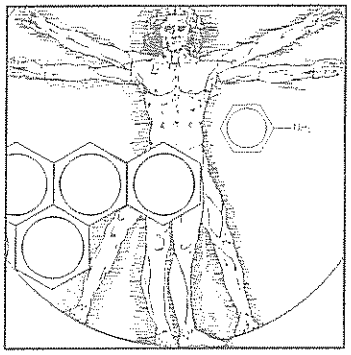


SOCIETY OF TOXICOLOGY

Communiqué

November/December 1995

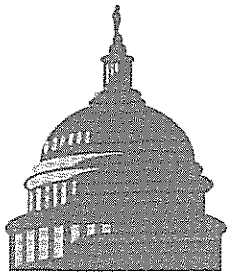
Final Night Reception Scheduled Thursday

The SOT Program Committee has scheduled four full days of cutting-edge scientific programs for the 1996 SOT Annual Meeting. The program will culminate on Thursday, March 14, with the Awards Ceremony and Final Night Reception, (held on Wednesday evening in 1995). The Awards Ceremony, which will begin at 6:30 p.m., will honor this year's award recipients and promises to have a new and exciting format. At 7:00 p.m., attendees will move next door to the Final Night Reception. The Reception is free to all and is an enjoyable way to sample Pacific realm cuisine while socializing with your colleagues. Be sure to note these changes on your calendar, so that you may join in the celebration to mark the conclusion of another successful meeting.

Substantial Membership Growth for 1995

Between 1991 and 1995, the membership in the Society of Toxicology grew at an annual rate of about 5% per year to 3880 members. In 1995, SOT received 532 membership applications. This represents an increase of nearly 14% over the number of applications submitted to SOT in 1994. Of the 532 applications received in 1995, 64% were submitted after the release of the new simplified membership application form and the decision by SOT Council to eliminate the $50 application fee. Thanks go to both the Membership Committee and Council for implementing these changes that resulted in such a dramatic increase in applications. If you know someone who is interested in becoming a member of the Society of Toxicology, please use the new membership application located in the back of your 1995-1996 Membership Directory, or contact the SOT Headquarters office. The next application deadline is **April 1, 1996.**

Watching Washington: Superfund



Key Provisions, Reauthorization/ Appropriation

SOT is actively working to ensure adequate authorization and appropriation levels for the Superfund Basic Research Program. SOT coordinated a conference call in which all Superfund Research Program Directors were invited to participate. Strategies on both the authorization and appropriations fronts were discussed. At the time of this writing, a Superfund Basic Research Pro-

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This edition of the Communiqué contains information for the SOT Annual Meeting:

- **Sponsorship Opportunities**
- **Placement Service**
- **Symposia, Workshops & Roundtables**
- **Continuing Education Courses**

Record High Abstract Total!

The totals are in, and it looks as if 1996 will be a record year. The headquarters office has received and processed 1,699 abstracts! According to our records this is the second highest total that the office has ever received (1704 in 1993 in New Orleans). The Program Committee will be working hard during the month of November to put together informative and thoughtful sessions. Acceptance letters, confirming the session type and the day and time scheduled, will be mailed during the latter part of December. If you have not received a letter by January 2, 1996, please contact **Nell Dillard** at SOT Headquarters.

INSIDE

Jack H. Dean, Ph.D.
1995-96 President of the Society of Toxicology

PRESIDENT'S MESSAGE

HORIZON 2000

THE SOCIETY OF TOXICOLOGY'S LONG-RANGE PLANNING ACTIVITY

This newsletter article describes results of your Society's 1995 Long-range Planning Activities, which I will term Horizon 2000.

A meeting was held to start this process on May 11-12, in Alexandria, Va. and included your elected officers, Council, **Shawn Lopez** from Headquarters, and two Arthur D. Little (ADL) Consultants. The ADL consultants were engaged because of their previous experience with this process in nonprofit and scientific societies to assist with the planning, facilitation and reporting of the meeting. After a draft Long-range Plan (LRP) was developed, a second meeting was held in Herndon, Va. on September 22 facilited by **Drs. Bus** and me. The participants at this meeting included Council, Shawn Lopez, and the chairpersons and leadership from the various committees whose activities are impacted by the Long-range Plan.

The process used by ADL is based on three key elements of successful planning. The first is the creation of a shared view of major external issues or trends that will impact the future success of this Society. These key issues establish the boundaries within which the SOT must successfully operate in the future. The second element of the LRP is the creation of a credible and desirable picture of the organization productively operating within these boundaries in the future. This picture of the future is composed of strategic initiatives to be implemented for the future to exist as described. Finally, the third element of planning is the establishment of more pathways to be followed in order to get to the desired future. Simply described, this process involves "Writing the History of the Future" and is done using an approach involving identification of key milestones associated with the strategic initiatives.

Prior to the first meeting, ADL interviewed the participants as well as previous Council members and identified issues and external trends all felt were facing the Society. Based on this interview process, and ADL's experience with other professional/learned organizations, the results were cast in terms of eleven specific trends believed to have potential impact on the Society.

At our first LRP meeting, we were asked to prioritize each trend by rating (1) its impact on the Society and (2) the ability of the Society to influence the trend. The following eight trends scored high in at least one of the two measures and were selected for focus in the years ahead:

- (1) Need for basic and applied research to improve risk assessment,
- (2) lack of public understanding of toxicology,
- (3) shrinking research funding sources,
- (4) changing employment demographics and employment needs,
- (5) use of animals in research,
- (6) changing computing and communications technologies,
- (7) need to strengthen international relations, and
- (8) need for a stable and broad financial platform.

Continued on page 18

FUTURE SOT ANNUAL MEETINGS

1996:	*March 10-14 Anaheim, California*
1997:	*March 9-13 Cincinnati, Ohio*
1998:	*March 1-5 Seattle, Washington*

What Do My Dues Do?

By SOT Treasurer, Mary Davis

It's that time again. Dues are due by **December 15**. Dues invoices were mailed in the middle of October (if you haven't received your invoice, please contact SOT Headquarters).

So what happens to your dues?

Of the Full and Associate member $131 dues payment, $86 goes to your journal subscriptions: *Fundamental and Applied Toxicology* and *Toxicology and Applied Pharmacology*. The remaining $45 goes to support SOT programs and run the Society. SOT members give their time to the Society, serving on the committees that accomplish the Society's goals.

SOT reimburses committee members' travel expenses (economy class only, lodging booked by our meeting manager for favorable rates). Committee meetings add to the cost of running the Society, but ensure participation by a broad spectrum of our members. SOT staff members support the committees, keep the Society's records in order, its books straight, and the management running smoothly. The staff produces the directory of members, Annual Meeting materials, and the Communiqué, as well as the ballots, dues renewal notices and just about everything else the Society sends out.

The Society's portion of your dues accounts for about 7% of SOT's income. The remaining income comes from the Annual Meeting (registration, continuing education courses, exhibits), sales of the Society's journals, Corporate Associate dues, contributions to the Society (those to the Toxicology Education Foundation are handled separately), and miscellaneous income such as advertising in the Communiqué, sales of Continuing Education syllabi, and rental of mailing lists. Some of our programs, such as the Placement Service and the Resource Guide, have fees to offset the expenses of the program.

SOT's largest revenue and expense item is the Annual Meeting. The cost of the meeting (not including exhibits, CE or placement) is about $163 per registrant. As a Society member, you can register for $155 (by January 19). The exhibits, nonmember registrant fees ($255), and Continuing Education courses generate enough income to pay for the balance of Annual Meeting expenses and to support the Society's other programs — making the public aware of the science of toxicology, reaching the next generation of toxicologists with our intern and minority programs, working with Congress on issues important to our members, and other long-term goals of the Society (listed in **Jack Dean's** article on page two of this Communiqué).

If you have questions concerning the Society's programs and/or your dues, please feel free to call our Headquarters office.

1996 Membership Dues Deadline: December 15

Dues Waiver Policy

Employment:

Any SOT member in good standing whose employment is temporarily interrupted may apply for a waiver of dues for a period up to one year. A dues waiver may be renewed for an additional year upon reapplication.

Members should submit to the SOT Executive Director, a written request that includes a description of most recent employment history.

Requests for dues waivers will be maintained confidentially and will be individually reviewed by the chairman of the Membership Committee.

Members granted dues waivers will continue to receive the SOT newsletter, journals and will be permitted to submit abstracts and register for the Annual Meeting at the membership rate.

Retirement:

Full and Associate members who have retired from active work in toxicology may apply for Retired Status. Retired members pay no dues but retain full membership benefits and may elect to subscribe to the Society's journals at the discounted member rate. Requests for Retired Status are due at SOT Headquarters by **December 15.**

The *Society of Toxicology Communiqué* is published 5 times annually in Reston, Virginia for members of the Society of Toxicology.

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Jay I. Goodman, Ph.D.
Deadlines for Upcoming Issues:
December 3, 1995
April 3, 1996
June 3, 1996
August 3, 1996

Society of Toxicology

35th Annual Meeting

Anaheim Convention Center

March 10-14, 1996

Why Come to Anaheim? *Views from SOT's Southern California Chapter Members*

For many people, Anaheim means either Disneyland or a variety of chili pepper. When asked for the Southern California perspective on why SOT members should come to Anaheim next March for the Annual Meeting, many of the nature-lovers among us also immediately listed opportunities for sailing, swimming, fishing and watching the sun set into the Pacific Ocean from sandy beaches, all within a short distance (by California standards) from the Anaheim Convention Center. Exploring local canyons, mountains and deserts seems to be another popular leisure activity for Southern California SOT Chapter members and their families. Still others frequent the artist colonies and gourmet restaurants in Laguna Beach—south of Anaheim, and La Jolla—north of San Diego. The newly-emerging wine country of Temecula in northeast San Diego County was also mentioned several times.

The nice variety of sight-seeing bus tours and the Ensenada, Mexico cruise described in the 1996 Annual Meeting Preliminary Information booklet are definitely good values for those who prefer planned social events and to let others do the driving. If you want to experience Southern California as the locals do when the meeting is not in session, you might also want to consider renting a car at some point and obtaining the "insider's" list of restaurants and lesser-known activities being compiled for meeting participants by the Southern California SOT Chapter.

Good weather can almost be guaranteed, but nobody was willing to do that as El Nino has been playing tricks on us in recent years. Comfortable walking or hiking shoes and a warm sweater or jacket should be all you will need; *however, we suggest that everyone might also pack some light rain protection to ensure sunny skies over Southern California during the Meeting.*

We look forward to your arrival.

Placement Service

For the Annual Meeting, the Placement Service will be housed at the Anaheim Marriott located across the street from the Anaheim Convention Center. If you would like Placement Forms, please contact **Nell Dillard** at SOT Headquarters.

Sponsorship Opportunities

Event sponsoring opportunities are available for the 1996 SOT Annual Meeting and include student, minority program, and general session events. 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 4,000 SOT members); and through signage on-site. If you are interested in sponsorship, please contact **Clarissa Russell** at SOT Headquarters for a list of available opportunities.

SOT/EUROTOX Debate

Resolved: Dose Setting for Carcinogenicity Studies Should Be Based on the Maximum Tolerated Dose.

The SOT/EUROTOX Debate held at the 1995 EUROTOX Congress in Prague will be repeated at the 1996 SOT Annual Meeting in Anaheim, California. This year's debate discusses the advantages and disadvantages of testing for carcinogenicity at the maximum tolerated dose (MTD). According to internationally accepted test guidelines, the highest dose level in carcinogenicity studies should be sufficiently high to elicit signs of minimal toxicity without substantially altering the normal life span due to effects other than tumors. It has been argued that the use of the MTD will maximize the likelihood of detecting carcinogens, thus adjusting for the insensitivity of the model. Also testing at the MTD will provide a benchmark that allows comparisons of potency between carcinogens. On the other hand, the use of the MTD concept has been criticized strongly. The kinetic behavior of the test chemical may be different at the MTD compared to lower doses. Also, the mechanism of action operating at the MTD may be different from that at lower doses. In addition, animal welfare issues and increased demand on resources have been brought forward against the MTD requirement.

The discussant for the motion is **Eugene E. McConnell** (SOT) and the discussant against the motion is **Iain F.H. Purchase** (EUROTOX).

Symposia

Sphingolipids - The Enigmatic Lipid Class: Biochemistry, Physiology, and Pathophysiology

Chairpersons: R.T. Riley and K.A. Voss, USDA, Athens, GA

Sponsored by the Food Safety and Mechanisms Specialty Sections

The "sphingo" in sphingolipids comes from the fact that in 1884 J.L.W. Thudichum found sphingolipids to be "Sphinx-Like" in that they were an enigma. While still an elusive class of lipids, research on complex sphingolipids, free sphingoid bases, and sphingolipid degradation products in signal transduction pathways, and as mediators of cell growth, differentiation, and cell death has been rapidly expanding. Recently, sphingolipid metabolites have been demonstrated to modulate cellular calcium homeostasis and cell proliferation via interaction with specific cellular receptors. Also, disruption of sphingolipid metabolism has been implicated in several animal diseases and human cancer by toxins that are currently the focus of a FDA long term tumor study. This symposium will focus on (i) the role of sphingolipids as important nutrients and contributing factors in disease, (ii) the involvement of disrupted sphingolipid metabolism in animal disease and cellular deregulation associated with exposure to inhibitors of ceramide synthase, (iii) glucosphingolipids as mediators of cell cycle progression and stress responses, and (iv) the role of sphingoid base metabolites and the ceramide cycle in expression of genes regulating cell growth, differentiation, and apoptosis.

Speakers:

- A.H. Merrill, Jr., Emory University School of Medicine, Atlanta, GA
- R.T. Riley, USDA, Athens, GA
- J.J. Schroeder, Michigan State University, East Lansing, NJ
- J.A. Shayman, University of Michigan, Ann Arbor, MI
- S. Speigel, Georgetown University, Washington, DC

Mitochondrial-Mediated Cell Injury

Chairpersons: K.B. Wallace, University of Minnesota, Duluth, MN and D.P. Jones, Emory University, Atlanta, GA

Sponsored by the Mechanisms Specialty Section

Mitochondria are central to cellular energy metabolism, redox control, osmotic regulation, pH balance and cytosolic Ca2+ homeostasis. Thus, chemical-induced mitochondrial dysfunction can have diverse effects on extramitochondrial functions, and considerable effort is often required to distinguish between toxic mechanisms occurring directly through mitochondrial targets and those in which mitochondria dysfunction only plays a modulatory role in cell death is caused by damage to extracellular targets. Mitochondria are generally susceptible to damage from oxidants and electrophiles as well as lipophilic cations and lipophilic weak acids. Of particular interest, the mitochondria contain a small genome which is essential for mitochondrial function and not well protected against DNA damage. Consequently, accumulated mitochondrial DNA damage can contribute to chronic toxicity even if short-term studies do not reveal mitochondrial dysfunction. Mitochondrial dysfunction is often organ-specific because the mitochondrial phenotype is cell specific with regard to enzyme and tranporter content, subcellular localization and mitochondrial volume density within cells. Variations in mitochondrial content and characteristics are also known to occur with chronic hypoxia, aging, and other pathophysiologic conditions so that risk of toxicity due to agents affecting mitochondria is likely to vary considerably in association with other health-related parameters.

Speakers:

- G. Cortopassi, University of California-Davis, Davis, CA
- J.T. Eells, Medical College of Wisconsin, Milwaukee, WI
- V.M.C. Madeira, University of Coimbra, Portugal
- J.L. Stevens, W. Alton Jones Cell Science Center, Lake Placid, NY
- K.B. Wallace, University of Minnesota, Duluth, MN

Oxidative Stress and Glutathione Redox Status in Mechanisms of Developmental Embryotoxicity

Chairperson: C. Harris, University of Michigan, Ann Arbor, MI

Sponsored by Mechanisms and Reproductive & Developmental Specialty Sections

Chemical agents known to cause persistent anatomical and/or functional birth defects, have also been known to generate free radicals and reactive oxygen species (ROS). The uncontrolled production of ROS or free radicals, coupled with inadequate antioxidant defenses, creates conditions of oxidative stress which have been proposed as the primary insult through which many teratogenic lesions may be produced. Reactive oxygen species are reported to regulate embryonic development by providing signals for cell proliferation, differentiation and the initiation of apoptosis. Glutathione (GSH), low molecular weight thiols and related enzymes comprise a major antioxidant and radical scavenging defense system in most cell types. Glutathione also serves an important role in maintaining the proper cellular redox environment for control of normal gene expression and regulation of biochemical functions. It is probable that the disturbances in redox and antioxidant status that occur in response to chemical insult and environmental extremes are sufficient to alter genetic and biochemical functions and disrupt development. This symposium will explore the role and function of GSH status in the preimplantation and postimplantation embryo with respect of chemically-induced oxidative stress and describe several biochemical and molecular consequences resulting from the altered redox state. Phenytoin embryotoxicity will be reviewed with respect to the ability of the conceptus to metabolize the compound to free radicals, the role of GSH in mediating this response, and the cellular and molecular alterations elicited by exposure. The session will conclude by evaluating the connection between ROS, cellular antioxidant functions, and control of programmed cell death involving products of the bcl-2 gene family.

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Symposia

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Speakers:

- C. Gardiner, University of Northern Colorado, Greeley, CO
- C. Harris, University of Michigan, Ann Arbor, MI
- D.M. Hockenbery, Fred Hutchinson Cancer Research Center, Seattle, WA
- P.G. Wells, University of Toronto, Toronto, Ontario

Recombination and Genome Rearrangements: Involvement in Carcinogenesis and Genotoxic Endpoints

Chairperson: R.H. Schiestl, Harvard School of Public Health, Boston, MA

Sponsored by the Molecular Biology and Carcinogenesis Specialty Sections

To predict a potential carcinogenic activity of chemicals from genetic toxicology assays it seems important to use a genetic endpoint that is involved in carcinogenesis. In addition to point mutations, DNA recombination and genome rearrangements causing deletions, gene amplifications and translocations are involved in carcinogenesis and in most genetic diseases. Tumor suppressor genes can be removed by deletion events, proto-oncogenes can be turned on after deletion events join them to expressed loci and loss of heterozygosity may uncover the phenotype of recessive mutations. Mutations causing a high frequency of carcinogenesis such as p53, ataxia telangiectasia, Werners syndrome and Blooms syndrome increase genetic instability causing a high frequency of recombination and genome rearrangements. Assays for recombination exist in yeast and in Drosophila. Assays in both organisms have been validated to some extent and they identify recombinagens. New assays have been developed in human cells and in vivo in mice. Deletion events in yeast, in human cells and in the mouse are inducible by carcinogens including carcinogens that are negative in the Salmonella (Ames) assay and in most other short term tests. This symposium will feature presentations on the effects of mutations causing a high frequency of cancer on recombination and genome rearrangements and the molecular characterization of these events. The second part of the symposium will feature an overview of assays detecting such recombination events, their validation status and advantages of their use in genetic toxicology.

Speakers:

- R. Monnat, Jr., University of Washington, Seattle, WA
- R.H. Schiestl, Harvard School of Public Health, Boston, MA
- T. Tlsty, UCSF, San Francisco, CA
- F.K. Zimmermann, Darmstadt Institute of Technology, Darmstadt, Germany

Drug Metabolic Enzymes in Developmental Toxicology

Chairperson: M.S. Miller, University of Tennessee, Knoxville, TN

Sponsored by the Molecular Biology and Reproductive & Developmental Toxicology Specialty Sections

Although much is known about the metabolism of environmental toxicants in adult organisms, little information exists on the role of cytochrome P450 (CYP) enzymes during development. The developing organism is remarkably dynamic, presenting a constantly changing metabolic profile as various enzyme systems are activated or repressed. This may explain the markedly different sensitivities to various toxicants that are exhibited throughout the developmental period. The application of molecular biological methods has provided important information on the roles of these enzymes in modulating the response of the developing organism to toxicological exposures. The first talk will focus on the identification and role of CYPs during early organogenesis, particularly on how these enzymes influence the response of the conceptus and early embryo to toxic chemicals. The second presentation will discuss the identification of CYPs expressed during human development, as many of the enzymes present in adults are not expressed in the fetus. The third speaker will discuss the developmental consequences of loss of expression of particular CYP enzymes, focusing on recent studies employing knockout mice to examine the role of CYP1A1 during development. The last two talks will discuss some of the short and long term consequences of *in utero* exposures to toxic chemicals and the role of CYP in modulating the toxic response of the developing organism. The first of these will focus on the role of CYP2E1 in human fetuses during late gestation and the response of this enzyme to inducing agents such as alcohol. The last talk will discuss the role of CYP1A1 in the activation of the *Ki-ras* oncogene following *in utero* exposure to carcinogens as a mechanism for lung tumor formation in a pharmacogenetic mouse model.

Speakers:

- F.P. Guengerich, Vanderbilt University, Nashville, TN
- M.R. Juchau, University of Washington, Seattle, WA
- M.S. Miller, University of Tennessee, Knoxville, TN
- D.W. Nebert, University of Cincinnati, Cincinnati, OH
- J.L. Raucy, The Agouron Institute, La Jolla, CA

Brain Metallothioneins: The Role in Physiology and Pathology

Chairperson: M. Aschner, Bowman Gray School of Medicine, Winston-Salem, NC

Sponsored by the Neurotoxicology Specialty Section

The objective of this symposium is to define the role of brain metallothioneins (MTs) both in brain physiology and pathology. MTs are small, cysteine-rich, metal-binding proteins that are expressed in all eukaryotes that have been examined. In mammals, 2 isoforms, MT-I and MT-II, are expressed in most organs and they are regulated by a number of metals, hormones, and xenobiotics. Recent studies have revealed a brain-specific isomer, MT-III. Proposed functions attributed to brain MTs include detoxification of metals and their storage, zinc storage for the demands of cell differentia-

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Symposia

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tion and proliferation, metal transfer, and scavenging of free radicals. The existence of brain-specific isoform of MT-III also suggests that it might have important neurophysiological functions, especially in the utilization of zinc as a neuromodulator. This idea is reinforced by the potential involvement of MT-III in a number of neurodegenerative disorders, and its depletion in humans afflicted by Alzheimer's disease, and recent observations on the in creased sensitivity of MT-III "knockout" mice to kainate-induced seizures. The specific aims of this symposium are: 1) to review the physiologic functions and biochemical properties of MTs, 2) examine the distribution of brain MT with particular emphasis on cell-specific localization (neurons vs. glia), 3) to discuss MT gene responsiveness upon brain injury, and 4) to discuss the potential role of MTs in the etiology of neurodegenerative disorders.

Speakers:

- M. Aschner, Bowman Gray School of Medicine, Winston-Salem, NC
- A.I. Bush, Harvard Medical School, Charlestown, MA
- M.G. Cherian, University of Western Ontario, London, ON, Canada
- C.D. Klaassen, University of Kansas Medical Center, Kansas City, KS
- R. Palmiter, University of Washington, Seattle, WA

Dietary and Environmental Estrogens and Antiestrogens: Complex Issues

Chairpersons: W. Helferich, Michigan State University, East Lansing, MI, S. Safe, Texas A & M University, College Station, TX, and J. Yager, Johns Hopkins University, Baltimore, MD

Sponsored by the Food Safety and Carcinogenesis Specialty Sections

Many dietary chemicals have been classified as estrogens and antiestrogens. The estrogenic potential of plant chemicals (phytoestrogens) was first described approximately fifty years ago when it was observed that sheep grazing on clover showed clinical signs of hyperestrogenism. The symptoms included: Milk excretion from virgin females, milk excretion from castrated males and infertility. Although phytoestrogens are weak estrogen agonists they are consumed by both animals and humans at levels high enough to elicit estrogen responses in experimental animal models. Additionally, it has been speculated that these weak agonists may act as antagonists to endogenous estradiol and act beneficially with regard to certain chronic diseases such as estrogen-dependent breast cancer. Asian populations which consume high levels of phytoestrogens in foods, such as soy and its derived products, have a relatively low incidence of breast cancer and other hormone-dependent cancers. Since the majority of human breast cancers are dependent on estrogen, it appears the consumption of an estrogen agonist would present some risk rather than be preventative in women consuming phytoestrogens. This paradox of consumption of foods containing phytoestrogens and decreased levels of breast cancer will be discussed by the first two speakers. Recently chemicals which act as aromatic hydrocarbon receptor (AhR) agonists have been shown to be antiestrogenic in both in vivo and in vitro models. Potential mechanisms for the antiestrogenicity of these compounds will be discussed by the third speaker. Various environmental agents can alter the metabolism of both xenoestrogens and endogenous estrogens. The fourth speaker will discuss the role of increased metabolism to catechols and the resulting increased oxidative damage in estrogen-induced carcinogenesis.

Speakers:

- W. Helferich, Michigan State University, East Lansing, MI
- J. Liehr, University of Texas Medical Branch, Galveston, TX
- M. Messina, Consultant, Port Townsend, WA
- S. Safe, Texas A & M University, College Station, TX

Immunotoxicity of Medical Devices

Chairpersons: K. Rodgers, University of Southern California, Los Angeles, CA and J.T. Zelikoff, New York University Medical Center, Tuxedo, NY

Sponsored by the Immunotoxicology Specialty Section

The ability of a medical device to interact with the immune system currently involves assessment of the immunogenic potential and biocompatibility of the device or an extract of the device. However, implants are often in the body for extended periods of time and/or are placed by a surgical procedure that in and of itself will generate an acute inflammatory response. This symposium will discuss studies that have been performed to evaluate: the immunogenicity of various devices that consist of several different compositions (i.e., silicone, metals, and latex) in contact with different anatomical sites; the ability of a device to modulate an inflammatory response generated by a surgical procedure or trauma; and the response of the body to a material left in place for extended periods of time. This symposium will bring together scientists from many different disciplines to begin to identify and fill in the gaps in this area.

Speakers:

- C.G. Frondoza, Johns Hopkins University, Baltimore, MD
- J.J. Jacobs, Rush Medical College, Chicago, IL
- P.C. Klykken, Dow Corning Corporation, Auburn, MI
- K. Rodgers, University of Southern California, Los Angeles, CA
- V.J. Tomazic, FDA, Rockville, MD

Aquatic Pollution-Induced Immunotoxicity in Wildlife Species

Chairpersons: R.W. Luebke, US EPA, Research Triangle Park, NC and J.T. Zelikoff, New York University Medical Center, Tuxedo, NY

Sponsored by the Immunotoxicology Specialty Section and Society of Environmental Toxicology and Chemistry

At present, immunotoxicity studies are, with few exceptions, conducted under laboratory conditions and nearly all of these studies are done in laboratory rodents. As such, many toxicologists are only vaguely aware

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Symposia

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of the immunotoxicity studies done under the more natural condition of environmental exposure to pollutants. The purpose of this symposium is threefold: the dissemination of information on the immunologic health of selected wildlife species in contaminated habitats; to demonstrate the plausibility of using altered immune responses of directly-exposed species as a biomarker to predict the effects of toxic environmental pollutants; and to foster collaboration between field and laboratory immunotoxicologists. The first speaker is Peter Hodson, president of SETAC. He will address trends in aquatic pollution and provide specific examples based on pulp mill effluents. The next three speakers will discuss the effects of polluted environments on feral populations of fish (Mohamed Faisal), birds (Keith Grasman) and seals (Peter Ross) living in these contaminated environments. The final speaker (Judy Zelikoff) will discuss how well laboratory immunotoxicological studies in wildlife species compare with data generated in field studies. All of the speakers in this symposium are actively involved in evaluating immune function in wildlife species under field or laboratory conditions and are uniquely suited to discuss the ecological, immunological and logistical aspects of these studies.

Speakers:

- M. Faisal, The College of William and Mary, Gloucester Point, VA
- K.A.Grasman, Wright State University, Dayton, OH
- P.V. Hodson, Queens University, Kingston, ON, Canada
- P.S. Ross, Seal Rehabilitation and Research Centre, Pieterburen, The Netherlands
- J.T. Zelikoff, New York University Medical Center, Tuxedo, NY

Modulation of T-Helper Cell Populations: Potential Mechanisms of Respiratory Hypersensitivity & Immune Suppression

Chairpersons: M.J. Selgrade, US EPA, Research Triangle Park, NC and D.A. Lawrence, Wadsworth Center for Labs & Research, Albany, NY

Sponsored by the Immunotoxicology and Inhalation Specialty Sections

There are two major subdivisions of CD4+ helper T lymphocytes which regulate different sets of immune responses. Th1 cells produce interleukin (IL) 2 and γinterferon as well as other cytokines, mediate delayed-type hypersensitivity responses, provide help for complement-fixing antibodies, activate macrophages, and may be particularly important in responding to viral and tumor antigens expressed on cell surfaces. Th2 cells produce a different array of cytokines including IL-4 and IL-5, which promote IgG1, IgA, and IgE responses, and enhance eosinophil differentiation. Th2 cells are more important in responding to parasitic infections and the generation of immediate-type hypersensitivity responses, including reactions to allergens and some types of asthma. The balance between Th1 and Th2 cells is affected by infections, aging, hormones, and toxic substances. Such alterations may impact the outcome of infectious, neoplastic, allergic, and autoimmune diseases. It is apparent that one way in which chemicals might produce immunotoxic effects is via modulation of T helper cell populations. This symposium presents examples of several agents which appear to act in this manner and describes both underlying mechanisms & impacts on susceptibility to and expression of infectious & allergic disease. (This abstract does not reflect EPA policy.)

Speakers:

- M.I. Gilmour, University of North Carolina, Research Triangle Park, NC
- I. Kimber, ZENECA, Ltd., Macclesfield, Cheshire, UK
- D.A. Lawrence, Wadsworth Center for Labs & Research, Albany, NY
- M.R. Schuyler, VA Medical Center, Albuquerque, NM
- M.J.K. Selgrade, US EPA, Research Triangle Park, NC
- S.E. Ullrich, M.D. Anderson Cancer Center, Houston, TX

Repair of DNA Damage: Mechanisms and Consequences

Chairperson: W.M. Baird, Purdue University, West Lafayette, IN

Sponsored by the Carcinogenesis Specialty Section

Numerous chemicals exert toxic effects through their interactions with DNA. These genotoxic agents range from drugs used in chemotherapy to many classes of environmental carcinogens such as alkylating agents, combustion products, compounds from plants and dye intermediates. These interactions can result in the induction of mutations that can lead to cancer, teratogenesis and a number of other deleterious effects. A major determinant of whether such toxicological consequences occur is the ability of the individual to repair this damage to DNA prior to DNA replication and the fixation of a mutation. To understand the consequences of exposure to genotoxic compounds, it is essential to understand how DNA damage is repaired. It is now recognized that DNA repair is not uniform throughout the genome but occurs selectively in certain areas. This selection is dependent upon the type of DNA damage induced as well as the area of the genome. The symposium is designed to provide an introduction to repair in the genome overall and to describe repair within specific genes and DNA strands and its relationship to transcriptional activity. The recent development of approaches for examining repair at specific sites in the DNA of the genome using ligation-mediated PCR will be described. Overall, this symposium will provide a thorough, contemporary overview of DNA repair and its role in the response to exposure to genotoxic agents.

Speakers:

- W.M. Baird, Purdue University, West Lafayette, IN
- P.C. Hanawalt, Stanford University, Stanford, CA
- V.M. Maher, Michigan State University, East Lansing, MI

Molecular Biomarkers in Environmental Toxicology

Chairperson: J.D. Groopman, Johns Hopkins University, Baltimore, MD

Sponsored by the Carcinogenesis Specialty Section

In recent years, the great advances in our understanding of the mechanisms of action of toxicants and carcinogens has spurred the development of molecular

Symposia

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biomarkers for use in risk assessment in individuals. These biomarkers extend across the spectrum from markers of internal dose, biologically effective dose, and host susceptibility factors to specific genetic targets. Experimental models have been critical for the development of these molecular biomarkers and these studies are providing valuable data for extrapolation issues relating data obtained in an experimental setting to that which occurs in people. Recent examples of these types of studies include the link between aflatoxin exposure and liver cancer and exposure to benzene and a number of adverse human health outcomes. As this research continues, there will be an ever increasing push to translate experimental findings for other carcinogens to population-based investigations. The combination of mechanistic studies, epidemiology and risk assessment offers great potential to understand the potential for health impact from exposures to environmental agents. Thus, these studies are central to modern risk assessment technologies. Finally, these studies are being used to develop clinical intervention protocols for high risk individuals.

Speakers:

- G.S. Bailey, Oregon State University, Corvallis, OR
- J.D. Groopman, Johns Hopkins University, Baltimore, MD
- F.F. Kadlubar, National Center for Toxicological Research, Jefferson, AR
- M.T. Smith, University of California, Berkeley, CA
- G.N. Wogan, Massachusetts Institute of Technology, Cambridge, MA

Osteotoxicity and Intervention Protocols

Chairpersons: E. Jeffery, University of Illinois, Urbana, IL and M.H. Bhattacharyya, Argonne National Laboratory, Argonne, Il

Sponsored by the Metals Specialty Section

The majority of the body burden of xenobiotic minerals such as lead, fluoride, and strontium is found associated with the skeleton. Bone has long been recognized as a storage site for xenobiotic minerals. The possibility that these xenobiotics might be toxic to bone or even be released during bone resorption to produce systemic toxicity, is a relatively recent consideration. When industrial chemicals or new drugs are screened for toxicity, no evaluation of osteotoxicity is required. Development of therapies for osteoporosis is currently a very active area in the pharmaceutical field. In this area, chemicals are specifically chosen for their effects on bone physiology, and methods have evolved to evaluate osteotoxity. Our first symposium speaker is a highly respected member of the bone research community who will provide detailed insight into the role of vitamin D in normal bone growth and remodeling. This topic will feed directly into the second presentation, which addresses the osteotoxicity of lead, focusing on the cellular and molecular biology of lead interactions with the vitamin D endocrine system. Cadmium osteotoxicity will be addressed next, with unique insights provided at all levels, from humans to whole animals to organ and cell culture systems, including a view toward identifying susceptible populations. The final presentation addresses the issue of therapeutic protocols for treating osteoporosis, providing insight into current treatment options and toxicological and pharmacological aspects of developing new protocols that meet FDA guidelines.

Speakers:

- M.H. Bhattacharyya, Argonne National Laboratory, Argonne, IL
- H.F. DeLuca, University of Wisconsin, Madison, WI
- E. Jeffery, University of Illinois, Urbana, IL
- J.G. Pounds, Wayne State University, Detroit, MI
- N.A. Sacco-Gibson, Procter & Gamble Pharmaceutical, Cincinnati, OH

Regulation of Cell Proliferation and Apoptosis in Cancer

Chairperson: D.G. Kaufman, University of North Carolina, Chapel Hill, NC

Sponsored by the Carcinogenesis Specialty Section

Abnormal regulation of the life cycle of cells is a major feature of neoplasia. Most malignancies are characterized by abnormalities of cell proliferation, typically a capacity for persistent and excessive proliferation, often at accelerated rates. In addition, abnormalities of cell death, often manifested as cell immortality, are another common feature of neoplasia. This symposium will provide a broad perspective on these abnormalities in preneoplastic and neoplastic cells and it will delve into mechanisms by which they contribute to cancer. In broad perspective these alterations of cell proliferation and apoptosis will be considered for hepatocarcinogenesis. This will span the issues of carcinogen dose, risk assessment, and the alterations of cell cycle regulatory proteins within emerging liver neoplasms. The features and mechanisms of cell death will be considered and morphological manifestations will be linked to molecular mechanisms. This will be further explored with regard to alterations of levels of ionized cellular calcium and the induction of newly identified genetic pathways leading to induced cell death. Mechanisms underlying these phenomena will be explored with regard to the failure of the G1/S and G2/M cell proliferation checkpoints during carcinogenesis. The abnormalities of these protective mechanisms will be linked to the progressing genetic instability that develops early in carcinogenesis and potentiates further genetic changes, abnormalities of cell senescence and reexpression of telomerase. The vulnerability of cells to chemical carcinogens when they are treated in early part of the S phase will also be considered. Mechanisms for this vulnerability will be explored with regard to the vulnerability of replicating DNA to carcinogen adduction. In addition, studies will be considered which involve efforts to identify sequences and genetic loci in genomic DNA that are replicated in early S phase and may be critical DNA targets for carcinogenesis.

Speakers:

- T. Goldsworthy, CIIT, Research Triangle Park, NC
- D.G. Kaufman, University of North Carolina, Chapel Hill, NC
- W. Kaufmann, University of North Carolina, Chapel Hill, NC
- B. Trump, University of Maryland, Baltimore, MD

Workshops

Risk Assessment and Risk Management of Worker Exposures To Pesticides: The Next Generation

Chairperson: J.C. Lamb, Jellinek, Schwartz & Connolly, Inc., Arlington, VA
Sponsored by the Regulatory Affairs and Legislative Assistance Committee

This workshop is designed to inform SOT members of significant new developments in pesticide worker exposure assessment, risk assessment, and risk management. Pesticide risk assessment and risk management are undergoing a dramatic evolution as the regulatory agencies move away from conventional NOAEL point estimates of hazard and similar point estimates of exposure towards use of probabilistic models that estimate distributions of hazard and exposure. The first speaker will describe the hazard data that are developed for worker risk assessments and changes in how they are being used in risk assessments. The second speaker will explain the current default assumptions that apply to pesticide worker exposures and risk assessments and ways to improve the measurements and assumptions about exposure. The third speaker will describe the current databases, such as the Pesticide Handlers Exposure Database (PHED) and new models, incorporating Monte Carlo Estimations, that are used to generate estimates of exposure for workers. The fourth speaker will focus on how the US EPA is currently using these exposure and hazard data to make risk assessment and risk management decisions for pesticide workers and the implications of Monte-Carlo-base risk assessments on the risk management process. The last speaker will describe similar regulatory decisions made by the California EPA.

Speakers:

- P. Fenner-Crisp, US EPA, Washington, DC
- R.I. Krieger, UC Riverside Entomology, Riverside, CA
- J.C. Lamb, Jellinek, Schwartz & Connolly, Inc., Arlington, VA
- C. Lunchick, Jellinek, Schwartz & Connolly, Inc., Arlington, VA
- J. Ross, University of California, Riverside, CA

The Use and Misuse of Toxicology Evidence in the Courts

Chairpersons: G.S. Edwards, Toxicon Associates, Natick, MA and F. Welsch, CIIT, Research Triangle Park, NC
Sponsored by the Roundtable of Toxicology Consultants and the Committee on Public Communications

In recent years several instances of perceived misuse of scientific evidence have engendered calls for reform concerning qualifications of expert witnesses and admissibility of their testimony. The 1993 Supreme Court Daubert decision (a case alleging that the anti-nausea drug Bendectin® caused birth defects) changed the previous standards for consideration of expert depositions. The Federal Judicial Center recently published The Reference Manual for Scientific Evidence to augment that decision and to help judges facing complex scientific issues. This book provides guidelines to aid judges in deciding on the qualifications of expert witnesses and the admissibility of their testimony. The first speaker is the author of the Manual's chapter on toxicology. Others on the program will discuss examples of the use and misuse of toxicology evidence, ethical considerations for expert witnesses, the evolving standards for scientific evidence, and a practical primer for toxicologists serving as expert witnesses. The purpose of this workshop is to familiarize SOT members with the emerging legal standards for scientific evidence, particularly as they apply to toxicology. Furthermore, the objective is to provide SOT members with some advice about what to expect should they be called upon to provide an expert opinion.

Speakers:

- J.S. Cecil, Federal Judicial Center, Washington, DC
- D.L. Eaton, University of Washington, Seattle, WA
- B.D. Goldstein, UMDNJ-Robert Wood Johnson Medical School, Piscataway, NJ
- J.C. Lamb, Jellinek, Schwartz & Connolly, Inc., Arlington, VA
- W. W Schwarzer, U.S. District Court, San Francisco, CA

The IPCS Collaborative Study on Neurobehavioral Screening Methods

Chairperson: V.C. Moser, US EPA, Research Triangle Park, NC
Sponsored by the Neurotoxicology Specialty Section

The International Programme on Chemical Safety (IPCS) sponsored a collaborative study to evaluate the utility of neurobehavioral test methods for identifying neurotoxic chemicals. The goal was to determine the intra- and inter-laboratory reliability of a functional observational battery (FOB) and an automated assessment of motor activity. These test methods are currently recommended to screen chemicals for neurotoxic potential in the U.S., and these results are timely in light of ongoing efforts to harmonize testing guidelines worldwide. This study included four laboratories in the U.S. and four in Europe, each of which evaluated the effects (dose-response and time-course) of seven prototypic chemicals following both acute and 4-week exposures. These data provide important information regarding the reliability, sensitivity, and robustness of neurobehavioral screening methods over a range of laboratory conditions. The results of the chemical tests indicated that all participating laboratories generally could detect and characterize the effects of known neurotoxicants, in spite of differences on specific endpoints. Control data were quite similar for some endpoints, but varied greatly for others. This workshop will 1) provide the background and study design of this collaborative effort; 2)focus on the presentation of the data, concordance of the results across laboratories; and 3) provide opportunity for discussion on issues raised regarding the conduct and interpretation of neurotoxicity screening studies.

Speakers:

- G.C. Becking, IPCS, WHO, Research Triangle Park, NC
- B.M. Kulig, TNO Nutrition and Food Research Institute, Rijswijk, The Netherlands
- R.C. MacPhail, US EPA, Research Triangle Park, NC
- V.C. Moser, US EPA, Research Triangle Park, NC

Workshops

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Development of Fluorescent Markers for Assessing Cell Injury

Chairpersons: L.D. Fechter, University of Oklahoma, Oklahoma City, OK and D. Acosta, University of Texas, Austin, TX

Sponsored by the Neurotoxicology and In Vitro Specialty Sections

The development of sensitive and selective fluorescent markers provides new opportunities for assessing adverse effects of toxicants on cells, cellular organelles, tissue slices, and organotypic cultures. Markers have become available for studying cellular pH, a variety of critical ions, competency of cell membranes, and mitochondrial and lysosomal function among others. The initial lecture will review basic principles underlying the use of these markers and will focus on a number of well established and new fluorescent markers that are of particular interest to toxicologists. The presentations that follow will exemplify the application of such markers under specific culture conditions and will identify confounding factors and necessary controls for interpretation of the outcomes. Workshop participants will discuss the utilization of fluorescent dyes in combination with confocal and traditional fluorescence microscopy in isolated cells and cell cultures, tissue slices, organotypic cultures, and in vivo. Participants will discuss the assessment of cellular pH and calcium, characterization of mitochondrial function and cell topology and the use of green fluorescent protein as a reporter gene in toxicology. The purpose of this workshop is to discuss the development of fluorescent markers, to highlight their use, to discuss their limitations and problems in interpretation and to note new developments in this rapidly expanding area.

Speakers:

- W.D. Atchison, Michigan State University, East Lansing, MI
- K. Blanchard, Brown University, Providence, RI
- J.A. Connor, Lovelace Institute for Basic and Applied Medical Research, Alburquerque, NM
- R. Haugland, Molecular Probes, Inc., Eugene, OR
- J.J. Lemasters, University of North Carolina, Chapel Hill, NC

Entry of Women into Early Clinical Trials: Update on Preclinical and Clinical Issues

Chairpersons: R.E. Morrissey, Schering-Plough Res. Ins., Lafayette, NJ and F.A. Mielach, Aspen Biomedical Consulting, N. Bethesda, MD

Sponsored by the Reproductive & Developmental Toxicology and Regulatory Specialty Sections

Recently, the FDA removed restrictions on enrollment of women of childbearing potential into clinical trials for development of drugs and biologics. This action will permit evaluation of possible gender differences with respect to toxicity and efficacy of new agents. In traditional drug development, FDA required that women be enrolled in clinical trials after the submission of nonclinical reproductive and developmental toxicology studies, generally performed in parallel with Phase 2 clinical trials. However, for life-threatening indications such as AIDS, because of the different risk/benefit profile for potential therapies, FDA has permitted early enrollment of women, before submission of any reproductive studies. This Workshop will include timely presentations of FDA and European regulatory perspectives on timing of enrollment of women into early clinical trials, and the preclinical data that pharmaceutical manufacturers are developing to support these studies. Additional speakers will discuss the impetus within the women's community to enroll women earlier in clinical trials, the physician viewpoint on this initiative, and potential institutional and ethical concerns.

Speakers:

- T.M. McGovern, The HIC Law Project, New York, NY
- R.E. Morrissey, Schering-Plough Res. Ins., Lafayette, NJ
- A. Scialli, Georgetown University Medical Center, Washington, DC
- L.A. Sherman, FDA, Rockville, MD
- B. Ullrich, Fed. Inst. of Drugs, Berlin, Germany

Implementation of EPA Revised Cancer Assessment Guidelines: Incorporation of Mechanistic and Pharmacokinetic Data

Chairpersons: N.P. Page, ToxaChemica, International, Gaithersburg, MD and D.V. Singh, US EPA, Washington, DC

Sponsored by the Carcinogenesis, Risk Assessment, and Veterinary Specialty Sections

The EPA Cancer Assessment Guidelines were introduced in 1986 and had a profound impact on the conduct of cancer assessments in EPA and internationally. With the advances in understanding of the carcinogenic processes, it became apparent that revisions of the guidelines were needed to promote better utilization of biological data that has been evolving. In particular, there has been great interest in using pharmacokinetics and mechanism data wherever possible to replace the default use of surface area scaling and the linearized multistage quantitation procedures. The EPA undertook an extensive evaluation of its guidelines with input from national and international scientists. At the 1994 SOT annual meeting the main scientific issues were debated in an SOT forum. That SOT critique was considered by the EPA in its revision process. The revised guidelines are now in final form and undergoing implementation. The intent of this workshop is to provide hands-on experience in implementing the revised guidelines. The revision process will be described along with a discussion as to the types of mechanistic data that are needed to exploit the guidelines. Two case studies will be presented to illustrate the use of the revised cancer risk assessment guidelines with real data. Finally, a panel of representatives from industry, State and federal agencies, and the international community will discuss the guidelines with audience participation.

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Workshops

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Speakers:

- M. Andersen, ICF Kaiser, Morrisville, NC
- R. Conolly, CIIT, Research Triangle Park, NC
- W. Farland, US EPA, Washington, DC
- C. Frederick, Rohm & Hass Company, Spring House, PA
- J.I. Goodman, Michigan State University, East Lansing, MI
- G. Lucier, NIEHS, Research Triangle Park, NC
- J. Stratton, State of California, Sacramento, CA
- H. Yamasaki, IARC, Lyon, France

Identification of Respiratory Allergens: Introduction

Chairpersons: I. Kimber, ZENECA, Ltd., Cheshire, U.K. and M.J. Selgrade, US EPA, Research Triangle Park, NC
Sponsored by the Immunotoxicology and Inhalation Specialty Sections

A variety of chemicals and proteins can sensitize the respiratory tract. Among these are materials of industrial importance including certain diisocyanates, acid anhydrides, reactive dyes, and enzymes. Currently, there exist no widely accepted or well validated methods for the prospective identification of respiratory allergens. Most progress has been made with guinea pig methods where sensitizing potential is usually measured as a function of changes in pulmonary function induced following sensitization and challenge. However, these methods are usually prohibitively expensive, particularly for screening purposes. A number of alternative approaches are under consideration and will be the subject of this workshop. There will be short reviews of the nature of the health problems associated with occupational respiratory sensitization, chemical structure activity analysis as a tool for detecting pulmonary allergens, approaches used to test for respiratory allergens in guinea pigs, and alternative approaches using mice. Finally, regulatory issues and needs in this area will be reviewed. There will then be open discussion of the relative merits and limitations of the approaches described, their appropriateness for various industrial and regulatory situations, and research and development needs. (This abstract does not reflect EPA policy.)

Speakers:

- I.L. Bernstein, The Procter & Gamble Company, Cincinnati, OH
- M.H. Karol, University of Pittsburgh, Pittsburgh, PA
- I. Kimber, ZENECA, Ltd., Cheshire, U.K.
- M.K. Robinson, The Procter & Gamble Company, Cincinnati, OH
- K. Sarlo, The Procter & Gamble Company, Cincinnati, OH
- M.J. Selgrade, US EPA, Research Triangle Park, NC

New Developments and Applications of Diverse Experimental Animal Models Selected for Specific Toxicologic Research Needs

Chairpersons: R. McClellan, CIIT, Research Triangle Park, NC and G. Henningsen, USEPA, Littleton, CO
Sponsored by the Veterinary and Risk Assessment Specialty Sections and the Committee on Animals in Research

This Workshop is designed to broadly discuss the selection or development and the application of improved animal models for toxicology, based upon biomolecular, cellular and other physiological traits. The proper choice of experimental animal models is a key factor that enables toxicologists to better extrapolate observed effects to humans and other target species. Selecting the most appropriate model also becomes critical as toxicologists further investigate specific cellular and molecular mechanisms or modes of action of toxicants, thereby affording more confidence for ascertaining relevance of toxic responses and risks to health. Several exemplary models exist, which will be described and contrasted with alternative animal models, whereby an appropriate species has been specifically matched to a health issue or toxicological problem. Speakers will discuss the development or selection of specific animal models recently used to investigate: 1) toxicokinetic and clinical relevance of primate, swine, and rodent models for new concerns of methanol neurotoxicity, 2) essential attributes of surrogate species used to evaluate ecotoxicologic effects and risks in wildlife, 3) use of juvenile swine, versus rodents, as improved indicators of heavy metal bioavailability in children, and 4) refined development and use of transgenic animals to better assess pharmacological and toxicological effects of new drugs and environmental carcinogenic risks.

Speakers:

- D. Dorman, CIIT, Research Triangle Park, NC
- A. Fairbrother, Oregon State University, Corvallis, OR
- D. Liggitt, University of Washington, Seattle, WA
- R. Tennant, NIEHS, Research Triangle Park, NC
- C. Weis, US EPA, Denver, CO

Toxicological Foundations of Ecological Risk Assessment

Chairpersons: A.J. Nordone, Consultox, Limited, Damariscotta, ME and I. Tinsley, Oregon State University, Corvallis, OR
Sponsored by Regulatory Affairs & Safety Evaluation Specialty Section

During the 1980s, ecological risk assessment had played a secondary role to human health concerns. In a 1990 report on appropriate priorities and future strategies, EPA's science advisory have recommended that as much importance be attached to reducing ecological risk as human health risk. Since then ecological risk assessment methodology has developed rapidly, and it is now the primary focus of the EPA's Risk Assessment Forum to prepare the very first guidelines for ecological risk assessment. This workshop will demonstrate current, state-of-the-art ecological risk assessment methods. Emphasis will be placed on

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Workshops

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the use of toxicological information in the ecological risk assessment and risk management process. Both field and laboratory studies that can enhance these processes will be described. The significance of the proposed guidelines and their potential impact upon present and future-ecological risk assessment methods will be discussed.

Speakers:

- M.J. Hooper, Clemson University, Pendleton, SC
- H.M. Ohlendorf, Sacramento, CA
- G.W. Suter, Oak Ridge National Laboratory, Oak Ridge, TN
- W. van der Schalie, USEPA, Washington, DC

Toxicological Implications of Co-exposure to Ultraviolet Light and Pharmaceuticals

Chairpersons: A. L. Kraus, The Procter & Gamble Company, Cincinnati, OH and R. E. Osterberg, US FDA, Rockville, MD

Sponsored by the Regulatory and Safety Evaluation Specialty Section

Historically, phototoxicity surfaced with sulphonamides and tetracyclines in the 1940s - 1960s. Recent evidence of photoactivity from a variety of drug classes and the separate but concerning increasing incidence of skin cancer has elevated concerns of combined drug-ultraviolet light interactions. As a result, there are increasing regulatory requests for phototoxicology data. Some of these requests are for data from models designed to predict possible human response, while others are from models with limited, if any, human health response correlates. Given the expansion of awareness to phototoxicities with compounds such as psoralins, phenothiazines, and more recently, fluoroquinolones, significant discussion on the use of screening procedures and development tests is under way. While some models appear to provide helpful correlates to potential human response (i.e., photoirritation and photallergy), others are less tested and more controversial (i.e., photocarcinogenicity). This session will overview available approaches in photochemistry, photoirritation, photoallergy, photoimmunology, and photocarcinogenicity. The presentations and group discussions will seek to identify models of significant value and areas of uncertainty or concern that could be aided by additional research. While this workshop will provide an overview of this emerging area with primarily a U.S. FDA and drug product perspective, discussion may apply to other areas.

Speakers:

- P.R. Bergstresser, University of Texas, Dallas, TX
- P.D. Forbes, Argus Research, Horsham, PA
- G.F. Gerberick, Procter & Gamble, Cincinnati, OH
- I.E. Kochevar, Harvard University, Boston, MA
- A.L. Kraus, Procter & Gamble, Cincinnati, OH
- H.V. Sheevers, US FDA, Rockville, MD

Roundtables

Proposition 65--What's Happening to the Science?

Chairperson: J.N. Boyd, Corning Incorporated, Corning, NY

Sponsored by the Regulatory and Legislative Assistance Committee

The California Safe Drinking Water and Toxics Enforcement Act of 1986, commonly referred to as Proposition 65, states: "No person in the course of doing business shall knowingly and intentionally expose any individual to a chemical known to the state to cause cancer or reproductive toxicity without first giving clear and reasonable warning to such individual." Either the state or private citizens may bring suit against those businesses whose processes or products allegedly result in exposures in excess of "no significant risk levels" (NSRLs) for carcinogens or 1/1000 of the NOEL for reproductive toxicants. In this the tenth year since the law was enacted, a number of legal and technical issues remain unresolved. Of particular interest to toxicologists are: (1) criteria for establishing NSRLs and NOELs and (2) exposure assessment methodology and assumptions. These are critical components in determining compliance or noncompliance for a product or process. Presenters will include attorneys involved in both prosecuting and defending Proposition 65 cases and toxicologists involved in resolution of the underlying scientific issues. They will discuss:

1) Use of tabulated Tumorigenic Dose 50 (TD50) values in an expedited method for estimating carcinogen potency and NSRLs,

2) the regulatory advantages of the expedited method,

3) uncertainty and ambiguity in the application of exposure assessment criteria in establishing compliance for specific products,

4) the role of scientific and nonscientific criteria in enforcement.

Speakers:

- M. Corash, Morrison & Foerster, San Francisco, CA
- D. Roe, Environmental Defense Fund, San Francisco, CA
- L. Stone, The Procter & Gamble Company, Cincinnati, OH
- L. Zeise, CAL-EPA, Berkeley, CA

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An SOT Workshop at the 1995 Annual Meeting

Roundtables

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Should Benchmark Doses Be Used in Human Health Risk Assessments?

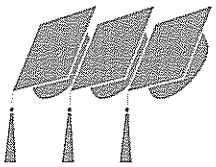
Chairperson: T. B. Starr, Environ Corporation, Raleigh, NC
Sponsored by the Risk Assessment Specialty Section

The pros and cons of using benchmark doses in place of traditional No Observed Adverse Effect Levels (NOAELs) in determining "safe" levels of exposure to toxic substances merit careful consideration by the toxicology community. This methodology, proposed for use in regulatory decision-making for noncarcinogenic toxic effects, employs dose-response data to estimate the parameters of a flexible mathematical dose-response model. An example is the Weibull model, which in turn is used to derive "benchmark" doses, i.e., conservative lower confidence bounds on the exposure levels associated with fixed levels of response, such as 1% or 5%. These dose estimates often lie below the observable response range.

Specific topics for this roundtable discussion include model selection, appropriateness of data use, statistical properties of benchmark dose estimates, model sensitivity, extent of conservatism, potential alternative approaches, and mechanistic considerations.

Speakers:

- B.C. Allen, ICF Kaiser, Morrisville, NC
- R.J. Kavlock, US EPA, Research Triangle Park, NC
- J.A. Moore, Institute for Evaluating Health Risks, Washington, DC
- J.L. O'Donoghue, Eastman Kodak Company, Rochester, NY
- T.B. Starr, Environ Corporation, Raleigh, NC



Continuing Education Courses

Continuing Education courses on both basic and advanced topics will be offered on Sunday, March 9.

Courses descriptions were included in the September/October Communiqué and can be obtained through the SOT Fax on Demand Line at (508) 230-2015.

- *Advanced Topics in Toxicokinetics*
- *Apoptosis: Recent Advances in Detection and Regulation*
- *Toxicant Effects Mediated by Steroid and Other Receptors: Modulation of Gene Expression and Other Cellular Responses*
- *Epidemiology for Toxicologists*
- *The Cell Cycle: Influence on Toxic Responses*
- *New Approaches for Studying Cytochrome P450-Dependent Toxicant Metabolism*
- *Aquatic Toxicology and Human Health Risk Assessments: Shared Metabolic Pathways, Shared Mechanisms of Action, Plus Data at the Bottom of the Dose Response Curve*
- *Mitochondrial Injury in Toxicology*
- *The Female Reproductive System - How to Assess Potential Toxicity*
- *Quantitative Uncertainty Analysis in Risk Assessment: Monte Carlo Techniques*
- *De-Regulation of ras Signaling by Toxic Chemicals*
- *Applications of PCR Technologies to Molecular Toxicology*

Watching Washington

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gram fact sheet is in the process of being developed and Program Directors are encouraged to use the fact sheet as talking points in any correspondence or contact with Members of Congress.

On October 18, 1995, Representative **Michael Oxley** (R-OH), Chairman of the Commerce, Trade, and Hazardous Materials Subcommittee introduced legislation to reauthorize and reengineer the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, otherwise known as "Superfund." Senator **Robert C. Smith** (R-NH) introduced the Senate Republicans' version of Superfund Reauthorization (S.1285) on September 29, 1995. Congress is expected to consider Superfund Reauthorization this year, as the program's taxing authorities expire at the end of 1995. The current timetable is to complete action by mid-November.

Retroactive Liability

Rep. **Oxley's** bill includes a partial repeal of retroactive liability for a select class of small businesses, and Rep. **Oxley** is reportedly pushing for a full repeal if he can find a way to pay for it. This particular provision has already prompted criticism from the Clinton Administration and EPA Administrator **Carol Browner**. In an effort to encourage private parties to clean up waste sites and avoid litigation, the House bill also includes a provision that would allow some companies to apply for a government rebate of up to 50 percent of their cleanup costs.

Recognizing the challenge of paying for a repeal of retroactive liability and a rebate allowance, Sen. **Smith's** bill does not include a repeal provision. The Senate bill does, however, include a 50 percent tax credit to help defray the cost of cleanup for waste dumped prior to 1980.

NIEHS Superfund Basic Research Program

Originally authorized in 1986 as part of the Superfund Amendments and Reauthorization Act, the Superfund Basic Research Program is a university-based program of basic research funded through the Environmental Protection Agency (EPA) and implemented by the National Institute of Environmental Health Sciences (NIEHS). The Program provides research grants to allow biomedical research scientists to collaborate with engineers and ecologists to study the human health effects of hazardous substances in the environment and aid in risk assessment and risk management techniques.

Authorized funding levels for the Superfund Basic Research Program suffered a tremendous cut in Senator **Smith's** Superfund Reauthorization legislation. Senator **Smith's** bill reauthorizes this program at $20 million. This is $15 million (43%) below the program's last authorized level in 1994. The Senate reauthorization level virtually destroys this program.

The House bill does not authorize a specified funding level for the Superfund Basic Research Program. Instead, it authorizes a total sum of approximately $250 million for the Hazardous Waste Superfund and leaves funding decisions within these categories to EPA and the Appropriations Committee. However, because of the relatively small authorization amount for the Superfund and the broad array of programs and activities that fall under this section, the Superfund Basic Research Program will be competing for a relatively small amount of money that will very likely result in a cut from 1994 authorized levels.

FY 1996 Appropriations

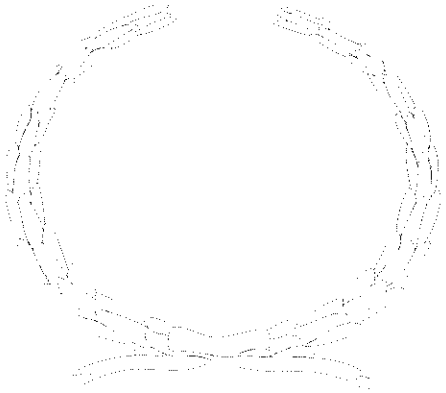
The Senate, led by Senator **Christopher Bond** (R-MO), Chairman of the Senate VA-HUD-Independent Agencies Appropriations Subcommittee, and the House, led by Rep. **Jerry Lewis** (R-CA), Chairman of the House VA-HUD-Independent Agencies Appropriations Subcommittee, each cut $300 million from Superfund, maintaining that Superfund is a program in need of substantial overhaul. This cut resulted in an appropriation of approximately $1 billion for the Superfund program for FY 1996.

NIEHS Superfund Basic Research Program

The House VA-HUD-Independent Agencies FY 1996 Appropriations bill recommended $31.5 million for the NIEHS Superfund Basic Research Program ($4.2 million less than FY 1995 and $1 million less than the President's request) and the Senate bill recommended $16 million ($19.7 million less than FY 1995 and $16.5 million less than the President's request).

Both the House and Senate versions passed the House and Senate floors, respectively. Differences will be worked out by a conference committee before the bill is voted on again by each chamber and then sent to the President for his signature. It is unclear whether the President will sign this funding legislation in light of OMB Director **Alice Rivlin's** comment that this legislation "would threaten public health and the environment..."

If you would like further information on Superfund Reauthorization or Appropriations, please call **Shawn Lopez** at SOT Headquarters.



SCALA AWARD NOMINATIONS

Nominations are being solicited for the 1996 Robert A. Scala Award and Lectureship in Toxicology. This annual award honors the work of industry toxicologists and promotes continued outstanding scientific contributions to the field by industrial organizations. Letters of proposal can be sent to **Victoria Leyton**, EOHSI, P.O. Box 1179, Piscataway, NJ 08855-1179, (908) 445-0202. The deadline for receipt of proposals is **December 15, 1995.**

TWO NEW BURROUGHS WELLCOME FUND AWARDS AVAILABLE

In recognition of the growing concern over fungal diseases and infections, the Burroughs Wellcome Fund has established the Molecular Pathogenic Mycology Award Program to support investigators who have made a commitment to research on the basic pathogenesis of fungi. Two types of awards are offered for 1996:

Scholar Award of $400,000, payable over five years, primarily intended for investigators who are at the associate professor level and have made significant contributions to understanding the basic molecular biology of pathogeneic fungi.

New Investigator Award of $150,000, payable over three years, primarily intended for junior researchers who have made a commitment to the study of pathogenic fungi.

The awards are aimed at fostering the use of a variety of modern scientific techniques—taken from molecular biology, fundamental biochemistry, immunology, pharmacology, and genetics — to advance knowledge of pathogenic fungi. At least one Scholar Award and one New Investigator Award will be made during 1996.

Candidates for both awards must be U.S. or Canadian citizens or permanent residents. Application materials should be submitted to: Molecular Pathogenic Mycology Award Program, Burroughs Wellcome Fund, 4709 Creekstone Drive, Suite 100, Morrisville, NC 27560-9771 by **January 15, 1996.** Awards will be selected by May 15, 1996, and the awards will begin on July 1, 1996.

THE MT. DESERT ISLAND BIOLOGICAL LABORATORY ANNOUNCES NEW INVESTIGATOR TOXICOLOGY AWARDS FOR SUMMER 1996

The Mount Desert Island Biological Laboratory (MDIBL) is an independent marine and freshwater biological station located on the coast of Maine near the mouth of the Bay of Fundy. It is the largest cold water laboratory in the eastern United States, and the relatively undisturbed ecology of the surrounding area provides a unique setting to investigate a wide range of biological problems. The Center for Membrane Toxicity Studies (CMTS), funded by a NIEHS Marine and Freshwater Biomedical Science Grant, is an integral component of the international group of scientists at the MDIBL who investigate a variety of fundamental problems of interest in biomedical sciences, in particular, comparative cellular and molecular transport physiology. The Laboratory offers the nearly unique opportunity for M.D.'s and Ph.D.'s to interact daily in a close-knit biological laboratory setting, directing their collective and cooperative attentions to solving fundamental mechanisms of toxicology of relevance to human health, in this case, membrane and cell pathologies produced by heavy metals and other environmental pollutants.

The CMTS provides funding for pilot studies for post-doctoral 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 1996 summer session is **January 15, 1996**. Mail applications to the Mount Desert Island Biological Laboratory, Department CMTS, Box 35, Old Bar Harbor Road, Salsbury Cove, ME 04672.

State Societies Target Science Literacy in Schools

By Vincent Castranova, Animals in Research Committee

A number of state organizations are active in producing and distributing materials to students and teachers which portray the value of biomedical research and the continued need for responsible use of animals in toxicology.

The North Carolina Association for Biomedical Research has produced a colorful booklet that describes the importance of animal research. This booklet entitled "What's the Point of Biomedical Research?" targets middle and high school students.

"The Lucky Puppy" is a coloring workbook for children 6-9 years of age. It demonstrates how animal research is used by veterinarians to treat pets. This workbook of activities and puzzles was developed by the North Carolina Association for Biomedical Research in association with the Pennsylvania Society for Biomedical Research.

The Massachusetts Society for Medical Research in association with the Pennsylvania Society for Biomedical Research and other groups has developed a health and science calendar for elementary students. This poster-sized calendar features a different health or science topic (such as infectious disease, dental health, product safety, and nutrition) each month. Activities outlined in an accompanying teacher's guide include hands-on experiments, health tips, and discussion of career opportunities.

"Bio Rap" is a series of newsletters for grades 6-8 produced by Connecticut United for Research Excellence (CURE). This newsletter includes articles, puzzles, and activities organized around a given topic with an accompanying teacher's guide. Topics covered thus far are: rabies, feline leukemia, Lyme disease, AIDS, product safety, and cancer. CURE is beginning an effort to distribute this newsletter nationally. The Society of Toxicology is among the organizations providing financial support for this project.

"Animals in Science: A Resource Guide" is a publication by the Pennsylvania Society for Biomedical Research which provides information for teachers and librarians concerning the use of animals in science.

The SOT Animals in Research Committee would be happy to assist you in obtaining any of these materials. For assistance contact the committee chairperson, **Vincent Castranova.**

Animal Models Shed Light on Human Disease

By Vincent Castranova, Animals in Research Committee

Recent reports describe the development of new animal models that have yielded results which may impact the prevention or treatment of a number of human diseases.

A team of researchers at the Universite Louis Pasteur has developed a strain of mice which are susceptible to insulin-dependent diabetes mellitus. **Dr. Mathis** and colleagues found that insulin-dependent diabetes mellitus occurs when T_1 lymphocytes invade the pancreas and destroy insulin-producing Langerhans cells. T_2 lymphocytes were not protective as once believed. These French scientists speculate that this form of diabetes may be combated by using antibodies against T_1 lymphocytes rather than supplementing T_2 cells.

Dr. Slotkin and colleagues at Duke University have used a rat model to link maternal smoking with increased risk of sudden infant death syndrome (SIDS). Their data indicate that newborn rats exposed as fetuses to nicotine alone were unable to adjust to periods of oxygen deprivation (as experienced in sleep apnea) and often died due to failure to produce adrenaline and noradrenaline. In contrast, control pups were able to survive periods of low oxygen tension by producing stress hormones which stimulate heart rate. These data suggest that pregnant women should not only forgo smoking but should also refrain from use of nicotine patches.

Dr. Robinson and colleagues at the Southwest Foundation of Biomedical Research found that the Brazilian opossum, like humans, spontaneously develops cutaneous malignant melanoma in response to UV light. As with humans, only a fraction of UV-exposed opossums develop skin cancer. This research team from San Antonio hopes to breed susceptible and resistant strains of opossums and examine genetic components of the disease as well as test the effectiveness of various chemotherapies.

Research teams lead by **Drs. Alarie** and **Karol** at the University of Pittsburgh and **Drs. Frazer** and **Castranova** at NIOSH have developed a guinea pig model which mimics the fever, leukocytosis, labored breathing, pulmonary edema, and activation of pulmonary phagocytes reported in organic dust toxic syndrome. This model has been used to identify etiologic agents, such as endotoxin, in various agricultural dusts. It has also been used to test the effectiveness of various techniques to remove endotoxin from cotton dust prior to commercial use in textile mills.

HORIZON 2000

THE SOCIETY OF TOXICOLOGY'S LONG-RANGE PLANNING ACTIVITY

Continued from page 2

Based on the trends and the priorities, the meeting participants were asked to draft a picture of the Society (future vision) in the year 2000 and beyond. We were also asked to write a vision statement illustrating the future position of the Society with respect to each of the prioritized trends. A unified vision statement was developed as follows:

"The overall vision of the Society is to be the leading organization worldwide for stimulating state-of-the art science in toxicology; translating and communicating the results of scientific investigations to members, media, government and the public; promoting sound regulatory practice and policy; and representing the scientific and professional interest of its members. The Society will achieve this vision through a combination of products and services that reflect its status as both a learned and professional society, including the most highly respected journal, meetings and educational offerings."

Working in small break out groups, strategics initiatives were developed to address the priority trends. The "History of the Future" was written as milestones and individual time-lines for each of the strategic initiatives.

The draft LRP was presented to the leadership of our committees. At the second meeting, the participants evaluated these priorities by asking (1) is the priority stated correctly, (2) are the strategic initiatives and pathways appropriate, (3) are there additional pathways that should be included, (4) which committee(s) should implement the initiatives, (5) what is the appropriate timetable for implementation, and (6) what milestone should be used to gauge success? Comments were recorded, the pathways were slightly revised and supplemented with action steps in order to provide a starting point for strategic discussions within the committees.

What I will now describe in the text that follows are each of the strategic initiatives relative to current trends or issues, potential impact and future vision.

#1 Need for Basic and Applied Research to Improve Risk Assessment

Current Trends/Issues: Public policy decisions continue to be made using regulatory toxicology methods and risk assessment processes that do not fully integrate the state-of-the-art.

Potential Impact: The profession may appear to be ineffective in applying the appropriate methods and in influencing public policy.

Future Vision: The Society will provide a forum for the cooperative discussion of risk assessment procedures and a platform for validation of methods.

#2 Public Understanding of Toxicology

Current Trends/Issues: The general public's understanding of the role of toxicology as a science, as a component of public policy decisions, and as a source of benefit to society is poorly understood.

Potential Impact: A general lack of awareness and respect for the profession - possible difficulties in recruiting top students to the field.

Future Vision: The Society will have access to federal and state legislators and will have programs in place to provide scientific guidance to the appropriate use of toxicological data in structuring and/or reviewing key legislation. The Society will have a working relationship with the media and will have a mechanism to provide expert commentary to reporters seeking a scientific perspective in their articles. The Society will have programs to communicate toxicological principles to public school children. The Society will have educational programs available for allied professionals who need to better understand toxicology. Where appropriate, the Society will engage in cooperative programs with other organizations and public agencies to maximize the impact of its communications.

#3 Shrinking Research Funding Sources

Current Trends/Issues: The academic community is an important part of the Society and an important resource in achieving the Society's objectives. However, academia is facing declining government support for research.

Potential Impact: If academics are under-funded, they may be less able or unable to participate in the Society.

Future Vision: The Society will have a working relationship with public and private funding agencies and will establish mechanisms to communicate the need for (and benefits of) basic and applied research in toxicology. The Society will serve as a source of scientific input to decisions on levels of funding and allocation of funding among alternative areas of toxicological investigation. The Society will testify in Congress on issues where there is a need for the science of toxicology to be represented.

#4 Changing Employment Demographics and Training Needs

Current Trends/Issues: Toxicology employment demographics are changing. Government, industry, and academic investment in building capability in toxicology has already leveled off and may decline in the years ahead.

Potential Impact: Lower or negative growth in Society membership.

An imbalance in employment supply vs. demand. A higher level of unemployment for toxicologists, including mid-career and older professionals; and more toxicologists taking early retirement.

Future Vision: The Society will maintain an ongoing forecast addressing the balance of supply and demand for degreed toxicologists. This forecast will be a resource for members, students, universities and business.

#5 Use of Animals in Research

Current Trends/Issues: Animal rights groups continue to be very pro-active in influencing public opinion regarding the scientific use of laboratory animals, including targeting school-age children and their teachers.

Potential Impact: If the animal rights activists succeed in influencing legislation, the impact on the Society and profession could be substantial, including major constraints on the methods and practices of toxicology.

Future Vision: SOT will establish relationships and will support groups that are successful in publicizing the benefits of animals in research. The Society's membership will be fully educated in the use of animals in research and will be actively informing the local community of the benefits derived from the use of animals in research.

#6 Computing and Communications Technologies

Current Trends/Issues: The rapid evolution of computing and communications technologies is profoundly changing the distribution of scientific information.

Potential Impact: This trend will continue to impact both scientific publications and meetings. New electronic methods of receiving publications and information are likely to displace conventional methods. There is uncertainty over the nature and venue of professional meetings in the future.

Future Vision: The Society will be among the most advanced organizations in the utilization of computing and communications technologies to manage its infrastructure and serve its members. SOT will meet its communication needs through the electronic format.

#7 Strengthen International Relations

Current Trends/Issues: Global trade barriers are falling. Companies are becoming increasingly international in scope. Universities have increasing foreign student populations.

Potential Impact: The needs of the members of the Society may change as their professional lives are impacted by working abroad, dealing with international regulations, etc.

Future Vision: The Society will be the leading organization representing the interests of members worldwide, providing a platform for the exchange of information worldwide, and maintaining an integrated approach to understanding toxicological concerns worldwide.

#8 A Stable and Broad Financial Platform

Current Trends/Issues: The financial condition of the Society has improved dramatically in recent years. However, there is still some concern that the Society is too dependent upon the Annual Meeting as a revenue source.

Potential Impact: The Society may find itself underfunded if the Annual Meeting attendance should drop.

Future Vision: The Society will have revenues of $6 million with no more than 50% from the annual meeting, the other 50% will come from new products and services.

In future columns, I, and **Dr. Bus** to follow, will spend time discussing the strategic initiatives to address these trends, their implementation pathways and the action steps that will be used. We hope you support SOT's Horizon 2000 (Long-range Plan) and will provide specific comments and input as it is rolled out in more detail in the articles that follow. Be certain that your SOT is on the move!

Jack H. Dean, President

SOT Placement Center - A Continued Asset To SOT Members

The mission of the SOT Placement Service is to "promote and facilitate employment opportunities for members of the Society of Toxicology." This expectation was exceeded at the 1995 Annual Meeting in Baltimore.

The Placement Center processed 436 candidates for employment and managed 120 job postings in 1995. Of the total candidate pool, over 84% had PhDs or were doctoral candidates, with 70% having had some job experience. Of the employers, 31% were from industry, 26% from academia, 16% from consulting firms, 12% from contract labs, 8% from nonprofit organizations and 7% from government. Many employers attend the annual meetings to take advantage of the recruiting opportunities provided by the Placement Center.

Analysis of the 1995 Placement Center data provided some useful insights into toxicological job trends and the role of the Center. About 35% of the candidates were toxicologists with over 5 years of experience showing that the Center is much more than a clearing house for entry level positions and post-docs. There were a significant number of positions in the area of risk assessment, various environmentally related areas, regulatory affairs and quality assurance. The high number of postings in these areas may suggest a shortage of qualified candidates and could be an opportunity for future crossover by classical toxicologists. There were few postings for academic teaching positions, indicating an under-utilization of the Center in this employment area. About 30% of the candidates were non-US citizens which is leading the Placement Committee to investigate better ways to best meet the issues and special needs of these individuals. This quantitative information will be used to provide better Placement Center service in the future. Identifying employment trends will also provide guidance to educators in aligning programs with current employment needs and future trends.

Employers continue to view the Placement Center as a low cost opportunity to screen a concentrated pool of candidates concerned about their careers. The size and variety of the candidate pool provides an ideal forum for employers to search for and find an employee that meets the needs of their position. In addition, the opportunity to meet with candidates one-on-one provides for an efficient interview process. The Placement Center continues to make changes to ensure that logistical challenges are kept to a minimum and the needs of employers are met.

Comments on and suggestions for improving the placement process are always welcomed and should be directed to the Placement Committee, c/o the SOT Headquarters.

Postdoctoral Position in Immunotoxicology/ Immunopharmacology

Postdoctoral position in immunotoxicology/ immunopharmacology are available immediately to study the role of cAMP-mediated signal transduction on T-cell regulation. Specifically, the inhibition of cAMP activated transcription factors and regulated genes by cannabinoid compounds. The successful candidate will join a multifaceted biochemical/molecular research team. Experience in one or more of the following areas is highly desired: immunology, biochemistry, cell or molecular biology. Send curriculum vitae including names and phone numbers of three references to:

Dr. Norbert E. Kaminski
Department of Pharmacology and Toxicology
B440 Life Sciences Building
Michigan State University
East Lansing, MI 48824
Phone: (517) 353-3786
FAX (517) 353-8915

Assistant/Associate/Full Professor Molecular Biology/Toxicology

The Division of Toxicology, Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences is recruiting a full-time tenure track faculty position to join the growing division at the Assistant, Associate or Full Professor level. Requirements include: a Ph.D. or equivalent degree, postdoctoral training, and a productive record of quality research. Applicants should be utilizing molecular approaches to solve basic problems in any area of toxicology or pathophysiology. Individuals are expected to develop an independent research program with extramural funding. Applicants applying at the Associate or Full Professor level should have extramural funding. Excellent opportunities are available for collaborative research with other UAMS faculty and adjunct faculty at the National Center for Toxicological Research located nearby. A competitive start-up package, and research space in a newly constructed research building are available. Send CV, a brief research prospectus and the names of three references to:

Rick G. Schnellmann, Ph.D.
Division of Toxicology, Slot 638
University of Arkansas for Medical Sciences
Little Rock, AR 72205
Phone: (501) 686-8883
Fax: (501) 686-8970

Applications received before December 1, 1995 are assured of consideration. *UAMS is an equal opportunity/affirmative action employer.*

Mid-Atlantic Chapter

The spring meeting of the Mid-Atlantic Chapter of SOT was held on April 19, 1995 in Morristown, NJ. Concurrent with the traditional morning poster session, a mini workshop on talking to the public about the use of animals in toxicology was held. **Jayne Mackta**, Executive Director of the New Jersey Association for Biomedical Research, was the featured speaker at the workshop. Meeting participants were enthusiastic about the addition of a small-scale conference to the program and this feature will likely be incorporated into future meetings of the Chapter.

Three graduate students received awards for the quality of their poster presentations at the spring meeting. **Joanna Matheson** (NYU Medical Center) won first place for her poster "Possible Immune Mechanism for Cadmium-Induced Kidney Damage." **Susan Goldstein** (Rutgers University) won the second place award for her poster "Induction of Barrett's Esophagus and Esophageal Cancer with a Combination of Surgery and Carcinogen Treatment in Rats." Third place was given to **Ilona Jaspers** (NYU Medical Center) for her poster "Induction of IL-8 and Nitric Oxide Release by Airway Epithelial Cells upon Exposure to Ozone." Each student received a plaque and a cash award provided by Hoechst-Celanese to defray the costs of a future scientific meeting.

The afternoon program began with **Dr. Roger O. McClellan** (CIIT) receiving the Mid-Atlantic Chapter's Ambassador of Toxicology award. The award is given annually to an individual who has advanced the understanding of the science of toxicology on a national and international basis. Dr. McClellan gave a presentation in which he outlined the history of risk assessment and exhorted toxicologists to become more involved in the process. Following Dr. McClellan's talk, **Dr. Paul Newton** (Pharmaco LSR) introduced the scientific symposia "Inhalation Toxicology: What's in the Air?." Speakers included **Drs. Richard Schlesinger** (NYU Medical Center), **Carroll Snyder** (NYU Medical Center), **Bruce Stuart** (Schering-Plough), and **Michele Medinsky** (CIIT).

Northeast Regional Chapter

The Northeast Regional Chapter of the SOT announces its new officers for May, 1996:

President-Elect:..... William P. Beierschmitt

Vice President:..... Susan G. Emeigh Hart

Councilor:..... Jose E. Manautou

Congratulations to the winners.

South Central Chapter

The 1995 annual meeting of the South Central Chapter of the SOT, held October 13 at the University of Mississippi Medical Center in Jackson, attracted over 30 presentations and 100 participants from the five state region made up of Arkansas, Louisiana, Mississippi, Oklahoma, and Tennessee. The Conference was hosted by **Dr. Durisala Dessiah**, Chapter President and Professor of Neurology at UMMC. **Dr. James Bus**, President-Elect of the SOT, presented a keynote lecture entitled, "Perspectives of a Chemical Industry Toxicologist on the Chlorine Issue." Awards were presented to **R.S. Mangipudy** (NE Louisiana University) for the best platform presentation by a student, to **T. Ito** (University of Mississippi Medical Center) for the best non-student, non-faculty presentation, and to **N. Halmes** (University of Arkansas for Medical Sciences) for the best poster presentation by a student. Student travel awards, that support research visits by students to other regional laboratories, were given to **Ms. Swarupa** to work with **Dr. Daniel Casciano** at the National Center for Toxicological Research. Also, **Ms. Prathibha Rao** received a travel award to undertake studies with **Dr. Beverly Lyn-Cook** at NCTR.

UPCOMING CONFERENCES

■**3rd Congress of Toxicology in Developing Countries,** November 19-23, 1995, Cairo International Conference Center, Egypt, Dr. Amira Eldefrawi, International Advisory Committee, University of Maryland School of Medicine, (410) 706-3564, Fax: (410) 706-3564 or Secretary General Dr. Sameeh Mansour, Cairo, Fax: 011-202-337-0931.

■**The Commission Veterinarian/Equine Medical Director, A Short Course,** November 28-December 1, 1995, Maxwell H. Gluck Equine Research Center, University of Kentucky, Lexington, KY, Dr. Thomas Tobin, (606) 257-3739, Fax: (606) 257-5169. *This course is directed towards Commissioned Veterinarians and other interested industry professionals and is approved for 16.25 hours of continuing education credit by the American Veterinary Medical Association.*

■**Toxicology of Inflammation and Reproductive Agents,** November 30 - December 1, 1995, Montreal, Quebec, Dr. B. Virgo, (709) 737-7903.

■**Society for Risk Analysis,** December 3-6, 1995, Honolulu, HI, Richard J. Burk, Jr., (703) 790-1745.

■**AIHC'S 1995 Annual Meeting: Managing The Risk Revolution: Balancing Science and Policy,** December 6, 1995, ANA Hotel, Washington, DC, AIHC (202) 833-2131, Fax: (202) 833-2201.

■**NRC Symposium: New Approaches for Assessing the Etiology and Risks of Developmental Abnormalities,** December 11-12, 1995, National Academy of Sciences Auditorium, Washington, DC, Ms. Linda Leonard, (202) 334-2993, Fax (202) 334-1393.

■**Western Pharmacology Society's 39th Annual Meeting,** January 27- February 1, 1996, Granlibakken Conference Center, Lake Tahoe, CA, Dr. Ralph Purdy, WSP President, Department of Pharmacology, College of Medicine, University of California, Irvine, CA 92717, (714) 824-7653, Fax: (714)824-4855, E-mail: repurdy@uci.edu.

■**AAPS Workshop on Polymorphism of Drug Substances: Manufacturing, Formulation, Analytical, Stability, Bioavailability and Regulatory Affairs,** Crystal Gateway Marriott, Arlington, VA, AAPS, (703) 548-3000, Fax: (703) 684-7349, E-mail: meetings@aaps.org.

■**Academy Toxicologic Sciences (A.T.S.) Annual Meeting,** March 10-14, 1996, Anaheim, CA, John A. Thomas, Ph.D., University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78284-7722, (210) 567-2007, Fax: (210) 567-3070.

■**Society of Toxicology (SOT),** March 10-14, 1996, Anaheim Convention Center, Anaheim, CA, (703) 438-3115, Fax: (703) 438-3101, E-mail: sothq@toxicology.org.

■**AAPS Western Regional Meeting,** March 18-19, 1996, San Jose Convention Center, San Jose, CA, AAPS, (703) 548-3000, Fax: (703) 684-7349, E-mail: meetings@aaps.org.

■**American Society of Pharmacology & Experimental Therapeutics - The Experimental Biology Meeting,** April 14-18, 1996, Washington, DC, Ms. Kay Croker, ASPET, 9650 Rockville Park, Bethesda, MD, 20814-3995.

■**AAPS Workshop on the Impact of Technology Changes on Regulatory Methods for Pharmaceuticals,** April 18-19, 1996, Crystal Gateway Marriott, Arlington, VA, AAPS, (703) 548-3000, Fax: (703) 684-7349, E-mail: meetings@aaps.org.

■**Symposium on the Pharmacokinetics/ Pharmacodynamics in the Developing System & Impact on Risk Assessment,** April 21-23, 1996, Arkansas' Excelsior Hotel, Little Rock, Arkansas, John F. Young, NCTR, Jefferson, AR, 72079.

■**Mid-America Toxicology Course,** April 21-26, 1996, The University of Kansas Medical Center, Courses Director: 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.

■**First International Symposium on Cosmetic Efficacy,** April 28-29, 1996, Marriott-Marquis Hotel in New York City, NY, Katherine Wagner (212) 305-2714.

■**AAPS/FDA/USP Workshop on Scaleup of Transdermal Drug Products,** April 29-May 1, 1996, Crystal Gateway Marriott, Arlington, VA, AAPS, (703) 548-3000, Fax: (703) 684-7349, E-mail: meetings@aaps.org.

PUBLICATIONS OF INTEREST

■**Course on Experimental and Clinical Neurotoxicology at Department of Nutrition Sciences**, May 27-31, 1996, University of Oporto, Portugal, Dr. Ana Paula Augusto, Curso Ciencias da Nutricao, University of Oporto or Rua Dr. Roberto Frias, 4200 Porto Portugal, Fax: (351-2-5504143..

■**Teratology Society 36th Annual Meeting**, June 22-27, 1996, Keystone, CO, Carol Lemire, (301) 571-1841, Fax: (301) 571-1852, E-mail: clemire@act.faseb.org or ekagan@act.faseb.org.

■**RASS VI, IUTOX-International Union of Toxicology**, August 30- September 8, 1996, Royal Garden Village, Hua Hin, Thailand, RASS Secretariat, Malmfors Consulting AB, Vastmannagatan 48, S-113 25 Stockholm/Sweden, +46 8 31 19 90; Fax: +46 8 30 11 33.

■**Third International Conference on Neuroprotective Agents, Clinical and Experimental Aspects**, September 8-12, 1996, Villa Monestero, Varenna, Lake Como, Italy, Bruce Trembly, M.D., Chief Neurosurgery, VA Medical Center, Togus, MA 04330, (207) 623-8411, ext. 5053, Fax: (207) 623-5766 or William Slikker, Jr., Ph.D., Director, Division of Neurotoxicology, NCTR/FDA, Jefferson, AR 72079, (501) 543-7203, Fax: (501) 543-7745, E-mail: wslikker@fdant.nctr.fda.gov.

■**2nd World Congress on Alternatives and Animal Use In The Life Sciences**, October 20-24, 1996, Utrecht, The Netherlands, World Congress Alternatives 1996, FBU Congress Bureau, P.O. Box 80.125, 3508 TC Utrecht, The Netherlands, +31.30.53.5044/2728, Fax: +31.30.53.3667, E-mail: 1.donkers@pobox.ruu.nl.

■**Seventh North American ISSX Meeting**, October 20-24, 1996, Hotel del Coronado, San Diego, CA, ISSX, P.O. Box 3, Cabin John, MD 20818 USA, Fax: (301) 983-5357.

■*Basic Concepts in Pharmacology, A Student's Survival Guide, By Janet L. Stringer, M.D.*, McGraw-Hill Companies, Health Professions, P.O. Box 182615, Columbus, OH 43272-7046, (800) 262-4729, Fax: (212) 512-2252.

■*Casarett & Doull's Toxicology, The Basic Science of Poisons*, Curtis D. Klaassen, McGraw-Hill Companies, Health Professions, P.O. Box 182615, Columbus, OH 43272-7046, (800) 262-4729, Fax: (212) 512-2252.

■*Clinical Pharmacology, Third Edition*, Edited by Melmon, Morrelli, Hoffman, & Nierenberg, McGraw-Hill Companies, Health Professions, P.O. Box 182615, Columbus, OH 43272-7046, (800) 262-4729, Fax: (212) 512-2252.

■*Fundamentals of Aquatic Toxicology: Effects, Environmental Fate, and Risk Assessment, Second Edition*, Edited by Gary Rand, Ecological Services Inc., North Palm beach, Florida, Taylor & Francis, 1900 Frost Road, Suite 101, Bristol, PA 19007, (800) 821-8312, Fax: (215) 785-5515.

■*Geriatric Pharmacology*, By Bressler & Katz, McGraw-Hill Companies, Health Professions, P.O. Box 182615, Columbus, OH 43272-7046, (800) 262-4729, Fax: (212) 512-2252.

■*Goodman & Gilman's The Pharmacological Basis of Therapeutics, Ninth Edition*, Editors-in-Chief: Joel G. Hardman, Ph.D. & Lee E. Limbird, Ph.D. McGraw-Hill Companies, Health Professions, P.O. Box 182615, Columbus, OH 43272-7046, (800) 262-4729, Fax: (212) 512-2252.

■*Official Methods of Analysis of AOAC International, 16th Edition - on CD-ROM*, AOAC International, 200 Wilson Blvd., Suite 400-GG, Arlington, VA 22207-3301, (800) 379-2622, Fax: (703) 522-5468.

■*The Toxicity of Anticancer Drugs*, Edited by Powis & Hacker, McGraw-Hill Companies, Health Professions, P.O. Box 182615, Columbus, OH 43272-7046, (800) 262-4729, Fax: (212) 512-2252.

COUNCIL HIGHLIGHTS

Following, are the highlights of the September 21, 1995 Council Meeting:

1. Council voted to support the National Health Research Fund proposal being reintroduced by Senators Hatfield and Harkin. This proposal provides a dedicated source of additional funding for the National Institutes of Health.
2. Council voted to sponsor, in name only, the International Business Communications conferences on Molecular Toxicology and Risk Assessment, scheduled for February 12-16, 1996.
3. Council has asked the Society's newly retained legislative advocacy firm, Capitol Associates, to monitor and provide information to the SOT membership on the following legislative issue areas: Delaney Clause, Risk Assessment, Superfund, Animals in Research, and Research Training and Funding.
4. Council will propose the following Bylaws revisions to the membership:
   - The Continuing Education Committee will be increased from six to nine members; three members will be appointed annually for a three-year term.
   - In addition to chemicals, the Regulatory Affairs and Legislative Assistance committee will now keep Council abreast of new developments that concern the regulation of "drugs, biologics and devices."
   - Failure to pay dues within 12 months from the end of the calendar year, for which assessed, shall result in forfeiture of membership. Currently, membership expires at the end of the calendar year.
5. Council is developing an informational brochure to distribute to those not familiar with SOT and to include with copies of SOT position papers.
6. A full and exciting scientific program is scheduled for the last day of the SOT Annual Meeting, Thursday, March 14, and will be followed by the 1996 Annual Meeting Awards Ceremony and Final Night Reception.

SOT CHANGES ITS E-MAIL ADDRESS

Please affix the attached label to the back of your Membership Directory. The Society's Internet E-mail address was changed from a commercial name to an organization name. This address is active and is accepting all messages.

E-Mail:
73162.506@CompuServe
or
sothq@toxicology.org

AFFIX LABEL TO YOUR SOT DIRECTORY.

ADMINISTRATIVE UPDATE

Best wishes to **Nell Durrett** who was married to **Matthew Dillard** on October 7, 1995 in Richmond, Virginia. She has returned to the office after a three week vacation and will continue to work with the Program and Placement Committees. She will be using the name Nell Dillard if you need to contact her with any questions.