Mixtures Specialty Section

A mixture of business, social, and news

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From the President

While the holiday activities are all around us, the leadership team of Mix SS is getting ready for the SOT 2023 annual meeting. Meeting in person last year was wonderful after two years of virtual meetings, but we missed seeing many old friends who were still not able to travel in 2022. We are looking forward to seeing all of the members of Mix SS in-person in Nashville and catching up on what is happening in the field of mixture risk assessment. This year Mix SS was the primary endorser for a workshop and a symposium at the annual meeting (for details on the sessions, please see page seven of the newsletter). Both of the sessions deal with the use of NAMs to characterize toxicological interactions. On pages four and five of the newsletter we have an article on why NAMs are expected to play a big role in future assessments the risks posed by combined exposures. Last year, Mix SS...

From the President cont'd

…formed new committees including Communications, Webinars, Membership, and Fundraising. If you interested in joining any our existing committees or new committees, please contact any of the Mix SS officers. Speaking of officers, thanks to the work by our past president Dr. Mansi Krishan we have a great slate of candidates for our 2023-24 leadership positions. Please be sure to vote when the election is held in January. Next year will also see a revised Mixture's Specialty page on the SOT website. The initial version of the new pages looks great (check out the new logo on page seven) due to the work of our ad hoc grad student representative Dr. Brianna Rivera and incoming vice president Dr. Courtney Roper. Also, if you have not done so already, please follow the Mix SS LinkedIn page. We use the page to share updates and announcements of Mix SS activities and mixture issues.

In closing, I would like to quote, and strongly affirm, Tom Webster's (Mix SS president 2020-2021) thoughts on the field of mixture risk assessment.

> "I believe that mixtures research has a crucially important and bright future and one that is interdisciplinary, bringing together toxicologists, epidemiologists, exposure scientists, mathematical modelers, statisticians, risk assessors and others. The SOT Mixtures Specialty Section is actually one of the few professional organizations that specializes in this field of research. Please invite your colleagues to join us!"

Sincerely,

Paul S. Price, PhD
President, Mix SS (2022-2023)

Recent and Upcoming Webinars

"Combined Effects of Chemical Mixtures Are Predictable for the Whole Transcriptome - a Proof of Concept Toxicogenomic Study With Zebrafish Embryos."

Wibke Bush, PhD | Group Leader, iTox-Integrative Toxicology | Helmholtz-Centre for Environmental Research

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A Population-based Human in vitro *Approach to Quantify Inter-individual Variability in Responses to Chemical Mixtures."*

Lucie Ford | Graduate student | Texas A&M University

The Risk Assessment Specialty Section (RASS) hosts monthly webinars and twice a year, RASS graciously teams up with MixSS to co-host seminars at the intersection of risk assessment and mixtures toxicology. The September webinar was a split session featuring two of our MixSS Top Abstract award winners from the 2022 SOT Annual Meeting – Dr. Wibke Busch and Lucie Ford. Both speakers presented research on the use of new approach methods to estimate mixture-based effects. Wibke Busch presented her work on dose and exposure time integrated toxicogenomic approaches in a zebrafish model. Lucie Ford presented her work on characterizing inter-individual variability using an in vitro lymphoblast model derived from diverse human populations.

Access these presentations and other past MixSS webinars HERE.

The next RASS-MixSS webinar is on January 11, 2023 (3PM EST) and the speaker will be Dr. Andreas Kortenkamp from Brunel University London.

NAMs and Mixture Hazard Assessment

New Approach Methodologies (NAMs) have been proposed for use in chemical hazard assessments, however, NAMs are likely to have an even greater use in assessments of mixtures. The advantages of NAMs identified in a recent report from the European Food Safety authority include: a focus on effects in humans by measuring effects in human cells and tissues, a focus on molecular mechanisms rather than apical effects, and the discrimination of the roles of kinetics and dynamics in dose response.

These factors are very relevant for the study of the toxicity of mixtures. In the evaluation of the toxicity of a single chemical, the concordance of kinetic and dynamic effects between animal models and humans is only required for a single chemical; however, concordance is required for multiple chemicals in mixture assessments. As a result, the probability of animal models failing to predict human toxicity is greater for the assessment of the toxicity of mixtures than single chemicals and measuring toxicity in test systems that are closer to humans will have a greater benefit for mixture hazard assessments than single chemical assessments.

While the current system of managing risks posed by chemicals is based on the similarity of apical endpoints across different chemicals (dose additivity being more likely to occur when two chemicals have a common endpoint or affect a common organ or system), the ability to accurately predict a mixture's toxicity is greatly increased by information on the mechanisms of action of the chemicals. A recent EFSA workgroup meeting proposed a decision tree for assigning chemicals to assessment groups based on mechanistic data from both NAMs and animal models (see figure). In addition, Adverse Outcome Pathways (AOPs) that are based on findings from NAMs can be helpful in assessment approaches for chemicals with a common apical effect. It has been suggested that dose additivity is indicated when two chemicals have a common molecular initiating event and response addition when they only have a common apical endpoint. The ability to separately characterize the kinetics of chemicals is required for use of NAMs that only characterize the dynamic portion of dose response. This has led to the….
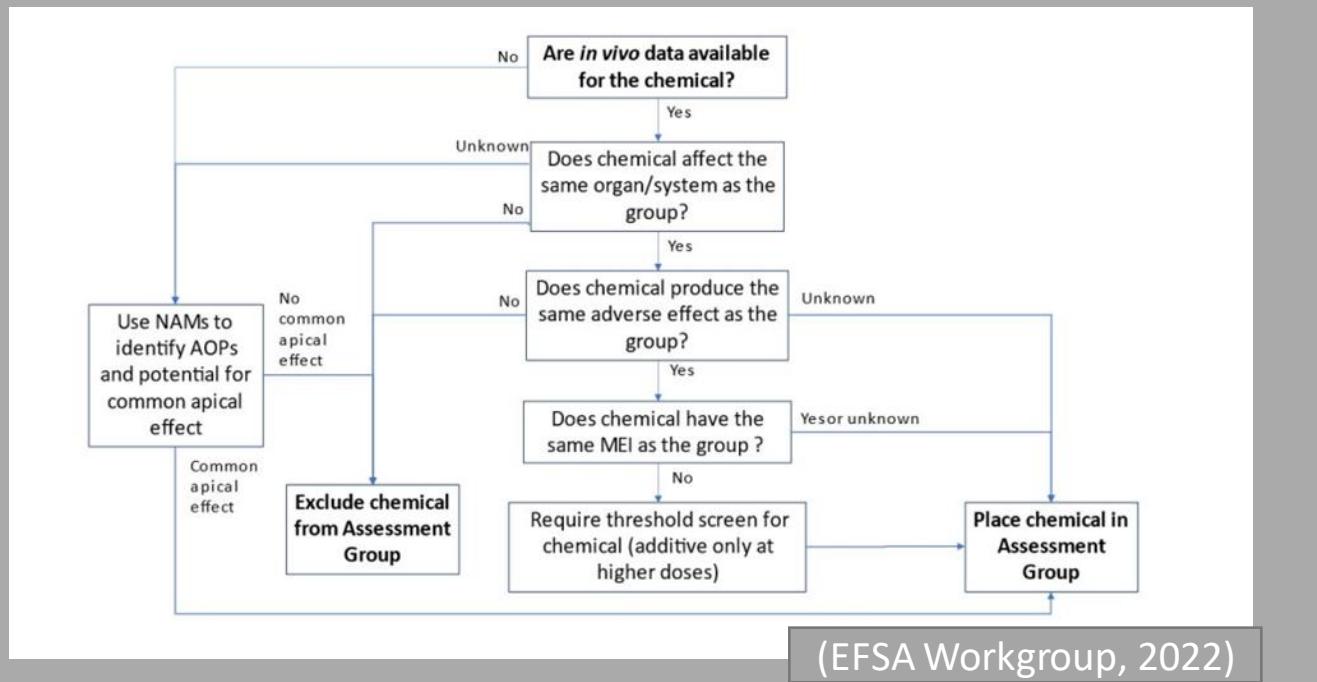
(EFSA Workgroup, 2022)

Cont'd from pg 4

…development of high throughput models of chemical's kinetics. The ability to separately characterize the kinetic and dynamic portions of dose response is very useful in characterizing chemical interactions. Interactions such as potentiation, inhibition, synergy, and antagonism between chemicals can be divided into interactions that occur in the kinetic and the dynamic portions of dose response of chemicals. Kinetic interactions between two substances are dependent on the ability of one or both chemicals to change the ADME (adsorption, distribution, metabolism, or excretion) capacity of an individual. By focusing on kinetics separately from dynamics, NAMs encourage the investigation of how one chemical can change the relationships between internal and external doses in a second chemical. The understanding of dynamic interactions is also supported by NAMs. Dynamic interaction can be characterized using AOP networks that are defined using the result of NAMs.

In summary, the development of NAMs provides opportunities for the improvement of the assessment of the toxicity of mixtures by providing relevant data on the mechanisms of action of chemicals in a mixture. Because of this potential, sessions on NAMs and mixtures were accepted in the 2022 and 2023 SOT meetings.

–Paul S. Price, PhD
President, Mix SS (2022-2023)

References: EFSA International Workshop on RA of Combined Exposure to Multiple Chemicals. EFSA Supporting Publications, 2022, 19(7), 7422 E. Development of a Roadmap for Action on New Approach Methodologies in Risk Assessment. EFSA Supporting Publications, 2022, 19(6), 7341E. Assessing the toxicity of mixtures of chemicals. In Statistics in Toxicology. Edited by Daniel Krewski and C. Franklin, 1991, pp. 559-591. Cordon and Breach, New York. Adverse Outcome Pathways to Support the Assessment of Chemical Mixtures. In Chemical Mixtures and Combined Chemical and Nonchemical Stressors, pp. 177-201. Springer, Cham, 2018. Adverse outcome pathway networks II: network analytics. Environmental toxicology and chemistry 37, no. 6 (2018): 1734-1748.

2022-2023 Officers

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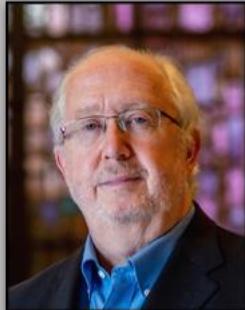
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Greylin Nielsen

Don't forget to vote in our upcoming election!! Be on the lookout for an email ballot from MixSS soon.

☑ VOTE

Positions up for election include:

- Vice-President Elect
- Secretary/Treasurer
- Junior Councilor
- Postdoctoral Representative
- Graduate Student Representative

Looking Ahead: SOT 2023

Proposal Review Process

In late April, 2022, the Mix SS Program sub-committee began pre-review for SOT 2023 session proposals. During this initial round of review, the sub-committee was able to provide feedback to strengthen several "pre-proposals," as well as offer advice on potential speakers for various topics, etc.

After SOT's session proposal deadline on May 16th 2022, the sub-committee received a total of five proposals that included a Continuing Education course, workshops and symposiums. Each proposal was reviewed and scored based on 1)How well the session was developed 2)If the speakers' professional perspective was balanced 3)Scope 4)Relevancy to mixtures 5)Whether the session was timely and not redundant to past sessions.

MixSS Endorsed SOT 2023 Sessions

After the Program sub-committee submitted their preferences for Annual SOT sessions endorsed by MixSS, SOT has accepted the following as MixSS endorsed sessions (see full program for more details):

Symposia: Monday, March 20th, 2023: 1:45 to 4:30 PM, Room 205
"New Approach Methodologies to Evaluate Botanical Safety"

This symposia will provide an overview of the current regulatory landscape for botanical products, discuss gaps and ongoing efforts to improve or design new methodologies, and highlight successes and challenges associated with study design, method development, and data interpretation of these approaches.

Workshop: Tuesday, March 21st, 2023: 1:00 to 2:30 PM, Room 205
"Challenges and Future Directions in NAM Applications to Mixtures Risk Assessment"

This workshop identifies the current usefulness and limitations of NAMs for informing regulatory risk assessment of mixtures and discusses emerging methodologies to address these challenges.

Have a topic you'd like to see endorsed by the Mix SS in the future?

Submit your ideas HERE

SOT **62nd Annual Meeting**
& ToxExpo • Nashville, TN
March 19–23, 2023

For the Trainees

The Mixtures Specialty Section (MixSS) provides awards supporting **graduate students** and/or **postdoctoral fellows** involved in research related to the **toxicology of mixtures**. The MixSS will recognize outstanding Student and Postdoc research presented at SOT 2023.

Application Deadline: January 31st

The winners will receive:
- **achievement plaque**
- **cash award**

For more information please see:
https://www.toxicology.org/groups/ss/mix/Awards.asp

WE ARE CURRENTLY PLANNING:

A virtual event to honor **Jane Ellen Simmons** and her contributions to mixtures research and dedication to training young scientists.

Graduate students and **post-docs** will be given the opportunity to present their research and receive a **travel award** towards attending an SOT annual meeting.

HELP US RECRUIT EMERGING TOXICOLOGISTS!

SOT ToxScholar program supports presentations to increase awareness of toxicology as a science and as a career field.

At institutions that are
- Primarily undergraduate
- With a high proportion of undergraduates from underrepresented groups
- In developing countries

We need YOU to be a ToxScholar. Apply for funding.

Faculty United for Toxicology Undergraduate Recruitment and Education (FUTURE) Committee

Join us for our **2nd annual mixtures research mentoring event** at SOT 2023!

New Logo Alert!

As part of the effort led by SOT's creative team, the Mixtures Specialty Section was given the opportunity to redesign our website and logo. Officers of the Mixture Specialty Section decided to focus on the integration of three central themes to mixtures toxicology: non-chemical stressors, cumulative exposure, and chemical interactions. The three different colors in the logo represents the integration and influence of these factors on human and environmental health.

Important Upcoming Dates

March 27-31, 2023 . . . . **SOT Nashville 2023**

August 1, 2022 . . . . Registration and Housing opened

January 3-11, 2023 . . . . Late-breaking abstract submission period (Late-Breaking Poster Sessions will take place on Thursday of SOT).

January 31st, 2023 . . . . Mixtures SS Best Overall and Best Student/Postdoc Awards Deadline

Are you on LinkedIn? Now we are too! Connect with the Mixtures Specialty Section on LinkedIn to stay up to date on Specialty Section announcements, SOT Annual Meeting deadlines, and upcoming webinars.

Find the MixSS LinkedIn Page HERE

Editors: Rachel Dee | Allison Phillips