NATIONAL CAPITAL AREA CHAPTER
SOCIETY OF TOXICOLOGY NEWSLETTER
Electronic Edition

December 2006 Issue 22

Renew Your SOT and NCAC Membership at
http://www.toxicology.org/script/loginredirect2.asp?page=dues

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 annual meeting of the SOT.

MESSAGE FROM THE PRESIDENT

The Nation's Capital Chapter of the Society of Toxicology has been involved in a lot of very exciting activities. We recently had our Fall Symposium on "Computational Toxicology." Thanks go to Gary Burin for putting together a very informative program. It was well attended and all of the speakers were excellent. You can find out more information about the symposium in this newsletter. And watch for news about our spring symposium which will take place on May 23, 2007, at NIH. Our spring symposium includes a student poster competition so encourage all eligible students to apply. Another great opportunity for students will be our Career Day that will occur on January 31, 2007 at the University of Maryland, Baltimore Campus. It will be an excellent opportunity for graduate and post doctoral students to meet toxicologists from all the job sectors and to learn valuable strategies for finding a job. You can get more information on this event in the newsletter and on our website. Our chapter is also very involved with K-12 activities. We are planning to give out several awards at local County Science Fairs and to sponsor some grants for high school science teachers. More information will be made available on our website.

If you would like to become more involved with the NCAC, please let myself or one of the other officers know. We are looking for candidates to fill some of the officer positions on the NCAC board. I encourage you all to become more involved. It's a great way to meet other toxicologists and to contribute to the field of toxicology.

Please note that we will be having a NCAC dinner night at the 2007 SOT meeting on Tuesday (March 27th). The location and time will be posted on our website and please let us know if you are interested in attending this function.

Suzanne Fitzpatrick
301-827-4591

MESSAGE FROM THE NEWSLETTER EDITOR

This issue of the NCAC newsletter contains some of the usual features such as the reports from our president, student representative, and abstracts from the December symposium on “Computational Toxicology”. In addition, there is section on the Toxicology Scholar Program. The main purpose of the SOT sponsored program is to have professional toxicologists and advanced graduate students inform undergraduate students about the educational and career opportunities in toxicology. Please see page 4 for more details about this program which are provided Devon Graham.

The NCAC has a number of exciting events planned in 2007 including the upcoming career day and the spring symposium. In addition, the following local events may be of interest to the

at the White House Homeland Security Council, is giving a presentation on February 7th and this event is being hosted by the Association of Government Toxicologists. His presentation is titled "**What's new with Avian Flu**?" and his talk will take place in the Small Dining Room Uniformed Services University of the Health Sciences Bethesda, MD. For more details please visit the AGT website (http://www.agovtox.org/).

Another interesting local meeting is **The 32nd Annual Winter Meeting of The Toxicology Forum**, January 30-February 1, 2007, at the Westin Embassy Row Hotel, Washington, DC. The meeting will be covering topics such as 1.) Manufactured Nanoscale Materials: Identification and Management of Potential Risk 2.) Perchloroethylene (PERC): Approaches to Evaluating Uncertainty in Health Risk Assessment 3.) Evidence based toxicology: Are we ready? Furthermore, the meeting will be providing updates on "Toxicogenomics and Predictive Toxicology (NAS/NRC Report)" and "Emerging Approaches to Toxicity Testing and Risk Assessment" just to name a few. For more details, please go to this website (http://www.toxforum.org/html/winter_meeting.html).

Please feel free to contact me with seminars or upcoming not-for-profit events in Virginia, Maryland and the District of Columbia that may be of interest to toxicologists in our area. Please send these announcements to my attention (Michael.Orr@fda.hhs.gov), as we are very willing to publicize upcoming events.

If you are interested in joining NCAC, an application for membership can be found at the end of the newsletter. Feel free to distribute this edition of the newsletter to colleagues who may be interested in joining our local chapter. The cost is nominal ($20 for full membership, $10 for student membership) and membership in the local chapter is an excellent introduction to local activities in the toxicology field. Additional information on our local chapter can be found at our website (http://www.toxicology.org/isot/rc/ncac/default.htm).

Mike Orr
301-796-1604

MESSAGE FROM THE STUDENT REPRESENTATIVE

It's that time of year again! Our annual **Student Day** will be held on **Wednesday, January 31st, 2007**, at the University of Maryland, Baltimore County campus. This year's program is entitled "Life after Graduation: Career Opportunities for Toxicologists", and will include speakers from government, academia, industry, public health and more. Did we mention that registration is *free* if you RSVP prior to the event? Well, it is, so please make plans to join us then. Fliers and registration information are circulating now, so if you have not received anything yet, please let us know. In fact, you can now contact the student representatives via a new centralized email account: **ncac.student@gmail.com**. We look forward to hearing any questions, comments or concerns you might have regarding student activities in the NCAC. We are also able to bring any issues before the SOT's Student Advisory Committee, which oversees student involvement in the Society, so do not hesitate to contact us. We'll see you on the 31st!

Chris and I look forward to meeting each of you at this year's symposia. If you have any comments, questions or suggestions, please feel free to contact us at dgrah001@umaryland.edu or shethcm@vcu.edu.

Devon Graham and Christopher Sheth

Toxicology Scholar Program

Devon Graham, a Ph.D. student from the University of Maryland, Baltimore, was awarded a travel grant via SOT's Toxicology Scholars Program. The program is designed to promote awareness of toxicological research to undergraduate students in liberal arts colleges that offer little or no toxicology training. Devon visited her *alma mater*, Allegheny College, in Meadville, Pennsylvania, where she spoke to students and faculty in two different settings. The first was at a research seminar in which Devon described her work based on the neurotoxic effects of methamphetamine in drug-tolerant rodents. She also spoke to students to an upper-level biology class about both her research and career and educational opportunities in toxicology. In view of the success of this event, NCAC members are encouraged to take advantage of the Toxicology Scholars Program. Information regarding the application can be found at http://www.toxicology.org/ai/eo/toxscholar.asp. Please feel free to contact Devon at dgrah001@umaryland.edu for more information on the visit or on the program itself.

EXECUTIVE COMMITTEE MEMBERS

National Capital Area Chapter – Society of Toxicology

President:	Suzanne Fitzpatrick (’06-’07) US FDA 301-827-4591 sfitzpat@oc.fda.gov
Vice-President/ President-Elect	Gary Burin (’06-’07) Technology Sciences Group Inc. 202-828-8980 gburin@tsgusa.com
Immediate Past President	Harry Milman ('05-'06) ToxNetwork.com 301-871-6714 hmilman@verizon.net
Secretary:	Deborah Burgin (’06-’09) US Environmental Protection Agency 202-566-0269 burgin.deborah@epa.gov
Treasurer:	Jennifer Weeks Sekowski ('05-‘08) US Army CHPPM 410-436-8774 jennifer.sekowski@us.army.mil
Councilors:	Michael Orr ('06-'09) US Food and Drug Administration 301-796-1604 michael.orr@fda.hhs.gov
	Lynn Flowers (‘04-‘07) US EPA 202-564-1537 Flowers.lynn@epa.gov
	Thomas Flynn (‘05-‘08) US Food and Drug Administration 301-827-8382 thomas.flynn@fda.hhs.gov
Student Representative	Devon Graham (’06-’07) University of Maryland 410-550-1532 dgrah001@umaryland.edu
Student Vice- Representative	Christopher Sheth (’06-’07) Virginia Commonwealth University shethcm@vcu.edu

ABSTRACTS FROM DECEMBER, 2006 NCAC-SOT SYMPOSIUM

The NIH Chemical Genomics Center: Generating datasets for computational toxicology

Christopher P. Austin, M.D. Director
NIH Chemical Genomics Center
National Human Genome Research Institute
National Institutes of Health

Assessment of toxicity has traditionally been *in vivo*, but such studies are low-throughput, often costly, and inconsistently predictive of human toxicity. *In vitro* approaches would potentially be less costly and time consuming and more easily connected to molecular mechanisms, but would have to be correlated to *in vivo* data to be useful. To evaluate the utility of cellular proxies for *in vivo* toxicity, the National Toxicology Program (NTP), the NIH Chemical Genomics Center (NCGC), and the Environmental Protection Agency (EPA) have established a collaboration to generate data on the effects of known toxicants in cell-based and cell-free assays relevant to toxicity. A collection of 1408 compounds assembled by the NTP is being tested by the NCGC using Quantitative High Throughput Screening (qHTS) across multiple assays of cellular toxicity and biochemical/genetic pathways implicated in toxic responses, using human and rodent cell lines derived from tissues commonly affected by organ toxicity. The data generated show that qHTS produces reliable, reproducible, and interpretable data across the 1408 compounds in multiple cell lines with different assay readouts. The collaboration is now being expanded to a greater number of compounds, including structurally-related compounds that differ in toxicological activity as well as active ingredients in pesticide formulations of interest to the EPA, and to a greater number of readouts and assay conditions. Data are being deposited into PubChem for use by research community.

Emerging Non-clinical QSAR Predictive Toxicology Applications for Pharmaceuticals at the FDA

Joseph Contrera, Ph.D.
Center for Drug Evaluation and Research
U. S. FDA

Abstract Not Available

ETHICAL Computational Toxicology: Its use and application in the Pharmaceutical Industry

Nigel Greene, Ph.D.
Drug Safety Research & Development
Pfizer Global Research and Development
Groton/New London Laboratories

Social demands to ensure the public safety of new drugs whilst maintaining a steady flow of new and more effective medicines presents the pharmaceutical industry with the a significant challenge of identifying and managing the risks presented by an increasingly large number of novel compounds. Often initial assessments of safety are made in the absence of high quality toxicology data as generating this data would take many years and millions of dollars for each compound under review. As a result, the industry has been seeking ways to prioritize these new compounds according to their potential for adverse effects to humans.

Computational approaches to hazard identification and risk assessment offer significant

advantages but their application is not without its drawbacks. On the positive side, these types of approaches to hazard assessment are very fast and cheap to run once they have been successfully implemented. In addition, these approaches offer a highly attractive public relations solution in view of the increasing demands to refine, reduce or replace animals in laboratory experiments. However, questions still exist about their ability to accurately distinguish between toxic and non-toxic molecules and their effectiveness in ensuring public safety.

This presentation will highlight recent experiences in the practical application of computational toxicology in a pharmaceutical company. It will illustrate how structure-based approaches can be applied to complex toxicological endpoints such as hepatotoxicity, and look at using high through-put assay data to predict toxicity and finally how these approaches are being used to aid in decision-making (e.g. development, risk management, exposure controls, and prioritization of biological testing).

The use of QSAR Analysis in the Safety Evaluation of Food Additives and Botanicals.

Luis Valerio, Ph.D.
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety, FDA, College Park MD

The safety of chemical entities added to conventional food falls under the regulatory auspices of the Center for Food Safety and Applied Nutrition (CFSAN), Office of Food Additive Safety (OFAS) at the U.S. FDA. Assessing the safety of food additives is important to ensuring public health by avoiding human exposure to potentially harmful substances. Carcinogenesis is often considered the most sensitive endpoint in toxicological review of food additives, and the Federal Food Drug & Cosmetic Act (21 U.S.C. 348) provides a clause (Delaney) (section 409(c)(3)(A)), which does not permit a food additive to be deemed safe if it is found to induce cancer when ingested by man or animal. The regulatory requirements for testing the carcinogenic potential of a food additive depend on a number of factors established within the regulatory framework. Some food additives under review at OFAS are found to have insufficient experimental evidence to assess carcinogenic potential. Moreover, it is well known that many active constituents from botanical (plant-derived) materials have not tested in long-term animal studies such as a rodent cancer bioassay. Therefore, there is a need for the development and validation of an efficient, reliable, and sensitive methodological approach for use in screening the thousands of untested chemicals natural and synthetic for the most sensitive endpoints, such as carcinogenicity. A key tool emerging to support the risk management of this issue is predictive toxicological software programs employing quantitative structure-activity relationship (QSAR) modeling using pre-existing data and characteristics of chemical structural attributes of subject compounds. At CFSAN/OFAS, several QSAR software programs are currently under evaluation for their performance and use in predicting the rodent carcinogenic and genotoxic potential of small organic compounds directly added to or migrating into the food matrix from food packaging materials. These programs include MultiCASE ToxLite, MDL-QSAR, and Oncologic. Predictions are taken into consideration using a weight-of-evidence approach with other relevant information such as exposure, chemical structural alerts, and available biological data found to be appropriate for a safety assessment. Examples for the application of QSAR analysis at OFAS will be given in relation to substances reviewed for safety in the Food Contact Notification Program, and the results of a QSAR evaluation study on the predictive performance of MDL-QSAR in screening naturally occurring dietary constituents from edible plant-based food and toxic botanical materials. Finally, the presentation will review the utility and limitations of these QSAR software programs as a regulatory decision support tool for screening and prioritizing the carcinogenic risk of ingredients added to food.

Prediction of pharmaceutical clinical adverse effects using QSAR software and a relational database constructed from FDA/CDER and MDL-Elsevier PharmaPendium Records

Ed Matthews, Ph.D.
Center for Drug Evaluation and Research
FDA, Rockville MD

The Informatics and Computational Safety Analysis Staff (ICSAS) at FDA's Center for Drug Evaluation and Research (CDER) has created a new database of pharmaceutical adverse effects (AEs) detected in clinical trials and Agency post market surveillance programs. The database currently contains ~9,500,000 AE drug records from FDA/CDER's post market surveillance, including the Spontaneous Reporting System (SRS, 1969-1997) and Adverse Event Reporting System (AERS, 1998-2006). It also contains labeling and literature AE data from Mosby's Drug Consult (2,000 drug monographs), Meyler's Side Effects of Drugs (40,000 references), and DRUGDEX (MicroMedex). All of these AE data are linked to a common medical thesaurus of ~11,500 terms derived from MedDRA (Level 3) and SRS COSTAR vocabularies. The AEs are also linked to the drug generic name (~4,000 drug products); chemical structure (mol and SMILES format); and the pharmaceutical drug class, clinical indications, and receptor targets. Retrieval of these data was greatly facilitated using MDL/Elsevier's new PharmaPendium™ software which was developed as a concept product of the CRADA between FDA/CDER and MDL Information Systems. Our AE database is being configured using weight of evidence (WoE) paradigms in order to identify drug products with biologically and statistically significant AE findings. To account for variations in the AE reports in the SRS and AERS databases due to different patient populations for each drug, we estimated patient exposure based on the number of reports for each drug expressed as a percentage of the total number of reports in the AE database. A positive finding for a single AE endpoint required a significant increase in the observed frequency of reporting over the expected frequency of AEs. To simplify the complexity of the AE findings for the different organ systems, the AEs were clustered and bundled according to the relative concordance of the observations of inactive and active molecules. The WoE AE database is then being used to construct quantitative structure-activity relationship (QSAR) models to predict the AEs of untested chemicals. QSAR models are being constructed using the *MC4PC* program (MultiCASE, Inc.); the pharmacological activities of the drugs are being predicted using *BioEpisteme* program (Prous Science). The first phase of this project has focused on developing AE data sets and QSAR models for the liver and kidney organ systems and results are presented for the liver. The long range goal of this investigation is to have AE QSAR models for all of the major organ systems.

Environmental chemical hazard prediction by high-throughput screening and genomics approaches in the ToxCast program of the US Environmental Protection Agency

Keith Houck. Ph.D
National Center for Computational Toxicology
Office of Research and Development
US EPA
Research Triangle Park NC

Abstract Not Available

Applying data mining approaches to predictive toxicology

Chihae Yang, Ph.D
Leadscope Inc.

Dublin Ohio

Abstract Not Available

NATIONAL CAPITAL AREA SOT, ANNUAL STUDENT DAY SYMPOSIUM

Mark your calendar-

Topic: **"Life After Graduation: Career Opportunities for Toxicologists"**

Location: University of Maryland Baltimore County, Catonsville, MD

Date: January 31, 2007

Registration is **FREE** if received by 5:00 pm January 30th.

TREASURERS REPORT

November 14, 2006

I. Official checking account balance (10/30/06 statement): $16,550.17

II. Not yet reflected in bank statement (as of 11/14/06)

New memberships $40.00
full (1)- $20, student (2)- $20

III. Unofficial Balance as of 11/14/06: $16,590.17

Respectfully Submitted,
Jennifer W. Sekowski
14 November, 2006

National Capital Area

MEMBERSHIP APPLICATION

Name: _____

Affiliation: _____

Address _____

_____

City: _____

State: _____ Zip Code: _____

Area Code: _____ Phone: _____FAX:_____

E-mail: _____

Membership Type _____ Full Member ($20) _____ Student ($10)

Please check the most appropriate responses:

SOT Member

_____ Yes

_____ No

Highest Degree Attained

_____ A.S.
_____ B.A.
_____ B.S.
_____ D.V.M.
_____ D.V.M./Ph.D.
_____ M.D.
_____ M.D./Ph.D.
_____ M.P.H.
_____ M.S.
_____ M.A.
_____ Ph.D.
_____ Sc.D.
_____ V.M.D.
_____ V.M.D./Ph.D.

Type of Affiliation

_____ Academia
_____ Consulting
_____ Contract Lab
_____ Government
_____ Industry-Chemical/Petroleum
_____ Industry- Pharmaceutical
_____ Industry- Other
_____ Other- _____

Please complete the information above and send with a check, money order or credit card (payable to [specific RC], no POs) to the address below. The chapter to which you are applying will review your application and you will be notified within 30 days. Those not accepted will receive a full refund. *Current RC members: please do not use this form since your renewal dues are billed annually through SOT.*

Payment Type: Money Order_____ Check _____ Credit Card _____
Credit Card # _____ Exp date _____
Name on Card _____

Send to:

Jennifer Weeks Sekowski, Treasurer
US Army
CHPPM ATTN MCHBS TS THE, 5158 Blackhawk Road
Aberdeen Proving Ground, MD 21010