National Capital Area Chapter
Society of Toxicology Newsletter
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R. Mitkus, Editor

CHAPTER MISSION STATEMENT

The National Capital Area Chapter of the Society of Toxicology (NCAC-SOT) was established to provide a regional focus for scientists of all disciplines interested in toxicology. The Chapter acts to:

- Sponsor and co-sponsor symposia on current issues in toxicology
- Provide an annual award to an outstanding student in toxicology to assist in attending the annual meeting of the SOT
- Maintain communication with the National SOT regarding current toxicology and regulatory concerns
- Sponsor Regional Chapter events at the SOT Annual Meetings

MESSAGE FROM THE PRESIDENT

Greetings from the President's chair, and Happy Fall/Winter!

It has been a busy few months for the National Capital Area Chapter. Our Fall Symposium on Green Chemistry was a great success. We had speakers covering a broad spectrum of topics, from the small (chemical development) to the very large (public policy). Our Vice-President, Cal Baier-Anderson has written a wonderful summary, please take the time to read it and, in the event you were not able to attend the symposium, learn more about this emerging hot topic. Also part of our Fall Symposium was a Student Career Panel ("Job Opportunities – what are they and how do you find them?"). This luncheon discussion panel was primarily for graduate students and post-docs, but of great interest to everyone in the audience. Our student and post-doctoral representatives did an outstanding job of pulling this panel together, and have written a summary that appears later in the newsletter.

The Student Career Panel was just part of our effort to reach out to graduate students. Letters were sent to many faculty members this fall, asking for help in "recruiting" students and post-docs. Perhaps you received one? Our chapter has a long history of offering programs, travel awards, and other activities for graduate students and post-docs. At $10/year, student membership is a bargain, and provides a number of opportunities. Our fall and spring symposia are free to student members. They provide a forum for students to present their research, with awards via poster competitions. These awards include the Bern Schwetz Travel Award to offset costs of travel to the annual SOT meeting. Unfortunately, participation has been somewhat less than overwhelming. As the next generation of toxicologists and leaders in the field, the NCAC is a great to get involved and network with local, national, and even international toxicologists. Are you a graduate student, or do you know one, who wants to interact in a high impact/low pressure setting? Maybe you are interested in a little extra help attending the annual meeting? If so, there are a number of mechanisms for participating. Check out the NCAC website, ToXchange, or the NCAC groups on Facebook Twitter, or LinkedIn for announcements. We look forward to getting to know you!

Of course, everyone is looking forward to the annual meeting in San Francisco. We will be having our traditional get together, details are in the works. And, we are actively working on our Spring Symposium; our topic will be Systems Toxicology. Our tentative date is May 10 at the Lister Hill auditorium. I do hope you will be able to join us both in San Francisco, and back here in the DC area. Until then, I wish everyone a happy and healthy fall, winter, and holiday season.

Laurie E Roszell, DABT, PhD
NCAC-SOT President

MESSAGE FROM THE GRADUATE STUDENT AND POSTDOC REPRESENTATIVES

Hello NCAC students and postdocs! We, your student representatives, Colleen McLoughlin and Anna Schlappal, and your postdoc representative, Linnzi Wright, are excited to share news from the fall symposium and hope you are having a great fall semester!

At the fall NCAC symposium we hosted a lunchtime career panel, with particular focus on finding jobs for students and postdocs. Panel members included author Elizabeth Grossman, University of Maryland professor Dr. Rosemary Schuh, Charles River Laboratories Senior Regional Manager Thomas Claggett, Dr. Chris Sheth from EPA, Dr. John Warner of the Warner Babcock Institute for Green Chemistry, Dr. Mark Thompson from DuPont Haskell Global Centers for Health and Environmental Sciences, and Dr. Margaret H. Whittaker Managing Director and Chief Toxicologist of ToxServices LLC. Panelists provided a lively discussion and insight on topics ranging from their personal experiences in finding jobs, to networking (if you are not already on, join linkedin!), and even negotiating salaries.

We would love to hear from students and postdocs about ideas you have for ways we can better serve you. You can also contact us personally, Colleen: mcloughlince@vcu.edu or Anna: aschlapp@umd.edu. We began work over the summer to expand the methods of communication for members with the chapter leadership, in addition to ToXchange, you can find our facebook group (SOT National Capital Area Chapter), or follow us on Twitter (@SOTNCAC)! A recent addition is we now also have a group on Linkedin!

We can't to hear from you and are looking forward to an exciting year for NCAC students!

Colleen E. McLoughlin
Student Representative
VCU

Anna Schlappal
Student Vice-Representative
UMD

Linnzi Wright, PhD
Postdoctoral Representative
US Army

NCAC-SOT EXECUTIVE BOARD MEMBERS

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2011 Fall Symposium Addresses Green Chemistry and the Role of Toxicology

- by Cal Baier-Anderson

The fall symposium, held on September 29th at Lister Hill Auditorium on the NIH campus, featured speakers discussing the essential role that toxicologists play in implementing green chemistry principles. Green chemistry is defined as the design of chemical products and processes that reduce or eliminate the use or generation of hazardous substances. Identifying hazards is, of course, the province of toxicology. The symposium speakers described the origins of green chemistry, the importance of engaging toxicologists to understand chemical hazard, the challenges of implementing green chemistry, and how communication and collaboration can strengthen chemical design and innovation.

John Warner, "Father" of Green Chemistry

John Warner, President and Chief Technology Officer, Warner Babcock Institute for Green Chemistry, opened the symposium by describing his early research in chemistry, leveraging synthetic pathways based in natural processes. As a young, prominent researcher with Polaroid, John developed thousands of new molecules. But it was the recognition that as a chemist he knew nothing about the hazards that might be associated with the chemicals he was designing that led John to work with Paul Anastas, currently an Assistant Administrator at EPA, to develop the guiding principles of Green Chemistry[1], with an emphasis on designing out hazard.

Hazard reduction is an active approach to pollution prevention. Using nature as muse, it is possible to develop useful chemicals and synthetic processes that are benign by design. Chemists need to work with toxicologists to understand hazard, and hazard mechanisms so that they can redesign chemicals to eliminate the hazard. This can and must be done in a way that preserves functionality and is cost competitive. And, in fact, green chemistry is being successfully implemented right now. John described founded the Warner Babcock Institute for Green Chemistry LLC to prove green chemistry can be good business. His company solves real-world problems for business customers using green chemistry and to date has more than 200 patents.

John's work demonstrates that it is much more expensive to manage hazardous chemicals than those that are safer by design. And yet, green chemistry still constitutes only a small percentage of the chemicals marketplace, so there is enormous potential. To expand will require the expansion of green chemistry training. John helped found the first green chemistry PhD program at University of Massachusetts, and since then green chemistry has been integrated into many other programs. And many of these programs include basic toxicological training for green chemists. John also advocates licensing for chemists.

Steve Devito, USEPA, Designing out Hazard

Steve Devito, trained as a medicinal chemist and a registered pharmacist, described principles of chemical design for hazard reduction. Steve's training emphasized how compounds interact with biological elements to cause toxicity and how chemical design can be manipulated to reduce negative interactions. He noted that great strides have been made in the implementation of several green chemistry principles (for example, minimize derivatization, use catalytic reagents, improve energy

[1] http://www.epa.gov/sciencematters/june2011/principles.htm

efficiency), while hazard reduction lags behind. Industrial chemistry can learn from advances in hazard reduction made by the pharmaceutical industry.

Steve provided numerous examples the design of safer chemical molecules (which are described in more detail in the book *Designing Safer Chemicals*[2]). He emphasized that understanding the mechanism of toxicity of a chemical can help chemists make structural modifications to mitigate the toxicity. A classic example is the difference in toxicity between ethylene glycol ethers and propylene glycol ethers. Ethylene glycol ethers (EGE) are associated with a suite of reproductive, developmental, kidney, thymus and blood effects that are not found with the propylene glycol ethers. The propylene glycol ethers (PGEs), even at much higher exposure levels, do not cause these effects. The difference is the placement of a methyl group; EGE primary alcohols are metabolized in the liver by alcohol and aldehyde dehydrogenases, forming the toxic alkoxyacetic acid metabolites. In contrast, PGE secongary alcohols are metabolized in the liver by cleavage of the ether linkage by mixed function oxidases to form propylene oxide and an alcohol.

Another concept that is useful in green chemistry is that of isosteres[3] which are widely employed by medicinal chemists, but perhaps not as much by industrial chemists. In pharmaceutical design, the purpose of exchanging one isostere for another is to enhance the desired properties of a compound, and minimize toxicity without making significant changes in chemical structure.

Mark Thompson, Dupont, Integrating Green Chemistry into Chemical Design and Manufacture

That green chemistry holds great promise to revolutionize product design and engineering is not in dispute. The challenge is in its implementation. While successes have been documented, solutions come in fits and starts. Mark Thompson described Dupont's commitment to green chemistry but also provided a dose of reality, explaining that breakthroughs come, but at a cost. Research takes time and money to develop chemicals that are functional, yet less toxic. This is particularly true for the agricultural pesticides, which, by design are intended to be poisonous to specific species. Understanding toxicological mechanisms is critical to designing molecules that exhibit specificity and minimize harm to non-target species. Dupont has found success in characterizing toxicological targets and exploiting species specific differences. One example of this are rhyanodine receptors, which regulate muscle and nerve activities by modifying levels of internal calcium in these cells. Both mammals and insects have rhyanodine receptors, but there are species-specific differences that can be used to guide insecticide design. Insecticides that target insect rhyanodine receptors have proven to be very effective with low mammalian toxicity.

Dupont has also developed a tool that helps researchers identify potential hazard and exposure concerns associated with chemicals. The tool draws on 1400 public databases, and includes consideration of public perception. The tool is coupled with a visualization system that provides a visual description of the concerns associated with each chemical that facilitates the rapid comparison of chemicals. Dupont researchers use this tool to understand and anticipate concerns and risk reduction needs.

Margaret Whittaker, ToxServices, Characterizing Green Chemicals

A board-certified toxicologist and risk assessor, Margaret Whittaker is president of the consulting company ToxServices. In addition to providing quantitative risk assessment services, Margaret also

[2] *Designing Safer Chemicals,* edited by Roger Garrett and Stephen DeVito. Washington: American Chemical Society, in fall 1997.
[3] Isosteres are molecules or ions of similar size containing the same number of atoms and valence electrons, e.g., O2-, F-, Ne, http://www.chemicool.com/definition/isosteres.html

conducts hazard evaluations and alternatives assessments to screen products, fragrance formulas and chemical classes for chemicals that may pose risks to human health or the environment, and to help clients identify safer alternatives.

Margaret described frameworks for hazard evaluation and alternatives assessment, and tools that are particularly helpful. Margaret emphasized the importance of the UN Globally Harmonized System of Classification and Labeling[4] that is applied in Europe and increasingly, the US, to characterize and rank hazard.

There are many tools available to assist toxicologists with hazard characterization. These include predictive software applications such as DEREK and TOPKAT, which are quite expensive tools that are mostly used by Pharma. But there are several tools provided by government agencies that are very useful, such as the Analog Identification Model (AIM), ChemID Plus for analog identification, and TEST software for hazard evaluation. Both TEST and AIM are offered by the EPA[5] and ChemID Plus is available through the National Library of Medicine.[6] The OECD Toolbox[7] is a collection of QSAR methods that address a variety of mechanisms and endpoints such as sensitization, carcinogenicity, genotoxicity, skin and eye irritation and aquatic toxicity. Margaret also emphasized the importance of including an evaluation of ecological criteria in the hazard evaluation. In addition to the OECD Toolbox, the EPA has a set of tools known as EPI Suite [Estimation Program Interface (EPI) Suite[8]] to characterize physicochemical properties, perform ecological evaluation and estimate environmental fate and transport.

Elizabeth Grossman, Journalist, Communicating Green Chemistry and Hazard Concerns

As an investigative journalist, Elizabeth Grossman writes frequently about controversies in toxicology. And it was this interest in toxicology that led to research green chemistry, and subsequently, her acclaimed book, *Chasing Molecules: Poisonous Products, Human Health and the Promise of Green Chemistry*. In her talk, Elizabeth emphasized the need for communication with journalists. Journalists are rarely allowed to speak with scientists, instead being funneled to public relations staff for whom it may be a challenge to explain complex scientific issues. Thus, interviews turn into a bad game of "telephone", where facts get warped and distorted as they filter down the chain. Elizabeth emphasized that accurate translations of complex scientific issues are best achieved through direct engagement between journalists and scientists.

Robert Peoples, American Chemistry Society, Green Chemistry Institute, Collaborating to Advance Green Chemistry

Robert Peoples is director of the American Chemical Society Green Chemistry Institute, and in this capacity promotes the implementation of green chemistry principles. As Robert explained, this means modeling chemistry on natural processes, which occur at ambient temperature and pressure, with water as the solvent, no waste, and active biodegradation. It is imperative that we as a global community grapple with the "grand challenge" of addressing such problems as energy, water, food, environment, poverty, terrorism & war, disease, education, democracy and population in a sustainable manner. Finding sustainable solutions will require that we establish effective lines of communication among scientists and engineers to implement green chemistry and engineering.

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[4] Also known as the "Purple Book", available here: http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html
[5] TEST is available at: http://www.epa.gov/nrmrl/std/cppb/qsar/#TEST, AIM is available at: http://aim.epa.gov/default.cfm?CFID=65536806&CFTOKEN=22296474&jsessionid=5a309cdc81f62f2fb4745f8517f7335a6844
[6] ChemID Plus is available at: http://chem.sis.nlm.nih.gov/chemidplus/
[7] The OECD Toolbox is available at: http://www.oecd.org/document/54/0,3746,en_2649_34379_42923638_1_1_1_1,00.html#An_overview_of_Phase_2
[8] EPI Suite is available at: http://www.epa.gov/oppt/exposure/pubs/episuite.htm

Robert emphasized that different perspectives can be bridged to everyone's benefit. It will take the collective efforts of academia, (education and invention), government (enabling, protecting) and industry (innovation, implementation) to find sustainable solutions.

Looking forward, Robert proposed a plan to bolster green chemistry research and implementation. In the short-term, there is a need to train existing technical and leadership professionals. Curriculum change is necessary, and while this has already begun, there is more work to do. A longer-term effort will involve communication with the public, so that they understand the meaning and value of green chemistry. In the meantime, the green chemistry market continues to expand, and will be a key to creating a more sustainable future.

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The 12 Principles of Green Chemistry

(http://www.epa.gov/sciencematters/june2011/principles.htm)

The 12 Principles of Green Chemistry, originally published by current EPA Assistant Administrator Paul Anastas, Ph.D. and John Warner, Ph.D. in Green Chemistry: Theory and Practice (Oxford University Press: New York, 1998), provide a road map for chemists to implement green chemistry.

The twelve principles are:

- **Prevention:** It's better to prevent waste than to treat or clean up waste afterwards.
- **Atom Economy:** Design synthetic methods to maximize the incorporation of all materials used in the process into the final product.
- **Less Hazardous Chemical Syntheses:** Design synthetic methods to use and generate substances that minimize toxicity to human health and the environment.
- **Designing Safer Chemicals:** Design chemical products to affect their desired function while minimizing their toxicity.
- **Safer Solvents and Auxiliaries:** Minimize the use of auxiliary substances wherever possible make them innocuous when used.
- **Design for Energy Efficiency:** Minimize the energy requirements of chemical processes and conduct synthetic methods at ambient temperature and pressure if possible.
- **Use of Renewable Feedstocks:** Use renewable raw material or feedstock rather whenever practicable.
- **Reduce Derivatives:** Minimize or avoid unnecessary derivatization if possible, which requires additional reagents and generate waste.
- **Catalysis:** Catalytic reagents are superior to stoichiometric reagents.
- **Design for Degradation:** Design chemical products so they break down into innocuous products that do not persist in the environment.
- **Real-time Analysis for Pollution Prevention:** Develop analytical methodologies needed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
- **Inherently Safer Chemistry for Accident Prevention:** Choose substances and the form of a substance used in a chemical process to minimize the potential for chemical accidents, including releases, explosions, and fires.

NCAC-SOT Treasurer's Report – November 17, 2011

by
Jessica Ryman-Rasmussen, Treasurer

Account activity since last report

(Dated May 31, 2011 in July 2011 Newsletter)

May 31, 2011 (Closing balance)				17007.02
Debits				
	Spring Symposium	Speaker travel	300.65	
	Fall Symposium (September 29, 2011)	Registrations 955.00 Expenses (Caterer, travel for one speaker*) 1449	494.00	
	Total		794.65	
Credits				
	Dues (renewals and new members)		50.00	
	Misc. deposits**		1530.00	
	Total		1580.00	
October 31, 2011* (Closing balance)				17792.37

*Most recent bank statement in my possession.

*Does not include travel claim (150.31) for one speaker that hasn't yet been reimbursed. Also does not include travel for speakers who have not yet submitted travel claims.

**October ledger from SOT not available to identify sources of deposits.

LABORATORY DIRECTOR, MEDLAB CONSULTING LLC, RALEIGH, NC

We are in search of a PhD board-certified in Toxicology or Chemistry, for example, to serve as Laboratory Director for High Complexity POLs across the country with minimal time requirements for good reimbursement. Please fax CV to 919-443-1272 or call Jeanne Crowle at 919-630-9499.

NATIONAL ACADEMY OF SCIENCES WORKSHOP

Emerging Technologies for Measuring Individual Exposomes
December 8-9, 2011
House of Sweden
2900 K Street NW
Washington, DC 20007

This workshop will take a close look at emerging technologies that can be used to gather individual exposure information based upon external and internal measurements. Presentations and discussions will explore which of the technologies are "ready now" and which are still "emerging" for use in environmental health research. Particular attention will be paid to the relative advantages and disadvantages of external and internal measurements for characterizing individual exposomes and for performing EWAS. Recent proof-of-concept studies will be highlighted and bioinformatic tools will be discussed. This synthesis should inform researchers and policy makers about the critical roles that the exposome concept and new technologies can play in understanding the origins of human diseases.

This workshop will be Webcast. Instructions on how to register for and access the Webcast will be available approximately 1 month before the workshop dates.

http://nas-sites.org/emergingscience/workshops/individual-exposomes/