National Capital Area Chapter
Society of Toxicology Newsletter

Electronic Edition

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Editor—Gary Burin

DON'T FORGET TO REGISTER EARLY FOR THE SOT ANNUAL MEETING
REGISTER AT https://www.eshow2000.com/toxexpo/registration.cfm

Message from the President by Sid Green

This is the first opportunity I have had to communicate with you by way of our newsletter. First let me begin by thanking those members of the chapter who have seen fit to participate in the chapter's activities, either by serving on committees, or participating in or otherwise helping with the symposia and student's day. I would also like to say that I am fortunate to have the group of officers, including the student representatives, who are currently working with the chapter. They have truly done an outstanding job.

We have been very busy attempting to make certain you view the chapter as a valuable asset. One of the activities that takes the most planning and time is the symposia/students day. I know that surprised no one, but I make that point to solicit your help when called on to either suggest speakers, topics, or help in making those events successful. One of the ways you can help is by attending the sessions. Most have agreed that the topics over the past years have been extremely interesting, but that has not really translated into increased attendance. If you have a suggestion for a topic, give Dr. David Kram a call or contact any of the officers of the chapter.

SOT headquarters has requested we name a Web Liaison person to work with headquarters to keep our chapter's site current and posted with information that helps the members and showcases our chapter's activities. Dr. Thomas Flynn of the FDA has accepted that role and we intend to improve on our website with his able assistance. Please free to make any suggestions you may have to Tom or any of the officers of the chapter.

Also the organizers of the national meeting have soliciting our help in making the Education Committee's efforts a success at the Annual Meeting in Baltimore on March 21-25. Your response to this solicitation was truly outstanding. Members volunteered as Mentors (escorting, explaining the meeting, subject matter) for the teachers expected to attend. Others offered to make presentations at the Education Committee's program. These presentations will address something that is of interest to the state of Maryland.

So you see, there are lots of ways you can help the chapter, and I encourage you to make an effort to do so. We are really here to serve you, and I happen to think we best serve when we have an active and interested membership.

NCAC-SOT Executive Board Members – 2003-2004

President:	Sidney Green ('03-'04) Howard University 202-806-9748; sidgreen@howard.edu
Vice-President/ President-elect:	David Jacobson-Kram ('03-'04) Food and Drug Administration 301-594-5671; jacobsonkram@cder.fda.gov
Immediate Past President:	Susan Makris ('03-'04) Environmental Protection Agency 703-305-5222; makris.susan@epa.gov
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Treasurer:	Laurie Roszell ('02-'05) US Army CHPPM 410-436-8774; laurie.roszell@apg.amedd.army.mil
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Student Representative	Robert Mitkus ('03-'04) University of Maryland 410-706-5153; rmitk001@umaryland.edu
Student Vice- Representative	Melinda Pomeroy ('03-'04) Virginia Polytechnic Institute and State University 540-231-1887; mpomeroy@vt..edu

Note: Ben Fisher (Covance Laboratories), who was elected to the position of Councilor (Newsletter Editor) in May 2003, resigned this position due to extensive job-related responsibilities. Gary Burin (Technology Sciences Group), who was also on the May 2003 ballot, has agreed to step into this role and will serve as Newsletter Editor through 2006. The Executive Board extends heartfelt thanks to both Ben and Gary for their service to the NCAC-SOT!

Fall Symposium

Topic: **Animal Models for Safety and Efficacy Testing of Agents that can not be Tested in Humans**

Location: Howard University, Towers Auditorium,Washington, DC
Date: November 18, 2003

The goal of this symposium was to help educate toxicologists and generate discussion about the use of animals safety and efficacy testing when the conduct of such studies in human populations would be considered unethi This regulation, often called the "Animal Rule" was published in the Federal Register in May of 2002. This regulation specifies that animal studies alone can be used to demonstrate effectiveness when: 1. The pathophysiological mechanism for the toxicity of the substance (chemical, biological, radiological, or nuclear) its treatment or prevention is well understood, 2. The drug effect is demonstrated in two animal species, unless species has been well characterized, 3. The endpoint in animal studies is clearly related to the human endpoint, PK/PD data are available to allow selection of an effective human dose. Examples of drugs and biologicals approved under the animal rule were presented.

Speakers and presentation titles:

Tracey MacGill, Ph.D., US FDA -- **Use of Animal Models When Ethics Prohibit Use of Human Subjects: Examples and Challenges**

The recent heightened threat of biological, chemical, radiological or nuclear attacks by terrorists has resulted in a critical need to develop medical countermeasures against these agents. The approval of a new drug product by the U. S. Food and Drug Administration (FDA) requires "substantial evidence", that is, a demonstration of safety for use in humans and efficacy for the specified indication under the conditions of use. Historically, the requirement of substantial evidence has been met through the conduct of adequate and well-controlled clinical studies. It is widely accepted that intentional exposure of human volunteers to the extreme toxicity of threat agents would be unethical. Natural or accidental exposures are rare, making it infeasible to conduct clinical trials for many of the threat agents. For these reasons, the FDA promulgated 21 CFR 314 Subpart I (the "Animal Efficacy Rule") in 2002. Under this rule, animal data may be accepted as primary evidence of efficacy and used in conjunction with human safety data as the basis of approval, when specific criteria can be met. Under this rule the development of validated animal models of human disease and the ability to interpret and extrapolate animal pharmacodynamics data to effective exposure in humans will be critical for development of drug countermeasures. This presentation will describe the Animal Efficacy Rule, current strategies for using the Rule, and challenges that may be encountered in the development and approval of products under the Rule.

Daniel P. Maher, Ph.D., Ph.L., Catholic University of America -- **Certainty and Benefit in Medical Research Human Beings**

This paper argues that the effort to make medicine scientific leads to a fundamental difficulty for any effort to articulate adequate ethical standards for research on human beings. Admiration for scientific certainty entails a depreciation for any kind of thinking or judgment that is not scientifically verified or verifiable. This depreciates in particular the cognitive value of the moral standards that place limits on the conduct of medical research. From the perspective of the standards of scientific certainty, any moral judgment tends to appear as a more or less arbitrary constraint imposed by those who have political or social power to define what is morally acceptable. This fundamental difficulty undermines confidence in the very standards and goals that govern the practice of medicine. The essay concludes with a summary of three sorts of arguments that have been proposed to justify medical research on human beings in virtue of the benefits that may be

hoped to arise from it.

David Green, Ph.D., US FDA -- **Rising to the Challenge – the FDA's New Rule Using Animal Efficacy Da Approval of New Drugs and Biologics**

In response to the public need to make available countermeasures to various threat agents that may be used by terrorists, FDA published the document titled, "New Drug and Biological Products: Evidence Needed to Demonstrate Effectiveness When Human Efficacy Studies Are Not Ethical or Feasible" or so-called "Animal Rule." This new standard for the approval of drugs and biological products is a challenge to both the FDA and developers of new therapeutics. It is a challenge to FDA in terms of maintaining its high standards, particularly for measures of clinical efficacy, while departing from traditional methods and also for developers to be innovative and diligent in satisfying the criteria as set forth by FDA. A wide variety of drugs and biologics are potentially subject to the new rule, as medical countermeasures will be used in a diverse set of situations and involve various clinical populations. Previously drugs and biologics that were used as countermeasures could only be authorized for use under an IND. This process was difficult and cumbersome to use in emergencies. Fundamentally under the rule, animals will substitute for people to determine the efficacy countermeasures to threat agents and these findings will be extrapolated from animals to people. To perform this task in a scientifically valid fashion requires a careful consideration of several factors such mechanisms of action for the toxin and therapeutic as well as relative pharmacokinetics and pharmacodyanmics between species. The rule sets out basic principles to follow in devising and conducting studies including the use of GLP procedures. Although a challenge to implement, the first approval using the animal rule was pyridostigmine for pretreatment against poisoning by the nerve agent soman.

Doris Snow, Ph.D., Dynaport Corporation -- **Product Development Challenges When Applying the Anima**

The Animal Rule has provided biodefense vaccine manufacturers an incredible opportunity to obtain licensure of unique products; however, with opportunity, comes many challenges. The Animal Rule is not a means to obtain accelerated approval, nor does it provide a short cut to licensure. There are many product development challenges, including design strategy challenges, facility challenges, manufacturing challenges, and clinical trial design challenges. It is important to identify and develop relevant animal models, and design studies that will support the label indication. It is essential to plan early and communicate frequently on the design and purpose of pivotal animal studies with the FDA.

Stephen Hundley, Ph.D., US FDA -- **Ciprofloxacin and Inhalation Anthrax: Primate Model for Effectiven**

FDA approved ciprofloxacin, a fluoroquinolone antimicrobial, for Inhalational Anthrax indication in late August, 2000. This approval preceded the final promulgation of the "Animal Rule" in May, 2002. The ciprofloxacin submission by Bayer Pharmaceuticals in part consisted of a rhesus monkey study conducted in late summer and fall of 1990 by the United States Army Medical Research Institute of Infectious Diseases (USAMRIID). The USAMRIID study demonstrated that rhesus monkeys exposed by inhalation to weaponized anthrax spores in quantities representing 5- to 10-fold the LD_{50}, and were treated with ciprofloxacin for 30 days had survival rates equivalent to concurrent groups of monkeys dosed for the same timeperiod with doxycycline or penicillin (Friedlander, et.al., J. Infect. Dis., 167:1239-1242, 1993). Experimental data with rhesus monkeys as far back as 1956, and accidental exposure cases to humans from Sverdlovsk, USSR, in 1979, indicated that the pathophysiology of inhalational anthrax in rhesus monkeys

was similar to the human case studies from Sverdlovsk.

The persistence of anthrax spores in the lung and mediastinum for several weeks following inhalation exposure and continued dosing with antimicrobials was confirmed in the USAMRIID study based on one of ten monkeys that survived during the 30-day post-anthrax spore exposure period while being administered ciprofloxacin but died due to anthrax within six days of the cessation of ciprofloxacin therapy. Similar observations were made in the case studies from the Sverdlovsk incident with other antimicrobials. These data suggested to the FDA that ciprofloxacin therapy needed to be for 60 days following inhalation exposure to anthrax spores. Plasma ciprofloxacin levels were determined in rhesus monkeys on five different days of dosing during the 30-day dosing period (125 mg, bid 12 hours). The peak and trough plasma levels for ciprofloxacin were similar to plasma values from human patients receiving 500 mg, bid 12 hours, for previously approved indications. Therefore, the approved indication for Inhalational Anthrax is 500 mg, bid, 12 hours for 60 days. The approval justification states the following: "Ciprofloxacin serum concentrations achieved in humans serve as a surrogate endpoint reasonably likely to predict clinical benefit and provide the basis for this indication." The experiences with the Inhaltional Anthrax indication impacted the development of the "Animal Rule" with regard to the types of animal studies required to demonstrate effectiveness for disease states with high mortality rates that cannot be feasibly or ethically evaluated in human clinical trials.

John Carley, Ph.D., US EPA – **Grappling with the Acceptability of Already- Completed Third-Party Hum Research at EPA**

Abstract not available.

Jack Fowle, Ph.D., US EPA -- **Computational Toxicology: Application to Human Health**

Many challenges prevent EPA for accurately knowing the true nature of risk from exposure to environmental chemicals and other agents so EPA must use assumptions and other policy choices in its risk assessments. Several recent technological advances now make it possible to develop molecular profiles using genomic, proteomic and metabonomic methods in order to identify the impacts that chemicals have on living organisms or the environment. Parallel to efforts in genomics there have been major advances in computer speed and access to data It is now possible to develop ways to evaluate the vast amounts of information created by the omic" technologies using data mining tools made possible by rapid advances in computational storage capacity and speed. These are being harnessed by EPA in its Computational Toxicology program to understand the cascade of events from exposure to disease and to provide tools, methods and models to improve risk assessment by developing ways to prioritize and rank chemicals for testing and to make the testing process more efficient. The application of computational toxicology to endocrine disrupting compounds was used to illustrate how the approach can improve ways to understand chemical transformation and metabolism, exposure indicators, dose metrics to better define toxicologically relevant doses, and how it can be used to characterize toxicity pathways to understand and predict how xenobiotics interact with biological systems. The goals are to improve quantitative structure activity relationship (QSAR) and other computational approaches, to develop pollution prevention strategies by developing the means to estimate potential impacts a candidate chemical may have after release into the environment, and to develop high throughput screening approaches as a rapid efficient means to provide preliminary data to rank chemicals for testing and evaluation. The challenges facing EPA in terms of resources, matching needed expertise with current capabilities and understanding how to interpret genomic data and linking the science to inform decision was also described. It was noted that in order to be able to use genomics data for risk

assessment EPA needs to ensure
relevance, and the approaches have to be feasible, not only technically but within the context of EPA's laws, resources and politics.

Student Day

Topic: **2003 Career Enhancement Day for Graduate Students and Post-Docs: Skills You Can Use for Your Future: Interviewing**

Location: Howard University Hospital Complex, Cancer Center, Washington, DC
Date: November 19, 2003

Topics and speakers:

Interviewing skills for a Position at a State Organization
Kent Carlson, PhD, Biologist, OPP/Biopesticides and Pollution Prevention Division, USEPA; former Toxicologist/Environmental Specialist, Maryland Department of the Environment

State toxicology positions offer the potential to experience regional, state-wide, and local issues. For this reason, they are often highly desired as a training ground for a career in toxicology. State budgetary deficits have constrained the number of toxicology positions, however, and available positions are highly competitive. Utilizing the appropriate approach in interviews is critical, therefore, for successfully obtaining a State Toxicologist position. Opportunities, requirements, and interviewing tips for the position of Toxicologist with the Maryland Department of the Environment will be discussed.

Interviewing skills for an Academic Assistant Professor Position (Teaching primary, research secondary) *Robert Resau, PhD*, The Community College of Baltimore County

There are numerous and varied colleges and universities where teaching is the primary responsibility of the faculty member and research is secondary. Some of these institutions do not expect any research effort at all. Others require research involving undergraduates, and still others expect occasional publications from the faculty member. These differences are very substantial, and require that the candidates for any given position know which alternatives they prefer, and investigate the specific characteristics of the institution offering the position. This presentation explores how to use such information to best advantage in the interview.

Interviewing skills for an Academic Post-doctoral Position *Marion Ehrich, PhD, DVM, D.A.B.T.*, Virginia-Maryland Regional College of Veterinary Medicine, President, Society of Toxicology

The purpose of post-doctoral training is to provide the new toxicologist with experience as a semi-independent investigator, to ease the transition to an independent investigator. Responsibilities are considerably greater than those of a graduate student, and may include exploring new frontiers for his/her mentor, managing a project (including laboratory personnel working on the project), and/or contributing to proposals that increase laboratory funding. Post-doctoral training is best done in a new environment, so the interviewer will ask why the applicant chose to do post-doctoral training, why this particular position is of

interest, what the applicant can bring to the laboratory, the expectations of the applicant while employed as a post-doctoral research associate, and plans that go beyond the post-doctoral appointment. In addition to answering these questions to the best of the applicant's ability, it is important that he/she be honest about date available. To come to the interview with knowledge of current and past work of the laboratory contributes to creating a favorable impression.

Interviewing skills for an Academic Assistant Professor Position (research primary, teaching secondary) *John Groopman, PhD,* Chair, Department of Environmental Health Sciences, Johns Hopkins University

Abstract not available.

The Federal Hiring Process and What Interviewers Can and Can not Ask by Law

Angela Mosby, Human Resources Officer, Region III, USEPA *Robert J. Mitkus, Sr.*, Deputy Director, Office of Communications and Government Relations, Region III, USEPA

This presentation will provide an overview of the federal and EPA hiring system and process, merit systems principles, prohibited personnel practices, OPM interviewing research, the EPA interview process and the types of questions encountered therein.

HIRED! Interviewing with Power, Polish and Presence

Nancy Grimshaw, CCP, PHR, Office of Human Resource Services, University of Maryland Baltimore

We've all heard that you never get a second chance to make a first impression. This session will give you practical advice on how to interview at your best by overcoming everything from nerves, to tough questions to a bad hair day. Find out why "taking up space" isn't just for astronauts; it may help get you noticed! Learn effective practice techniques to increase confidence. We'll even solve the problem of how to dress for interviews in "office casual" environments.

Interviewing skills for a Research Position in Industry

James C. Lamb, IV, Ph.D., D.A.B.T., Senior Vice President, The Weinberg Group Inc.; former Senior Vice-President, Blasland, Bouck & Lee, Inc. (BBL Sciences)

Abstract not available.

Interviewing skills for a Research Post-doctoral Position in the Federal Government

Robert J. Mitkus, Sr., Deputy Director, Office of Communications and Government Relations, USEPA

Angela Mosby, Human Resources Officer, USEPA Region III

Research indicates that past performance is an accurate indicator of future performance. As an extension of this, we will discuss types of interviews; benefits; how to plan for a logical, structured interview; identifying

needed job skills for positions and describing them in objective, behavioral terms; guidelines for developing questions; common interview questions; steps in conducting successful interviews; and how to handle difficult interviewing situations.

Treasurer Report by Laurie Roszell

The following report details the income and expenses incurred as a result of the Fall Symposium and Student Day (November 18-19, 2003), and summarizes the current status of NCAC-SOT assets.

Meeting-related income:

		No.	Received
Registration:			
	Symposium		
	Members		
	Regular (35)	18	$ 630
	Student (0)	6	$ 0
	Non-Members		
	Regular (45)	48	$2160
	Student (10)	5	$ 50
	Student Day		
	Members (5)	8	$ 40
	Non-Members (10)	3	$ 30
Membership			
	Regular (20)	3	$ 60
	Student (10)	1	$ 10
	Total income:		$2980

Meeting-related expenses:

Secretarial/Postage:	$ 24.00 (Fall newsletter, Symposium)
Printing (program)	$ 0.00
Speaker(s):	$ 474.10
Room rental	$ 0.00
Catering:	$1428.75
Audio/visual	$ 0.00
Poster boards	$ 0.00
Speaker gifts	$ 93.78
Total meeting expenses:	$ 2020.63

Net meeting income: $959.37

Current Assets:

Checking account (11/28/2003):	$ 4538.14.92
Annual net assets (Nov 2003):	$ 5464.39

Survey - Informal Social Gathering of NCAC-SOT Members at SOT Meeting in Baltimore by Rob Mitkus

Many of us are familiar with regional chapters sponsoring and advertising a gathering of its members at SOT each year, and why should we be any different! Indeed holding the 43rd Annual Society of Toxicology Meeting in Baltimore, MD provides our regional chapter members with a perfect opportunity to gather together in an informal and relaxing atmosphere. As a result, the Executive Board has decided to look into holding a lunch or dinner away from the Baltimore Convention Center for NCAC members at SOT in March. We would like to get an idea of the level of your interest, however, before making any plans. If you would, kindly email Rob Mitkus at rmitk001@umaryland.edu by Jan. 31 to let him know if you would be interested in attending either a lunch or a dinner at one of Baltimore's many local restaurants during our next national meeting. Thanks!

Student Travel Awards for SOT Meeting in Baltimore

The NCAC-SOT offers full-time graduate students and post-doctorate students an opportunity to compete for the Bern Schwetz Student Travel Award (a cash award for the support of student travel to the annual SOT meeting). NCAC-SOT student members who are interested in submitting an application can consult the SOT website and/or contact Dr. Katherine Squibb for information.

NCAC-SOT Membership

Over the past year, membership in NCAC-SOT has increased substantially. In December 2002, there were a total of 56 members; in December 2003, the number had increased to 245 members. This is partly related to the fact that headquarters SOT maintains the membership records for its regional chapters. This method of doing business has several tangible benefits for NCAC-SOT and its members. SOT provides members with annual notification that membership fees are due in December, provides on-line renewal capabilities, takes secure credit card payments, and immediately deposits membership renewal fees into the NCAC-SOT checking account. Annual membership fees for NCAC-SOT are only $20 for regular memberships and $10 for full-time students. These negligible fees (which may be less than your weekly Starbucks budget!) are used to fund two fantastic symposia each year, and to support a myriad of student activities, including career enhancement programs and student awards. If you have not yet renewed your regional chapter membership, please do so today! If you already renewed your SOT membership and forgot to renew your NCAC-SOT membership at the same time, or if you are not a member of SOT, then contact Rosibel Alvarenga at Society of Toxicology, 1821 Michael Faraday Drive, Suite 300, Reston VA 20190, phone: 703-438-3115, e-mail: sothq@toxicology.org or rosibel@toxicology.org. It's never too late to renew your NCAC-SOT membership for 2004!

2004 NCAC-SOT Symposium Schedule

Put these dates on your calendar now! The NCAC-SOT Spring Symposium will be held on June 8 and the Fall Symposium will be held on November 2 at the National Library of Medicine, Lister Hill Auditorium, Bethesda, MD. Topics for the meetings will be announced soon.

Student Day will be November 3rd this year.