From the International Academy of Toxicologic Pathology
An Affiliate of the IFSTP

I.A.T.P. Recognizes Bernie Wagner, M.D. for his Distinguished Career in Toxicologic Pathology

The International Academy of Toxicologic Pathology co-sponsored a symposium in honor of the lifetime achievements of one of the founding fathers of toxicologic pathology, Bernard M. Wagner, M.D. at the New York Medical College, September 22-23, 2003. The international symposium, entitled: ***Chemical Safety Assessment: Contributions of Toxicological Pathology and Mechanistic Investigations***, was organized by I.A.T.P. Fellow, Gary Williams, M.D., Professor of Pathology at NYMC. Dr. Wagner was bestowed the title of Honorary Fellow of the I.A.T.P., the first to receive this honor. The I.A.T.P. is a global organization of leaders in the field of toxicologic pathology, drawing its Fellows from industry, government and academia from Europe, Asia and North America.

I.A.T.P. Sponsors Symposium on Contemporary Issues in Toxicologic Pathology At the 5th International Symposium of the IFSTP, Hosted by the JSTP in Japan

The International Academy of Toxicologic Pathology is sponsoring an afternoon symposium at the International Conference Center Kobe, Japan, on Sunday, February 15, 2004. An international team of I.A.T.P. Fellows and guests will present lectures on a wide range of topics, including cancer, immunopathology, endocrine disruption and the role of brown adipose tissue in humans. Speakers include Drs. Gary Williams, John Seely and Michael Iatropoulos from American, Joseph Voss and Pieter Wester from Europe, and Hiroyuki Tsuda from Japan. Professor Charles Capen will provide closing comments.

STP Membership Committee Report Summary for Winter 2004 Scope

STP Membership Committee, Thomas Dorr (Chair)

The Membership Committee recently reviewed 16 applicants and made recommendations to the Executive Committee resulting in the addition of 10 Full, 3 Associate, and 3 Student Members to the STP.

For the ongoing Member-get-a-member campaign, 10 current STP members were cited as influential in the applicants' decisions to apply for membership.

The Membership Committee and AIM have recently provided pathology training programs with access to The Scope newsletter in order to give students early exposure to the benefits of membership in the STP and current information on the activities of the society. The newsletter was sent to contact people at US and Canada-based training programs along with a cover letter requesting that it be made available for review by pathology residents, graduate students, and veterinary students interested in pathology.

The Membership Committee made recommendations to the Executive Committee regarding the policy for honorary members. In addition to the benefits for honorary members outlined in the STP bylaws, the Membership Committee recommended adding the right to vote and waiver of registration fees to the annual STP meeting for honorary members. These recommendations have been reviewed and approved by the Executive Committee.

The STP would like to thank the following people, and their supporting companies, for their participation in the STP-Sponsored session at The Society of Quality Assurance (SQA)'s 19th Annual Meeting.

Jane Hollingsworth, EPL
Dr. Roy Kerlin, Pfizer Global Research and Development
Dr. Jeffrey Wolf, EPL
Dr. Darrell Toumari, Schering-Plough Research Institute
Dr. Mark Butt, Charles River

This year's STP session was entitled, "Toxicologic Pathology: Current Compliance Considerations." Dr. Jeffrey C. Wolf presented "Good Laboratory Practice Considerations in the Use of Fish Models." The second presentation, "Society of Toxicologic Pathology Position on Histopathology Data Collection and Audit Trail: Compliance With 21 CFR Parts 58 and 11" was given by Dr. Darrell Tuomari. The remainder of the session was devoted to a question and answer time, "Ask the Pathologist." Panelists included Drs. Jeff Wolf, Darrell Tuomari, Mark Butt, and Roy Kerlin.

If any STP members would be interested in participating in the STP-Sponsored session at the 2004 SQA meeting (Reno NV, April 25-29), please contact the STP/SQA Liaison, Lynda Lanning (lyndal@otsuka.com or 240-683-3378).

Thanks! Lynda

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Rockville, MD 20850
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REPORT TO IFSTP

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DATE: 10/02/2004

1) NATIONAL SOCIETY: Society of Toxicologic Pathology

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REPORT TO IFSTP

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2) NUMBER OF MEMBERS: see www.toxpath.org

Please provide a membership list of your Society to the Office of the Secretary General

3) ACTIVITIES: RECENT AND PLANNED:

Meetings, Symposia, Interactions with other Societies; Dates, Location, Estimated Attendance;
Type of Activity: Educational, Regulatory, Publications, etc.)

NOTE: Please use second page to insert data, if needed.

Recent: The Membership Committee recently reviewed 16 applicants and made recommendations to the Executive Committee resulting in the addition of 10 Full, 3 Associate, and 3 Student Members to the STP.

The Fundraising Committee is in the process of contacting potential sponsor for the 2004 Annual Meeting to be held in Salt Lake City, Utah. In addition the Committee is also contacting organizations to renew or establish new Organizational Membership within the Society. It's through the continued support of organizations that STP is able to achieve its mission and goals play an intricate role in fostering training and recognition of toxicologic pathologists.

Planned: Annual General Meeting, Salt Lake City, USA June 13-17, 2004
The 23rd Annual Meeting of the Society of Toxicologic pathology topic is *Hepatotoxicity* and will be held at the Grand America Hotel in Salt Lake City, Utah.

Issues: Strategic Plan: Many of the goals of the previous strategic plan have been accomplished, and although we made some progress on a new plan last year, it has languished a bit asother issues took priority. The Executive Committee (EC) at the October meeting decided that a clear strategic plan was vital to aid decision making on a number of issues. Therefore we decided to lengthen the February EC meeting to accommodate strategic plan discussions and hire a facilitator, Pat Walker Hichman of Tecker Associates, to ensure that a draft strategic plan was formulated during that time period. I look forward to that meeting and to sharing the outline of a draft plan with the membership for approval in the months ahead.

REPORT TO IFSTP

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Fundraising: STP is about to embark on a capital fundraising endeavor to generate significant dollars to increase training opportunities for pathologists. We became aware that ACVP was also planning a similar capital campaign to increase funding for educational opportunities for veterinary pathologists. We formed a subcommittee of individuals from STP (Drs. Wanda Haschek-Hock, Bruce McCullough, and John Robertson) and ACVP (Drs. Gary Cockrell, Ricardo Ochoa, and Reid Patterson) to determine whether the two organizations should work together to define a capital campaign and solicit funds, as many of the sources for funding for the two groups would be identical. The unanimous opinion of the subcommittee was that the two groups should work together on this endeavor; both the ACVP Council and STP EC approved this commitment this fall. The subcommittee was then tasked with determining
the specifics of the combined effort, and presenting recommendationsto the leadership of both organizations by February. We will be providing you updates as those recommendations are received.

Liaison report: American College of Veterinary Pathologists
Liaison: R. Keith Harris
23 February 2004

The ACVP Council has met twice since my last report, once in November 2003 in Banff in conjunction the College's annual meeting, and once by teleconference on 12 February 2004. Primary issues addressed by Council, and of interest to the STP membership, were:

1. **Newly Elected Officers.** The results of the 2003 elections were announced. New officers are:

   President: Linda Munson
   Vice President/President Elect: Keith Harris
   Secretary/Treasurer: Derek Mosier (effective in November 2004)
   Councilor: Robert Hall

   Primary STP contacts are Linda Munson (President) and Paul Stromberg (Secretary/Treasurer until November 2004). Linda plans to meet with the STP EC at the Society's annual meeting in June 2004.

2. **Joint STP/ACVP initiative to coordinate funding for training.** A joint STP/ACVP committee met in September 2003 and January 2004 in an effort to better coordinate the fund raising activities of the two organizations. Members of this committee are: John Robertson, Gary Cockerell, Wanda Haschek-Hock, Bruce McCullough, Ricardo Ochoa, and Reid Patterson. The committee has drafted a proposal for an "ACVP/STP Coalition for Veterinary Pathology Fellows" establishing an industry-funded training program projected to support 15 new residency and PhD training positions. ACVP Council is currently evaluating the proposal.

3. **Salary/Compensation Survey**. The College conducted an on-line salary/compensation survey in December 2003 - January 2004. Over 600 College members responded, which represents a slightly better response than occurred in the last survey, conducted on paper in 1998. Results of the survey should be available on the College's web site and in the College's newsletter in March or April 2004.

10 February 2004

Society of Toxicologic Pathology Liaison Report to the STP External Affairs Committee

STP Liaison: David Eisenbrandt, Dow AgroSciences, Indianapolis
Affiliate Organization: CropLife America

CropLife America (CLA) is an organization representing the major manufacturers, formulators and distributors of crop protection, pest control and biotechnology products (http://www.croplifeamerica.org). CLA promotes sound legislation and science-based regulation, promotes increased understanding of the value of crop protection products, encourages the use of sound science in the research, development and regulatory processes and also addresses issues affecting the safe use of pesticide products. The CLA Human Health & Risk Assessment Round Table (HART) reports through the Registration Committee to the Technical, Legal, Legislative and Communications Oversight Council of CLA. The Chair of the HART group is Abraham Tobia of Bayer CropScience and the Vice-Chair is Frederick O'Neal of DuPont Crop Protection. The CLA staff representative for HART is Angelina Duggan. The HART group meets six times each year and closely coordinates with similar expert groups in Europe and Canada.

Continuing issues for CLA HART scientists are the U.S. EPA's Draft Final Guidelines for Carcinogen Carcinogen Risk Assessment as well as the Supplemental Guidance for Assessing Cancer Susceptibility from Early-life Exposure to Carcinogens. The latter proposes adjusting the calculation of lifetime risk from exposure to non-threshold carcinogens based on estimated exposure during the first two years of life by a 10x safety factor and the next 13 years of life by a 3x safety factor.

CLA HART scientists have provided comments in response to the U.S. EPA proposal (March 4, 2003, 68 Federal Register, 10238) "National Agenda for the Environment and the Aging: Setting Priorities for Research and Education to Address Environmental Hazards That Threaten the Health of Older Persons." CLA emphasized that it is both inappropriate and inaccurate to generalize that environmental exposures result in infirmity in old age or that past exposures are the primary cause of declining health in aging populations. CLA suggested that investigations for aging populations should be

prioritized to identify lifestyle factors, physiologic processes and genetic pre-dispositions to diseases generally associated with aging populations.

Other ongoing issues for CLA HART scientists are related to existing and planned regulatory guidelines for testing of chemicals for potential health effects. Working groups are actively addressing significant issues related to developmental neurotoxicology studies, endocrine 'disruption' test methodologies, 28-day inhalation toxicity studies, developmental thyroid toxicology, immunotoxicology and developmental immunotoxicology.

Opportunities for STP actions in support of CLA are:

1. Publish the STP Commentary "Pathologic Assessment in Developmental Neurotoxicity Testing" (Jortner et al.) which was in a final draft version in July, 2001 after a great deal of time and effort.
2. Approximately 12,500 mammals are now used to conduct the required health effects test guidelines to register a pesticide. A majority of these animals (78%) are use in reproductive and developmental studies. Additional requirements and test guidelines are being considered that will significantly increase the use of animals for registration studies. STP should be instrumental in influencing regulatory agencies in the development of a more rational approach to product safety testing as compared to the current paradigm of continually adding to a long list of endpoints.

Handout 1D

International Life Science Institute **February 2004**

by Dr. Charlotte Keenan

HESI HIGHLIGHTS

- 2 scientific sessions were presented at the 2004 annual ILSI meeting
    - "Adverse Drug Reactions – A Threat to Public Health", covering the topics of hypersensitivity, adverse reactions in the pediatric population, animal model systems and pharmacogenetics.
    - "Conducting a Comprehensive Evaluation of the Human Allergenic Potential of Novel Proteins", covering international guidelines, sequence homology, digestive stability, animal models and case studies.
- **A workshop that will consider the biological consequences of DNA adducts, modifiers of DNA adduct levels and of their ultimate effects, and how data for DNA adducts can be utilized in mechanistic studies and in the risk assessment process will be held on April 13-14, 2004, in Washington, DC.**
- **The HESI Committee on Genomics has published 13 technical and overview papers detailing the outcome of its 2.5 year collaborative research program a special mini-monograph published as part of the journal, EHP Toxicogenomics. The journal will be available in hard-copy in March but these articles are available for download now via EHP's in-press website.**
- **HESI will be sponsoring the ILSI workshop held in conjunction with the American College of Veterinary Pathologists annual meeting. This year the topic will focus on Immunotoxicology.**

RSI HIGHLIGHTS

1. Toxicology and Risk Assessment
    - Children's Health - Development of a Framework for Assessment of Risks to Children from Exposure to Environmental Agents. **In 2003, five papers were published in *Environmental Health Perspectives,* comprising the products of the 2001 RSI workshop that developed a conceptual framework for assessing children's risks from environmental exposures to pathogens, radioactive substances and chemicals such pesticides, commodity chemicals, pharmaceuticals and environmental comntaminants. (The papers are available through EHP Online at http://ehp.niehs.nih.gov/).**
2. Model Peer Review Center of Excellence
3. Framework for Evaluating Human Relevance of Mode of Action of Animal Tumors, with Special Attention to Peroxisome Proliferator-induced Tumors in

Rodents - The PPAR alpha Subgroup has prepared a report providing an evaluation of the current state-of-the science with regard to the carcinogenic potential of PPAR alpha agonists and an update on the understanding of the mode(s) of tumorigenic action in the liver, Leydig cell and pancreatic acinar cell. Subgroups made presentations at the 2003 SOT meeting and manuscripts prepared for a supplement of Critical Reviews in Toxicology (Nov 2003).

4. Application of the Enhanced Mode of Action Analytical Framework to Genotoxic Carcinogenicity and Noncancer Endpoints
5. Issues in the Design and Interpretation of Chronic Toxicity and Carcinogenicity Studies in Rodents – **The document being developed by the working group will be completed in 2004. OECD is incorporating the RSI work on dose selection into its test guidelines and guidance documents.**
6. Testing of Fibrous Particles: Short-term Assays – **A working group paper has been drafted, and the group will complete its work by summer 2004**.
7. Application of Toxicogenomics Technology and Bioinformatics in Toxicological Research and Risk Assessment - **RSI is considering a project that would contribute to meeting the educational needs for scientists and decision-makers in all sectors. More specifically, the project would start with detailed educational material already developed by academic and regulatory scientists and would "package" this material into a flexible and easily accessible format (e.g., an online interactive format).**
8. General Principles for Evaluating the Utility and Application of Screening Assays
9. Use of Non-tumor Data in Cancer Risk Assessment - An expert working group convened by RSI has identified a number of general principles for the use of data other than bioassay tumor incidence in cancer risk assessment. The principles are drawn in part from case studies prepared by the working group on benzene, 1,3-butadiene and vinyl chloride. The paper presenting the principles and case studies was published in the Journal of Regulatory Toxicology and Pharmacology in March/April, 2003.
10. Cumulative and Aggregate Risk Evaluation System (CARES™) – a tool to evaluate short-term, intermediate and lifetime scenarios for dietary-food, dietary-drinking water and other exposures to pesticides for the purpose of characterizing risk. The tool will be managed by ILSI Research Foundation.

More detail can be found on the web site - www.ilsi.org and click on "entities" to find HESI and RSI.

Report to the STP Executive Committee
Activities of the National Toxicology Program (NTP)

http://ntp-server.niehs.nih.gov

Feb 19, 2004

NTP Satellite Symposium on Hepatic Pathology

The NTP will sponsor a satellite symposium on Saturday, June 12, 2004, before the start of the Society of Toxicologic Pathology Annual Meeting. The annual meeting is scheduled for June 13-17, 2004. The format for the satellite symposium will the same as the one held in Savannah in 2003.

Cases will be available on a web site prior to the meeting and audience response units (for audience voting and instant display of the results) will be provided during the satellite symposium. The emphasis for the cases will be hepatic lesions although non-hepatic lesions will also be included.

Persons interested in attending can obtain information on-line at www.toxpath.org or send a message to stp@toxpath.org

Public Meeting Set to Discuss NTP Vision

The last decade of the 20th century and the turn of the 21st century have produced dramatic technological advances in molecular biology and computer science. In an effort to determine how best to incorporate these new scientific technologies into its research and testing strategies and to broaden scientific knowledge linking mechanism and disease, the NTP has developed a vision. The NTP Vision for the 21st Century is to move toxicology from a predominately observational science at the level of disease-specific models to a predominately predictive science focused upon a broad inclusion of target-specific, mechanism-based, biological observations. The NTP plans to develop a roadmap or framework to guide the program in implementing its vision. The goal of the roadmap is to position the NTP strategically at the forefront of toxicology in providing scientific data and its interpretation for public health decision-making.

The NTP held a public meeting on Thursday, January 29, 2004, to receive comment on the Vision and input for developing a roadmap. The NTP desires broad participation in developing the roadmap and invites the public comments. In developing the roadmap and milestones toward achieving the vision, the NTP seeks input on issues raised by the following questions:

1. What scientific information should the NTP be producing and what technical capabilities should the NTP have by 2008? By 2013?

2. How do you envision that the refinement/replacement of classical toxicological

studies with mechanism based assays will impact on the evaluation of public health hazard

3. How can we best structure the NTP to provide this information and to ensure its optimal utilization in the protection of public health?

4. . What resources will be needed to realize this vision and how long will it take?

Background information (NTP Vision document) is posted at http://ntpserver.niehs.nih.gov/ (*select* NTP Vision Public Meeting *under* What's New?).

NTP Board of Scientific Counselors Technical Reports Subcommittee Review of Draft Technical Reports

The NTP Board of Scientific Counselors Technical Reports Review Subcommittee peer reviewed 6 draft NTP Technical Reports of NTP rodent toxicity and carcinogenicity studies and 1 draft report of carcinogenicity studies in 2 fish models at its meeting on Feb 17 - 18, 2004 at the National Institute of Environmental Health Sciences (NIEHS). The reports reviewed included:

TR#	Chemical	Uses and Occurrence
494*	Anthraquinone	Intermediate in dye manufacture
520	3,3',4,4',5-Polychlorinated biphenyl 26 (PCB 126)	Insulating fluid for electronics
521	2,3,7,8, Tetrachloro-*p*-dibenzene dioxin (TCDD)	Byproduct of combustion and smelting
525	2,3,4,7,8-Pentachlorodibenzofuran (PeCDF)	Byproduct of incineration and combustion
526	Dioxin mixture: (PCB 126, TCDD and PeCDF)	Insulator and combustion byproduct
527	Malachite Green & Leucomalachite Green	Dye; antifungal for fish
528**	1,2,3-Trichloropropane 2,2-Bis(bromomethyl)-*p*-1,3-propanediol Nitromethane	Paint and varnish remover Flame retardant Fuel additive, synthesis intermediate and solvent

***** The Subcommittee reviewed the draft NTP Technical Report on Anthraquinone in May 1999. Subsequent to that peer review, the tested anthraquinone was found to contain a 0.1% contaminant. As a result, additional mutagenicity and metabolism studies were conducted and the findings from those studies are included in the revised draft report. The Subcommittee will evaluate the results from the follow-up studies, use that information to re-examine the carcinogenicity findings from the 2-year studies and make a recommendation on the carcinogenicity of anthraquinone.

****** Studies of these compounds are being done in two species of fish (Medaka and Guppy)

The draft reports are available for public review, free-of charge though ehpOnline (http://ehp.niehs.nih.gov). A limited number of printed reports are available from Central Data Management at the NIEHS (Tel: 919-541-3419, fax: 919-541-3687, CDM@niehs.nih.gov).

Report on Carcinogens (RoC) Public Meeting

The NTP held a public meeting on January 27-28, 2004, to receive public comment on the current process for reviewing nominations for listing in or delisting from the RoC and on the current listing criteria used for evaluating the nominations. The purpose of this meeting is to obtain input and provide all interested parties the opportunity to express their views and/or to comment on the views expressed by others. A panel that included NTP staff, representatives of the NTP Board of Scientific Counselors and the NTP Executive Committee received the public comments and participate in the discussion.

NTP Requests Nominations for Future Evaluation for Listing/Delisting in the RoC

The NTP solicits and encourages the broadest participation from interested individuals or parties in nominating agents, substances, mixtures, or exposure circumstances for listing in or delisting from the RoC. Nominations should contain a rationale for the listing or delisting and appropriate supporting background information and relevant data (e.g., journal articles, NTP Technical Reports, Interagency Agency for Research on Cancer listings, exposure surveys, release inventories) when possible. Nominations should be directed to the address below.

Contact Information: Dr. C. W. Jameson, Head, Report on Carcinogens, NIEHS/NIH, 79 Alexander Dr., Room 3118, P. O. Box 12233, MD EC-14, Research Triangle Park, NC 27709; T: (919) 541-4096; F: (919) 541-0144, e-mail: jameson@niehs.nih.gov

Scientific Advisory Committee on Alternative Toxicological Methods (SACATM)

The next meeting of the SACATM will be held on March 10-11, 2004, at the Hyatt Regency Hotel, One Bethesda Metro Center, Bethesda, Maryland 20814. The meeting begins each day at 8:30 a.m. until adjournment and is open to the public with attendance limited only by space available.

Chartered in January 2002, the SACATM replaced the Advisory Committee on Alternative Toxicological Methods. The SACATM advises the Director of the NIEHS, the Interagency Coordinating Committee on the Validation of Alternative Methods, and the NICEATM on priorities and directives related to the development, validation, scientific review, and regulatory acceptance of new or revised toxicological test methods and on ways to foster partnerships and communication with interested parties.

Individuals who plan to attend are asked to register with Dr. Kristina Thayer, Executive Secretary [NTP Liaison and Scientific Review Office, NIEHS, P. O. Box 12233, Research Triangle Park, NC 27709. T: (919) 541-5021, fax: (919) 541-0295, or e-mail: thayer@niehs.nih.gov].

Agenda and details of the meeting are announced in the Federal Register and posted on the NTP web site (http//:ntpserver@ niehs.nih.gov *select* What's New).

PhRMA Liaison Report to STP-EC

By D. Tuomari, 20 FEB 04

PhRMA-DruSafe (Drug Safety Subsection)

My contact at PhRMA (Pharmaceutical Research and Manufacturers of America) is now Michael Garvin. Dr. Tim Anderson (Pfizer) is the Chair of DruSafe. Ruth Lightfoot (Glaxo-SmithKline) is the Vice-Chair. Dr. Bruce McCullough (Aventis) is the Secretary. A new position that has been created at PhRMA, which will interact, with DruSafe is that Lisa (Alisia) Miles has been appointed the Director of Emergency Preparedness, to help counter terrorism with biological or chemical agents.

Throughout the past months, I have forwarded various information documents that PhRMA has sent me to the STP-EC. In addition, I sent to PhRMA some updates on STP activities, including a copy of the STP comments on the tissue list issues raised by the VICH GL 37 guideline. I will continue to provide detailed discussions to STP-EC based on the PhRMA workshops when I am able to attend or receive notes/slides.

There was a DruSafe/FDA Genotoxicity Workshop held Nov. 19-20, 2003. The main motivation for this meeting was the perceived change in FDA-CDER guidance to follow-up on the unique *in vitro* positive genotoxicity findings from the previously accepted ICH guidelines. In particular was the use/role of the Syrian Hamster Embryo (SHE) cell transformation assay in different divisions of the FDA-CDER. Genotoxicity data from three cases, all with some positive findings were presented and discussed. The general conclusions indicated the need to use of sound scientific judgment and a weight of evidence approach. In general they conclude that repeat dose clinical trials could proceed in all three of the cases presented, without additional studies. However, additional studies are necessary to better understand the mechanism of action of significance of positive findings. There was general agreement that short-term carcinogenicity studies could be accelerated to continue clinical development in parallel. The majority indicated that the SHE cell transformation assay should not be a requirement to proceed with clinical development; and in the case of a positive chromosomal aberration assay, the SHE cell assay was NOT an appropriate follow-up assay.

Workshop conclusions/generalizations about the weight of evidence included:

- The use of cytogenetic analysis from the subchronic studies may be useful in assessing the relevance of a positive *in vitro* assay.
- Careful assessment of *in vitro* cytotoxicity was necessary for interpretation of positive genotoxicity results. Positive *in vivo* results were unlikely in the absence of toxicity.
- Perception that sometime the course of action is more dependent on what the FDA wants verus the belief of what is scientifically most appropriate. For example, *in vivo* UDS is often chosen as a follow-up assay, without consideration as to whether it is the most appropriate.

- Simply accumulation an increasing number of negative assays is NOT a defensible approach for the weight of evidence.
- Equivocal results should be repeated for reproducibility. If the compound causes a reproducible equivocal/weak positive result, then consider a fourth ICH test.

There was a major difference of opinion concerning the validity of risk assessments based on the *in vitro* concentrations that gave positive results versus *in vivo* plasma levels which were associated with negative results and the extrapolation of those results to the projected human blood levels. The FDA-CDER did NOT support these types of risk assessments. In contrast, some PhRMA people emphasized that this contributes to the understanding of safety margins.

One very IMPORTANT conclusion was that positive *in vitro* genotoxicity results combined with an increased tumor incidence in the rodent bioassay do NOT necessarily equate to a genotoxic carcinogen. One also needs to consider tumor site, tumor type, and mechanistic evidence.

Four questions were raised by the workshop:

1. Is the ICH genotoxicity guidance in need of revision?
2. Should ICH guide data interpretation?
3. Are there better follow-up assays to *in vitro* positives than the SHE cell assay?
4. What data gaps need to be filled in order to make better use of other endpoints (e.g. value of cytogenetic endpoints from subchronic studies?

Currently, DruSafe is preparing a position paper concerning the use of SHE cell transformation assay.

DruSafe will participate in FDA-CDER Scientific Rounds which are held approximately monthly. Scheduled topics included: screening strategies for selecting drug candidates (emphasis on genotoxicity assays); role of mechanistic studies in drug development; screening for QT effects; and biologic drug development.

Liaison Report, Society of Quality Assurance
January 2004

Prepared/submitted by: Lynda Lanning

EC ACTION ITEM: No action items at this time.

SQA NEWS

The Society of Quality Assurance (SQA)'s 20th Annual Meeting will be held April 25-29, 2004 in Reno, Nevada. This year's STP session is entitled, " Toxicologic Pathology: Current Practices, Digital Trends and Compliance Implications." Dr. Glenn Elliott will be presenting " Good Laboratory Practice Considerations in Clinical Pathology." Our second presentation, " Digital Imaging in Pathology: Compliance Strategies " will be given by Dr. Noel Dybdal. The remainder of the session will be devoted to a question and answer time, "Ask the Pathologist." Panelists will include Drs. Glenn Elliott, Noel Dybdal, Reid Patterson and Michael Connor. The SQA Annual Meeting Planning Committee is very excited about our session and attendance is expected to be high. [The preliminary program for the meeting is listed below.]

In addition, the STP's organization poster will be displayed during the meeting in the Poster area.

U.S. Regulatory Updates

The Computer Validation Initiative Committee (CVIC) submits comments to the United States Food & Drug Administration on FDA's Draft Guidance for Industry on Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical Current Good Manufacturing Practice.

Comment to Docket: 2003D-0386 (PDF file)

New FDA Guidance is available for public comment - Providing Regulatory Submissions in Electronic Format--General Considerations

The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Providing Regulatory Submissions in Electronic Format--General Considerations." The draft guidance discusses general issues common to all types of electronic regulatory submissions and updates the guidance of the same name, issued in January 1999. The update now includes information for the Center for Devices and Radiological Health (CDRH), the Center for Food Safety and Applied Nutrition (CFSAN), and the Center for Veterinary Medicine (CVM) and reflects advances in technology as well as lessons learned from experience with electronic submissions received over the past several years.

Docket No. 2003D-0465, CDER 2000152. Draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format--General Considerations; Availability. Page 60395 [FR Doc. 03-26571] [TXT] [PDF] [PRE-PUB] Comments December 22, 2003
http://www.fda.gov/OHRMS/DOCKETS/98fr/2003D-0465-gdl0001.pdf
http://www.fda.gov/OHRMS/DOCKETS/98fr/2003D-0465-gdl0001.doc

CROMERRR UPDATE

David Schwarz, EPA, Office of Environmental Information, has confirmed that CROMERRR (EPA's proposed Cross Media Electronic Reporting and Record-Keeping Rule) will not likely be forwarded to OMB (Office of Management and Budget) until at least January 2004.

IMPACT:
CROMERRR (reporting portion) was not issued in 2003. The final rule most likely will not be issued until mid-2004 at the earliest.

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Annual Meeting Sessions

Concurrent session topics are tentative and subject to change. Please check back often for updates.

Last update: Tuesday, 20 January 2004

Session descriptions and a registration form are available in the PDF Registration Brochure. Online registration also is available.

Tuesday, 27 April 2004

7:30 - 8:30
Continental Breakfast with with Exhibitors and Posters

8:30 - 10:30
Opening Plenary
2004 President's Address
3rd Annual QA Journal Award Presentation
Keynote Presentation: Patti Wood
Chair: P. Bork

10:30 - 10:45
Beverage Break with Exhibitors and Posters

10:45 - 12:00
Session A —

RQAP-GLP Examination Saturday, 24 April 2004

SQA Skills Forum
Training Documentation
Chair:
K. Hackett-Fields
Session B —
SQA Skills Forum
Reporting Audit Findings
Chair: J. Goeke
Session C —
SQA Skills Forum
Measuring the Performance of the Quality Assurance Unit
Chair: G. Furrow
Session D —
SQA Skills Forum
Auditing Tools I:
Design of GXP Audit Checklists
Part 1 of 2, continued in Session O
Chair: M. Finkes

12:00 - 1:30
Lunch
History of SQA Presentation

1:30 - 3:00
Session E — GCP
Regulatory Update — Clinical
Chair: M. Kaiser
Session F —
EPA-GLP
Regulatory Update —
EPA-GLP
Chair: M. Morris
Session G —
FDA-GLP
Ethical Issues in Non-clinical Drug Development
Chair: M. Christian
Session H — Special Interests
Medical Device Topics
Chair: D. Bridges

3:00 - 3:30
Beverage and Snack Break with Exhibitors and Posters

3:30 - 5:00
Session I — GCP
Monitoring Safety of Drugs after Marketing Authorization
Chair:
R. Huddleston
Session J —
EPA-GLP
Development Cycle of Pesticides
Chair: D. Green
Session K — FDA-GLP
Regulatory Update —
FDA-GLP
No Special Interests Session at this time
Chair: J. Goeke

5:00 - 8:00
SQA Peripheral Meetings: Regional Chapters, Committees and Specialty Sections

Wednesday, 28 April 2004

7:30 - 8:30
Continental Breakfast with Exhibitors and Posters

8:30 - 10:00
Session L —
SQA Skills Forum
How to Train the QA Professional
Chairs: B. Lawler, D. Garvin
Session M —
SQA Skills Forum
How to Write an Audit Report
Chair: C. Carson
Session N —
SQA Skills Forum
Measuring the Performance of the QA Professional
Chair: G. Furrow
Session O —
SQA Skills Forum
Auditing Tools II: Completeness & Efficiency
Part 2 of 2, continued from Session D
Chair: E. Humes

10:00 - 10:30
Beverage Break with Exhibitors and Posters

10:30 - 12:00
Session P — GCP
Accreditation of Clinical Trials and Research Programs
Chair: A. Hudson
Session Q —
EPA-GLP
Techniques for Auditing FieldNotes Electronic Field Study Data
Chair: R. Daniel
Session R —
FDA-GLP
21 CFR Part 11 Guidance: What Does it Mean to Me?
Chair: S. Grunwald
Session S — Special Interests
Scientific Archiving
Chair: A. Bosau, D. Talerico

12:00 - 1:30
Lunch

1:30 - 3:00
Session T — GCP
It is Time to Rename QA — Novel Approaches to GCP QA
Chair:
R. Hattemer-Apostel
Session U —
EPA-GLP
Registration of "Pesticides" in Europe, a Daily Challenge
Chair: S. Broughton
Session V —
FDA-GLP
Managing Multisite and Multinational QA Units
Chair: B. Patterson
Session W — Special Interests
A Collation of Computer Compliance Conundrums
Chair: L. Beacham

3:00 - 3:30
Beverage and Snack Break with Exhibitors and Posters

3:30 - 5:00
Session X — GCP
Improving Sponsor/CRO Collaborations
Chair: P. Becker
Session Y —
EPA-GLP
Don't Gamble with Compliance — Updates on CROMERRR, ELAB/NELAC and OPP Electronic Submissions)
Chair: R. Peterson
Session Z —
FDA-GLP
Animal Health Issues
Chair: M. Reimers
Session AA — Special Interests
Biopharma-ceuticals
Chair:
A. Plocinski

5:30 - 9:00
Dinner and Entertainment
(Optional Event — Separate registration will be offered online)

Thursday, 29 April

7:30 - 8:30
Continental Breakfast

8:30 - 10:30
Session BB
GCP Roundtable Discussions
Chair: M. Laszek
Session CC
EPA-GLP Roundtable Discussions
Chair: B. Foy
Session DD
FDA-GLP Roundtable Discussions
Chair: R. Siconolfi
Session EE
Special Interests Roundtable Discussions
Chair: P. Royal

10:30 - 11:00
Beverage Break

11:00 - 12:00
Session FF — GCP
QA Management Philosophies II
Chair: M. Laszek
Session GG —
EPA-GLP
Pesticide Exposure Studies
Chair:
J. Normansell
Session HH —
FDA-GLP
GLP Interfaces with GCP and GMP
Chair: D. Harris

Session II —
Special Interests
Toxicologic Pathology: Current Practices, Digital Trends and Compliance Implications
Chair: L. Lanning

12:00 - 1:30
Lunch

1:30 - 3:30
Closing Plenary

Roundtable Consensus Reporting
The information gathered during the Roundtable Discussions will be collated, evaluated, and reported to the attendees in a general session.

Regulatory Reply Session
Regulatory Representatives will have the opportunity to comment on the scenarios and consensus information discussed during the Roundtable Discussions. The scenarios to be discussed will be presented to the Regulatory Representatives before the meeting.

U.S. EPA and U.S. FDA Representatives Invited