SOT Annual Meeting:
Baltimore, Maryland,
March 5-9, 1995

This edition of the
Communique contains
the Annual Meeting:
Sponsorship Opportunities
Placement Service
Symposia Descriptions
Continuing Education Listing

Fundamental and Applied
Toxicology to Increase
Number of Issues per Year;
Manuscript Handling Fees
Eliminated

Beginning in 1995, Fundamental
and Applied Toxicology will be
expanded from the current eight to
ten issues per year. It is anticipated
that this change will shorten the
publication time for accepted
manuscripts by approximately one
month. The Board of Publications
intends to publish Fundamental and
Applied Toxicology on a monthly basis
as soon as possible, to further
shorten the publication time for
accepted manuscripts and to
increase the desirability of the
journal to institutional subscribers.
In addition, the SOT and Academic
Press have agreed to discontinue
the manuscript handling fee
(currently $100.00) for both of the
Society's journals, Fundamental and
Applied Toxicology and Toxicology
and Applied Pharmacology, beginning
with the 1995 publication year. SOT
members are encouraged to use
their two journals to report signif-
ificant research findings and to
publish other items and comment-
aries of interest to toxicologists.

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PLSIDENT'S MESSAGE

Plans for the 1995 Annual Meeting are progressing rapidly now that abstracts have been received and organized into sessions. This complex job is performed by the Program Committee which, through their insight and wizardry, is able to discern themes among the more than 1600 abstracts received. We should all extend sincere appreciation to Barbara Beck, Kim Boekelheide, Kevin Driscoll, Peter Goering, Charlene McQueen, Stanley Omaye, Tom Petry, Deborah Rice, and Glenn Rush, under the leadership of Jack Dean and Jim Bus, for the many hours reading, sorting, and organizing our abstracts into the exciting and stimulating sessions we anticipate at the Meeting.

This year, we received 1668 abstracts, which allows us to make some predictions about the meeting. As you can see in the graphic to the right, based upon trends of the past 15 years, we can expect over 4000 registrants at the Meeting. Last year, the prediction was remarkably accurate, coming within 2% of the actual number (4100 predicted, 4176 registrants!)

The Annual Meeting provides an opportunity for exchange of scientific information, renewing friendships, extending contacts, and continued education. Look on pages 6-14 for a preview of the symposia, workshops and roundtables scheduled for March 5-9. I am also enthusiastic about the introduction of some new social functions to provide increased opportunity for networking and for recognition of achievements in toxicology. We are planning to sponsor a general reception at which we will acknowledge and honor those with outstanding achievement in toxicology. In addition, a special function is being planned for current and previous student awardees, allowing them an opportunity to renew acquaintances and to catch up on career developments.

I look forward to personally greeting you in Baltimore.

Sincerely,

Meryl H. Karol, Ph.D.
President
MHK@VMS.CIS.PITT.EDU   FAX: (412) 967-6611

P.S. We SOT members, like other busy scientists, have many deadlines to meet. Sometimes deadlines are missed and excuses are received. Below are my favorite excuses:

TOP 10 REASONS WHY AN ABSTRACT WAS NOT RECEIVED ON TIME

10. The Federal Express truck was hijacked.
9. The dog ate my disk.
8. I was called for jury duty on the O.J. Simpson case.
7. My gel didn't harden.
6. I needed more time to make the data fit the theory.
5. The irritant turned out to be the technician.
4. I developed astigmatism and thought the deadline was Oct. 11.
3. My reserve unit was sent to Haiti.
2. I developed dermatitis from the Abstract form.
1. I was too engrossed reading the Communiqué.
Scientists and Indirect Costs

This article first appeared in slightly modified form in the July 1994 Newsletter of the American Society for Cell Biology and was reprinted in the Newsletter of the American Association of Immunologists. The version below will be printed in the newsletter of the American Association of Anatomists. It is reprinted here with permission.

In this article Dr. Samuel Silverstein, President of the Federation of American Societies of Experimental Biology and a member of the American Society of Cell Biology, asserts that Scientists and the Federal government should scrutinize indirect costs. In particular, he indicates there should be an emphasis on requiring that scientists receive a higher quality of services from their institutions in order to increase the productivity in biomedical research that can result from the use of the funds. Suggestions and comments on this topic from the membership of SOT are encouraged, and these will receive consideration for publication in a future issue of our Newsletter. Send your written opinions to: Indirect Costs Issue, SOT Newsletter, c/o Shawn D. Lopez, Executive Director, Society of Toxicology, 1767 Business Center Drive, Suite 302, Reston, VA 22090.

The expenses incurred by universities in support of research are legitimate and necessary for the conduct of research. The Federal government recognizes this and reimburses each university for these expenses in proportion to the fraction of all research at the university that is government supported. These reimbursements are known by the

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IN VITRO Toxicology Specialty Section Formed

The Society of Toxicology is pleased to announce the formation of a new Specialty Section: the In Vitro Toxicology Specialty Section. The overall goals of this Specialty Section are to serve as a resource and act as a focus for the Society of Toxicology in activities relating to in vitro toxicology; to conduct educational activities to better inform the members of the Society of current developments and issues in the field of in vitro toxicology; and to recognize outstanding contributions to the field. The proposed areas of interest to this subsection include, but are not limited to: understanding the relationship between in vitro and in vivo models; exploring the application of in vitro methods to predict target organ toxicity, identifying potential toxicological hazards, classifying hazardous materials, understanding mechanisms of toxicity; promoting the process of validation of new methodologies, and establishing the infrastructure required to attain that goal (including databanks, chemical banks, and standards for quality control); defining the regulatory issues relating to in vitro toxicology and contributing to the international harmonization of in vitro toxicology; and encouraging the development of innovative methodologies for in vitro toxicity testing. If you would like further information on this new section, please contact Dr. John Frazier (513) 256-3600, fax (513) 258-2197.

SOT Council Approves "Tissue Slices" Satellite Meeting

At their September 1994 meeting, the SOT Council approved the "Second Symposium on the Use of Tissue Slices: In Vitro Models of Toxicology and Biotransformation" as a satellite to the 1995 SOT Annual Meeting in Baltimore. The Symposium is scheduled for Saturday, March 4, from 9:00 am - 5:00 pm.

The topic, tissue slices, addresses an area of increasing interest to toxicologists as well as to scientists in pharmacology and biotransformation. Speakers will include academics, corporate scientists and a representative of the regulatory community (FDA). This diverse group will discuss the topic of the tissue slice model with sufficient variety to appeal to a wide audience. For more information, please contact: Paul M. Silber, In Vitro Technologies, Inc., at (410) 455-1242.
COMMUNIQUE COMMENTARY

Shall We Continue To Sepulcher SOT Abstracts?
By Valerian E. Kagan, Ph.D.
Department of Environmental and Occupational Health, University of Pittsburgh

Shall we continue to sepulcher abstracts of SOT meetings? The 33rd Annual SOT Meeting in Dallas (March 1994) was my first as a new 1993 member of our Society. The scientific program of symposia, poster and platform sessions was overwhelmingly exciting and covered the hottest topics. Not only was I impressed by the great scientific and educational forum, but I was also very proud to be part of the community of toxicologists. I am sure that the important results brought to the meeting are of great interest not only for participants and for society members, but also for a significantly broader audience of our colleagues working in closely related and in remote fields. But, what if they were not present at the meeting? Could they have access to these materials? I believe this would not be easy. The 1994 Toxicologist, an official publication of the SOT, contained more than 1,700 abstracts of the meeting. It is available only to SOT members and to registrants of the meeting. These abstracts are not available in international data sources (e.g., in current contents). While other societies use their journals for publicizing and disseminating abstracts of their meetings, SOT with its two official society journals, for some reason prefers to issue a special publication which is an informational graveyard.

I am sure that the 1995 SOT Meeting in Baltimore will be even more exciting than the previous one. The abstracts for the meeting are in the review process now. The abstracts for the forthcoming ICT-VII in Seattle are due in January, 1995. It may not be too late to arrange to publish the 1995 abstracts in special issues of the Society journals, i.e. to use the SOT journals to the benefit of both society members and a broader scientific community (non-society members).

IN MEMORIAM

Hermann Druckrey, 1904-1994

Hermann Druckrey died unexpectedly on August 7, just a few days after his 90th birthday, in Freiburg, Germany. As a long-term member of the Society of Toxicology, Professor Druckrey was well known through his outstanding studies in pharmacology, toxicology and chemical carcinogenesis.

Hermann Druckrey was born in the city of Greifswald, in Mecklenburg-Vorpommern, into a family of pharmacists. He received his M.D. degree in 1931 from Universities of Giessen Heidelberg and Leipzig. His postgraduate training was in pathology at the University of Prag, and his training in biochemistry at the University of Goettingen was under the Nobel laureate H. Windaus and with the 1939 Nobel laureate, A. Butenandt. During World War II, he served as Medical Officer; after 2 years as a prisoner of war he continued his academic career at the University of Freiburg.

In 1949 he published, together with the physicist K. Kupfmueller, his first book on “Dose and Effect” (Dosis und Wirkung) in which he clearly delineated the principles of the toxic and pharmacologic effects of drugs. In the same year, he was appointed Professor and Director of the Laboratories of the Hospital for Surgery. He was now in a position to initiate in-depth studies on the dose-response relationship in chemical carcinogenesis. This led to the development of the principle of the “summation effect” with the widely recognized and accepted formula D=dtN. Professor Druckrey’s research group grew considerably and the transfer to the Max-Planck Institute for Immunology in Freiburg enabled this team to undertake large-scale chemical and biochemical studies, and bioassays on the organotropism of carcinogenic N-nitroso compounds. These studies still serve as guidelines for structure-organotropic carcinogenicity of nitroso compounds.

In 1974, Hermann Druckrey retired from the Max-Planck Institute and the University to his home in Merzhausen near Freiburg. He remained in contact with many of his friends and colleagues in chemical carcinogenesis and, until recently, he followed closely the literature and many of us were rewarded with his constructive advice and thoughts to our publications. Hermann Druckrey was a prolific writer. He published several books and about 500 scientific articles. In 1973, the Japanese Association for Cancer Research and in 1979, the American Association for Cancer Research recognized his outstanding research in carcinogenesis by awarding him with honorary memberships and in 1984 the University of Hamburg awarded him with a Dr.med.h.c.

Hermann Druckrey will be missed by his many friends in Germany and throughout the scientific world.

In Memoriam
Joseph P. Nachtman, Ph.D.
Roger W. Worlund
Virginia L. Zolatzian, Ph.D.
Edward Fairchild, Ph.D.
Ralph Clinton Wands

November/December 1994
Speaking of Animal Use
By Andrea Hubbard, SOT Animals in Research Committee

Some years ago my colleagues and I at the University of Connecticut were asked to teach an Environmental Toxicology course to a group of nonscientists. In the middle of my lecture on “biologic variation” and the difference between human and animal responses to toxicants, I was aggressively challenged about the use of animals in predicting xenobiotic toxicity. I couldn’t find the words to express my beliefs and did not do a good job in convincing the class of appropriate use of animals in research. This incident prompted me to become an active member in a statewide group, Connecticut United for Research Excellence (CURE), which sends scientists and nonscientists into the classroom to address concerns about animal use in research. Through this organization, I have developed reasonable responses to individuals who were unsure about the value of animals in research. Listed below are two of these responses.

Joseph Murray, Nobel Laureate, 1990, states that in his first attempts at kidney transplants, 15 died; in his second attempts, 6 died; in his third attempts, 1 died; and in the fourth attempts, none died. The first three tries were with animals; the fourth try was with a human being. The American Humane Association estimates that between 17.6 and 29.2 million dogs and cats are put to death by animal care and control agencies annually. At best estimates, only 1% of these animals are used in biomedical research. The other 99% are put to death because their owners do not claim them. In addition, the following states have a Pound Law where pound and shelter animals cannot be made available for research: Connecticut, Delaware, Hawaii, Maryland, Maine, Massachusetts, New Jersey, New Hampshire, New York, Pennsylvania, Rhode Island, Vermont and West Virginia.

I am interested in learning how other scientists handle questions about animal use and would like to use a column in the SOT newsletter as a medium for exchanging ideas and thoughts. If you have had any experiences similar to mine and have developed good answers to some of the tough questions on animal use in research, please let me know (FAX: 203-486-4998 or Hubbard@UCONNNVM.UConn.Edu). I will share your comments in upcoming articles.

In Vitro Toxicology
By Wai Nang Choy and Harry Olson, SOT Animals in Research Committee

In vitro techniques have always been used at early stages of drug development. In addition to a preliminary cytotoxicity test, cultured cells are often used to screen for cytotoxic agents (e.g. cancer drugs). Liver cells and liver slices from human and other species are used for comparative drug metabolism studies as related to enzyme induction and metabolite identification. Results of these studies are sometimes used to select the appropriate animal species for multidose toxicity studies.

For risk assessment, the role of in vitro toxicology is traditionally confined to hazard identification (e.g. genetic toxicology for the identification of genotoxic carcinogens). However, data from in vitro studies may also be used for interspecies risk extrapolation based on the “parallelogram” or the “four-corners” approach of risk assessment. In this proposal, human health risk can be extrapolated from in vitro human studies (e.g. tissue culture, biomarkers), based on toxicity correlations between in vitro human studies, in vitro animal studies, and in vivo animal studies. The addition of in vitro data for interspecies risk extrapolation is an improvement of the current practice of using in vivo data (e.g. body weight, body surface area, safety factor) alone.

Future Developments

With almost an unlimited number of combinations of cell types, tissues, organs and toxicity endpoints, it is certain that many new in vitro testing techniques will be developed in the near future. The usefulness of these in vitro tests for safety evaluation, however, is dependent on the results of their validation studies. It is conceivable that continued refinements of a few in vitro tests, accompanied by advances in tissue culture and molecular biology, will lead to new in vitro testing strategies that are capable of providing sufficient information for safety evaluation. In the interim, the use of animals in pharmaceutical testing will continue, and wise decisions should be made to minimize their use.

LITERATURE AVAILABLE
The SOT Animals in Research Committee has assembled a compilation of literature concerning the use animals in research. If you are interested in receiving this information, please contact SOT Headquarters at (703) 438-3115; Fax: (703) 438-3113.
Society of Toxicology
Baltimore Convention Center

1995 Annual Meeting

The Society of Toxicology will hold its 34th Annual Meeting at the Baltimore Convention Center, Baltimore, Maryland. The SOT meeting is the largest toxicology program in the world, attracting more than 4500 attendees. This year's meeting includes innovative science and quality research in a comprehensive program. The Preliminary Program, which includes a registration form, hotel, and travel reservation forms, will be sent to members in December. Continuing Education course descriptions were included in the September/October newsletter; symposia, workshops and roundtables descriptions are published in this newsletter; special sessions will be described in the January/February newsletter. The Final Program and Abstracts will be mailed to members in February.

Sponsorship Opportunities

Event sponsoring opportunities are available for the 1995 SOT Annual Meeting. Events to be sponsored include student, minority program, and general sessions. Cosponsoring opportunities are available for as little as $500. Participating companies will be recognized in the on-site SOT Program, Calendar and Exhibitor Directory (distributed to 4000+ attendees); the January/February and May/June SOT newsletters (mailed to 3,600 SOT members); and through signage on-site. If you are interested in SOT sponsorship, please contact Clarissa Russell at SOT Headquarters for a list of available opportunities.

Placement Service

For the Annual Meeting, the Placement Service will be housed at the Sheraton Inner Harbor Hotel located adjacent to the Baltimore Convention Center. If you would like Placement Forms, please contact SOT Headquarters at (703) 438-3115.

Annual Meeting Symposia

MORBIDITY AND MORTALITY FROM ACUTE INCREASES IN URBAN PARTICULATE

Chairpersons: J.L. Maunderly, Inhalation Toxicology Research Institute, Albuquerque, NM and R.O. McClellan, Chemical Industry Institute of Toxicology, Research Triangle Park, NC
Sponsored by the Inhalation Specialty Section

Recent epidemiological studies have raised questions about the effects of environmental particle exposures for which we presently have few answers. Several studies have demonstrated associations between short-term fluctuations in ambient urban particle concentrations and daily mortality rates. Other studies have shown associations between ambient particle concentrations and changes in respiratory function and other indicators of respiratory morbidity. Cause-effect relationships, in contrast to indirect associations, have not been proven, but the current weight of evidence tends to implicate particles directly. Although heavy particle exposures are known to present health hazards, the concentrations associated with these newly-recognized effects are often within current air quality standards and the magnitude of the concentration fluctuations associated with the effects are small and common. Previous human exposures and toxicological studies have not predicted these effects, nor does our present knowledge explain causal mechanisms. The public health and regulatory implications of these issues are huge, particularly in view of EPA's impending review of the National Ambient Air Quality Standard for PM10. This issue demands an immediate interactive investigative response from the epidemiology and toxicology communities. This symposium will familiarize attendees with the issues, current knowledge, and research opportunities.

Speakers:
- D.L. Costa, U.S.E.P.A., Research Triangle Park, NC
- D.W. Dockery, Harvard School of Public Health, Boston, MA
- J.L. Maunderly, Inhalation Toxicology Research Institute, Albuquerque, NM
- R.O. McClellan, Chemical Industry Institute of Toxicology, Research Triangle Park, NC
- G. Oberdorster, University of Rochester, Rochester, NY
- J.D. Spengler, Harvard School of Public Health, Boston, MA

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BIOLOGICALLY-BASED, QUANTITATIVE RISK ASSESSMENT OF NEUROTOXICANTS
Chairperson: W. Slikker, Jr, National Center for Toxicological Research/FDA, Jefferson, AR
Sponsored by the Neurotoxicology, Risk Assessment, and Regulatory and Safety Evaluation Specialty Sections

The need for biologically-based, quantitative risk assessment procedures for non-cancer endpoints such as neurotoxicity has been discussed in reports by the United States Congress (Office of Technology Assessment, OTA), National Research Council and a federal coordinating council. According to OTA, current attention and resources allocated to health risk assessment research are not commensurate with its impact on public health and the economy. Methods to include continuous rather than dichotomous data for neurotoxicity endpoints, biomarkers of exposure and effects, pharmacokinetic and mechanistic data have been proposed for neurotoxicity risk assessment but require further review and validation before acceptance. The purpose of this Symposium is to examine procedures to enhance the risk assessment process for neurotoxics and to discuss techniques to make the process more quantitative. Accordingly, a review of the currently used safety-factor risk assessment approach for neurotoxics will be provided along with specific examples of how the process may be enhanced with the use of the benchmark dose approach. The importance of including physiologically-based pharmacokinetic data in the risk assessment process and specific examples of this approach will be presented for neurotoxicants. The role of biomarkers of exposure and effect and mechanistic information in the risk assessment process will also be addressed. Finally, quantitative approaches with the use of continuous neurotoxicity data will be demonstrated and the outcomes compared to those generated by currently used risk assessment procedures.

Speakers:
- M.E. Anderson, ICF Kaiser K.S. Crump Division, Morrisville, NC
- D. Bellinger, Children’s Hospital, Boston, MA
- K.S. Crump, ICF Kaiser Engineers, Ruston, LA
- W. Slikker, Jr, National Center for Toxicological Research/FDA, Jefferson, AR

IS CARNITINE A KEY TOXICOCHEMICAL TARGET?
Chairperson: J.E. Garst, Alamogordo, NM
Sponsored by the Food Safety and Mechanisms Specialty Sections

Increasingly R-(L)-carnitine (Cn) and/or short-chain O-acyl Cn esters (SCCn) are reported to ameliorate various adverse effects of diverse chemicals and drugs, including halothane, 2,4,5-T, MPTP, valproic acid, adriamycin, aflatoxin B1, and even hyperbaric oxygen. Besides affecting chemical/drug-induced toxicity, Cn and its SCCn esters can protect against metabolic diseases such as Reye’s syndrome, diabetic nephropathy, and even Alzheimer’s disease. Moreover, the toxicity of various substances seems mediated in part by actions that alter carnitine and/or its enzymes. These include CO, various heavy metals, and the antibiotic cephaloridine. Cn and its esters may play a direct role in homeostasis, influencing protein translocation and function and physiological signaling pathways involving calcium ion flux, calpains II, and protein kinase C. This symposium will explore new avenues suggesting that the Cn system may be a key toxicological target. The first speaker will review the biochemistry and function of Cn. The second speaker will review Cn biosynthesis, deficiency (CnD), and its growing use in clinical medicine. The third speaker will review work from the juvenile visceral stenosis (jvs) CnD mouse. Besides showing signs similar to Reye’s syndrome in humans, these mice show an increased expression of c-jun and c-fos proto-oncogenes. The fourth speaker will review evidence of protection by SCCn esters against radial-mediated loss of enzyme activity and against DNA-strand breakage. These data associate SCCn (carnitine acetyltransferase?) with prevention of programmed cell death or apoptosis. By revealing how Cn changes can explain the tumorigenicity of peroxisome proliferating agents (PPA), the last speaker will explore whether Cn might participate in a signaling system by which a cell responds to the organism’s external environment.

Speakers:
- L.L. Bieber, Michigan State University, East Lansing, MI
- M.E.T. Boerrigter, Harvard Medical School & Beth Israel Hospital, Boston, MA
- J.E. Garst, Alamogordo, NM
- C.J. Rebeutche, University of Iowa, Iowa City, IA
- T. Saeki, Kagoshima University, Kagoshima, JAPAN

CELL CYCLE CONTROLS AND CARCINOGENESIS
Chairperson: T.L. Goldsworthy, CIIT, Research Triangle Park, NC
Sponsored by the Molecular Biology Specialty Section

Significant progress has been made in understanding the cellular and molecular basis of cell growth and division. Cell cycle progression is controlled by both positive and negative growth regulators. Factors regulating cell division (cyclins, kinases, growth factors) and a series of cell cycle checkpoints have been identified. Loss of maintenance of checkpoints and cell cycle controls leads to altered cell growth and genetic instability and gene mutation. It is increasingly apparent that many, if not all, toxicants exert many of their carcinogenic actions by directly or indirectly perturbing the cell cycle. To better understand toxicant-induced perturbations on the cell cycle and carcinogenic process, this symposium will focus on (1) DNA repair and cell-cycle specific gene mutation, (2) interference of cell cycle checkpoint control in preneoplastic cells, (3) G2 cell cycle checkpoint perturbations, (4) altered expression of cyclins and kinases in chemical carcinogenesis, and (5) receptor-mediated and intercellular/extracellular growth factor signals in mutagenesis and carcinogenesis.

Speakers:
- J.G. Babish, Paracelsian, Inc. and Cornell University, Ithaca, NY
- T.L. Goldsworthy, CIIT, Research Triangle Park, NC
- G.W. Lucier, NIEHS, Research Triangle Park, NC
- R.S. Paules, Growth Control and Cancer Group, NIEHS, Research Triangle Park, NC
- R.J. Preston, CIIT, Research Triangle Park, NC
- T.D. Tisty, University of North Carolina, School of Medicine, Chapel Hill, NC

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INTERSPECIES TOXICOLOGY: MOLECULAR BASIS OF DIFFERENTIAL RESPONSE
Chairperson: C.L. Walker, U.T.M.D. Anderson Cancer Center, Smithville, TX
Sponsored by the Carcinogenesis and Molecular Biology Specialty Sections

Recently, attention has been focused on the differences that exist in interspecies responses to toxicant exposures. The objective of this symposium is to present timely examples wherein a molecular approach has been used to evaluate toxicant response in animal models and how data from these models can be extrapolated to other species, including humans. Information has begun to emerge that key enzyme systems involved in activation and detoxification of chemicals and their regulation differ at the molecular level in different species, leading to difficulties in the interpretation of toxicity data when extrapolating across species. The issue of how the metabolism of compounds can act as a determinant of toxicity in various species will be addressed by the first speaker. Many animal models utilizing recoverable transgenes have been used to study genetic damage induced by toxic agents. In the second talk, the relationship between genotoxicity data obtained in transgenic animals of different species and the disadvantages and advantages of the various transgenic model systems available will be addressed. The third speaker will cover specific examples of carcinogen specificity in the spectrum of ras family oncogene mutations in various species and tumor types. The last of the four speakers will discuss issues relating to the use of molecular techniques to establish the relevance of animal models to the human disease, using breast cancer as a paradigm for extrapolating carcinogenicity data across various species.

Speakers:
- R.N. Hines, Wayne State University School of Medicine, Detroit, MI
- G.S. Provost, Stratagene, La Jolla, CA
- G.D. Stoner, The Ohio State University Comprehensive Cancer Center, Columbus, OH
- S. Sukumar, The Johns Hopkins University School of Medicine, Baltimore, MD
- C.L. Walker, UT MD Anderson Cancer Center, Smithville, TX

ENDOCRINE MODULATION OF REPRODUCTION
Chairpersons: R.E. Chapin, NIEHS, Research Triangle Park, NC and G.P. Daston, Procter & Gamble, Cincinnati, OH
Sponsored by the Reproductive and Developmental Specialty Section

Hormones are biologically active at exceedingly low concentrations, a characteristic that allows efficient endocrine signaling at distant target tissues. This characteristic may also render the target cells susceptible to exogenous agents that either mimic or block the action of an endogenous hormone. The nature of the response to these exogenous toxicants is target-and life-stage-dependent. There has been a great deal of publicity recently regarding the potential for certain synthetic chemicals to act as estrogen mimetics. Recent research has expanded our understanding that other hormonal systems may also be affected by toxicants; that adverse responses are varied and may be permanent; and that there may be a large number of exogenous agents with the potential to act via hormonal disturbance. The purpose of this symposium is to present current information about the potential for interaction of various agents with hormonal systems controlling reproductive function and development. The first talk illustrates with results from a widely-used herbicide the role of endocrine disruption in mammary carcinogenesis. The second talk will describe the prevalence and effects of naturally-occurring estrogens in the diet. The third talk will describe new research demonstrating the existence of environmental agents with anti-androgenic activity. The fourth talk will document the influence of thyroid status on testicular development, illustrating that reproductive function may be controlled by endocrine factors not traditionally considered to be part of the reproductive system. Together, these talks will demonstrate the potential for toxicant-induced disruption of a variety of hormonal control points.

Speakers:
- R.E. Chapin, NIEHS, Research Triangle Park, NC and G.P. Daston, Procter & Gamble, Cincinnati, OH
- R.A. Hess, University of Illinois, Urbana, IL
- C. Hughes, Duke University Medical Center, Durham, NC and Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, NC
- W.R. Kelce, ManTech Environmental, Research Triangle Park, NC
- J.T. Stevens, Ciba Crop Protection, Greensboro, NC

COMPARTMENTATION OF GLUTATHIONE: IMPLICATIONS FOR THE STUDY OF TOXICITY AND DISEASE
Chairpersons: C.V. Smith, Baylor College of Medicine, Houston, TX and D.P. Jones, Emory University School of Medicine, Atlanta, GA
Sponsored by the Mechanisms Specialty Section

That glutathione plays many roles in biological protective mechanisms has been recognized for decades. Conjugates, disulfides, and other glutathione-derived products also have been studied as biomarkers of the chemical natures or specific identities of key metabolites of toxic agents and such studies have been crucial in the delineation of the nature of the interactions of proximal toxics with target biomolecules. Despite the extensive evidence implicating the depletion and/or oxidation of glutathione in a wide variety of human and experimental toxicities, critical examination of such studies frequently indicates that injury is not related simply to glutathione status. Glutathione is compartmentalized at several levels and this compartmentalization appears to exert considerable influence on the relationships between glutathione depletion or oxidation and onset of injury. Although compartmentalizing is usually viewed from the perspective of different intracellular pools, the significance of extracellular glutathione in functionally important pools is gaining appreciation. As the factors affecting the interactions of intracellular pools with extracellular pools are delineated, studies in humans can be designed and interpreted with greater precision and utility.

Speakers:
- T.M. Guenther, University of Illinois College of Medicine, Chicago, IL
- D.P. Jones, Emory University School of Medicine, Atlanta, GA
- L.H. Lash, Wayne State University School of Medicine, Detroit, MI
- B.H. Lauterburg, University of Berne, Berne, Switzerland
- C.V. Smith, Baylor College of Medicine, Houston, TX

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MECHANISMS OF INFLAMMATORY LIVER INJURY: ADHESION MOLECULES AND CYTOTOXICITY OF NEUTROPHILS

Chairpersons: R.A. Roth, Michigan State University, East Lansing, MI and H. Jaeschke, The Upjohn Company, Kalamazoo, MI

During recent years, increasing experimental evidence suggested that hepatic nonparenchymal cells, in particular Kupffer cells and neutrophils, can contribute significantly to the pathogenesis of liver injury in various chemical toxicities. Indeed, neutrophils are central to the mechanism of injury after hepatic ischemia-reperfusion and endotoxemia. In this symposium, an overview of critical aspects of neutrophil-dependent liver injury will be presented. Molecular mechanisms of neutrophil arrest, adhesion and stimulation in the microvasculature will be discussed. Cytokines such as TNFα and IL-1, as well as lipid peroxidation products, play important roles in neutrophil recruitment and activation. Mechanisms by which activated neutrophils injure rat hepatocytes will be considered. Interactions between neutrophils and contractile perisinusoidal, fat-storing cells and their role in hepatic microvascular failure will be explored. Results of these and other investigations are leading to increased understanding of the complex interactions between neutrophils and tissues that result in injury.

Speakers:
- M.G. Clemens, The Johns Hopkins School of Medicine, Baltimore, MD
- P.F. Caney, Michigan State University, East Lansing, MI
- H. Jaeschke, The Upjohn Company, Kalamazoo, MI
- C.W. Smith, Baylor College of Medicine, Houston, TX

INTERACTIONS BETWEEN IMMUNE AND NON-IMMUNE CELLS IN IMMUNOTOXICOLOGY

Sponsored by the Immunotoxicology Specialty Section

It is increasingly apparent that cells and factors outside of the traditional definition of ‘immune’ cell are intimately involved in both normal immune function and immunotoxicity. Evaluation of information derived from immunotoxicological studies, particularly in vivo studies, in the absence of an understanding of the potential non-immune influences, often leads to an incomplete understanding of the biological response in question. An obvious example of this is the role of overt stress on host immune function in which neuroendocrine influences play a significant role in the ultimate immune status of the host. This symposium will address the role of key cells not classically considered a part of the immune system, but intimately involved in immunological processes. Specific topics which will be covered by the speakers will include: 1) the influence of leukocytes, particularly Kupffer cells, on hepatocyte function, 2) a discussion on the immunologic potential of keratinocytes in the context of skin pathophysiology, 3) the complex interactions between the central nervous system and the immune system, and lastly, 4) the global influence of endothelial cells on immune function. The specific goals of this symposium are to familiarize the audience with the inter-communicative nature of immune process, discuss the importance of exploring alternative hypothesis in interpreting immunotoxicological studies, and finally to stimulate collaborative research in the area of immunotoxicology.

Speakers:
- A.L. Baldwin, University of Arizona, Tucson, AZ
- R.E. Billings, Colorado State University, Ft. Collins, CO
- G.J. Harry, National Institute of Environmental Health Sciences, Research Triangle Park, NC
- J.D. Laskin, UMDNJ-Robert Wood Johnson Medical School, Piscataway, NJ

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SECOND MESSENGERS: THEIR ROLE IN IMMUNOTOXICITY

Chairperson: N.E. Kaminski, Michigan State University, East Lansing, MI

Sponsored by the Immuno-Toxicology Specialty Section

The objective of this symposium is to describe the role of second messengers in immune regulation and how changes in intracellular signaling by immunotoxic agents result in immune dysfunction. Several well characterized immunotoxicants will be discussed in the context of the signal transduction pathways they disrupt and the immunological functions which are consequently altered. Changes in immunocompetence following chemical exposure has been established for a wide variety of unrelated agents. For the vast majority of immunotoxic compounds thus far identified, it is clear that disruption of normal immune function is mediated through direct interactions between the agent or its metabolite and immunocompetent cells. Regardless whether this interaction occurs at the level of the cell membrane or at intracellular sites, basic regulatory processes mediated by second messengers are often altered ultimately resulting in immunologic dysfunction. For a number of immunotoxic compounds, the specific disruptions in intracellular signaling they produce have now been identified, leading to a basic understanding of their mechanism of action. Equally important, through the application of some of these agents as biological probes, tremendous insight has been gained pertaining to which intracellular signaling processes control which cellular functions. Although a number of signaling pathways common to all cell types have been identified, the actual functional processes they control may differ remarkably from cell-type to cell-type. Each of the speakers will focus on the role of specific signal transduction pathways and how their perturbation by chemicals results in altered immunocompetence.

Speakers:
- S.W. Burchiel, The University of New Mexico, College of Pharmacy, Albuquerque, NM
- M.P. Holtsapple, Dow Chemical Company, Midland, MI
- N.E. Kaminski, Michigan State University, East Lansing, MI
- J.A. Ledbetter, Bristol-Meyers Squibb, Seattle, WA
- J.W. Putney, Jr., NIEHS, Research Triangle Park, NC

SELECTIVE PROTEIN COVALENT BINDING AND TARGET ORGAN TOXICITY

Chairpersons: S.D. Cohen, University of Connecticut, Storrs, CT and J.A. Hinson, University of Arkansas Medical Sciences, Little Rock, AR

Sponsored by the Mechanisms Specialty Section

Protein covalent binding by xenobiotic metabolites has long been associated with target organ toxicity but mechanistic involvement of such binding has not been widely demonstrated. Modern biochemical, molecular and immunochimical approaches have facilitated identification of specific protein targets of xenobiotic covalent binding. Such studies have revealed that protein covalent binding is not random but selective with respect to the proteins targeted. Selective binding to specific cellular target proteins may better correlate with toxicity than total protein covalent binding. Current research is directed at characterizing and identifying the targeted proteins and clarifying the effect of such binding on their structure, function and potential roles in target organ toxicity. This symposium will first describe the approaches employed to detect and identify the targeted proteins. Next, the association of selective protein covalent binding by acetylamphen and 2,5-hexanedione will be discussed in the context of specific cellular perturbations which may contribute to the target organ toxicity. Formation of xenobiotic-protein adducts with immunogenic properties in drug hypersensitivity and autoimmune will also be described as an additional means by which selective protein covalent binding may mediate toxicity.

Speakers:
- R. Boekelheide, Brown University, Providence, RI
- S.D. Cohen, University of Connecticut, Storrs, CT
- E.A. Khairallah, University of Connecticut, Storrs, CT
- L.R. Pohl, NHLBI, NIH, Bethesda, MD
- N.R. Pumford, University of Arkansas for Medical Sciences, Little Rock, AR

GAP JUNCTIONAL COMMUNICATION FOR DRUG DISCOVERY AND DEVELOPMENT

Chairperson: J.E. Trosko, Michigan State University, East Lansing, MI

Sponsored by the Carcinogenesis Specialty Section

The rationale for this symposium is to present a new conceptual strategy for both toxicity testing of new chemicals and new chemo-preventive/chemotherapeutic drug development for cancer prevention and management. It is based on a series of experimental observations over the last 30 years that dysfunctional gap junctional intercellular communication (GJIC) appears to correlate with the neoplastic phenotype, as well as other toxicological endpoints. With recent developments in the cloning and characterization of the family of highly conserved gap junction genes and their protein products (connexins), as well as in the development of new techniques to measure, functionally, gap junctions, it appears that GJIC is a crucial process needed for the regulation of normal growth control, differentiation and adaptive functions of differentiated cells. Chemical tumor promoters, growth factors, oncoproteins and hormones have been linked with the down-regulation of GJIC, while several tumor suppressor genes, antitumor promoters and anti-oncogenic inhibitors have been shown to up-regulate GJIC. In addition, transfection with connexin genes into non-communication tumor cells have been shown to up-regulate GJIC and restore growth control. Three different, but interrelated, presentations will address how the study of GJIC could be useful in toxicology studies of non-genotoxic chemicals, in drug development for chemotherapeutic and chemoprevent of cancers and in potential gene therapy of cancer.

Speakers:
- P.P. Mehta, University of Miami School of Medicine, Miami, FL
- C.C.G. Naus, The University of Western Ontario, London, Ontario, Canada
- R.J. Ruch, Medical College of Ohio, Toledo, OH
- J.E. Trosko, Michigan State University, East Lansing, MI

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Symposia

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MOLECULAR MARKERS IN THE EVALUATION OF CHEMOPREVENTIVE AGENTS

Chairpersons: M.A. Pereira, Medical College of Ohio, Toledo, OH and M.A. Nelson, University of Arizona, Tucson, AZ
Sponsored by the Carcinogenesis Specialty Section

Chemopreventive agents against various cancer types have been identified in laboratory animal models of carcinogenesis. These agents are awaiting evaluation in human clinical studies. Also, the efficacy needs to be determined for numerous other potential cancer chemopreventive agents that are either analogues of already identified compounds or active in vitro screening assays. The testing of these agents in human clinical studies can best be accomplished by evaluation of their modulation of molecular markers, biomarkers and/or intermediate endpoints of the carcinogenic process. Hence, agents could be distinguished that prevent or reverse the carcinogenic process prior to the occurrence of cancer. Molecular markers and biomarkers are required in laboratory efficacy studies so as to have the identification of new chemopreventive agents driven by mechanistic considerations. The use of intermediate and precancerous endpoints would allow the preclinical studies to identify agents that will be evaluated in human studies using similar precancerous endpoints. The first presentation will discuss the application of surrogate endpoint biomarkers in chemoprevention studies, the next two will give examples in animal models and the last two will present discussions of clinical studies.

Speakers:
- R.A. Lubet, NIH, NCI, DCPC, Bethesda, MD
- M.A. Nelson, University of Arizona, Tucson, AZ
- M.A. Pereira, Medical College of Ohio, Toledo, OH
- D. Sidransky, Johns Hopkins University, Baltimore, MD
- C.D. Stoner, The Ohio State University Comprehensive Cancer Center, Columbus, OH

WATER CHLORINATION: ESSENTIAL PROCESS OR CANCER HAZARD?

Chairpersons: R.J. Bull, Battelle Pacific Northwest Laboratory, Richland, WA and L.S. Birnbaum, HERL, USEPA, Research Triangle Park, NC
Sponsored by Mechanisms, Risk Assessment and Carcinogenesis Specialty Sections

Chlorine has been successfully used for the control of waterborne infectious disease. In the 1970s, it was found that chlorine reacted with natural organic matter present in surface waters to produce disinfection by-products (DBPs). Concern focussed initially on the trihalomethanes (THMs), but a wide variety of DBPs are now known to result from chlorination. Divergent estimates of the risk posed by DBPs come from the available toxicological and epidemiological data. The purpose of this symposium is to determine if there is a convergence of toxicological and epidemiological data on this issue. If not, critical questions for research will be identified. The first presentation will discuss the available analytical epidemiological studies. Second, pharmacokinetic, mechanistic and modeling information on the prototypical DBP, chloroform, will be presented. A contrast will be drawn with data on brominated THMs to determine if a dependable model can be developed for this class of DBP. The fourth presentation will deal with the carcinogenic properties of the potent mutagens that are produced by chlorination. The final presentation will discuss the haloacettes, carcinogenic DBP whose concentrations approach and occasionally exceed those of the THMs. The impact that these results should have on public policy will form the basis of the closing discussion.

Speakers:
- R.J. Bull, Battelle Pacific Northwest Laboratory, Richland, WA
- B.E. Butterworth, CIIT, Research Triangle Park, NC
- K.J. Cantor, National Cancer Institute, Bethesda, MD
- R.A. Pagram, USEPA, Research Triangle Park, NC
- J.B. Rase, Department of Marine Sciences, University of South Florida, St. Petersburg, FL
- J.Tuomisto, National Public Health Institute, University of Kuopio, and Finnish Cancer Registry, Helsinki, Finland

TOXICANT-INDUCED ALTERATION OF GENE EXPRESSION

Chairpersons: C.McQueen, University of Arizona, Tucson, AZ and R.F. Novak, Wayne State University, Detroit, MI

A variety of stimuli such as growth factors, cytokines, and hormones, as well as physical, chemical or metabolic events, including oxidative stress and altered Ca²⁺ homeostasis, alter signal transduction pathways either through receptor-mediated signaling pathways or through other signaling processes. These signaling events frequently culminate in changes in gene expression. Whereas enhanced gene expression occurs through transcriptional activation, mediated by the binding of transcription factor(s) to the 5' regulatory region of the gene, there exist numerous examples in which down regulation of gene expression also occurs. This symposium will feature presentations on the enhanced expression and suppression of gene expression in different systems in response to chemical agents, the mechanism(s) underlying altered gene expression and the potential role of this cellular response in modulating toxic injury and cellular homeostasis.

Speakers:
- W.E. Greenlee, Purdue University, West Lafayette, IN
- R.F. Novak, Wayne State University, Detroit, MI
- M. Runge-Morris, Wayne State University, Detroit MI
- D.J. Thiéole, University of Michigan Medical School, Ann Arbor, MI

SOT Symposia at the Annual Meeting.
Workshops

THE MAXIMUM TOLERATED DOSE (MTD) FOR INHALATION BIOASSAYS: TOXICITY VS OVERLOAD

Chairpersons: P.E. Morrow and G. Oberender, University of Rochester, Department of Environmental Medicine, Rochester, NY
Sponsored by the Inhalation Specialty Section

High concentrations of inhaled particles can result in a state of lung particle overload characterized by decreased particle clearance and an excessive buildup of particles in the lung. Lung particle overload in rats is associated with adverse responses including inflammation, fibrosis and lung tumors, however, other changes indicating the MTD has been exceeded may not be apparent. In this respect, it needs to be decided if additional inhalation-specific MTD guidelines are needed or whether alternative approaches should be considered. The primary purpose of this workshop is to subject the concept of MTD for particular inhalation studies to intensive discussion by a panel of experts. The first speaker will provide a historical and conceptual perspective of the MTD. This will be followed by two presentations discussing features of chronic inhalation study design and exposure-response relationships including implementation of the MTD. The final speaker will consider the problems of MTD interpretation for scientists and regulators. A panel discussion will be conducted to address key issues regarding inhalation MTD's including the relevance to low level exposures of responses (i.e. tumors) observed under conditions of lung particle overload and the development of guidelines for design of chronic particle inhalation studies.

- K. Driscoll, The Procter & Gamble Company, Cincinnati, OH
- J. Haseman, NIEHS, Biometry and Risk Assessment Program, Research Triangle Park, NC
- C. Hobbs, Inhalation Toxicology Research Institute, Albuquerque, NM
- P. Morrow, University of Rochester, Department of Environmental Medicine, Rochester, NY
- G. Oberender, University of Rochester, Department of Environmental Medicine, Rochester, NY
- V. Vu, USEPA, Office of Pollution Prevention & Toxics, Health Environmental Review Division, Washington, D.C.

NATIONAL TOXICOLOGY PROGRAM STUDIES: PRINCIPLES OF DOSE SELECTION AND APPLICATIONS TO MECHANISTIC BASED RISK ASSESSMENT

Chairperson: G. W. Lucier, National Institute of Environmental Health Sciences, Research Triangle Park, NC

The National Toxicology Program (NTP) was chartered in 1978 to coordinate toxicological research and testing activities within the Department of Health and Human Services. The NTP has characterized the toxicity of hundreds of chemicals primarily in rodents, under relatively standardized test conditions. The doses selected for use in these studies have generally been set sufficiently high to maximize the ability of the various assays to detect an adverse health effect. The use of animal data collected for hazard identification purposes in the derivation of quantitative risk assessments for both cancer and non-cancer endpoints has created discomfort with the assays, and stimulated attempts to restructure the tests to produce data more appropriate for this new purpose. Aside from the need to better define the lower end of the dose response relationship, the criteria for selection of the top most dose are also continually questioned. The merits of making basic changes in the toxicology study paradigm to accommodate the increasing use of these data for risk assessment are worthy of further debate, and other approaches to these problems need to be considered. The purpose of this workshop is to provide an overview of factors that are currently considered important in selection of doses for NTP studies, to describe some of the confounding factors that can result from the indiscriminate use of bioassay data in quantitative risk assessment, and to suggest ways in which information from mechanistic studies or studies of biomarkers of exposure of effect might be used to better advantage in risk assessment.

TOXICOLOGICAL IMPLICATIONS OF MICROSONAL ENZYME INDUCTION IN THE DEVELOPMENT OF NOVEL COMPOUNDS

Chairpersons: D.G. Robertson, Parke Davis Pharmaceutical Research, Ann Arbor, MI and P.S. Guzelian, Department of Medicine, University of Colorado, Denver, CO
Sponsored by the Mechanisms and Molecular Biology Specialty Sections

Induction of the cytochromes P450 is a common finding during pre-market evaluation of novel compounds. Over the past several years there has been an explosion of information on the biochemistry of P450's at both the gene and protein level. There is, however, a paucity of data on the significance of microsomal induction in experimental models as it relates to potential human exposure. All too frequently conclusions about the significance of induction are made on inadequate or erroneous information leading to decisions that may inappropriately result in discontinuation of a promising compound or visa-versa. Currently, within the pharmaceutical industry, there is no systematic approach to the development of inducers. Some companies refuse to develop inducers while others don't routinely screen for the effect. The primary focus of the workshop will be on the development of drugs, but the nature of the questions being addressed will give the workshop a broader scope. The emphasis will be on providing practical information about the toxicologic implications of microsomal induction and its relevance to humans. Topics covered will include induction and carcinogenesis, the significance of isozyme profiles and the utility of in vitro and transgenic models.

- P. Guzelian, Department of Medicine, University of Colorado, Denver, CO
- C. Omiecinski, Department of Environmental Health, University of Washington, Seattle, WA
- A. Parkinson, Department of Pharmacology, University of Kansas Medical Center, Kansas City, KS
- D.G. Robertson, Parke Davis Pharmaceutical Research, Ann Arbor, MI
- P. Watkins, General Clinical Research Center, University of Michigan Medical Center, Ann Arbor, MI
- S. Wrighton, Lilly Research Laboratories, Indianapolis, IN

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Workshops

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- J.R. Bucher, National Institute of Environmental Health Sciences, Research Triangle Park, NC
- E.M. Faustman, Department of Environmental Health, University of Washington, Seattle, WA
- J.I. Goodman, Michigan State University, East Lansing, MI
- G.W. Lucier, National Institute of Environmental Health Sciences, Research Triangle Park, NC
- C.J. Portier, National Institute of Environmental Health Sciences, Research Triangle Park, NC

FROM TEACHERS TO TOXICOLOGISTS: ANSWERING THE TOUGH QUESTIONS ABOUT ANIMAL RESEARCH

Chairperson: H.M. Olson, Sanofi Research Division, Collegeville, PA
Sponsored by the Animals in Research Committee and the Veterinary Specialty Section

It is becoming increasingly important for biomedical researchers to communicate the importance and value of their work to the general public and in particular to school students. Current deficiencies in science education and the lack of understanding of important scientific principles (e.g., dose-response, risk assessment) have resulted in large portions of the populace being susceptible to scientific misinformation and the efforts by animal activists to limit research activities. Several SOT groups have developed creative ways to communicate with the general public on important issues, including the value of animal research for human and animal health. Speakers will describe their experiences of giving presentations to various school age groups, speaking to community groups, or engaging in debates. The goal of this workshop is to illustrate three different approaches that SOT members have developed to convey the value of animal research.

- T.E. Eurell, Department of Veterinary Biosciences, University of Illinois, Urbana, IL
- S. Hermansky, Bushy Run Research Center, Export, PA
- A.K. Hubbard, Pharmaceutical Sciences, University of Connecticut, Storrs, CT
- H.M. Olson, Sanofi Research Division, Collegeville, PA

TECHNIQUES FOR QUANTIFYING UNCERTAINTY IN RISK ASSESSMENT

Chairpersons: M.L. Garpas, ChemRisk Division of McLaren/Hart, Cleveland, OH and M.L. Dourson, USEPA, Cincinnati, OH
Sponsored by the Risk Assessment Specialty Section

The various steps performed in conducting a risk assessment are accompanied by differing degrees of variability (e.g., randomness in a population) and uncertainty (e.g., lack of fundamental knowledge). This workshop will focus on approaches that can be used by a risk assessor for quantifying these uncertainties. The first speaker will discuss quantifying the uncertainty and variability in the concentrations of toxicants in the environment, their fate and transport, and the parameters of the exposure assessment. The second speaker will describe techniques of Monte-Carlo simulation and sensitivity analysis for characterization of estimates of tissue dose from toxicokinetic models. The next speaker will elaborate on uncertainty in dose-response by describing the relationship of tissue dose to short-term toxic effects such as mutagenicity, cytotoxicity, and induced cellular replication. The last speaker will describe the process of decision analysis in which Bayesian concepts of subjective probability can be used with probability trees and elicited expert judgments to address uncertainty in modeling carcinogenic potencies. Following the formal presentation, a discussion session will be directed at several key issues concerning the imprecision of risk numbers. Issues to be discussed include extrapolation of animal data to humans, Bayesian concepts compared to classical analysis, probabilistic analysis versus point estimates and resolution of conflicting data.

- R.B. Conolly, Chemical Industry Institute of Toxicology, Research Triangle Park, NC
- M.L. Dourson, USEPA, Cincinnati, OH
- J. Evans, Department of Environmental Health, Harvard School of Public Health, Boston, MA
- M.L. Garpas, ChemRisk Division of McLaren/Hart, Cleveland, OH
- T.E. McKone, Lawrence Livermore National Laboratory, Livermore, CA
- R.R. Reitz, ChemRisk Division, McLaren/Hart, Midland, MI

Roundtables

IS INGESTED INORGANIC ARSENIC (As) A "THRESHOLD" CARCINOGEN?

Sponsored by the Risk Assessment Specialty Section

Ingested As is a carcinogen; it has been proposed to act via a threshold or nonlinear mechanism. This roundtable will discuss the US and Canadian As risk assessments. It will consider the hypothesis that there is a threshold for As and implications for regulatory purposes. At the present time, the health effects and toxicological mechanisms of As are under intense scrutiny as the US EPA is in the process of developing a regulation for As in drinking water that could impact the regulation of As, which is ubiquitous in the environment. Some epidemiological evidence suggests that there is a threshold for As. These preliminary reports show no increase in cancer until the drinking water contains relatively high levels of As. Additional support is provided by metabolic studies which report that there is a saturation of detoxification pathways at high As exposure levels. There are also questions on the applicability of the Taiwanese data to the US population. These topics will be covered and open for discussion.

- W. Chappell, University of Colorado, Denver, CO
- H. Gibb, Office of Health and Environmental Assessment, Washington, D.C.
- H.R. Guo, RegNet Environmental Services, Washington, D.C.
- B. Meek, Environmental Health Center, Washington, D.C.

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PROTECTING THE FOOD SUPPLY FROM ENVIRONMENTAL CONTAMINANTS: SCIENTIFIC AND ECONOMIC CONSIDERATIONS

Chairpersons: N.M. Elsayed, Walter Reed Army Institute of Research, Washington, DC; University of California, Los Angeles, CA; and University of Nevada, Reno, NV and S.C. Fitzpatrick, Regulatory Affairs Consultant, Rockville, MD
Sponsored by the Food Safety & Risk Assessment Specialty Sections

The use of chemicals to increase productivity in many areas such as agriculture and industry, and their potential adverse effects on public health, constitutes a major conflict in today's society. This conflict gains greater proportion when economic growth and progress are weighed in. For example, the assumption used to assess risk is that compounds such as pesticide residues and veterinary drugs can potentially reach the food chain "at their highest permitted level over the lifetime of the consumer." Do these compounds remain bioavailable to the consumer long enough at high concentration? Another public concern is over air pollution and acid rain originating from mobile and stationary sources which most often lead to enactment of new regulations. Such regulations can be viewed, by some, as economic obstacles stifling growth and development, and by others as necessary to limit an otherwise uncontrollable environmental pollution. This conflict between protecting the environment and economic development is even stronger in developing countries where producing enough food for the society is thought to be more important than safety of the environment or the individual consumer. This symposium will bring together scientists, economists, regulators and safety advocates to discuss this timely issue.

- R. Ackerman, The Environment Department, The World Bank, Washington, D.C.
- B. Ames, University of California, Berkeley, CA
- N.M. Elsayed, Walter Reed Army Institute of Research, Washington, DC; University of California, Los Angeles, CA; and University of Nevada, Reno, NV
- S.C. Fitzpatrick, Regulatory Affairs Consultant, Rockville, MD
- R. McClellan, Chemical Industry Institute of Toxicology, Research Triangle Park, NC
- E. Silberfeld, University of Maryland, Baltimore, MD

A Survey conducted at the 1994 SOT Annual Meeting revealed the following about the attendants:

**Product Interest**
- Publications 34%
- Contract Svs. 33%
- Sup./Equip. 23%

**Type of Organization**
- Academia 44%
- Private Industry 37%
- Government 12%
- Military 1%
- Other 5%
Scientists and Indirect Costs

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misleading term, "Indirect Costs."

Many scientists believe that their institution is not providing services commensurate with the Indirect Costs recovered from research grants. However, most scientists do not know what services/expenses Indirect Costs are meant to cover, how they are calculated, and how Indirect Cost monies are spent. There are many reasons for this lack of understanding. Few institutions provide information to their faculty concerning these issues. The Public Health Service's grant instruction booklet (PHS form 398), which gives detailed information on items of such cosmic importance as the maximum number of characters allowed in the grant's title, provides no information on the services that institutions are expected to provide in return for Indirect Costs. The only mention of these costs is on page 32 of PHS form 398. It states "3. Indirect Costs—see Checklist-self explanatory."

How can we be expected to evaluate the services and/or what costs the institution incurs in delivering them? No wonder many scientists feel taken for a ride on Indirect Costs. No wonder they are often publicly and vociferously unsupportive of Indirect Costs. No one has taken the trouble to explain how Indirect Costs on hard won grants are determined, and how they benefit research. It will be impossible to convince either the public or our representatives in Congress that Indirect Costs are justified while thousands of scientists are telling them otherwise.

By and large, members of Congress are no better informed about Indirect Costs than scientists. Repeating over and over more loudly, and more stridently the litany that "Indirect Costs are legitimate expenses of research," without explaining these costs is neither good psychology nor good strategy. Moreover, it simply isn't working. Providing scientists with a copy of Revised Circular A21 is not an answer either. To understand this piece of regulatory gobbledygook in its unexpurgated form requires some acquaintance with law and accounting, as well as the patience of Job. To overcome these difficulties I believe we need a three-pronged educational effort.

First, FASEB should ask the National Institutes of Health to include an explanation of Indirect Costs in the instructions for applying for a Public Health Service Grant. This explanation should be written in ordinary English (i.e., the language spoke outside the Beltway), and should provide a general description of the services for which institutions receive Indirect Cost reimbursements, and therefore are expected to provide in return for receipt of these monies.

Second, the institutions should develop educational materials that inform scientists of the services provided, the frequency of these services, and the total cost of delivering them to each investigator. In this way investigators can learn whether the Indirect Costs on their grants pay for some/all of the services provided by their University. These materials should contain information on subjects as mundane as the frequency of janitorial services in the laboratory and laboratory; and as sophisticated as the range of high technology services (e.g., E-mail, libraries, access to data bases), available to each investigator. In addition, these educational materials should describe costs incurred for light, heat/cooling, chemical waste, radiation safety, the Institutional Review Board, the Animal Care Committee, the mailroom, the library, purchasing, personnel, interest on mortgages, etc. It might be well for the institution to estimate the proportion of the costs of conducting research that are paid by Indirect Costs, and the average Indirect Costs recovered per research employee or principal investigator. Without such information, it will be very difficult for scientists and/or administrators to evaluate whether the institution is providing services of comparable type and cost as other institutions in the same city/region, and for investigators to determine whether they are receiving good value for the Indirect Cost monies we raise.

Third, scientific societies should prepare a brief (c2 pages), statement on Indirect Costs for Congress. The statement should describe the societal essential functions for which Indirect Costs pay. For example, it should point out that Indirect Costs pay for the Institutional Review Board, thereby insuring ethical human experimentation, the Animal Care and Use Committee, thereby assuring ethical and humane treatment of animals, the chemical and radiation safety committees, thereby protecting the public-at-large and other scientists from irresponsible use and/or disposal of dangerous chemicals and radioactive materials, a purchasing department, thereby allowing institutions to negotiate optimal discounts for scientific supplies, accounting services, thereby allowing the government, the institution, and the individual investigator to track grant expenditures, security, thereby assuring the safety of graduate students whose experiments begin after dinner and end at 4 a.m., and library and central computational services, thereby making accessible to each investigator the collective knowledge of mankind. While scientists can argue that some services are delivered inefficiently or inadequately, scientists, Congress, and the public-at-large are unlikely to argue that ethical human and animal experimentation, safe disposal of toxic chemicals and radioactive compounds, bulk purchasing of supplies to obtain the best possible price, accurate and timely grants accounting, and library and computational services are unnecessary to the ethical, safe and cost effective conduct of research.

Fourth, at periodic intervals, NIH might send a team to each institution to determine whether the scientists are satisfied with the services provided and whether these services are provided in an efficient and cost effective manner. Alternately, each institution might form a committee composed of the scientists who use these services. This committee would report periodically to institutions and Federal granting agencies concerning the quality of the services provided.

In summary, between 29 and 41% of the total monies provided by each grant (i.e., 40 to 70% of direct costs), reimburse the sponsoring institution for services that are essential for the conduct of research, but over which scientists have little or no control. Clearly, it would be unworkable for scientists to negotiate with their institutions for services on a service-by-service basis. However, as consumers of these services scientists should be consulted regarding their satisfaction with them. Enlisting scientists' participation in evaluating the services supported by Indirect Costs will improve communication, enhance accountability, and most importantly, increase the efficiency with which Indirect Costs are expended in support of medical research and of improvements in human health.
Chlorine
Continued from page 1

compounds. This resulted in the formation of an ad hoc "Chlorine Issue Working Group" (J. Goodman, Chair, SOT Council Representative; J. Kehler, Mechanisms; J. Lamb, RALA; J. Moore, Risk Assessment; and J. Zurlo, CPC), which took the lead in developing a draft position paper. This was reviewed by Council, distributed widely for comments (e.g., to officers of Specialty Sections and Regional Chapters) revised pursuant to the comments received and re-reviewed by Council, and submitted to Fundamental and Applied Toxicology for publication. The multiple review processes resulted in constructive criticisms that improved the final product. In this manner, we were able to reach a broad consensus for our general statement of principles relative to the "chlorine issue." Our SOT position paper entitled "Toxicologic Principles Do Not Support Banning Chlorine" is in press, as Commentary, in Fundamental and Applied Toxicology.

Toxicologic Principles Do Not Support the Banning of Chlorine

A Society of Toxicology Position Paper

Proposals have been made to develop a national strategy for substituting, reducing or prohibiting the use of chlorine and chlorine-containing compounds based on the premise that such action would improve protection of human health and the environment (International Joint Commission, 1994, and U.S. Environmental Protection Agency, 1994). The Council of the Society of Toxicology (SOT), the governing body of the Society, views these proposals as being contradictory to the principles on which the science of toxicology is based.

The SOT is a professional organization composed of scientists (approximately 3,500) from academia, government, non-governmental organizations and industry who are engaged in various areas of toxicology. The toxicologist is specially trained to examine the nature of the adverse effects of chemical and physical agents on living organisms and the environment. Toxicologists investigate the mechanism of action of the agent under consideration and assess its potential to cause adverse effects.

The literal definition of toxicology - the study of poisons - is somewhat simplistic in that it implies that we know which substances are toxic and which are not. In fact, a truism that has endured for about five hundred years is that essentially every chemical, either alone or in combination with other chemicals - in sufficient doses - is capable of producing an adverse effect. In more familiar terms, the dose makes the poison. Chemicals may have beneficial effects at some doses and adverse effects at others. A responsibility of the toxicologist is to define the potential toxic effects that chemicals can induce and to determine the conditions of use that minimize or prevent these effects so that the beneficial attributes of chemicals can be realized safely.

Some chlorinated compounds may present a justifiable health concern and, indeed, some (e.g., DDT) have been banned. However, a comprehensive strategy to eliminate a class of chemicals containing a common element (e.g., chlorine) is simplistic and ignores the basic principles of toxicology that govern risk assessment. In addition, it is important to note that elimination of chlorine from the environment would be impossible because there are many naturally occurring chlorine-containing chemicals (including sodium chloride). The number of such that have been identified has expanded markedly in the past decade, e.g., 30 naturally occurring chlorinated chemicals had been identified in 1968 compared with 1,500 in 1992 (Wilkes et al., 1994).

We should continue to conduct research to identify the potential for chemicals to damage the environment and/or endanger human health, ideally before they are released. The risk from a chemical exposure can be predicted realistically only if there is adequate information about the intrinsic toxicity of the chemical (including dose-response data), the potential for exposure, and the capacity for the chemical to bioaccumulate and persist in the environment. Chlorinated chemicals not only differ substantially in their toxic potencies, but they also differ in their propensities to bioaccumulate and persist in the environment. Thus, the mere presence of an element, e.g., chlorine, does not automatically impart harmful properties to a chemical.

All chlorine-containing compounds are not equally hazardous. Therefore, SOT takes the position that a broad-based ban of the class of chemicals containing chlorine, or any other element for that matter, would be both irresponsible and unscientific. Such a prohibition would unnecessarily eliminate many beneficial chemicals from common use. For example, the chlorination of drinking water in the vast majority of U.S. water systems has prevented untold numbers of illnesses and deaths by killing pathogenic organisms found in the water supply. The formation of low levels of potentially toxic chlorinated compounds as a result of this process is certainly of concern and must be minimized.

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However, the estimated hazard posed by the trace amounts of these materials that are produced is insignificant compared to that from untreated water. Accordingly, the benefit of a chlorinated water supply vastly outweighs its estimated risks. Other essential uses for chlorinated compounds include hospital disinfection, plant protection and the production of countless consumer products, including pharmaceuticals and plastics. Therefore, before a ban of chlorinated compounds (or a marked reduction of their use) can be considered in a realistic context the feasibility of producing effective and less toxic substitutes must be demonstrated. The concern surrounding the use of chlorine and chlorine-containing compounds is related, at least in part, to the large amount of information that has been generated by research on the toxicities of some of the compounds in this class. However, a similar body of evidence does not exist (i.e., the studies have not been performed) for most alternative compounds. Thus, before changes are made, the consequences of elimination of a compound or the hazard of using another chemical to achieve the same end must be considered.

The Society of Toxicology supports a comprehensive objective approach to understanding the potential hazards of chlorine and chlorine-containing compounds. It recognizes that there is a substantial body of evidence that implicates some of these compounds as potential human and environmental hazards. It is also aware that other, nonchlorinated, chemicals have a similar or greater potential to cause harm. Consequently, the SOT takes the position that the most responsible and scientifically sound approach is to assess the toxicity of agents on a chemical by chemical basis, rather than target one class of chemicals (e.g., chlorine-containing compounds) for study and elimination. The determination of unacceptable should be based on scientific data that document the adverse effects of exposure and a weighing of the risks vs. benefits of using the chemical in question. Indeed, based upon sound principles of toxicology, rational and effective assessments of the potential toxicity of chemicals, including chlorinated chemicals, are currently taking place and rigid standards exist for registration of new products to which people will be exposed.

Presented on behalf of the Society of Toxicology, Meryl H. Karn, President, Society of Toxicology, 1767 Business Center Drive, Suite 302, Reston, VA 22090 USA

FOOTNOTES

1This document was prepared in consultation with the SOT ad hoc Chlorine Working Group. Members of the group were: J.P.

2Affiliations: JAM, Institute for Evaluating Health Risks, Washington, DC; JCL, Jelinek, Schwartz & Connolly, Inc., Washington, DC; JIG, Department of Pharmacology and Toxicology, Michigan State University, East Lansing, MI; JPK, Division of Pharmacology and Toxicology, University of Texas at Austin, Austin, TX; JZ, Department of Environmental Health Sciences, Johns Hopkins University, Baltimore, MD; and MHK, Department of Environmental and Occupational Health University of Pittsburgh, Pittsburgh, PA.

REFERENCES


U.S. Environmental Protection Agency's 1994 recommendations in the Pollution Discharge Prohibitions of the Clean Water Act Reauthorization, as transmitted to the Congress by the Executive Office, page 22, February 1994, EPA 880-R-94-007. (A copy of this may be obtained from the Society of Toxicology, 1767 Business Center Drive, Suite 302, Reston, VA 22090 USA)


POSITION PAPER PROCEDURES

The SOT Council Procedure for submitting Position Papers was included in the September/ October newsletter.

For further information or copies of the procedures, contact the SOT Headquarters at (703) 438-3115 or Fax (703) 438-3113.
POSTDOCTORAL POSITION

Postdoctoral position in toxicology to study the molecular biology of sulfotransferases and hepatic transport mechanisms. Expertise in molecular biology techniques is preferred. Send applications and names of three references to: Curtis D. Klaassen, Ph.D., Department of Pharmacology and Toxicology, University of Kansas Medical Center, Kansas City, KS 66160-7417, Telephone: 913-588-7714; Fax: 913-588-7501.

ASSISTANT PROFESSOR

Neuropharmacology/Neurotoxicology. The Department of Pharmacology, Toxicology and Therapeutics at the University of Kansas Medical Center invites applications for a tenure-track position at the Assistant Professor level. The applicant must have a Ph.D. or M.D. degree, with two or more years of postdoctoral experience. The successful candidate will be expected to establish an independent research program in molecular neuropharmacology/neurotoxicology and contribute to the teaching of graduate and medical students. The ideal candidate will have had training in pharmacology, neurosciences and molecular biology. Affiliations with the Center for Environmental and Occupational Health and the Mental Retardation Research Center are possible. Curriculum vitae and the names of three references should be sent to: Dr. S.J. Enna, Department of Pharmacology, Toxicology and Therapeutics, University of Kansas Medical Center, Kansas City, KS 66160-7417. The University of Kansas is an Affirmative Action/Equal Opportunity employer.

The Mt. Desert Island Biological Laboratory Announces New Investigator Toxicology Awards For Summer 1995

The Mount Desert Island Biological Laboratory is an independent marine and freshwater biological station located on the coast of Maine near the mouth of the Bay of Fundy. The Center for Membrane Toxicity Studies (CMTS), funded by a NIEHS Marine and Freshwater Biomedical Science Grant, is an integral component of the Mount Desert Island Biological Laboratory (MDIBL).

Fellowship Opportunity - The CMTS provides funding for pilot studies for postdoctoral as well as junior and senior level scientists to do research at MDIBL, either independently or in collaboration with CMTS investigators during the summer months (primarily June through September, although extended periods may be considered). Fellowship amount is based on individual needs and can include a stipend, laboratory space, housing, and funds for supplies and travel. To receive application materials please write to the address below or call the MDIBL at (207) 288-3605. The deadline to receive applications for the 1995 summer session is January 15, 1995.

The Mount Desert Island Biological Laboratory Department CMTS Box 35 Old Bar Harbor Road Salsbury Cove, ME 04672

BP Oil Company Becomes SOT Corporate Member

The Society of Toxicology is pleased to announce that BP Oil Company has become a Corporate Member of the Society. The Society gratefully acknowledges its Corporate Members and the programs that they make possible.

Corporate members of the Society of Toxicology receive the SOT journals: *Fundamental and Applied Toxicology*, and *Toxicology and Applied Pharmacology*, and SOT Annual Meeting publications.

If you would like information on becoming a Corporate Member, please contact Shawn Lopez at the SOT Headquarters Office (703) 438-3115.
PUBLICATIONS OF INTEREST

- Aquatic Toxicology: Molecular, Biochemical, and Cellular Perspectives. Edited by: Donald C. Malins, Gary K. Ostrander, Lewis Publishers, 2000 Corporate Blvd., N.W., Boca Raton, FL 33431, (407) 994-0555.

- Biotransformation, Volume 6. Edited by Dr. D.R. Hawkins, Head of Metabolism and Environmental Chemistry, Huntingdon Research Centre Ltd., the Royal Society of Chemistry, Tirpin Distribution Services Ltd., Blackhorse Rd., Leichworth, Herts SG6 1HN, UK. +44 (0)462 672555, Fax +44 (0)462 480947.

- National Research Council Recently Released Reports:
  - Manganese: Effects on the Nutrient Requirements of Food-Producing Animals;
  - Livestock Disease Eradication: Evaluation of the Cooperative State-Federal Bovine Tuberculosis Eradication Program;
  - Livestock Requirements of Poultry, Ninth Revised Edition;
  - Range and Rangeland Health: New Methods to Classify, Inventory, and Monitor Rangelands;
  - Managing Global Genetic Resources: Agricultural Crop Issues and Policies;

Copies of these reports can be ordered through the publisher, The National Academy Press, by calling (202) 334-3313 or toll free (800) 624-6242.

UPCOMING CONFERENCES


- 27th Annual STC Symposium, Molecular Toxicology: Biomarkers and Transgenic Models, December 1-2, 1994 Holiday Inn Crowne Plaza, 420 Sherbrooke Ave, W., Montreal, Quebec H3A 1B4, Gordon Krip Ph.D., Executive Director STC, P.O. Box 517 Beaconsfield, Quebec H9W 5V1, Canada.

- The Western Pharmacology Society Meeting, January 22-27, 1995, Maui, HI, James L. Way, Shelton Professor of Pharmacology & Toxicology, 304 Reynolds Medical Building, College Station, Texas 77843-1114, (409) 845-2817, Fax: (409) 845-0699.


- 5th International Symposium, February 20-24, 1995, Hannover Medical School, Germany, Dr. H.C. U. Mohr, Hannover Medical School, Institute of Experimental Pathology, Konstanty-Gutschow-Str. 8, D-30625 Hannover, Germany, (+49) 511-532-4522/23, Fax: (+49) 511-5350-155.

- Society of Toxicology Annual Meeting, March 5-9, 1995, Baltimore Convention Center, SOT Headquarters, (703) 438-3115, Fax: (703) 438-3113.

- Introduction Course on Food Toxicology, March 13-17, 1995, Dr. Almeida, Nutrition Department, Oporto University, 351-2-4102064, Fax: 351-2-4104143.

- British Toxicology Society Scientific Meetings: Altered Gene Expression in Toxicity, March 27 - 29, 1995, York; Dr. J.K. Chipman, Meetings Secretary, School of Biochemistry, University of Birmingham, Edgbaston, Birmingham B15 2TT, England.

- Mid-America Toxicology Course, April 23-28, 1995, Kansas City, Missouri, Curtis D. Klaassen, Ph.D., Professor of Pharmacology & Toxicology, University of Kansas Medical Center, Kansas City, KS 66160-7417, (913) 588-7714, Fax:(913) 588-7501.


- 3rd International Course on the Safety Assessment of Pharmaceuticals, May 7-12, 1995, Tarrytown Hilton, Janet Marino at The American Health Foundation, (914) 789-7140, Fax: (914) 592-6317.


- In Vitro Toxicology, September 6-8, 1995, Oxford, Dr. J.K. Chipman, Meetings Secretary, School of Biochemistry, University of Birmingham, Edgbaston, Birmingham B15 2TT, England.
CHAPTER NEWS

National Capital Area Chapter News

At its spring meeting on June 3, 1994 the National Capital Chapter sponsored a Conference on Aquatic Toxicology: (1) Use of Aquatic Organisms in Assessing Human Toxicology and (2) Ecotoxicology. The meeting was held at the Maryland Science Center in Baltimore's Inner Harbor and was cosponsored by the Association of Government Toxicologists. The program included talks on "The Use of Frog Embryo Teratogenesis Assay-Xenopus (FETAx) in Detecting Human Developmental Toxicants" by Dr. John Bante of Oklahoma State University, "Cancer Etiology and Prediction: Radical-induced DNA Base Modifications in Human and Aquatic Systems" by Dr. Donald Malins of the Pacific Northwest Research Foundation, Seattle, WA, "Immunotoxicology in Mammals and Fish" by Dr. Judith Zelikoff of NYU Medical Center, "Aquatic Toxicology and Ecological Risk Assessment" by Dr. Eric Silberhorn of Technology Sciences Group, Washington, D.C., "Heavy Metals and Metallothionen in Maine Mollusks" by Dr. Guri Roesijadi of the University of Maryland Chesapeake Biological Labs in Solomons, MD, and "Microbiological Contamination of Seafood" by Dr. Mary Losikoff of the FDA's Office of Seafood in Washington, D.C. The morning and afternoon session chairpersons were Dr. Lorraine Twerdok of GEO-CENTERS Inc. at Fort Detrick, MD and Dr. Gregory Smith of Wildlife International Ltd. in Easton, MD. The Program's overall chairman was the Chapter's Vice President/President-Elect, Dr. Robert J. Rubin of the Johns Hopkins School of Hygiene and Public Health. The Chapter would also like to express its gratitude to Mr. Henry Gardiner of the U.S. Army Biomedical Research and Development Laboratory (USABRDL) for financial support of the travel expenses of the invited speakers.

At the noontime buffet luncheon, Dr. Ted Farber, the outgoing President of the Chapter, was given a plaque and gavel honoring him for his outstanding contributions to the Chapter over the years. Also installed as the new incoming officers were President: Dr. Robert J. Rubin of Johns Hopkins, Vice President/President-Elect: Dr. Hary Salem of the Life Sciences Department of the U.S. Army, Aberdeen Proving Grounds, Treasurer: Dr. Alex Apostolou, a Consultant in Toxicology from Rockville, MD, Secretary: Dr. Lorraine Twerdok of GEO-CENTERS Inc., and Councilors: Dr. David Brusick of Hazelton Washington, Inc., Dr. Joy Cavagno of the USFDA, Dr. Bruce Fowler of the University of Maryland. At a subsequent Executive Committee meeting, Dr. Steve Patierno of George Washington University was also appointed as a Councilor to fill in for Dr. Fowler who is out of the country on a sabbatical.

On May 24-26, the Chapter also cosponsored a Conference on "Alternatives in The Assessment of Toxicity: Theory and Practice," held at the U.S. Army Edgewood Research, Development and Engineering Center at the Aberdeen Proving Ground, MD. Also, at the Chapter's September 13, 1994 Executive Committee Meeting program topics to be developed and sponsored during the coming year included (1) Reactive Oxygen and Antioxidants and (2) Biological Monitoring and Epidemiology.

ADMINISTRATIVE NEWS

1993-1994 ANNUAL REPORTS AVAILABLE

The Society of Toxicology 1993-1994 Annual Report is available upon request. Please contact Jackie Celcis at the SOT Headquarters office if you would like a copy.

MAIL DELAYS

Changes in U.S. Postal Service policies have caused unprecedented delays in 3rd Class mail delivery. Because the Communicaté is the primary communication tool of the Society, the November/December issue is being sent to you via 1st Class mail delivery.

1995 MEMBERSHIP DUES DEADLINE: DECEMBER 15TH

The SOT membership voted in 1994 to change the bylaws date by which dues must be paid in order to receive the SOT journals. Dues are due December 15th of the year preceding the dues year.

This change will enable the Society to pay the publisher of the journals only for the journals of those individuals continuing membership. In the past, the Society was obligated to pay journal fees for individuals who did not renew their membership and for which it never received payments.

If you have any questions concerning this change, contact the Headquarters office.