

Society of Toxicology Immunotoxicology Specialty Section NEWSLETTER

November 1996

President's Message

Peter Thomas, Ph.D.

For those of you that are undecided about attending the SOT meeting in Cincinnati on March 9-13, let me tell you what you will miss. The Immunotoxicology Specialty Section has put together another outstanding program of workshops and continuing education programs. The first of three workshops will focus on immunological biomarkers and how they can be used as a measure of exposure and human health risk. This program is chaired by Drs. Judith Zelikoff, Nancy Kerkvliet and Barbara Beck and is co-sponsored by the Risk Assessment Specialty Section. The second workshop will involve a discussion of the scientific and regulatory issues surrounding the new immunotoxicology testing guidelines advocated by EPA. This workshop is chaired by yours truly. The third workshop will focus on the use of flow cytometry in immunotoxicology testing and research. This program is chaired by Drs. Scott Burchiel and Greg Ladics. Our continuing education course this year will review neuroimmunology and its implications for toxicology. Dr. David Lawrence is the chair of this session.

In addition to these sessions, there will be numerous platform and poster presentations to attend as well. So don't let the weather stop you from coming to the meeting this year. I think you will agree with me that Scott Burchiel and his program committee should be commended for putting together an exceptional agenda for this year's national meeting. I look forward to seeing you in Cincinnati.

Newsletter Editors

Thomas T. Kawabata
Merck & Co., Inc.
WP-45-216
West Point, PA 19846
T: (215)652-3327
F: (215)652-7758
thomas_kawabata@merck.com

Judith T. Zelikoff
Institute of Environmental Medicine
New York Univ. Medical Center
Long Meadow Road
Tuxedo, NY 10987
T: 914-351-5624
F: 914-351-5472
judyz@charlotte.med.nyu.edu

New Section Officers:

President:

Peter Thomas
Hazelton Corning / Covance

Vice-President:

Scott Burchiel
Univ. of New Mexico

Vice-President Elect:

Kathleen Rodgers
University of Southern California

Secretary/Treasurer:

Judith Zelikoff
New York Univ. Medical Center

Student Representative

Cynthia Graham
Univ. of Pittsburgh

Councilors:

Gary Rosenthal
Somatogen, Inc.

Tom Kawabata
Merck & Co., Inc.

Dori Germolec
NIH/ERIS

Dan Wierda
Eli Lilly
(Past President)

Post Doctoral Fellows and Students:

**Presentation Awards for the 1997
SOT Meeting in Cincinnati**

**Entry Deadline January 31, 1997
(see the Awards Committee Announcement
for more details)**

Serabian strongly recommended that industry anticipate problems and talk to regulators prior to submission.

Serabian indicated that regarding the current status of immunotoxicity testing, there has been progress in the identification and validation of sensitive *in vivo* and *in vitro* screens to detect changes in the structural and functional capacity of isolated components of the immune system. However, there is a lack of consensus within the immunotoxicology community on (1) validated protocols, (2) test batteries and (3) the sensitivity, reproducibility and predictive value of various tests. CBER has given much thought to the future direction of immunotoxicity testing and feels that in determining the risk-benefit for biologic therapeutic agents, a specific battery of immunotoxicity tests may be of limited use and, therefore, the development of a framework for particular classes of products may be more useful for assessment of immunotoxic risk to humans.

Current Efforts on the Murine Local Lymph Node Assay - Dr. Ken Hastings

There is effort underway to gain FDA acceptance of the murine local lymph node assay (LLNA) as a stand alone assay for the prediction of the contact sensitization potential of chemicals. This assay would provide an alternative to guinea pig assays. Within the FDA it was felt that information was lacking with respect to pharmaceuticals. Dr. Hastings informed the ILSI Immunotoxicology Technical Committee that another validation study that has been planned to address this issue and to evaluate a number of pharmaceutical agents in the LLNA. The study is scheduled to begin in the near future as the compounds have been selected and the protocol agreed upon. This study will look at several pharmaceutical agents including penicillin G, streptomycin, hydroquinone, ethylenediamine, benzoyl peroxide. An irritant control, methyl salicylate, will also be included in the study. Participants in this international validation study include P&G, Zeneca, Unilever, DuPont and IITRI. Results of this validation study will be published in a peer-reviewed journal.

EPA

FIFRA Immunotoxicity Testing Guidelines

The EPA has revised its test guidelines for Series 870-Health Effects Test Guidelines which are for use by the Office of Pesticide Programs (OPP) and the Office of Pollution Prevention and Toxics (OPPT). The EPA states these guidelines have been harmonized with those of the OECD. The availability of these guidelines for public review was announced on June 20, 1996 in the Federal Register (Vol. 61, No. 120).

The Immunotoxicity Test Guidelines (870.7800) proposed immune function tests be carried out and used along with data from routine toxicity testing to provide more accurate information on hazard identification of immunotoxic potential. Specifically, the immune function assays that would be required by these guidelines are (1) the plaque

forming cell (PFC) assay in 30-day toxicity tests (either the endpoint of enumeration of plaque forming cells or ELISA to quantitate serum IgM levels can be used) and (2) phenotypic analysis of spleen lymphocytes and NK cells as assessed by flow cytometry in 90 day studies (a functional test for NK cells may be substituted). The public was given until mid-October to comment on the proposed guidelines.

A FIFRA Scientific Advisory Panel (SAP) meeting was held October 29 and 30 in Washington, D.C. to review Series 870 Guidelines and comment on statements from the public. Discussions on the Immunotoxicity Test Guidelines were in the afternoon on October 29. Sheryl Reilly opened the session on Immunotoxicity Test Guidelines with a history of the development of these guidelines. She then mentioned that they had received numerous public comments and, based on these comments, she introduced seven issues which needed to be addressed. The EPA requested the advice of the SAP on these issues.

Issue #1 was one of the most important issues and is the only issue which will be briefly summarized here. Public comments on the draft immunotoxicity guidelines questioned the appropriateness of including flow cytometric analysis as a required immune function test. After much deliberation among scientists at the EPA, it was decided that an amendment to the draft immunotoxicity guidelines should be made removing flow cytometric analysis as a required immune parameter. The questions posed to the panel regarding Issue #1 were (1) did the Panel agree on the proposed amendment to eliminate flow cytometric analysis as a required immune function assay and, if so, (2) which immune function parameters should be required? Two SAP members commented on this issue, Dr. Albert Munson and Dr. Peter Thomas. Both (1) agreed with the EPA's amendment to remove flow cytometric analysis as a required assay and (2) recommended including thymus weights (including thymus:body weight ratio), PFC assay and the NK cell assay as required immune function assays in the Immunotoxicity Testing Guidelines.

The remaining six issues as well as the SAP's comments on these issues will be in the transcripts of the FIFRA SAP meeting which will be available in the near future under docket number OPP 00434 (FRL-5367-1).

The next steps in this process include distribution of the transcripts to the SAP for review as well as incorporation of the SAP recommendations (based to an extent on comments from the public) into the draft guidelines. The revised guidelines will again be available for public comment and a notice of availability of this document will be posted in the Federal Register. After the public comments have been addressed, the Immunotoxicity Guidelines will most likely be finalized.

Proposed Test Rule for Hazardous Air Pollutants - Dr. Gary Timm

The EPA is proposing a test rule under section 4(e) of the Toxic Substances Control Act (TSCA) to require manufacturers and processors of 21 hazardous air

(not only that, you help your colleagues by giving them a one-class breather).

Please send the information about curricula, etc., and if anyone has any comments or other ideas regarding either of the above issues, please contact me at (T) 914-351-2300, (Fax) 914-351-5472, or (E) cohenm@charlotte.med.nyu.edu.

Membership Committee

Chairperson: Mitchell D. Cohen

By now, everyone should have received their respective page from the preliminary Immunotoxicology Specialty Section (IMTOX) directory. As I noted in the fax cover letter, the Membership Committee is in the process of putting together a directory of all our current members which will include each person's phone number, fax number, e-mail address, and a 2-3 keyword listing of their area of immunotoxicologic research. This directory will eventually be loaded into a web page so as to provide the general public access to all of our members. In addition, this directory will hopefully also be a useful tool for helping to recruit graduate students into the IMTOX Specialty Section. The completed directory should be available at the next SOT meeting in Cincinnati; if you will not be there, please let me know and a copy will be mailed directly to you. On a second matter, the Executive Committee has agreed with a suggestion that each member try to actively recruit one new member into the IMTOX Specialty Section over the course of 1997. Currently, we have 179 members. Increased membership will not only provide more political clout to our section, but will also help to increase the general coffers (\$\$\$\$\$\$\$!!!!). This added funding can then be put to good use, such as in increasing the value or numbers of awards that are handed out at the annual meetings. The procedures for application to SOT have been greatly simplified, so I encourage each IMTOX member to go out and recruit a fellow faculty/company worker, and especially graduate students, to join SOT and us. You can use the application form(s) found in the back of your newly-arrived '96-'97 SOT Membership directory (or photocopies of same; if anyone needs these forms, please let me know and I will forward them. If anyone has any comments or other ideas regarding either of these issues, please feel free to contact me at:

cohenm@charlotte.med.nyu.edu,
(T) 914-351-2300, or (Fax) 914-351-5472.

Methods Committee

Chairperson: Robert Leubke

The Methods Committee has discussed organizing a compendium of techniques and individuals who are willing to serve as consultants for the techniques. The compendium could be as simple as a list of methods and assays or as detailed as individual S.O.P.'s. Before proceeding, we need to determine the level of interest in this idea among the Specialty Section membership, as well as which members are willing to serve as contacts. Note

that our intention is to provide a list of individuals willing to help others troubleshoot problems, locate reagents, etc., rather than to identify individuals as the ultimate experts on a technique. The same applies to a compilation of SOP's; we have no intention of identifying any one method as the correct way to do an assay.

A list of techniques and contact individuals could easily be maintained in ASCII format and sent to requesters by email or FAX. Bob Luebke has agreed to do this if there is not another volunteer. The information will also be posted to the Immunotoxicology listserver, and submitted to the Immunotoxicology Section newsletter. Ultimately, if there is sufficient interest in a more detailed compendium (e.g., S.O.P.'s) and in the Specialty Section going hi-tech, a searchable database could easily be incorporated into an Immunotoxicology Specialty Section homepage.

Please address all feedback to Bob Luebke, preferably by email (luebke@her145.hcr.epa.gov); I will forward all responses to other members of the Methods Committee. For those without email, fax your response to Bob at (919)541-4284, or call (919)541-3672.

Program Committee for the 1998 SOT Meeting

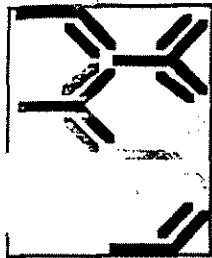
Chairperson: Kathy Rodgers (Vice President Elect)

Greetings from sunny California! We are doing well on getting ideas for our 1998 program. Dr. Robert House has submitted three excellent ideas. However, the program committee could use as many ideas as are available for symposia, round table discussions, workshops or courses for continuing education. If you have a suggestion or concept for an addition to the program, please contact myself [(213)226-4965] or one of the program committee members [M. Cohen (914)351-5277; J. Zelikoff (914)351-5624; I. Kimber 44625515408, D. Lawrence (518)474-0292, J. Barnett (190)632-2750; D. Frazier (617)252-9766] so that we can help you flesh it out, get in form for submission and present at the meeting of the entire Program and Executive Committees of the Immunotoxicology Subsection at the 1997 meeting of the Society of Toxicology. In addition, if any other persons would like to join the committee, please let me know. I look forward to hearing from you so that our program in 1998 will be representative of the joint effort of our entire discipline. Thanks in advance for your participation.

Student Representative

Cynthia Graham

As the first student representative to the Immunotoxicology Specialty section, I would like to open a line of communication, especially to other student members. I can be a liaison, voicing your concerns, needs, and hopefully, good news to other members of the section. I am hoping that the position of student representative will become a constructive addition to this section, and it can be with your help. Please contact me with any news or concerns through email at: ckgst1@vms.cis.pitt.edu; postal mail: c/o Department of Environmental and Occupational



Society of Toxicology Immunotoxicology Specialty Section NEWSLETTER

December 1995

President's Message

Peter Thomas
Vice-President and Chairman, Program Committee

Since Dan Wierda is a bit under the weather, I have agreed to take on some of his Specialty Section responsibilities. As I reported to you in the June Newsletter, the four programs sponsored by our Specialty Section will be presented at the national meeting in Cincinnati this Spring. They are:

- 1) Immunotoxicity of Medical Devices (symposium)
- 2) Aquatic Pollution-Induced Immunotoxicity (symposium)
- 3) Modulation of T-helper Cell Subsets: Potential Mechanism for Immune Suppression (symposium)
- 4) Identification of Respiratory Allergens (workshop)

Kevin Driscoll and Judith Zelikoff, both members of the National Program Committee, have informed me that all is on track with these programs for the upcoming national meeting in Anaheim. It looks like this will be another well attended meeting. The total number of abstracts for the Anaheim meeting is the second highest ever (New Orleans 1993 was the highest). On behalf of the Program Committee, I encourage you to attend the meetings, our symposia and the Immunotoxicology Specialty Section business meeting. It is clear that immunotoxicology continues to grow in importance and visibility on the national level. This is evident by the growth in both Specialty Section membership and in the number of programs we offer. Recognizing the limited meeting schedule, the Program Committee has assured us that it is doing everything possible to minimize the number of potential conflicts. No symposia are being scheduled for Thursday afternoon. Suggestions for improvements in this process can be made to either Kevin or Judith.

In addition to a strong scientific program, the Specialty Section is promoting other initiatives such as our 1996 Student Award Presentation being organized by George Shopp. Other concepts being discussed are the creation of a Specialty Section promotional brochure and soliciting outside articles for the Newsletter. Details of these will follow in a future newsletter.

Join me in wishing Dan a speedy recovery.

Peter Thomas

Section Officers:

President:
*Dan Wierda
Eli Lilly & Co.*

Vice-President:
*Peter Thomas
IIT Research Institute*

Vice-President Elect:
*Scott Burchiel
Univ. of New Mexico*

Secretary/Treasurer:
*Judith Zelikoff
New York Univ. Medical Center*

Councilors:
*George Shopp
Genentech*

*Gary Rosenthal
Somatogen, Inc.*

*Tom Kawabata
Procter & Gamble Pharmaceuticals*

*Michael Luster
NIEHS
(Past President)*

Newsletter Editors

*Thomas T. Kawabata
Procter & Gamble Pharmaceuticals
P.O. Box 538707
Cincinnati, OH 45253-8707
T: (513)627-1026
F: (513)627-1433
Kawabata.tt@pg.com*

*Judith T. Zelikoff
Institute of Environmental Medicine
New York Univ. Medical Center
Long Meadow Road
Tuxedo, NY 10987
T: 914-351-5624
F: 914-351-5472
judyz@charlotte.med.nyu.edu*

COMMITTEE REPORTS

Awards Committee (1996 SOT Meeting)

Chairperson, George Shopp

ANNOUNCEMENT 1996 Graduate Student/Postdoctoral Awards in Immunotoxicology Society of Toxicology

The Awards Committee of the Immunotoxicology Specialty Section of the Society of Toxicology will be granting up to five monetary awards at the Annual SOT meeting in Anaheim, in 1996. These awards will be in recognition of scientific excellence and achievement for the best papers in immunotoxicology submitted for presentation by graduate students and postdoctoral fellows. Candidates for these awards are requested to submit copies of their abstracts, all figures and data tables, summary, and conclusions, of their poster or platform presentation. The student or postdoctoral fellow must be the first author on the abstract. It is important that the submission be complete because the decision on the awards will be based on the written submission only, and not the actual presentation at the meeting. The submissions will be judged by the Awards Committee, and the winner will be announced at the annual meeting of the Immunotoxicology Specialty Section in Anaheim. All material should be submitted by February 1, 1996. Send to:

George Shopp, Ph.D.
Genentech
Mail Stop 9
460 Point San Bruno Blvd.
South San Francisco, CA 94080

Tel: 415-225-3713
Fax: 415-225-2797

Education Committee

Chairperson, Judith T. Zelikoff

We've been noticed! While the Committee still has not received much input concerning source references or course outlines for teaching immunotoxicology, there has been a great deal of interest from investigators all over the country beginning to teach immunotoxicology. Their major need is for a course outline and a place to get started. Since we never received enough information to formalize a course syllabus, I have been sending out the one which Mitchell Cohen and I developed and have used for our course in Environmental Immunotoxicology at New York University Medical Center. It seems to be working. It is exciting to think that "the word" is being carried to new, open minds. But we still need your help in "carrying the message" and sending successful course outlines to the Committee so we can formalize the program.

Concerning another aspect of education, the annual Virginia Beach Immunotoxicology meeting was held this past September and the turnout and presentations by

students and technical staff was again impressive. Off the record, I was particularly stirred by the large number of women attending this meeting and entering the field of immunotoxicology. Bravo!

Just a reminder, the Immunotoxicology Specialty Section is interested in having a student representative at its executive session. If you are interested please contact me by email at judyz@charlotte.med.nyu.edu or by fax (914-351-5624).

Regulatory Committee

Chairperson: Liz Sikorski

EPA

Roy Schoblad at the Office of Pesticide Programs reports that the EPA immunotoxicology testing guidelines have been drafted and the FIFRA Scientific Advisory Panel comments have been incorporated. Sheryl Reilly is currently integrating these guidelines into existing guidelines and harmonizing them with those of other subdivisions. The guidelines propose that chemical pesticides should undergo immunotoxicity testing that includes the standard assessment of extended histopathology, spleen and thymus weights and hematology. In addition, they are proposing that immunotoxicity testing of chemical pesticides include the sheep red blood cell assay, measurement of serum immunoglobulin, and flow cytometric analysis of the spleen. This document is not expected to come out until after the first of 1996. It should be noted that these guidelines are separate from those for biochemicals.

Gary Timm at the EPA's Office of Pollution Prevention and Toxicity has been working on proposed immunotoxicity test rules for analysis of twenty one hazardous air pollutants with the help of Vicki Dellarco (Office of Research and Development) and input from Mary Jane Selgrade (immunotoxicologist at EPA). He has discussed these proposed rules with industry and environmental groups. They are proposing that immunotoxicity testing of air pollutants include those parameters used in immunotoxicity testing namely, histopathology of bone marrow, spleen, thymus and lymph nodes (draining and distal), spleen and thymus weights, and hematology. In addition, they will recommend use of the sheep red blood cell assay as well as lung lavage. This document is awaiting in-house review and is not expected to come out until 1996.

ILSI

A summary of the Workshop on Immunotoxicology Testing and Risk Assessment (June 16-17, 1995) organized and sponsored by the Immunotoxicology Technical Committee of ILSI will be published in Food and Chemical Toxicology. Reprints of the article can be obtained by contacting Dr. David Neumann (FAX (202) 659-3617 or david@dc.ilsi.org) at ILSI's Health and Environmental Sciences Institute.

Immunotoxicity Testing and Risk Assessment: Summary of a 1994 Workshop
HESI Immunotoxicology Technical Committee
Food and Chemical Toxicology 33(10) 887-894

FDA

Dennis Hinton has indicated that the FDA is currently finalizing the draft of the immunotoxicity testing section of Redbook II. Regarding the content of this document, Hinton has stated that there is additional emphasis on allergy and hypersensitivity and that it contains information which will clarify issues that have generated controversy in the immunotoxicology community such as the use of maximum tolerated dose. The timetable for the release of the revised draft of the Redbook II has not been announced nor is there a projected date of publication.

SECOND CALL FOR ARTIFACTS

History of the Immunotoxicology Specialty Section

I have volunteered to be the historian for the Immunotoxicology Specialty Section. I would like to put together a portable poster that would be displayed at the annual meeting each year. The poster would highlight the historical development of the field of immunotoxicology and the growth of the specialty section with pictures and other memorabilia. I hope to keep it up-to-date with pictures taken at the meeting each year. I am in need of member to search their photo albums and files for pictures, that could be used for the poster. Also, any eptual ideas for the poster will be appreciated. Please your contributions to:

Dr. Nancy Kerkvliet
Dept. of Agricultural Chemistry
ALS 1007
Oregon State University
Corvallis, OR 97331

NEW IMMUNOTOXICOLOGY SPECIALTY SECTION LOGO DESIGN CONTEST

We would like to spruce up our Newsletter. We plan to change the logo on the newsletter that would best symbolize the Immunotoxicology Specialty Section. We have previously used the SOT Emblem. The drawing should be the size of the logo shown in this newsletter (upper left corner of front page). Please submit your entries to the following address by March 1, 1996 to be considered. We will post the drawings at the Specialty Section Meeting for a ballot vote. Any other suggestions for changes to the newsletter will be appreciated.

Newsletter Editors

Tom Kawabata and Judith Zelikoff

Tom Kawabata
Procter & Gamble Pharmaceuticals
Box 538707
Cincinnati, OH 45253-8707