Toxicologic Pathology and the Immune System

Co-Chairs: Susan A. Elmore, MS, DVM, DACVP, DABT, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, Patrick J. Haley, DVM, PhD, DACVP, Incyte Corporation, Wilmington, DE, and Jerrold M. Ward, DVM, PhD, DACVP, Global VetPathology, Montgomery Village, MD

The Society of Toxicologic Pathology (STP) will host a symposium on the fundamentals and recent innovations in the field of toxicologic pathology and the immune system. The focus of this international meeting is to correlate advances in the morphologic evaluation and interpretation of immunopathology findings with functional, cellular, and molecular knowledge in a series of plenary and poster sessions.

The major goal of the meeting is to provide an interactive program that allows for discussion of the current state of knowledge of immunopathology evaluations in conventional toxicology and specialized immunopathology studies. Foundational sessions will include fundamentals of Immune System Biology, including Basic Immunology, Functional Tests and Toxicologic Immunopathology; Innate Immunity; Acquired Immunity; Developmental Immunology; Challenges of Therapeutic Immunomodulation; and Issues and Observations Concerning Environmental Exposure to Immunotoxican.

The presentations will focus on a mix of standardized and contemporary pathology methods for immunopathology investigations. The meeting will also provide a unique forum to review the progress in the application of best practices for routine and specialized pathology evaluations of the immune system across the pharmaceutical, chemical, and academic worlds of pathology. An interactive panel discussion will explore the issues associated with differentiation of stress effects and immunotoxicity.

The traditional NTP Satellite Symposium, entitled Pathology Potpourri, in advance of the symposium will focus on the customary presentations of challenging lesions but will also include a presentation on proposed INHAND lymphoid nomenclature. Four continuing education sessions will be held on Sunday before the general sessions begin; Interacting with Regulatory Authorities: What to Do and What Not to Do; Novel Biomarker Discovery, Qualification, and Application in Drug Development: What’s New, What’s Used, and What’s New, Used & Successful; Ultrastructural Analysis and Toxicologic Pathology; and Histopathology of the Rodent Lymphoid and Hematopoietic Systems. A half-day Career Development Workshop: “Leaving the Rat Race: Consulting As a Career Choice in Toxicologic Pathology” will also be held on Sunday and the Career Development Lunchtime Series Monday will provide guidance on the use of professional networking in career development.

The immune system and its responses is one of the more complex and challenging arenas of toxicologic inquiry and regulatory concern, and this congress promises to be an opportunity to review and expand your knowledge in this important field. We hope you will join us for this exciting program in Denver.

Saturday, June 18

NTP Satellite Symposium: Pathology Potpourri
Centennial Ballroom A–D (3rd Level)
9:00 AM–4:30 PM

The object of this interactive symposium is to provide continuing education on interpreting pathology slides, to generate lively and productive conversation, and to have a good time. This symposium will also include presentations on proposed INHAND lymphoid nomenclature. During each talk, the speakers will project a series of images of lesions on one screen with a choice of diagnoses/answers on a separate screen. The members of the audience with wireless keypads will then vote and the voting results will be displayed on the screen. After each voting session, time is allowed for discussion.

9:00 AM–9:10 AM
Welcome and Introductory Remarks
Susan A. Elmore, MS, DVM, DACVP, DABT, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC

9:10 AM–9:40 AM
Bouillabaisse: A Sumptuous Medley of Proliferative Fish Lesions
Jeffrey C. Wolf, DVM, Experimental Pathology Laboratories, Inc., Sterling, VA

9:40 AM–10:10 AM
Proliferative Lesions in the Stomach and Duodenum of CD1 Mice
Andrew W. Suttie, BVSc, PhD, Covance Laboratories, Inc., Vienna, VA

10:10 AM–10:30 AM
A Kink in the Monkey’s Neck
Ingrid Pardo, DVM, MS, DACVP, Pfizer, Inc., Groton, CT

10:30 AM–11:00 AM
Break
Centennial Foyer (3rd Level)
11:00 AM–11:30 AM  My Skin Is Giving Me Problems  Torrie A. Crabbs, DVM, DACVP, Experimental Pathology Laboratories, Inc., Raleigh, NC

11:30 AM–12:00 NOON  New Rumors on Brain Tumors  Holly Kolenda-Roberts, DVM, PhD, Experimental Pathology Laboratories, Inc., Research Triangle Park, NC

12:00 NOON–1:30 PM  Lunch Break

1:30 PM–2:10 PM  Microcytes Are Not Created Equal  Greg S. Travlos, DVM, National Institute of Environmental Health Sciences, Research Triangle Park, NC and Kenneth S. Latimer, DVM, PhD, DACVP, Covance Laboratories, Inc., Athens, GA

2:10 PM–2:40 PM  The Funny Smell of Green Tea  Abraham Nyska, DVM, DECVP, FIATP, Consultant, Israel

2:40 PM–3:00 PM  2011, Year of the Rabbit...Eyes  JoAnn C. L. Schuh, DVM, PhD, DACVP, DABT, JCL Schuh, PLLC, Bainbridge Island, WA

3:00 PM–3:30 PM  Break  Centennial Foyer (3rd Level)

3:30 PM–4:00 PM  What’s in a Name: Valvulopathy or Valvular Endocarditis?  Ricardo Ochoa, DVM, PhD, DACVP, Pre-Clinical Safety Inc., Niantic, CT

4:00 PM–4:30 PM  Big Lymph Nodes, Big Problems  Jerrold M. Ward, DVM, PhD, DACVP, Global VetPathology, Montgomery Village, MD

7:00 PM–10:00 PM  Sponsored Reception  Mineral Hall D–G (3rd Level)

Continuing Education Credits

AAVSB RACE Provider #56

The CE Courses have been submitted but not yet approved for three and a half to four hours of Continuing Education credits (per course) in jurisdictions which recognize AAVSB RACE approval; however participants should be aware that some boards have limitations on the number of hours accepted in certain categories and/or restrictions on certain methods of delivery of Continuing Education. The Scientific Sessions have been submitted but not yet approved by AAVSB RACE program for 20 hours of Continuing Education credits in jurisdictions which recognize AAVSB RACE approval. The NTP Satellite Symposium has been submitted but not yet approved by the AAVSB RACE program for five and a half hours of continuing education credits in jurisdictions which recognize AAVSB RACE approval. Certificates of attendance will be provided at the conclusion of NTP, each CE course, and on Thursday for the scientific sessions. Please contact the AAVSB RACE program if you have any comments/concerns regarding this program’s validity or relevancy to the veterinary profession.

Continuing Education Courses

CE 1 (Sunday AM) 8:00 AM–12:00 NOON  Centennial Ballroom A–C (3rd Level)

Interacting with Regulatory Authorities: What to Do and What Not to Do  
Co-Chairs: Melissa Rhodes, PhD, DABT, GlaxoSmithKline, Research Triangle Park, NC and Hanan Ghantous, PhD, DABT, U.S. FDA, Silver Spring, MD

During the process of drug development, a Sponsor will need to interact with regulatory authorities (RA), such as the FDA, PMDA, and the EMA. In order to effectively interact with these agencies, the Sponsor must remember that the RA are partners in the drug development process. Similar to sponsors, RA have a genuine concern about the well being of the patients. Sponsors and patients will also benefit from the considerable institutional knowledge of RA about study designs, toxicity, pharmacology, and drug disposition of other drugs. This course will discuss how to effectively interact with the RA so that Sponsors and RA can gain the greatest benefit from their meetings.
8:00 AM–8:40 AM  Interacting with CDER  
Divisions of FDA  
Jeri El Hage, PhD, Aclairo PDG, Vienna, VA

8:40 AM–9:20 AM  Interacting with CBER  
Divisions of FDA  
Martin D. Green, PhD, U.S. FDA, Office of Vaccine Research and Review, Division of Vaccines and Related Product Applications, Rockville, MD

9:20 AM–10:00 AM  Interacting with the FDA: The “Animal Rule”  
Christopher Ellis, PhD, U.S. FDA, Center for Drug Evaluation and Research, Silver Spring, MD

10:00 AM–10:20 AM  Break  
Centennial Foyer (3rd Level)

10:20 AM–11:00 AM  Interacting with EMA  
Christopher Powell, FRCPath, GlaxoSmithKline, Ware, United Kingdom

11:00 AM–12:00 NOON  Interacting with PMDA  
Kazuichi Nakamura, DVM, PhD, Shionogi & Co., Ltd., Tokyo, Japan

CE 2 (Sunday AM) 8:00 AM–12:00 NOON  
Centennial Ballroom D (3rd Level)

Novel Biomarker Discovery, Qualification, and Application in Drug Development: What’s New, What’s Used, and What’s New, Used & Successful  
Co-Chairs: Jacqueline Tarrant, BVSc, PhD, DACVP, Genentech, San Francisco, CA, Dina Andrews-Cleavenger, DVM, PhD, DACVP, Amgen, Inc., Thousand Oaks, CA, and Dominique Brees, DVM, PhD, DACVP, Pfizer R&D, Sandwich, United Kingdom

Staying abreast of the biomarker field is no longer a pursuit of interest only to early drug discovery and safety scientists. The success of consortium driven biomarker discovery efforts and their recent approval by regulatory agencies has thrust the biomarker field to the forefront across all facets of drug development. Remaining up-to-date on the most promising novel biomarker discoveries, being alert to biomarkers currently seeking regulatory approval and understanding the utility and translational impact of newly approved preclinical safety biomarkers is a daunting task that falls primarily on the shoulders of safety pathologists. The first part of this course is aimed to highlight novel biomarker discovery efforts in carcinogenicity and genomics; two fields poised to revolutionize safety biomarkers in their respective fields. The second part of the course is devoted to revisiting recent advances, new regulatory submissions and examining the real world impact and utility of the more familiar renal and cardiac toxicity biomarkers. Practical aspects of study design, sample collection, techniques, analysis and interpretation will also be addressed to provide the participant with a well-rounded and applicable session.

8:00 AM–8:10 AM  Introduction  
Application of Emerging Genomic Biomarkers of Genetic Toxicity and Carcinogenesis for Chemical Cancer Risk Assessment  
Jiri Aubrecht, PharmD, PhD, Pfizer, Groton, CT

Despite the scientific progress in understanding of carcinogenicity, experimental approaches for assessing oncogenic risk associated with exposure to chemicals relies mainly on methods originally developed in the sixties and seventies. In many instances, the limited mechanistic insights provided by currently used approaches do not offer sufficient information to assess oncogenic risk to humans. Recent advances in molecular biology and bioinformatics have enabled interrogating cellular responses to chemical exposure on genomic level eventually leading to identifying molecular pathways and networks mechanistically involved in chemical carcinogenesis (system biology approach). Although systems approaches provide valuable biological insights, new experimental approaches are necessary to understand cross species differences in molecular pathways ultimately leading to better cancer risk assessment for humans. Here, we will discuss the development and potential application of systems biology-based approaches in chemical cancer risk assessment.

9:00 AM–9:45 AM  mRNA and microRNA as Biomarkers  
Igor Mikaelian, DVM, MSc, DACVP, Hoffman-La Roche, Nutley, NJ

Quantification of microRNA and mRNAs in body fluids is the latest biomarker frontier in drug safety assessment. Genomic biomarkers can be sensitively measured, show tissue-specific expression, utilize readily available and inexpensive reagents, and are less complex than the proteome. Interest in microRNAs has stemmed from these positive attributes in addition to stability, abundance, and the demonstration of early and pronounced elevations in response to different organ toxicities. The promise of these technologies will be reviewed at the light of in-house and published information related to monitoring of the cardiac function and cardiotoxicity.

9:45 AM–10:00 AM  Break  
Centennial Foyer (3rd Level)
10:00 AM–10:45 AM  New Urine Biomarkers of Renal Injury on the Horizon
Denise Bounous, DVM, PhD, DACVP, Bristol-Myers Squibb Company, Princeton, NJ

Biomarkers working groups comprised of members from pharmaceutical companies, academia, and government continue to develop, validate and seek regulatory approval for more specific and sensitive biomarkers of renal injury in nonclinical species and in humans. The initial panels of rat urine biomarkers submitted as consortium efforts and approved by regulatory agencies to monitor renal injury in rodent toxicology studies, continue to prove more sensitive and specific in detecting and monitoring kidney injury than the standard renal functional markers of serum creatinine and BUN. Additional markers and studies are continuing to be explored. Importantly, the regulatory acceptance of the rodent nephrotoxicity biomarkers has spurred questions around the broader use of markers in nonclinical studies as well as a large translational effort to extend improved nephrotoxicity biomarkers to patients in clinical trials supporting drug development efforts. Answers to questions around appropriate use, selection and application of the novel preclinical biomarkers as well as understanding which ones may be most translatable to clinical trials are beginning to evolve with time, continued use and shared experiences.

10:50 AM–11:35 AM  Cardiotoxicity Now: Existing and Emerging Biomarkers of Injury and Dysfunction
Brian Berridge, DVM, PhD, DACVP, GlaxoSmithKline, Research Triangle Park, NC

Risk management in drug development is an exercise in balancing the likelihood of a toxicity to occur in our target patient population with the ability to detect that toxicity early in its course. Cardiotoxicity is an important cause of drug development attrition and a significant concern for patient safety in clinical trials and even post-marketing. Nonclinical safety assessment has an important role in identifying risk, characterizing that risk, and working with clinical colleagues to design a relevant and sensitive translational biomarker strategy. This presentation will briefly review the spectrum of ways cardiotoxicity occurs in contemporary drug development and explore traditional and novel tools available for mitigating clinical risk.

11:40 AM–11:55 AM  “Hot Topic” Biomarker Interactive Discussion

Session participants are encouraged to bring controversial issues, ideas and questions surrounding current use and interpretation of any biomarker or methodology for input, alignment and opinions from colleagues and panel experts.

Career Development Workshop
Sunday, June 19
8:00 AM–12:00 NOON
Mineral Hall B–E (3rd Level)

Leaving the Rat Race: Consulting As a Career Choice in Toxicologic Pathology
(Free Event, registration required)

Co-Sponsors: Toxicologic Pathologists in Consulting (TOPIC) Interest Group, the STP Education Committee, and the STP Career Development and Outreach Committee (CDOC)

Co-Chairs: JoAnn C. L. Schuh, DVM, PhD, DACVP, DABT, JCL Schuh, PLLC, Bainbridge Island, WA, Brad Bolon, DVM, MS, PhD, DACVP, GEMpath, Inc., Longmont, CO (TOPIC), Kevin Keane, DVM, PhD, Huntington Life Sciences, East Millstone, NJ (Education Committee), Mike Conner, DVM, DACVP, Theravance, Inc., South San Francisco, CA, and Larry Fisher, DVM, PhD, DACVP, Cicero, IN (CDOC)

Advisor: Jon Werner, DVM, PhD, DACVP, Amgen, Thousand Oaks, CA (Web-Based Education Task Force)

So, you’ve been laid off! Or, maybe you just retired but still want to keep the cash flowing. Maybe all those mindless meetings are starting to get to you. Perhaps you are seeking new ways to use your special knowledge and skills. Even in this tight economy, becoming a full-time or part-time consultant in toxicologic pathology might provide you with an exciting and viable new career path. But, do you know what it takes, and do you have what it takes to successfully operate as a consultant? This workshop, led by long-time consultants with experience in anatomic and/or clinical pathology as well as management of preclinical programs, will help you answer these questions. Partially based on the compiled results of a questionnaire recently completed by members of TOPIC, this workshop will provide a practical approach for successfully planning, starting, and maintaining a consulting career. A panel discussion will allow the audience to interact further with consultant colleagues to gain the most benefit from their tips, tricks, troubles, and triumphs.
CE 3 (Sunday PM) 1:30 PM–5:00 PM  
Centennial Ballroom A–C (3rd Level)  
Histopathology of the Rodent Lymphoid and Hematopoietic Systems  

Co-Chairs: Cynthia L. Willard-Mack, VMD, PhD, Huntingdon Life Sciences, East Millstone, NJ, and Jerold M. Ward, DVM, PhD, DACVP, Global VetPathology, Montgomery Village, MD

This continuing education session will set the stage for the general meeting by providing a broad overview of histopathology of the lymphoid and hematopoietic organs and tissues. The first lecture is designed to provide attendees with a comprehensive review of normal morphology of bone marrow, thymus, spleen, lymph nodes and MALT as a basis for appreciating material in subsequent sessions. The use of specialized techniques important for the identification and observation of hematopoietic cells and tissues will be explored. Immunohistochemistry enables pathologists to study normal antigen expression in hematopoietic cells, identify cell populations in inflammatory lesions and diagnose hematopoietic disorders. In vivo intravital microscopy is an exciting recent modality that allows the activities of fluorescently labeled living cells to be observed in intact tissues in real time. Some of the more challenging aspects of diagnostic immunopathology will be discussed, including the differentiation of reactive and neoplastic lesions and the diagnosis of hematopoietic neoplasia in CD1 mice.

1:30 PM–1:35 PM  
Introduction

1:35 PM–2:20 PM  
An Integrated Overview of the Structure and Function of Lymphoid and Hematopoietic Organs

Cynthia L. Willard-Mack, VMD, PhD, Huntingdon Life Sciences, East Millstone, NJ

The histology of normal hematopoietic and lymphoid organs will be reviewed to provide the basis for recognizing and interpreting lesions in the immune system. The important role of fibroblastic reticular cells will be emphasized. The vascular and lymphatic elements that link these organs together into an integrated system will be discussed.

2:20 PM–2:50 PM  
The Utility of IHC in the Identification of Lymphohematopoietic Cells in Normal Tissues and Interpretation of Proliferative, Inflammatory, and Toxic Lesions

Jerold E. Rehg, DVM, DACVP, St. Jude Children’s Research Hospital, Memphis, TN
Immunophenotyping plays a key role in diagnosis and classification of hematolymphoid toxicity and proliferations. The immunologic profile of hematolymphoid proliferations may be assessed by flow cytometry or immunohistochemistry. Unfortunately, pathologists often have only paraffin embedded tissue with which to work. Cases of various hematolymphoid proliferations will be used to illustrate normal IHC markers for rodent hematopoietic cells and how IHC can help solve morphologic conundrums.

2:50 PM–3:15 PM  
**Break**  
Centennial Foyer (3rd Level)

3:15 PM–4:00 PM  
**The Role of Bone Marrow as a Hematopoietic and Secondary Lymphoid Organ**  
Irina Mazo, MD, PhD, Harvard Medical School, Boston, MA

Intravital microscopy (IVM) is a powerful in vivo tool to visualize and analyze cell behavior in both intra- and extravascular spaces during various physiological and pathological conditions. The talk will use the murine cranial bone marrow (BM) IVM model to characterize BM organization and topography and the marrow’s role as a hematopoietic and secondary lymphoid organ.

4:00 PM–4:30 PM  
**Differentiation of Hematopoietic and Immune System Reactive Lesions (Hyperplasias) from Neoplasias**  
Jerrold M. Ward, DVM, PhD, DACVP, Global VetPathology, Montgomery Village, MD

The immune system of rodents and other species provides a protective network of tissues and cells against endogenous and exogenous stimuli including toxins. This lecture will review the types of reactive lesions in spleen, lymph node, thymus and other tissues including hyperplasias. Differentiation of reactive lesions from early and full blown neoplasias will be illustrated and discussed.

4:30 PM–5:00 PM  
**Spontaneous Pathology of the Lymphoid and Hematopoietic System of Crl:CD-1 Mice**  
Alys E. Bradley, BSc, BVSc, MAnimSc, DipRCPath, FRIPH, MRCVS, FRCPath, Charles River Laboratories, Tranent, Edinburgh, Scotland

This talk will outline the common spontaneous background lesions seen in CD-1 mouse hematopoietic and lymphoid system organs in short-term, chronic and life-time studies. Lesions such as lymphocytic infiltrations, thymic lymphoid hyperplasia and lymphomas are common spontaneous background findings in Charles River CD-1 mice, yet may be unusual in other mouse strains.

**CE 4 (Sunday PM) 1:30 PM–5:00 PM**  
Centennial Ballroom D (3rd Level)

**Ultrastructural Analysis and Toxicologic Pathology**

Co-Chairs: Karamjeet Pandher, BVSc, PhD, DACVP, Pfizer Inc., Groton, CT and Henry Wall, DVM, PhD, DACVP, EPL, Inc., Research Triangle Park, NC

Electron microscopy is a powerful technique that can help illustrate the subcellular localization of toxic injury. It can serve to provide useful insights into the nature of the toxicologic insult, its mechanism, and may even help in risk assessment. As such electron microscopy can effectively compliment other molecular techniques in developing a comprehensive toxicologic assessment of a molecule. This continuing education course aims to re-enforce the technique for practicing toxicologic pathologists and to fill knowledge gaps vis-a-vis the latest advances in the field of electron microscopy. Following an introduction in ultrastructural landmarks, the speakers will attempt to highlight the role of ultrastructural investigations in variety of toxicologic processes. By drawing on specific case studies the speakers will attempt to elucidate the techniques, proper interpretation of electron microscopy data, and its synergies with various other investigative molecular techniques. Finally, latest advances in the field such as dual beam tomography and role in nanoparticle research will be discussed.

1:30 PM–1:35 PM  
**Introduction**

1:35 PM–2:05 PM  
**Introduction to Cellular Ultrastructure**  
Karamjeet Pandher, BVSc, PhD, DACVP, Pfizer Inc., Groton, CT

This short introductory presentation will focus on review of the commonly encountered subcellular organelles and structures that help navigation through the cell and identification of specific cell types.

2:05 PM–2:50 PM  
**Role of Ultrastructure Analysis in Preclinical Safety Evaluation: Interesting Case Studies**  
Jane Fagerland, PhD, DABT, Abbott Laboratories, Abbott Park, IL

Ultrastructural pathology data, while often considered merely “nice-to-have” information, can provide clear answers to toxicologic questions, and even point to underlying mechanisms such as mitochondrial toxicity that can be confirmed with further testing. Ultrastructural
evaluation intersects with other imaging methods and related technologies, such as laser capture microdissection or MALDI-mass spectrometry imaging, to correlate chemical information with morphologic findings. Case studies in which applications of transmission electron microscopy and associated imaging technologies were used to resolve preclinical safety issues will be presented.

2:50 PM–3:15 PM

**Break**
Centennial Foyer (3rd Level)

3:15 PM–3:45 PM

**Transmission Electron Microscopy Support of Preclinical Safety Studies**
Henry Wall, DVM, PhD, DACVP, EPL, Inc., Research Triangle Park, NC

This presentation reviews planning considerations for transmission electron microscopy (TEM) evaluations in support of toxicity studies. It will include relevant information that may facilitate the evaluation or interpretation of ultrastructural changes. Limitations on sample quality imposed by necropsy workflow procedures, and practical sampling procedures will be discussed. Common techniques to optimize sample quality for TEM and use of semi-thin sections to focus the ultra-thin section evaluation will be highlighted. Examples and brief discussion of the potential influence of artifacts on the interpretation of ultrastructural changes and the importance of clear consistent morphological criteria to aid the interpretation of test article-induced effects will be stressed.

3:45 PM–4:15 PM

**Ultrastructural Evaluation of Semen to Assess Effects of Exposure to Environmental Toxicants**
D.N. Rao Veeramachaneni, BVSc, MScVet, PhD, Colorado State University, Fort Collins, CO

Following toxicant exposures, seminal ejaculates may contain, in addition to sperm, somatic cells sloughed from testis, excurrent ducts, and accessory glands. Routine methods of semen evaluation do not permit characterization of subtle defects in sperm or definitive identification of denuded cells. Methods to process semen samples as biopsy material and evaluate them vis-à-vis corresponding tissue samples utilizing various light and transmission electron microscopic techniques will be presented.

4:15 PM–5:00 PM

**New Information from Large Tissues Volumes to the Smallest Structures of the Cell: What New Methods in Electron Microscopy Can Do for Your Research**
Richard Gursky, Sr. Applications Engineer, FEI Company, Hillsboro, OR

Looking at new techniques previously not associated with histology or toxicology this presentation will demonstrate how and why the techniques of Dualbeam™ tomography and STEM tomography can be used to find nanoparticles and other labeled materials in large volumes of tissue at very low concentrations. These techniques are also useful in visualizing, sometimes for the first time, the interaction of metals and polymers with cells and tissues and for examining the relationships of cells and organelles in new ways, with the help of newly developed instrument automation. Bringing these new and exciting methodologies to everyone will help shed light on some of our most commonly asked questions.

CE 5 (Sunday PM) 1:30 PM–5:30 PM

**Mineral Hall B–E (3rd Level)**

**Interacting with Regulatory Authorities: What to Do and What Not to Do**
Co-Chairs: Melissa Rhodes, PhD, DABT, GlaxoSmithKline, Research Triangle Park, NC and Hanan Ghaftous, PhD, DABT, U.S. FDA, Silver Spring, MD

During the process of drug development, a Sponsor will need to interact with regulatory authorities (RA), such as the FDA, PMDA, and the EMA. In order to effectively interact with these agencies, the Sponsor must remember that the RA are partners in the drug development process. Similar to sponsors, RA have a genuine concern about the well being of the patients. Sponsors and patients will also benefit from the considerable institutional knowledge of RA about study designs, toxicity, pharmacology, and drug disposition of other drugs. This course will discuss how to effectively interact with the RA so that Sponsors and RA can gain the greatest benefit from their meetings.

1:30 PM–2:10 PM

**Interacting with CDER Divisions of FDA**
Jeri El Hage, PhD, Aclain PDG, Vienna, VA

2:10 PM–2:50 PM

**Interacting with CBER Divisions of FDA**
Martin D. Green, PhD, U.S. FDA, Office of Vaccine Research and Review, Division of Vaccines and Related Product Applications, Rockville, MD
2:50 PM–3:30 PM
**Interacting with the FDA: The “Animal Rule”**
Christopher Ellis, PhD, U.S. FDA, Center for Drug Evaluation and Research, Silver Spring, MD

3:30 PM–3:50 PM
**Break**
Mineral Hall Foyer (3rd Level)

3:50 PM–4:30 PM
**Interacting with EMA**
Christopher Powell, FRCPaht, GlaxoSmithKline, Ware, United Kingdom

4:30 PM–5:30 PM
**Interacting with PMDA**
Kazuichi Nakamura, DVM, PhD, Shionogi & Co., Ltd., Tokyo, Japan

5:30 PM–7:00 PM
**STP Welcome Reception Sponsored**
Centennial Ballroom E–H & Foyer (3rd Level)

Monday, June 20

**Monday Morning**

7:00 AM–8:00 AM
**Continental Breakfast**
Centennial Ballroom E–H & Foyer (3rd Level)

7:00 AM–4:30 PM
**Exhibits and Poster Sessions Open**
Centennial Ballroom E–H & Foyer (3rd Level)

8:00 AM–8:10 AM
**Symposium Welcome**
Centennial Ballroom A–D (3rd Level)

8:10 AM–9:10 AM
**Keynote Address**
Centennial Ballroom A–D (3rd Level)

9:10 AM–12:00 NOON
**Session 1**
Centennial Ballroom A–D (3rd Level)

**9:10 AM–9:15 AM**
**Introduction**
Jerrold M. Ward, DVM, PhD, DACVP, Global VetPathology, Montgomery Village, MD

**9:15 AM–10:00 AM**
**Immunology for the Toxicologic Pathologist**
Paul Snyder, DVM, PhD, DACVP, Purdue University, West Lafayette, IN

**10:00 AM–10:40 AM**
**Break**
Centennial Ballroom E–H & Foyer (3rd Level)

**10:40 AM–10:55 AM**
**Student Speaker: RSV-Induced Airway Hyperreactivity Is Critically Dependent on the Complement C3a Anaphylatoxin and the Neuropeptide Substance P**
Monali Bera, MS, DVM, Children’s Hospital Boston, Boston, MA

**10:55 AM–11:15 AM**
**Functional Testing/Clinical Pathology Evaluation of the Immune System**
Denise Bounous, DVM, PhD, DACVP, Bristol Meyers Squibb, Princeton, NJ

**11:15 AM–12:00 NOON**
**Enhanced Histopathology of the Immune System**
Susan A. Elmore, DVM, MS, DACVP, DABT, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC
Monday Afternoon

Session 2
Centennial Ballroom A–D (3rd Level)
1:30 PM–5:00 PM

Innate Immunity

Co-Chairs: Paul Snyder, DVM, PhD, DACVP, Purdue University, West Lafayette, IN and Peter Ward, MD, University of Michigan, Ann Arbor, MI

This session will focus on aspects of Innate (non-specific) Immunity relevant to pathogenesis of disease, including recognition molecules, cells and effector mechanisms. Specific topics to be covered include: protective and harmful innate immune responses in sepsis mediated by IL-17A; evidence for cross talk between the complement system and toll-like receptors (TLR) during inflammation and; the role of dendritic cells at the interface between non-specific immunity and specific immunity. In each presentation, morphological and functional aspects of the innate immune responses will be covered.

1:30 PM–1:35 PM

Introduction
Paul Snyder, DVM, PhD, DACVP, Purdue University, West Lafayette, IN

1:35 PM–2:15 PM

Anatomy of Innate Immunity: Intravascular Immunity to Infection and Sterile Inflammation
Braedon McDonald, MD, PhD, University of Calgary, Calgary, AB, Canada

2:15 PM–2:55 PM

Adverse Functions of IL-17 in Experimental Sepsis and Endotoxemia
Peter A. Ward, MD, University of Michigan, Ann Arbor, MI

2:55 PM–3:25 PM

Break
Centennial Ballroom E–H & Foyer (3rd Level)

3:25 PM–3:40 PM

Student Speaker: Differential Expression of ATP-Binding Cassette Transporters in Activated Microglia: Implications for Cell Signaling During Neuroinflammation
Christopher Gibson, VMD, DACVP, Rutgers University, Piscataway, NJ

3:40 PM–4:20 PM

Cross talk between Complement and TLRs
Wenchao Song, PhD, University of Pennsylvania School of Medicine, Philadelphia, PA

4:20 PM–5:00 PM

Cellular Regulation of the Inflammatory Response
Peter Henson, PhD, University of Colorado Health Sciences Center, Denver, CO
Town Hall Meeting
Centennial Ballroom A–D (3rd Level)
5:30 PM–6:30 PM

Best Practices on Recovery Studies: The Role of the Pathologist
The Town Hall Meeting this year will be dedicated as an opportunity to provide member feedback to the SRPC Working Group that is preparing a guidance document on the recovery potential of histomorphologic changes observed in species routinely used in nonclinical toxicology studies. The group is working to review regulatory guidelines and make recommendations regarding why do recovery, when to have a study with a recovery, how to design a recovery arm, the potential outcomes of recovery and their interpretations, and a review of vaccine guidelines and concerns regarding delayed toxicity.

You are encouraged to attend this session and take the opportunity to provide your thought and concerns regarding this important topic.

6:30 PM–10:30 PM  Sponsored Reception
Capitol Ballroom 1–3 (4th Level)

Tuesday, June 21

Tuesday Morning
7:00 AM–8:00 AM  Continental Breakfast
Centennial Ballroom E–H & Foyer (3rd Level)

7:00 AM–12:15 PM  Exhibits and Poster Sessions Open
Centennial Ballroom E–H & Foyer (3rd Level)

Session 3
Centennial Ballroom A–D (3rd Level)
8:00 AM–12:00 NOON

Acquired Immunity
Co-Chairs: JoAnn C. L. Schuh, DVM, PhD, DACVP, JCL Schuh, PLLC, Bainbridge Island, WA and Gail Pearse, BVM&S, DACVP, GlaxoSmithKline, Ware, UK

Acquired immunity goes beyond innate immunity to provide controlled recognition and memory for specific antigenic challenges. Predominately involving activation of T and B cells, the resulting cellular- and secretory-mediated activity provides immediate and long-term host defenses. This session will highlight the biological advances in control of acquired immunity through T regulatory cells, the pathophysiology of effector cells and regulatory molecules in immunosuppression and hypersensitivity and allergy, and dysregulation that leads to loss of tolerance and autoimmune diseases.

8:00 AM–8:05 AM  Introduction
JoAnn C. L. Schuh, DVM, PhD, DACVP, JCL Schuh, PLLC, Bainbridge Island, WA

8:05 AM–8:40 AM  Regulatory T-Cells: Diverse Phenotypes Integral to Immune Homeostasis and Suppression
Richard Peterson, DVM, PhD, DACVP, GlaxoSmithKline, Research Triangle Park, NC

8:40 AM–9:15 AM  Immunosuppression: Upsetting the Balance
Curtis Maier, PhD, GlaxoSmithKline, Research Triangle Park, NC

9:15 AM–9:50 AM  Cytokine Pathways in Allergic Disease
Cara M. M. Williams, PhD, Pfizer Bio-Therapeutics R&D, Cambridge, MA

9:50 AM–10:05 AM  Student Speaker: Anchoring Gene Expression with Development of Hepatic Fibrosis in a Toxicant-Induced Fish Model of Hepatic Fibrosis
Arnaud Van Wettere, DVM, MS, DACVP, NCSU – College of Veterinary Medicine, Raleigh, NC

10:05 AM–10:40 AM  Break
Centennial Ballroom E–H & Foyer (3rd Level)

10:40 AM–11:15 AM  The Battle Within: Pathways and Regulation of Autoimmune Disease
Brad Bolon, DVM, MS, PhD, DACVP, GEMpath, Inc., Longmont, CO

11:15 AM–12:00 NOON  Panel Discussion: Stress Effects vs. Immunotoxicity
Paul Snyder, DVM, PhD, DACVP, Purdue University, West Lafayette, IN

Tuesday Afternoon  Free Time
Tuesday Afternoon

**Talk in Portuguese**

*Mineral Hall A (3rd Level)*

**12:30 PM–1:00 PM**

**Pathology Assessment of Embryo-Fetal Development Effects of Immunomodulatory Drugs in Cynomolgus Monkeys**

Evelyne Polack, DVM, MS, PhD, DACVP, Biogen Idec Inc., Cambridge, MA, USA

The cynomolgus monkey has become an increasingly important animal model for preclinical studies of biotechnology-derived therapeutics. This presentation will address the evaluation of potential effects of immunomodulatory human proteins on embryo-fetal development in cynomolgus monkey.

**Avaliação de Efeitos de Drogas Imunomodulatorias no Desenvolvimento Embrião-Fetal em Macacos Cynomolgus**

Evelyne Polack, DVM, MS, PhD, DACVP, Biogen Idec Inc., Cambridge, MA, USA

O macaco cynomolgus tem se tornado um modelo animal importante em estudos preclínicos no desenvolvimento de drogas derivadas de biotecnologia. Esta apresentação abordará a avaliação dos potenciais efeitos de proteínas imunomodulatorias humanas no desenvolvimento embrião-fetal em macacos cynomolgus.

**Evaluación de Efectos de Drogas Inmunomodulatorias en el Desarrollo Embrión-Fetal en Monos Cynomolgus**

Evelyne Polack, DVM, MS, PhD, DACVP, Biogen Idec Inc., Cambridge, MA, USA

El mono cynomolgus se ha convertido en un modelo animal importante para los estudios preclínicos de drogas derivadas de biotecnología. Esta presentación tratará de la evaluación de los efectos potenciales de proteínas inmunomodulatorias humanas en el desarrollo embrión-fetal en monos cynomolgus.

**Talk in Spanish**

*Mineral Hall A (3rd Level)*

**1:00 PM–1:30 PM**

**A Panoramic View on the Education and Training in Veterinary and Toxicologic Pathology in Brazil: The Role of the Latin American Society of Toxicologic Pathology, LASTP**

Maria Lucia Zaidan Dagli, DVM, MS, PhD, University of São Paulo, SP, Brazil

The aim of the presentation is to show a panoramic view of education and training in veterinary and toxicologic pathology in Brazil. Brazil has over 140 veterinary schools, distributed in practically all of its states; most of them are private schools. Disciplines of general pathology, animal pathology, pharmacology and toxicology make part of all educational programs; however, pathology of laboratory animals make part of the education program of only a few veterinary schools. Opportunities for training in veterinary pathology occur through animal pathology residence programs, or with post-graduation programs, which are nevertheless focused in educating for scientific research. The Latin American Society of Toxicologic Pathology, LASTP, has an important role in organizing training programs for professionals interested to work in this specific and important area of pathology.

**Una Visión Panorámica Sobre la Educación y Entrenamiento en Patología Veterinaria y Toxicológica en Brasil: El Papel de la Asociación Latinoamericana de Patología Toxicológica, LASTP**

Maria Lucia Zaidan Dagli, DVM, MS, PhD, University of São Paulo, SP, Brazil

El objetivo de la presentación es mostrar una visión panorámica de la educación y entrenamiento en patología veterinaria y toxicológica en Brasil. Brasil tiene más de 140 escuelas de veterinaria, distribuidas en prácticamente todos los estados; la mayoría de ellas son escuelas privadas. Disciplinas de la patología general, patología animal, farmacología y toxicología hacen parte de todos los programas educativos, sin embargo, la patología de los animales de laboratorio hacen parte del programa de educación de sólo una pocas escuelas de veterinaria.
Oportunidades de formação em patologia veterinária ocorrem a través de os programas de residencia em patologia animal, e com programas de posgrado, que, no entanto se centraren na educação para a investigação científica. A Sociedade Latino Americana de Patologia Toxicológica, LASTP, tem um papel importante na organização de programas de formação para os profissionais interessados em trabalhar em esta área especifica e importante da patologia.

Uma Visão Panorâmica Sobre a Educação e Treinamento em Patologia Toxicológica no Brasil: Papel da Associação Latinoamericana de Patologia Toxicológica, ALAPT
Maria Lucia Zaidan Dagli, DVM, MS, PhD, University of São Paulo, SP, Brazil

O objetivo desta apresentação é mostrar uma visão panorâmica da educação e treinamento em patologia veterinária e toxicológica no Brasil. O Brasil possui mais de 140 faculdades de medicina veterinária, distribuídas em praticamente todos os seus estados; muitas destas escolas são privadas. Disciplinas de patologia geral, patologia animal, farmacologia e toxicologia fazem parte de todos os programas educacionais; entretanto, a patologia de animais de laboratório faz parte do programa de somente algumas escolas de medicina veterinária.

A oportunidade de obter treinamento em patologia veterinária ocorre por meio de programass de residência em patologia animal, ou por meio de programas de pós-graduação, que estão, entretanto, focados em educar para a pesquisa científica e formar pesquisadores. A Associação Latinoamericana de Patologia Toxicológica, ALAPT, tem um importante papel na organização de programas de treinamento em patologia toxicológica para profissionais interessados em trabalhar nesta importante área específica da patologia.

Wednesday, June 22

Wednesday Morning
7:00 AM–8:00 AM
Continental Breakfast
Centennial Ballroom E–H & Foyer
(3rd Level)

8:00 AM–12:00 NOON
Session 4
Centennial Ballroom A–D (3rd Level)
The Immune System throughout Life
Co-Chairs: George A. Parker, DVM, PhD, DACVP, WIL Research Laboratories, Ashland, OH and Frieke Kuper, PhD, TNO, Zeist, Netherlands

The immune system is not a fixed entity, but instead goes through a progression of anatomical and functional changes starting with the fetus and newborn, progressing through adolescence and adulthood, and culminating in senescence. The basic anatomy and physiology of the immune system are genetically determined and depend heavily on endocrine and neural functioning. For example, life changes such as pregnancy and lactation have a significant impact on the immune system. Therefore, the effects of environmental factors and the efficacy of drugs differ with age/life stage and condition.

8:00 AM–8:10 AM
Introduction
George A. Parker, DVM, PhD, DACVP, WIL Research Laboratories, Ashland, OH

8:10 AM–9:00 AM
Changes in Lymphocyte Population with Age
Philippa Marrack, FRS, PhD, National Jewish Health, Denver, CO

9:00 AM–9:40 AM
Early Life Triggers of Developmental Immunotoxicity
Jamie C. DeWitt, PhD, East Carolina University, Greenville, NC

10:20 AM–10:50 AM
Immune Functioning in Non-Lymphoid Organs: The Liver
George A. Parker, DVM, PhD, DACVP, WIL Research Laboratories, Ashland, OH

10:50 AM–11:30 AM
Juvenile Immunotoxicity
Michael P. Holsapple, PhD, ILSI Health and Environmental Sciences Institute, Washington, DC
11:30 AM–12:00 NOON  
**Sensitive Periods during Adult Life: Pregnancy, Lactation**  
Frieke Kuper, PhD, TNO, Zeist, Netherlands

### Wednesday Afternoon

#### Responsible Authorship and Publication Practices
*Mineral Hall G (3rd Level)*  
12:15 PM–1:30 PM

An IATP and STP Sponsored Workshop and Panel Discussion

A 15-minute PowerPoint presentation will highlight issues related to authorship, order of authorship, what constitutes plagiarism and self-plagiarism, ethical issues, and conflict of interest related to manuscript preparation and submission. This session will include pointers on how to get your manuscript published, how to deal with reviewers’ comments, what constitutes a least publishable unit, and responsibilities of editors and associate editors. To stimulate audience discussion and to challenge the panel members, there will be practical and realistic case presentations, including when it is appropriate to include the pathologist as an author and how best to determine the order of authorship for publications produced by a committee or working group, such as INHAND documents. A box lunch will be provided by IATP for attendees who pre-register for the session. (Space is limited to 78 attendees, please visit the Registration Desk for availability.)

#### Session 5
*Centennial Ballroom A–D (3rd Level)*  
1:30 PM–5:00 PM

**Immunomodulation: How Much is Too Much?**

*Co-Chairs: Michael W. Leach, DVM, PhD, DACVP, Pfizer Inc., Andover, MA and Patrick J. Haley, DVM, PhD, DACVP, Incyte Corporation, Wilmington, DE*

This session will focus on a particularly challenging question in the world of emerging therapies. As targeting of specific receptor-mediated immunological and inflammatory pathways becomes more precise and selective modulation of immune mechanisms occurs, it becomes essential to ask the question “How much immunomodulation is too much?” Another question is “How much is enough?” How can we safely dial up intentional up-regulation of prophylactic drugs and adjuvants? The key challenge is identifying that level of immunomodulation, typically immunosuppression, which will result in a beneficial outcome. To meet this challenge a heightened understanding of the complex molecular relationships that exist for immune and inflammation pathways is required, as are more astute and contemporary methods for detecting and measuring changes to those pathways. The speakers in this session will attempt to define the risks and benefits of targeted immunomodulation as they apply to both large protein biologics and small molecules and how regulatory guidances may serve to guide researchers in the decision process.

1:30 PM–1:35 PM  
**Introduction**  
Michael W. Leach, DVM, PhD, DACVP, Pfizer Inc., Andover, MA

1:35 PM–2:20 PM  
**How Do We Apply Regulatory Guidances for Immunotoxicity to Immunomodulatory Drugs?**  
Ellen W. Evans, PhD, Pfizer Inc., Groton, CT

2:20 PM–3:00 PM  
**Small Molecule Immunomodulatory Drugs: Challenges and Approaches for Balancing Efficacy with Toxicity**  
Patrick J. Haley, DVM, PhD, DACVP, Incyte Corporation, Wilmington, DE

3:00 PM–3:40 PM  
**Break**  
Centennial Foyer (3rd Level)

3:40 PM–4:20 PM  
**Establishing the Carcinogenic Risk of Immunomodulatory Drugs**  
James Weaver, PhD, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD

4:20 PM–5:00 PM  
**The Yin and Yang of Immunomodulatory Biologics: Assessing the Delicate Balance between Benefit and Risk**  
Dimitry M. Danilenko, DVM, PhD, DACVP, Genentech, Inc., South San Francisco, CA
Thursday, June 23

Thursday Morning

7:00 AM–8:00 AM  Continental Breakfast  Centennial Foyer (3rd Level)

Session 6

Centennial Ballroom A–D (3rd Level)

8:00 AM–12:00 NOON

Environmental Toxicologic Pathology

Chair: Douglas C. Wolf, DVM, PhD, FIATP, ATS, U.S. Environmental Protection Agency, Research Triangle Park, NC

This session will focus on the impacts of environmental contaminants on the immune system and how they can affect public health and ecological systems. The first talk will overview the development and implementation of alternative cell-based, high throughput, evaluation systems for hazard identification and testing prioritization. The second talk will examine perfluorinated chemicals (PFCs), which are persistent in the environment and have been found in ground and surface waters. Epidemiologic studies suggest immune effects in humans and animal studies indicate PFCs target immune function and inflammatory responses. The third presentation will describe how air pollutants such as diesel exhaust particles, residual oil fly ash or its constitutive metals, can cause lung injury, inflammation, and potentiate allergic airway responses. The final presentation will describe the Deep Water Horizon spill, the largest oil spill and response action in U.S. history, with over 200 million gallons of crude oil released, and nearly two million gallons of dispersants applied. A diversity of biota were exposed, from deep ocean communities to coastal wildlife. A summary of the events of the spill, exposure pathways, and effects on wildlife including immune, endocrine, and population impacts will be presented.

8:00 AM–8:10 AM  Introduction  Douglas C. Wolf, DVM, PhD, FIATP, ATS, U.S. Environmental Protection Agency, Research Triangle Park, NC