



National Capital Area Chapter
Society of Toxicology Newsletter
- Electronic Edition -



July 2011

Issue No. 30
R. Mitkus, Editor

CHAPTER MISSION STATEMENT	1
MESSAGE FROM THE PRESIDENT	2
MESSAGE FROM THE GRADUATE STUDENT REPRESENTATIVES	3
NCAC OFFICERS LIST	4
2011 FALL SYMPOSIUM	5
SPRING SYMPOSIUM ABSTRACTS	5
TREASURER'S REPORT	8
POSITION ADVERTISEMENT	9
NORTH CAROLINA REGIONAL CHAPTER MEETNG	10
NIH GRADUATE SCHOOL OPEN HOUSE	11

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

Happy Summer to Everyone!

I am excited to have the privilege of serving as your president for the next year. First and foremost, thanks must be given to our outgoing officers. As President, Dr. Pamela Chamberlain ushered us through SOT's 50th anniversary year, which required NCAC participation in a number of activities not seen in a more "typical" year. These included receptions, special sessions at the national meeting, posters, a time capsule submission, and other events that I've probably forgotten. This was done with the help of the entire NCAC executive board, and through it all Pam was our fearless leader. Other officers whose terms have ended, and have ably supported NCAC-SOT over the past few years include Dr. Jennifer Sekowski, Dr. Thomas Flynn, and Dr. Matthew Smith. I want to welcome back the officers continuing their terms of service, as well as our new officers. There are four new faces within NCAC-SOT leadership. Dr. Cal Baier-Anderson is our new vice-President/President-elect, Dr. Linnzi Wright is our new Post-Doctoral Representative, Dr. Jessica Ryman-Rasmussen is our new Treasurer, and Ms. Anna Schlappal is our new Student Vice-Representative.

These new voices to the NCAC-SOT executive board have already brought some great ideas forward. For example, in addition to our communications through ToXchange (have you set up your profile yet?), we are now communicating via Facebook and Twitter. See the graduate student message for more information on how to link into these communities. I've been using ToXchange and Facebook and they are both great ways to exchange information. I haven't gotten to Twitter yet, but with the encouragement (and help) of our graduate students I'm sure I'll be there soon. Our goal is to reach as many people as possible. So whether it's through email, social media, snail mail or your ancient land line... we want you to be in the loop, and we want to hear from you!

In other events, Dr. Cal Baier-Anderson is planning a Fall Symposium focused on Green Chemistry. See the paragraph below for a complete description. This event will be held Thursday, September 29th at the National Library of Medicine's Lister Hill Auditorium; make sure to mark your calendars. Green Chemistry is a new topic for NCAC-SOT, but a timely one, and we look forward to seeing you there.

In addition to our Fall and Spring Symposia, NCAC-SOT will continue with our K-12 outreach activities. Our chapter has a long history of this outreach; our members have been and continue to be involved in science fairs, scouting activities, mentoring, and other educational programs. We already have a couple of events scheduled for the coming year, including the US Science & Engineering Festival (to be held on the Mall in Washington, DC). We will be asking for volunteers, so be looking for your invitation to volunteer (via our old and new communication mechanisms). Until then, I wish everyone a happy, healthy, and cool summer.

Laurie E Roszell, DABT, PhD
NCAC-SOT President

MESSAGE FROM THE GRADUATE STUDENT REPRESENTATIVES

Greetings NCAC students! I hope your summer is off to a good start! We, Colleen McLoughlin (student representative) and Anna Schlappal (student vice-representative) are very excited to be working together along with the executive committee! We look forward to representing you on the board and would like to hear any suggestions you may have for student events or ways for students to be involved in the chapter.

Mentors, we hope you will encourage your students to join and become involved in NCAC. The NCAC currently has a highly active member base; however we would like to have more student involvement. Joining NCAC as a student costs only \$10/year. There are a number of opportunities for students in the NCAC-SOT. In addition to our Fall and Spring symposia, we hold a yearly symposium focusing on topics of interest to students. These meetings provide a forum for students to present their research in a poster or oral presentation format, and network with local, national, and even international toxicologists. Additionally the NCAC offers several generous awards for poster competitions, including the Bern Schwetz Travel Award to offset costs of travel to the annual SOT meeting. The NCAC-SOT has members ranging from academia to private industry and federal sectors. The opportunity for expanded learning, varied experiences and professional connections makes the benefits of NCAC membership innumerable and invaluable.

We are also very excited to announce new ways to communicate with the NCAC leadership and members. In addition to ToXchange, you can find our Facebook group (SOT National Capital Area Chapter), or follow us on Twitter (@SOTNCAC)!

We are currently looking for student input on the student symposia as well as ideas/suggestions to create events that you would like to attend! Please take the time to give us feedback in this survey: <http://www.surveymonkey.com/s/3M7P6JK>.

You can also contact us personally, Colleen: mcloughlince@vcu.edu or Anna: aschlapp@umd.edu.

We can't wait 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

NCAC-SOT EXECUTIVE BOARD MEMBERS

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Upcoming Fall Symposium

On Thursday, September 29, 2011 the NCAC-SOT will host its Fall Symposium on “Green Chemistry”, to be held at Lister Hill Auditorium on the NIH Campus in Bethesda, MD. Green chemistry is the design of chemical products and processes that reduce or eliminate the use or generation of hazardous substances. Toxicologists have a vital role to play in the development of green chemistry, and the purpose of this symposium is to highlight the role of toxicology in green chemistry and to promote dialogue among scientists engaged in green chemistry activities. If you have any questions or suggestions, please contact the Symposium organizer, Cal Baier-Anderson at baier-anderson.caroline@epa.gov.

2011 Spring Symposium

Title: Current Trends in the Use of Non-Animal Data for Risk Assessment

Date: April 19, 2011

Location: NIH Lister Hill Center Auditorium, Bethesda, MD

Speakers and Abstracts

Abigail Jacobs, Center for Drug Evaluation and Research, USFDA – “Regulatory Use of Alternative Methods for Pharmaceuticals in the United States”

A wide range of alternative methods is used by drug developers during drug discovery to screen out undesired effects, such as an Ames positive, renal toxicity, cardiac toxicity, liver toxicity and phospholipidosis. Other alternative methods may be used during the development phase for drugs, such as genotoxicity, ocular corrosion, dermal corrosion, pyrogenicity, phototoxicity, dermal sensitization, liver metabolisms, and drug metabolic interactions. For regulatory drug development, a variety of in vitro methods is used most often to explain the mode of toxicity or help evaluate relevance to humans. There is flexibility in what kind of assays CDER/FDA can receive. However, the most challenging areas for replacing animals in drug development are being able to select the first dose of a drug for humans and being able to give persons thinking about getting pregnant or who becomes pregnant while on a drug, useful information. Most in vitro methods currently available have a number of limitations, including assessment of systemic effects and interactions, assessment of reversibility and late appearing effects, inability to mimic degradation in the stomach, metabolism (renal, and intestinal, as well as liver), and extrapolation from in vitro concentrations to in vivo doses.

The eventual goal is not to replace each current in vivo assay, one by one, but to apply new approaches.

Jack Fowle, Office of Pesticide Programs, USEPA – “Overview of OPP Use of Non-animal Data”

Thousands of regulatory decisions are made by EPA and others each year about the safety of commercial chemicals. Because pesticides are strong poisons the American public demands that their government make every effort to ensure that those pesticides in the marketplace won't hurt them or their pets or important plants and insects. Traditionally we have relied heavily on extensive animal testing to ensure that pesticides are safe. EPA is committed to developing alternative tests and recognizes that both scientific and political efforts are needed. This presentation will briefly discuss the use of non-animal data in OPP and the near-term efforts needed to develop and employ efficient means to screen large inventories of previously untested chemicals to identify those that require further testing and evaluation first. It will also describe the mid- to long-term efforts needed to build an enhanced understanding of toxicity pathways and human exposure to build hypothesis-based approaches to testing as well as the means to evaluate our confidence that the new testing approaches built on

alternative methods are at least as effective and protective of public health and the environment as the conventional testing approaches. This presentation will also describe efforts underway to work with partners throughout the world to advance a collaborative research agenda to develop the scientific basis for continuing to move to alternative tests.

Thomas Hartung, Johns Hopkins Bloomberg School of Public Health – “10 Years of ICCVAM: Challenges, Successes”

A decade of work to evaluate and implement alternative methods is a good moment to reflect on the achievements and the current process. The presenter had the privilege to work very closely with ICCVAM for almost seven years heading the European counterpart ECVAM. Europe and the United States further the development of new toxicological tools in different ways. While the replacement of animal tests has been promoted strongly in Europe over the last decades (following the 3Rs principles—reduce, replace, refine), in the United States the vision for a toxicology in the 21st century (Tox-21c), which was prompted by the National Research Council document only 4 years ago, dominates the discussion. In both cases, there is significant political support. However, while in Europe the horizontal animal welfare legislation from 1986 (which urges the use of 3Rs methods wherever possible) revised 2010 and cosmetics and chemical legislation are the primary drivers, in the United States it is mainly federal agencies, most prominently the U.S. EPA and more recently FDA; the former made the implementation of the NRC report their toxicity testing strategy only in 2009. This preempts such possible legislative measures as the reauthorization of the Toxic Substances Control Act (TSCA). The European implementation is characterized by substantial broad funding programs to develop 3Rs methods and can be termed a “bottom-up” approach; in contrast, the Tox-21 program represents a “top-down” approach, where programmed research is carried out and commissioned. It is postulated that the two approaches are two sides of the same coin, and instruct and complement each other. However, more importantly, if brought together they can result in a Human Toxicology Project and a real revolution in regulatory toxicology. The International harmonization of validation activities recently formalized as International Collaboration for Alternative Test Methods (ICATM) was a major step to increase efficiency and outreach to OECD, ICH and ICCR, the International organizations harmonizing testing approaches for chemical, drugs and cosmetics. This has resulted in strongly accelerated regulatory acceptance. At the same time, a relatively rigid process for validation has resulted, which requires substantial time and resources. The imperative comparison with the traditional test methods makes it difficult to improve the status quo. While the process was a proof of principle that International agreement on the usefulness of alternative methods and the possibility to substitute for traditional ones can be achieved, more complex hazards (e.g. systemic and chronic toxicities), new products (e.g. biological, cell therapies and nanomaterials) as well as new technologies (e.g. omics, high-throughput and image analysis) and integrated testing strategies represent challenges to this process. The hypothesis is put forward that formal validation needs to be complemented by other quality assurance processes for testing approaches not yet matured for formal validation. Evidence-based medicine might lend itself here as a role model.

Stan Barone, National Center for Environmental Assessment, USEPA – “Challenges and Opportunities in Putting High Throughput Chemical Risk Characterization into Real-world Practice”

Understanding of complex, interrelated environmental stressors and potential impacts on human and ecosystem health has grown tremendously in recent years. Basic and clinical sciences, however, have significantly outpaced risk assessment science. Insights into health and disease exist, but it is unclear how to incorporate this information into risk assessments with current methodologies. The practice of risk assessment will need to embrace a fundamental paradigm shift from a reliance on animal toxicology data derived primarily from rodent bioassays. The need for this shift is only made more immediate by the challenges of applying new types of data stemming from advances in computational toxicology and the huge volume of data that will be generated from the European Union’s Registration, Evaluation, and Authorization of Chemicals (REACH) Program. High throughput data will need to be translated into usable information to support science-based decisions in risk

assessment. The areas where this knowledge is expected to have the most impact is in defining toxicity pathways, informing risk assessors about interpretation of multiple modes of action for toxicity, and providing insight into human variability in key pathways and susceptible populations. The impacts of this information are expected to be qualitative and quantitative. For these new types of information to be incorporated quantitatively in risk assessments numerous challenges exist not the least of which is extrapolation from *in vitro* test systems to *in vivo* human health outcomes. However, the challenges are not insurmountable. The quantitative impacts of this new toxicity information will probably be seen first in cases of chemicals lacking significant data sets but for which toxicity fingerprints can be developed. (This abstract does reflect the Environmental Protection Agency policy).

Richard Judson, National Center for Computational Toxicology, USEPA – “Combined In Vitro and Modeling Approaches to Screening-level Risk Assessment”

The large number of untested chemicals in the environment is driving the need to develop methods to screen and prioritize chemicals for detailed testing. Here we describe a framework for estimating the human dose at which a chemical significantly alters a biological pathway *in vivo*, making use of *in vitro* assay data and an *in vitro*-derived pharmacokinetic model, coupled with estimates of population variability and uncertainty. The quantity we calculate, the Biological Pathway Altering Dose (BPAD), is analogous to current risk assessment metrics in that it combines dose-response data with analysis of uncertainty and population variability to arrive at conservative exposure limits. The analogy is closest when perturbation of a pathway is a key event in the Mode of Action (MOA) leading to a specified adverse outcome. Because BPADs are derived from relatively inexpensive, high-throughput screening (HTS) *in vitro* data, this approach can be applied to high-throughput risk assessments (HTRA) for thousands of data-poor environmental chemicals. We envisage the first step of HTRA to be an assessment of *in vitro* concentration-response relationships across biologically important pathways to derive Biological Pathway Altering Concentrations (BPAC). Pharmacokinetic (PK) modeling is then used to estimate the *in vivo* doses required to achieve the BPACs in the blood at steady state. Uncertainty and variability are incorporated in both the BPAC and the PK parameters and then combined to yield a probability distribution for the dose required to perturb the critical pathway. We finally define the BPADL as the lower confidence bound of this pathway-altering dose. This paper outlines a framework for using HTRA to estimate BPAD values; provides examples of the use of this approach, including comparison of BPAD values with published dose-response data from *in vivo* studies; and discusses challenges and alternative formulations. *This abstract does not necessarily reflect U.S. EPA policy.*

Martin Stephens, The Humane Society of the United States – “An NGO Perspective on Regulatory Acceptance of Non-animal Data and Related Issues” Abstract not provided.



NCAC-SOT Treasurer's Report – June 30, 2011

by
Jessica Ryman-Rasmussen, Treasurer

01/01/2011 (Opening balance)				20,008.57
Debits	Description	Notes		
	Fall Symposium (October 2010)	Recorded at SOT 1/20/2011; cleared on 2/23/2011	252.00	
	K-12 Outreach (March 2011)		105.30	
	Spring Meeting (March 2011)	Includes: Awards, hotel, printing expenses	5178.20	
	Fairfax Co. Science Fair (March 2011)		175.00	
	Spring Symposium (April 2011)	Includes: Awards, caterer, programs, poster boards	1888.00	
	Total		7598.50	
Credits				
	Dues (renewals and new members)		2900.00	
	Fall Symposium (October 2010)	Recorded at SOT 3/30/2011; cleared on 3/30/2011	166.95	
	Other	Deposits made by SOT to NCAC's account for which ledger is not yet available. Likely for NCAC SOT dues or Spring Symposium registrations paid directly to SOT.	1530.00	
	Total		4596.95	
May 31, 2011* (Closing balance)				17,007.02

*Most recent bank statement in my possession.

SCIENTIFIC PROGRAM MANAGER INTERNATIONAL LIFE SCIENCES INSTITUTE (ILSI)

ILSI North America seeks a Scientific Program Manager to provide scientific, technical, administrative and programmatic support to specific technical committees, subcommittees and/or project committees with ILSI NA. **Principal Responsibilities:** Committee Management (schedule meetings, prepare materials, coordinate committee activities, assist in activity status, monitor budgets, work with chairs to develop committee consensus for projects); and Scientific Responsibilities (stay abreast of relevant scientific/policy developments, assist in development of proposals/meeting materials/scientific publications, draft mission statements, establish and maintain coordination with key organizations). **Education:** Master's Degree in a scientific field such as toxicology, pharmacology or related field is required. Doctorate is beneficial. **Experience:** Minimum 5 years' relevant experience in a research organization/foundation, association, government agency, or consumer products industry. Specific experience in project management, scientific consulting and/or regulatory affairs is highly desirable. **KSAs:** Proven ability to function as a team member, develop and manage budgets, and perform hands-on project activities. Excellent written and verbal communication skills. Outstanding management/organizational ability. Proficient in MS Office.

Individuals interested in applying for this position should apply to HR@ilsa.org. ILSI is an EEO/Affirmative Action Employer M/F/D/V. To learn more about ILSI North America, go to <http://www.ilsa.org>.



North Carolina Society of Toxicology

2011 Fall Meeting

Date: Thursday, September 22, 2011

Meeting Theme: Epigenetics and Toxicology

Place: Rodbell Auditorium, NIEHS Campus, RTP, NC

Fall Meeting Activities Include:

Scientific Presentation by Experts in Epigenetics and Toxicology

Scientific Presentation by Winner of NCSOT President's Award for Research Competition

Career Panel Luncheon and Discussion for Postdocs and Students

Refreshments

Business Meeting (open to all)

Contact Michael Hughes (541-2169, hughes.michaelf@epa.gov) for more information

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Refreshments will be served

Learn about the variety
of evening courses.

Registration for
Fall 2011 will be
accepted.

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**from 4pm-7pm
on August 23, 2011
9101 Old Georgetown Rd.
Bethesda, MD 20814**