic Chemical Coexposures on the Urinary Excretion of Their Metabolites in Human Volunteers; Abstract #1012

Authors: Anne-Marie Vinggaard, Niels Hadrup, Mikael Pedersen, Kasper Skov, Line O. Bertelsen, Henrik Frandsen, Kristine G. Kongsbak, Julie Boberg, Ulla Hass; Title: Mixture Effects at Human Relevant Exposure Levels?; Abstract #1018d

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Mixing and Mingling at the Reception

Julia Rager and Nigel Walker

Kembra Howdeshell, Melanie Doyle-Eisele, and Dave Mattie

Sami Haddad and Axelle Marchand

Dave Mattie, Bruce Fowler, and Dave Herr

Tom Webster, Danielle Carlin, and Jane Ellen Simmons

Upcoming RASS/MixSS Webinar – Sept 10, 2014

Toxicology for Breast Cancer Prevention

Ruthann Rudel, Director of Research, Silent Spring Institute, Newton, MA

Exposure to chemicals that cause rodent mammary gland tumors is common, but few studies have evaluated potential breast cancer risks in humans. Our research program uses toxicology and exposure science to identify likely breast carcinogens and opportunities to reduce exposure. Our recent work was designed to facilitate measurement of biomarkers of exposure to potential breast carcinogens in breast cancer studies and biomonitoring.

We conducted a structured literature search to identify measurement methods for exposure biomarkers for 102 chemicals that cause rodent mammary tumors. To evaluate concordance, we compared human and animal evidence for agents identified as plausibly linked to breast cancer in major reviews. To facilitate future application of exposure biomarkers, we compiled information about relevant cohort studies.

We conclude that exposure measurement methods and cohort study resources are available to expand biomonitoring and epidemiology related to breast cancer etiology and prevention.

Upcoming Speaker:

Brenda Eskanazi (UC Berkeley) – February 11, 2015

Dr. Eskanazi is a neuropsychologist and epidemiologist whose long-standing research interest has been the effects of toxicants including lead, solvents, environmental tobacco smoke, dioxin, and pesticides on human reproduction (both male and female) and child development.

Past Speakers in the series:

Chirag Patel (Harvard Medical School) – Environment-Wide Association Studies to Connect Multiple Personal Exposures to Health, 1/8/14

Bette Meek (University of Ottawa, Canada) - International Experience in Addressing Combined Exposures: Increasing the Efficiency of Assessment, 9/11/13

Jack Harkema (Michigan State University) - Interface of Health Effects caused by the CardioMetabolic Syndrome and Exposures to Air Pollutant Mixtures, 4/10/13

To view previous webinars, visit the RASS website (https://www.toxicology.org/isot/ss/riskassess/downloads.asp)

Thank you to the MixSS membership for your speaker suggestions! Please send suggestions for future speakers to Kembra Howdeshell (howdeshellkl@niehs.nih.gov)

Bring a friend to MixSS

Melanie Doyle-Eisele, PhD
MixSS Councilor
Lovelace Respiratory Research Institute

The Mixtures Specialty Section is 1 of 27 opportunities you or your colleagues can be involved in throughout your career as a member of the Society of Toxicology. What makes the MixSS different from so many others is that we are "toddlers" at SOT compared to many – therefore, if you can give a few minutes now you can help develop the program that we want to become. The Mixtures Section provides a forum for the interaction of SOT members to discuss the impact of combination effects on current regulations, growing fields in science, and also immediately impacts research that is presented at national conferences.

If you know of a friend, neighbor, co-worker, or student that may be interested, please contact us (mdoyle@lrri.org). We welcome the opportunity to set up interactions with interested scientists and current members.

NOMINATE THE NEXT MIXSS OFFICERS

Nominations are open for the positions of vice president-elect, secretary/treasurer, councilor, 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 **Dave Mattie** (david.mattie@us.af.mil), with any nominations.

A short (1 paragraph) biosketch with the nominee's qualifications/interests is all that is needed. The past president will lead a nominations committee that will submit the slate of candidates to SOT by December 31, 2014. Membership will then vote to elect the 2014-2015 MixSS officers.

The time commitment is minimal for most positions (approximately 4-6 conference calls per year), while the rewards are *significant* – getting to know other mixtures researchers and contributing to the success of the MixSS!

Position descriptions:

Vice President-Elect (1 year followed by transition to vice president, president, and past president – 4 years total)

- Participate in teleconference meetings
- Administer Graduate Student/Post doc Award
- Present Student/Post doc Awards during MixSS reception
- Review and update by-laws

Secretary/Treasurer (2 years)

- Participate in teleconference meetings
- Prepare annual report for submission to SOT HQ (August 1)
- Take minutes at meetings
- Submit budget for annual meeting reception to SOT HQ
- Report on finances at SOT Annual Meeting MixSS Reception

Secretary/Treasurer (continued)

- Purchase plaques and ribbons for SOT Annual Meeting MixSS Reception
- Newsletter (optional)

Junior Councilor (1 year followed by transition to senior councilor position – 2 years total)

- Participate in teleconference meetings
- Work on increasing membership
- Work on increasing sponsorship

Post doctoral Representative (1 year)

- Participate in teleconference meetings
- Report MixSS-related events to PDA
- Provide postdoctoral perspective to MixSS activities

Graduate Student Representative (1 year)

- Participate in teleconference meetings
- Report MixSS-related events to GSLC
- Provide student perspective to MixSS

Upcoming Events

Exposome Workshop

Date: January 14-15, 2015

Location: NIEHS, Research Triangle Park, NC

Goal: What is the Exposome, what needs to occur to enable it, and how can/should it be implemented

Format: Small working groups will focus on the exposome from different angles: external exposure, internal exposure, biological response and systems biology, epidemiology, and analytical methodologies and informatics

Checkout the exposome webinar series at http://tools.niehs.nih.gov/conference/exposome_webinar_2014/

Next speaker: Paolo Vineis (Imperial College, London), "EXPOsOMICS - Causality and the Exposome Concept," September 11, 2014

Workshop: Statistical approaches to epidemiological studies of combined exposures/mixtures

Date: July 13-14, 2015

Location: NIEHS, Research Triangle Park, NC

Description: Epidemiologists and statisticians will discuss methods for evaluating associations between multiple chemical exposures and health effects.