

Saturday, June 21

NTP Satellite Symposium: Pathology Potpourri

9:00 AM–4:30 PM

(Free Event, Registration Required)

Chair: Susan A. Elmore, MS, DVM, DACVP, DABT, FIATP, NTP and NIEHS, Research Triangle Park, NC

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. 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, FIATP, NTP and NIEHS, Research Triangle Park, NC

9:10 AM–9:30 AM

NTP Non-Neoplastic Lesion Atlas

Mark Cesta, DVM, PhD, DACVP, NTP and NIEHS, Research Triangle Park, NC

9:30 AM–9:50 AM

An Unusual Lung Lesion in a Mouse

Margarita M. Gruebbel, DVM, PhD, EPL, Research Triangle Park, NC

9:50 AM–10:30 AM

Perplexing Vascular Lesions in Wistar Han Rats

Jessica S. Hoane, DVM, DACVP, Charles River Pathology Associates, Research Triangle Park, NC

10:30 AM–11:00 AM

Break

11:00 AM–11:30 AM

The ABCs of PEMD—Vaginal Cytology of the Rat and Mouse

Michelle C. Cora, DVM, DACVP, NTP and NIEHS, Research Triangle Park, NC

11:30 AM–12:00 Noon

A Puzzling Pancreatic Problem

Rachel Peters, DVM, DACVP, Takeda Pharmaceuticals International Co., Cambridge, MA

12:00 Noon–1:30 PM

Lunch Break

1:30 PM–1:50 PM

Eye-Catching Findings in the Rodent Retina

Kathleen A. Szabo, DVM, MS, DACVP, Charles River Pathology Associates, Research Triangle Park, NC

1:50 PM–2:10 PM

Looking Beyond Lymphoma

Bhanu P. Singh, BVSc, MS, DACVP, DABT, FIATP, Janssen Research and Development, LLC, Spring House, PA

2:10 PM–2:30 PM

Thrown Off Track by the Thymus

Jessica S. Hoane, DVM, DACVP, Charles River Pathology Associates, Research Triangle Park, NC

2:30 PM–3:00 PM

Angiomatous Lesions in Mesenteric Lymph Nodes

Schantel A. Hayes, DVM, PhD, DACVP, Charles River Pathology Associates, Research Triangle Park, NC

3:00 PM–3:30 PM

Break

3:30 PM–3:50 PM

An Unusual Retinal Lesion of the Fovea

Susan Elmore MS, DVM, DACVP, DABT, FIATP (for Dr. Kohji Tanaka), NTP and NIEHS, Research Triangle Park, NC

3:50 PM–4:30 PM

Nomenclature Challenges from the Endocrine INHAND Organ Working Group

Thomas Rosol, DVM, PhD, DACVP, Ohio State University, Columbus, OH

Sunday, June 22

Continuing Education Courses

CE 1 (Sunday AM) 8:00 AM–12:00 Noon

Biomarkers of Endocrine Effects and Reproductive Toxicity

Co-Chairs: Adam Aulbach, DVM, DACVP, MPI Research, Mattawan, MI; and David Honor, DVM, PhD, DACVP, AbbVie, Inc., Worcester, MA

The evaluation of endocrine and reproductive clinical pathology endpoints in nonclinical safety studies presents



a unique set of preanalytical, analytical, and interpretative challenges to the regulatory scientist. Regulatory guidance does not require the inclusion of these endpoints in traditional safety studies; however, they are sometimes incorporated without appropriate consideration for their use. These sessions will provide an overview of the current principles and approaches to assessing toxicity of the endocrine and reproductive systems with an emphasis on the appropriate selection and utility of endocrine biomarkers. Discussions will focus on regulatory requirements for the inclusion of these markers as well as strategies used in the pharmaceutical industry and drug development. These sessions will be of interest to both industry and regulatory pathologists and scientists.

8:00 AM–8:50 AM

Overview of Reproductive and Developmental Toxicology; Rationales for Testing

Alan Hoberman, PhD, DABT, ATS, Charles River Laboratories, Horsham, PA

8:50 AM–9:40 AM

The Use of Hormone Measurements in Preclinical Studies: Study Design, Analysis, and Interpretation

John C. O'Connor, PhD, DuPont Haskell Global Centers for Health and Environmental Sciences, Newark, DE

9:40 AM–10:15 AM

Break

10:15 AM–11:05 AM

Male Reproductive Toxicology, Evaluation of Inhibin B, and Future Directions

Robert E. Chapin, PhD, Pfizer, Inc., Groton, CT

11:05 AM–12:00 Noon

Reproductive Endocrinology and Toxicology in Nonhuman Primates

Mark Cline, DVM, PhD, DACVP, Wake Forest School of Medicine, Winston-Salem, NC

Career Development Workshop

Sunday, June 22

8:00 AM–12:00 Noon

Effective Communication of Pathology Results in Regulatory Studies

(Free Event, Registration Required)

Co-Chairs: Sabine Francke, DVM, PhD, FIATP, US FDA/CFSAN, College Park, MD; Emily Meseck, DVM, DACVP, DABT, Covance Laboratories, Inc., Madison, WI; Steven R. Mog, DVM, DACVP, US FDA/CFSAN, College Park, MD; Annette Romeike, Dr Med Vet, DACVP, FTAPath, Covance Laboratories SAS, Porcheville, France; and Charles E. Wood, DVM, PhD, DACVP, US EPA, Research Triangle Park, NC

Anatomic pathology endpoints in nonclinical safety studies have a central role in the safety/risk assessment for chemicals, food ingredients, devices, and drugs. The goal of this course is to present issues and recommendations for communicating pathology results of toxicologic safety studies more effectively with regulatory agencies. Topics of discussion are based on recent issues experienced by pathologists and toxicologists/pharmacologists at regulatory, industry, and contract pathology organizations and will provide a general overview of tools and strategies to effectively communicate pathology information for regulatory purposes. Several case study-based presentations will be given, followed by a panel discussion at the end of the session. Perspectives will be provided by a diverse group of speakers and panelists including non-pathologist regulatory reviewers, regulatory pathologists (EPA/FDA), as well as a US and European perspective of regulated industry pathologists (CRO and corporate pharma). Specific topics include pathology report issues addressed by regulatory (FDA) reviewers, peer review guidelines, terminology harmonization efforts such as INHAND and SEND, use of historical control data and web-based pathology resources. This information should provide a stimulating exchange for toxicologic pathologists and regulatory reviewers involved in safety evaluation.

8:00 AM–8:10 AM

Introduction/Overview: Communicating More Effectively in Pathology Reports

Sabine Francke, DVM, PhD, FIATP, US FDA/CFSAN, College Park, MD; and Charles E. Wood, DVM, PhD, DACVP, US EPA, Research Triangle Park, NC



8:10 AM–9:10 AM

Common Pathology Report Issues from a Nonpathologist Regulatory Reviewer's Perspective

Christopher Toscano, PhD, DABT, FDA/CDER/OND/DNP, Silver Spring, MD; and Lois Freed, PhD, FDA/CDER, Silver Spring, MD

9:10 AM–9:40 AM

Communicating with Regulators: OECD Peer Review Guidelines as a Case Example

Annette Romeike, Dr Med Vet, DACVP, FTAPath, Covance Laboratories SAS, Porcheville, France

9:40 AM–10:10 AM

Current Web-based Pathology Resources for Regulatory Study Reports

Steven R. Mog, DVM, DACVP, US FDA/CFSAN, College Park, MD

10:10 AM–10:30 AM

Break

10:30 AM–11:00 AM

The Role of Historical Control Data in the Interpretation of Nonneoplastic Pathology Findings in Preclinical Toxicology Studies

Emily Meseck, DVM, DACVP, DABT, Covance Laboratories, Inc., Madison, WI

11:00 AM–11:30 AM

Updates and Issues Related to INHAND and SEND Terminology Harmonization Efforts

Charlotte Keenan, VMD, CM Keenan ToxPath Consulting, Doylestown, PA

11:30 AM–12:00 Noon

Open Discussion

CE 2 (Sunday PM) 1:30 PM–5:25 PM

Scientific and Regulatory Considerations in the Safety Evaluation of Stem Cell-derived Therapies in Preclinical Studies

Co-Chairs: Basel Assaf, BVSc, PhD, Oregon National Primate Research Center, Beaverton, OR; and Timothy Bertram, DVM, PhD, DACVP, Tengion, Inc., Winston-Salem, NC

Stem cell-derived products have the potential to treat a diversity of medical conditions, many with unmet medical needs. The properties of stem cells, such as their differentiation and proliferative potential, pose safety concerns unique from those of small molecule drugs and other macromolecule biologics. These cellular products carry risks associated with localized host tissue response, long term persistence, ectopic tissue formation, differentiation to undesired cell and tissue types, off-target distribution, tumorigenicity, and immunogenicity. These risks are generally evaluated in preclinical studies as part of a comprehensive preclinical safety program prior to administration in humans. However, safety assessment for these products can be challenging due to inadequately defined host tissue responses to these products and due to the lack of standardized approaches in evaluating *in vivo* host responses. A primary goal of this session is to introduce this product class to the toxicologic pathology community and provide a forum for discussion of the scientific and the regulatory considerations in the evaluation of host responses to stem cell-derived therapies.

1:30 PM–2:05 PM

Stem Cell-Derived Cellular Therapy Products: Discovery to Translational Research

Mahendra Rao, MD, PhD, NIH Center for Regenerative Medicine, Bethesda, MD

2:05 PM–2:40 PM

Toxicologic Pathology Approaches in Evaluation of Stem Cell-Derived Cellular Therapy Products

Julia F. M. Baker, BVMS, Dip RC Path, MRCVS, Charles River Pathology Associates, Frederick, MD

2:40 PM–3:15 PM

FDA/CBER Regulatory Considerations in the Preclinical Evaluation of Cellular Therapy Products

Mercedes A. Serabian, MS, DABT, FDA/CBER, Rockville, MD



3:15 PM–3:50 PM

Break

3:50 PM–4:25 PM

Challenges in Evaluating the Tumorigenic Potential of Cell-Based Products

Alex Bailey, PhD, FDA/CBER, Rockville, MD

4:25 PM–5:00 PM

Industry Experience on the Preclinical Development, Challenges, and Tumorigenicity/Toxicology Testing of Stem Cell-Based Products

Jane Lebkowski, PhD, Asterias Biotherapeutics, Menlo Park, CA

5:00 PM–5:25 PM

Panel Discussion

CE 3 (Sunday PM) 1:30 PM–5:25 PM

Fundamentals of Translational Neuroscience in Toxicologic Pathology: Optimizing the Value of Animal Data for Human Risk Assessment

Co-Chairs: Alok Sharma, BVSc, MVSc, MS, PhD, DACVP, DABT, Covance Laboratories, Inc., Madison, WI; and James Morrison, DVM, DACVP, Charles River Pathology Associates, Durham, NC

Extrapolation of animal data to predict possible human outcomes is an elemental conundrum in drug discovery and development. This problem often is of particular significance when investigating therapeutic candidates with neuroactive properties or that induce structural alterations in the central nervous system (CNS), especially when the portfolio management process and/or regulatory review are given to individuals with limited or no formal training in neurobiology. This session is designed to impart fundamental information on basic neurobiological principles necessary for pathologists, toxicologists, and regulators to gain confidence in their abilities to translate CNS structural changes in test animals for risk assessment in humans. The last talk is included as a practical example regarding the application of such principles to address a current issue facing many pharmaceutical companies and regulatory agencies.

1:30 PM–2:10 PM

Structural-Functional Correlations in Neuropathology Evaluations: Rodents

Deepa Rao, BVSc, MS, PhD, DABT, DACVP, ILS/NTP, Research Triangle Park, NC

2:10 PM–2:50 PM

Structural-Functional Correlations in Neuropathology Evaluations: Non-Rodents

Ingrid Pardo, DVM, MS, DACVP, Pfizer, Inc., Groton, CT

2:50 PM–3:25 PM

Break

3:25 PM–4:05 PM

Pathology Considerations in Developmental Neurotoxicity (DNT) Testing

Robert H. Garman, DVM, DACVP, Consultants in Veterinary Pathology, Inc., Murrysville, PA

4:05 PM–4:45 PM

Neglected Factors that Confound Translational Neuroscience

Brad Bolon, DVM, MS, PhD, DACVP, DABT, ATS, FIATP, The Ohio State University, Columbus, OH

4:45 PM–5:25 PM

Polyethylene Glycol (PEG)-associated Vacuolation in Neural Cells and Its Impact on Development of PEG-Conjugated Therapies

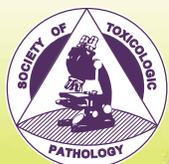
Wolfgang Kaufmann, Dr Med Vet, FTAPath, DECVP, FIATP, Merck KGaA, Darmstadt, Germany

CE 4 (Sunday PM) 1:30 PM–5:15 PM

The Art of Study Monitoring and Pathology Peer Review: How to Maintain a Relationship of Mutual Respect with CROs

Co-Chairs: Daniel Kemp, PhD, DABT, GlaxoSmithKline, Research Triangle Park, NC; and John Wilson, MS, GlaxoSmithKline, King of Prussia, PA

One of the most important decisions a company can make is to outsource the responsibility of conducting regulatory required studies. Therefore, oversight of this activity can be imperative to assure that adequate protection and safety are involved to maintain the quality and integrity of the resulting data. While the study director is ultimately responsible for the study, with proper oversight and communication the sponsor standards can still be met. Effective study monitoring and peer review through preparation, transparency, continuing education, and effective communication can help remediate unexpected findings, clarify discrepancies, and decrease the time for issue resolution within expedited timelines if a solid working relationship has been established with the contract research organization (CRO). Establishing a working



relationship with CROs may require visits to the facilities, an in-depth review of data, QA, AALAC, and laboratory procedures, and reviewing interim updates. It also requires an in-depth knowledge of individual CRO capabilities and study management skills. This CE course will focus on expectations of study monitors, peer review pathologists, CRO study directors, and CRO pathologists; and will offer skills to reduce program drift, late reporting, conflicting deadlines, and corrective actions. This would appeal to pharmaceutical, chemical, contract, and medical device industries.

1:30 PM–1:50 PM

Study Monitoring and Peer Review—An Overview

Daniel Kemp, PhD, DABT, GlaxoSmithKline, Research Triangle Park, NC

1:50 PM–2:30 PM

The Peer Review Process and Issue Resolution

Kevin McDorman, DVM, PhD, DACVP, Charles River Pathology Associates, Frederick, MD

2:30 PM–3:10 PM

The CRO Perspective on Study Monitoring and Pathology Peer Review

Fotini (Fay) Vlaseros, BSc, Charles River, Senneville, Quebec, Canada; and Luc Chouinard, DVM, DACVP, Charles River, Senneville, Quebec, Canada

3:10 PM–3:45 PM

Break

3:45 PM–4:25 PM

Study Monitoring—The Sponsor Perceptive

John Wilson, MS, GlaxoSmithKline, King of Prussia, PA

4:25 PM–5:15 PM

Regulatory Interpretation of Monitoring, Pathology Peer Review, and Multisite Studies

TBD

5:30 PM–7:00 PM

STP Welcome Reception

TRANSLATIONAL PATHOLOGY: Relevance of Toxicologic Pathology to Human Health

Scientific Co-Chairs: *Sabine Francke, DVM, PhD, FIATP, US FDA/CFSAN, College Park, MD; Mark Hoenerhoff, DVM, PhD, DACVP, NIEHS, Research Triangle Park, NC; and Lee Silverman, DVM, PhD, DACVP, Agios Pharmaceuticals, Cambridge, MA*

Toxicologic pathologists work in diverse settings studying changes elicited by pharmacological, chemical, and environmental agents and factors that modify these responses. This work involves the integration of pathology data into hazard identification, risk assessment, and risk communication frameworks that guide safety for potentially toxic substances. A central part of this process is the translation of pathologic effects in animal models to address specific issues in public health.

This symposium will focus on translational science and the relevance of toxicologic pathology to human health. Topics will include the predictive value of nonclinical models and how animal model and human endpoints inform each other. Progress in the development of new nonclinical animal models and other types of models will be discussed, highlighting areas where models are highly predictive of human endpoints and areas where alternative models are needed. Emerging technologies which have the potential to improve translational capabilities will also be presented, with an emphasis on advancements that will impact regulatory decision making in coming years. As the field of epigenetics is rapidly advancing, the role and utility of epigenetic endpoints in toxicologic pathology and their relevance to human health will be addressed. Environmental toxicologic pathology plays a critical role in understanding health impacts of environmental exposures; therefore, how pathology outcomes inform human health assessments and regulatory decisions will be discussed. Finally, as the incidence of comorbidities in the human population increases, there is a greater need to develop translational models that provide useful information on human populations with comorbidities; the challenges of developing such relevant animal models will be addressed. By the end of this symposium, the audience will have a better understanding of current trends and data needs in translational pathology and how the field of toxicologic pathology can leverage expertise and tools to meet these needs.



Monday, June 23

Scientific Sessions

Monday Morning

8:00 AM–8:05 AM

Symposium Welcome

Robert Sills, DVM, PhD, DACVP, FIATP, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, STP President

8:05 AM–8:10 AM

Introduction

8:10 AM–9:00 AM

Keynote Address: Translational Research and Development (TR&D) in the Context of Toxicology Pathology

Bruce D. Car, BVs, PhD, DACVP, DABT, Bristol-Myers Squibb Company, Princeton, NJ

Session 1

9:00 AM–12:00 Noon

Toxicity Concordance from Animals to Humans: How Predictive are Traditional Preclinical Studies of Adverse Effects or Toxicities in Clinical Studies?

Co-Chairs: Jeff Engelhardt, DVM, PhD, DACVP, FIATP, EPL, Inc., Camarillo, CA; Daniela Ennulat, DVM, PhD, DACVP, GlaxoSmithKline, King of Prussia, PA; and Sabine Francke, DVM, PhD, FIATP, US FDA/CFSAN, College Park, MD

Testing of xenobiotics in animals prior to human use has been a regulatory requirement since 1939. Since that time, safety testing has been an integral part of the development of regulated compounds such as pharmaceuticals, food additives, and environmental chemicals. As new chemicals or biologics and their targets have become more sophisticated or specialized, so have the questions regarding the reliability of the animal models. As translational toxicologic pathology relies on the predictive value of target organ toxicities identified in animal studies for responses in humans, robustness of the concordance between target organ toxicities identified as morphologic or biochemical changes in preclinical species and humans will be highlighted in this session. Limitations and advantages of animal models and traditional or nontraditional biomarkers for successful translation of preclinical study findings for clinical use will also be explored. For example, questions to be addressed are: do routine safety studies identify the

safety information needed by clinical investigators or are specific, hypothesis-driven studies needed? Are there better ways to interrogate toxicity data through the use of shared databases? What have we learned of early biomarkers and their concordance with tissue morphologic changes and their translational utility?

9:00 AM–9:10 AM

Overview: Setting the Stage for Translational Pathology

Jeff Engelhardt, DVM, PhD, DACVP, FIATP, Isis Pharmaceuticals, Inc., Carlsbad, CA

9:10 AM–9:50 AM

Nonclinical Safety Testing: Considerations of Current and Future Performance Characteristics

Thomas W. Jones, PhD, DABT, Eli Lilly and Company, Indianapolis, IN

9:50 AM–10:30 AM

Successful Integration of Nonclinical and Clinical Findings in Interpreting the Clinical Relevance of Rodent Neoplasia with a New Chemical Entity

Kirk Ways, MD, PhD, Janssen Research and Development, LLC, Raritan, NJ

10:30 AM–11:00 AM

Break

11:00 AM–11:20 AM

IQ-PSLG Nonclinical to Clinical Translational Safety Database Initiative

Thomas M. Monticello, DVM, PhD, DACVP, Amgen, Inc., Thousand Oaks, CA

11:20 AM–11:40 AM

Biomarker Development: "Burning Down the Haystack" to Find, Develop, and Qualify Translational Biomarkers

Daniela Ennulat, DVM, PhD, DACVP, GlaxoSmithKline, King of Prussia, PA

11:40 AM–12:00 Noon

Clinical Perspective on Novel Renal Safety Biomarker Utilization in Drug Development

Scott Adler, MD, AstraZeneca, Wilmington, DE



Career Development Lunchtime Series

12:30 PM–1:30 PM

Draft OECD Guidance on the GLP Requirements for Peer Review of Histopathology: A Panel Discussion

Presented by the STP Career Development and Outreach Committee

(Free Event, Registration Required)

Chair: Bevin Zimmerman, DVM, PhD, DACVP, Janssen Pharmaceuticals Research and Development, Spring House, PA

Panelists and audience members will discuss the Draft OECD Guidance Document on the GLP Requirements for Peer Review. This session will allow attendees to become more familiar with the guidance document and the potential impact it may have on the Peer Review Process.

Monday Afternoon

Session 2

1:30 PM–5:00 PM

Progress in Preclinical Testing for Translational Science

Co-Chairs: Glenn H. Cantor, DVM, PhD, DACVP, Bristol-Myers Squibb Company, Princeton, NJ; Jerrold M. Ward, DVM, PhD, DACVP, FIATP, Global Vet Pathology, Montgomery Village, MD; and Cory Brayton, DVM, DACLAM, DACVP, John Hopkins University School of Medicine, Baltimore, MD

Nonhuman animals used as human surrogates in preclinical testing and hypothesis-driven translational science have led to important medical and scientific breakthroughs. Preclinical (aka nonclinical) research in animals also has received scrutiny and criticism for insufficient relevance to human conditions. Current issues in the development of pharmaceuticals and biopharmaceuticals, and some new approaches in mouse models, will be presented. This session will focus on new findings and strategies to optimize preclinical translational research.

1:30 PM–2:15 PM

The Future of Preclinical Animal Models in Pharmaceutical Discovery and Development: A Need to Bring In Cerebro to the In Vivo Discussions

Jeffrey Everitt, DVM, DACVP, DACLAM, FIATP, GlaxoSmithKline, Research Triangle Park, NC

2:15 PM–3:00 PM

Translational Approaches to Using Genetically Diverse Mouse Populations Models to Understand and Predict Drug Toxicity in Humans

Alison Harrill, PhD, University of Arkansas for Medical Sciences, Little Rock, AR

3:00 PM–3:35 PM

Break

3:35 PM–4:15 PM

Extensive Double Humanization of Both Liver and Hematopoiesis in FRGN Mice

Markus Grompe, MD, Oregon Health and Science University, Portland, OR

4:15 PM–5:00 PM

Opportunities for Pathology in the Changing World of Translational Sciences and Biologic Modalities

Emanuel Schenck, DVM, PhD, MedImmune, LLC, Gaithersburg, MD

5:30 PM–6:30

Town Hall Meeting

Tuesday, June 24

Tuesday Morning

Session 3

8:00 AM–12:00 Noon

Emerging Technologies

Co-Chairs: Eric Blomme, DVM, PhD, DACVP, AbbVie, Inc., North Chicago, IL; and Gary Boorman, DVM, PhD, DACVP, FIATP, Covance Laboratories, Inc., Chantilly, VA

Emerging technologies offer exciting promise to address many diseases that have been refractory to traditional therapies, but also to improve toxicological assessment and human risk assessment. An increasing number of novel therapeutic approaches, such as oligonucleotide-based agents, antibody-drug conjugates, or new delivery systems, are in preclinical and clinical studies with some already approved by regulatory agencies. Likewise, a multitude of analytical technologies based on recent advances in molecular biology or engineering are available to evaluate exploratory compounds *in vitro* or *in vivo*. Discovery pathologists need to become familiar enough with these potentially useful technologies to offer salient advice on utility, data interpretation, or experimental designs. Pathologists involved in preclinical safety assessment also face new challenges associated with the interpretation of



frequently complex toxic changes of poorly characterized mechanisms and of unknown relevance to humans. This session will discuss the role that pathologists in the pharmaceutical industry can play in the identification, application, and development of emerging technologies to improve toxicity prediction and characterization, but also in the assessment of the safety of novel treatment modalities. This session is designed to provide a framework for pathologists to expand their contribution to this exciting but increasingly complex area of therapeutic development and safety assessment.

8:00 AM–8:55 AM

Evaluation of the Potential and Utility of New Technologies for Early Compound Characterization

Yvonne Will, PhD, Pfizer, Inc., Groton, CT

8:55 AM–9:45 AM

How Discovery Technologies Have Impacted Toxicology-Related Attrition and Influenced Regulatory Preclinical Assessment

Eric Blomme, DVM, PhD, DACVP, AbbVie, Inc., North Chicago, IL

9:45 AM–10:20 AM

Break

10:20 AM–11:10 AM

Antisense Oligonucleotides: The Promise and the Problems

*Kendall Frazier, DVM, PhD, DACVP, DABT, FIATP
GlaxoSmithKline, King of Prussia, PA*

11:10 AM–12:00 Noon

Recent Efforts in Prediction and Characterization of Adverse Effects on the Immune System

Ellen Evans, DVM, PhD, DACVP, Pfizer, Inc., Groton, CT

12:00 Noon–1:30 PM

Exhibitor Sponsored Lunch
For Registered Scientific Attendees

Tuesday Afternoon

Session 4

1:30 PM–5:00 PM

The Role of the Toxicologic Pathologist in Informing Regulatory Decisions and Guiding the Interpretation and Application of Data from New Technologies and Tools

Co-Chairs: Shashi Amur, PhD, US FDA/CDER, Silver Spring, MD; and Douglas C. Wolf, DVM, PhD, FIATP, ATS, Syngenta, Greensboro, NC

The use and application of data generated through the use of emerging technologies and novel tools holds great promise in aiding drug, food, and environmental safety assessments. After scientific and analytic validation of these new methods, integration of the validated methods within safety assessments is necessary for appropriate application in regulatory decision making. The first presentation will describe a new method which recapitulates the basic functions of an organ *in vitro*, organ-on-a-chip. The science behind this approach as well as some of the issues that would need to be addressed for its application in safety assessment will be described in this talk. The issue of verification and applicability of new technologies is very important to the regulatory community. The application of genomics, which is now widely used as a basic tool in science, is still in the early stages for safety assessment. Its application will be addressed in the second presentation. While new tools hold a lot of promise in aiding safety assessments, issues surrounding the application and interpretation of the classic indicators of adversity continue to be important. Evaluation of clinical chemistry, its interpretation, and translation relative to tissue responses will thus be addressed in the third talk. The second half of the session will address the development, qualification, and use of biomarkers and bioindicators for exposure, effects, clinical trial design and clinical response in drug development, clinical management, and risk management decisions from a regulatory perspective, followed by a panel discussion on issues relative to identifying and establishing biomarkers and bioindicators.

1:30 PM–2:00 PM

Organs-on-Chips

Anthony Bahinski, PhD, MBA, FAHA, Wyss Institute for Biologically Inspired Engineering at Harvard University, Boston, MA

2:00 PM–2:30 PM

Toxicogenomics for Safety Assessment

Weida Tong, PhD, US FDA/NCTR, Jefferson, AR



2:30 PM–3:00 PM

Evaluation, Correlation, and Interpretation of Clinical Pathology with Histopathology in Toxicity Studies

Nancy Everds, DVM, DACVP, Amgen, Inc., Seattle, WA

3:00 PM–3:35 PM

Break

3:35 PM–4:05 PM

FDA Perspective—Biomarkers as Drug Development Tools

Shashi Amur, PhD, US FDA/CDER, Silver Spring, MD

4:05 PM–4:35 PM

EPA Perspective—Exposure and Effects Prediction and Monitoring

Jon Sobus, PhD, US EPA, Research Triangle Park, NC

4:35 PM–5:00 PM

Panel Discussion on Issues around Biomarker Needs

Wednesday, June 25

Wednesday Morning

Session 5

8:00 AM–12:00 Noon

Epigenetic Endpoints in Toxicologic Pathology and Relevance to Human Health

Co-Chairs: Jim Hartke, DVM, PhD, DACVP, Celgene Corporation, Summit, NJ; and Mark Hoenerhoff, DVM, PhD, DACVP, NIEHS, Research Triangle Park, NC

Epigenetics is the study of heritable changes in gene expression caused by mechanisms that do not alter the underlying DNA sequence. Epigenetic alterations include histone modification, DNA methylation and acetylation, small interfering RNA (siRNA) mechanisms, and epithelial-stromal interactions, to name a few. While epigenetic mechanisms of carcinogenesis have been studied for decades, their application to drug development and discovery, risk assessment, hazard identification, and toxicologic pathology in general is relatively recent. It is becoming increasingly clear that epigenetic alterations not only play a role in cancer development, but also reproductive, developmental, and degenerative diseases in humans. How epigenetic mechanisms alter the biologic system to contribute to disease and toxicity is an area of ongoing and intense interest and research. This session will discuss the utilization of epigenetic endpoints in toxicity testing, and how they relate to human disease due to exposures in the process of reproductive, developmental,

degenerative, and neoplastic disease, and the assessment of these endpoints within the safety assessment and hazard characterization paradigms in toxicologic pathology for the study of human health.

8:00 AM–8:45 AM

An Integrated View of Epigenetics: Implications for Toxicologic Pathology

Jay I. Goodman, PhD, Michigan State University, East Lansing, MI

8:45 AM–9:25 AM

Investigating the Role of Epigenetics in Product Safety Assessment

Reza J. Rasoulpour, PhD, The Dow Chemical Company, Midland, MI

9:25 AM–10:05 AM

Epigenetic Changes in Cancers, Methodologies to Detect Them, and Potential Therapies

Stephen Baylin, MD, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD

10:05 AM–10:40 AM

Break

10:40 AM–11:20 AM

Chromatin Remodeling in Development and Disease

Michael C. Boyle, DVM, PhD, DACVP, DABT, Amgen Inc., Thousand Oaks, CA

11:20 AM–12:00 Noon

Epigenetics and the Microbiome

Theresa Alenghat, VMD, PhD, DACVP, University of Pennsylvania, Philadelphia, PA



Excel Tips and Tricks: Easy Ways to Quickly Visualize Your Pathology Data

12:00 Noon–1:30 PM

Sponsored by IATP and STP

(Free Event, Registration Required)

This interactive presentation will demonstrate ways to quickly visualize numeric pathology data primarily using Microsoft Excel. Although Excel's built-in graphing capabilities are limited compared to dedicated graphing programs, some of its functions are ideally suited to evaluating pathology data from toxicity studies. Registrants are encouraged to bring their computers along with the example Excel spreadsheet that will be emailed to registrants prior to the session. The session will begin by demonstrating methods to get data into Excel from Word and PDF documents and how to best format different types of data. Next, several methods of graphing will be demonstrated, including scatter plots and pivot charts. For scatter plots, the demonstration will include on-the-fly review, optimizing visualization, and annotating graphs. For pivot tables and charts, the demonstration will include pros and cons of pivot charts, flipping data to be pivot-ready, creating and modifying a chart, customizing a data table or chart for export to PowerPoint or Word, and annotating graphs and data. For data sets not easily graphed in Excel, alternative graphing programs will be mentioned. At the end of this session, attendees will have new tools to evaluate data for interpretation and presentations.

Wednesday Afternoon

Session 6

1:30 PM–5:00 PM

Environmental Toxicologic Pathology and Prediction of Human Health Risks

Co-Chairs: Charles E. Wood, DVM, PhD, DACVP, US EPA, Research Triangle Park, NC; Wanda Haschek-Hock, BVSc, PhD, DACVP, DABT, FIATP, University of Illinois, Urbana, IL; and David Malarkey, DVM, PhD, DACVP, NIEHS, Research Triangle Park, NC

Evaluating the impact of environmental factors on human health and disease is an integral part of translational science. For toxicologic pathologists, the study of environmental health effects and their mechanisms, and the use of this information in risk assessment and policy decisions, involves a range of different animal models and bioassays. Recently, there has also been increased interest in the use of higher-throughput alternative models, including *in vitro*

and computational approaches, for assessing human health hazards due to environmental agents. This session will focus on translational applications of data derived from different model systems used in hazard identification and risk assessment of environmental compounds. Specific areas of focus will include current regulatory issues in chemical safety, evaluation of environmental obesogens and metabolic disruptors, emerging approaches for testing of reproductive toxicants, comparative pathology of rodent lung tumors, and health effects of phycotoxins from harmful algal blooms.

1:30 PM–2:05 PM

Current and Emerging Issues in Chemical Safety

Jeffrey Morris, PhD, US EPA Office of Chemical Safety and Pollution Prevention, Washington, DC

2:05 PM–2:40 PM

Interface of Air Pollution, Diabetes, and the Metabolic Syndrome: Translational Studies on Health Effects

Jack Harkema, DVM, PhD, DACVP, Michigan State University, East Lansing, MI

2:40 PM–3:15 PM

Break

3:15 PM–3:50 PM

Rodent vs. Human Lung Cancer: The Good, the Bad, and the Ugly!

Arun Pandiri, BVSc&AH, MS, PhD, DACVP, EPL, Inc., Research Triangle Park, NC; and Samuel M. Cohen, MD, PhD, University of Nebraska Medical Center, Omaha, NE

3:50 PM–4:25 PM

Deriving Points of Departure and Performance Baselines for Predictive Modeling of Systemic Toxicity using ToxRefDB

Matthew Martin, PhD, US EPA National Center for Computational Toxicology, Research Triangle Park, NC

4:25 PM–5:00 PM

Health Effects of Phycotoxins from Harmful Algal Blooms

Olga M. Pulido, MD, MSc, ABPath, FIATP, University of Ottawa, Ottawa, Ontario, Canada

5:30 PM–5:50 PM

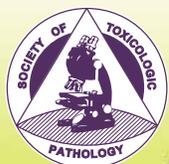
Awards Ceremony

5:50 PM–6:30 PM

Annual Business Meeting

7:00 PM–9:00 PM

President's Reception



Thursday, June 26

Thursday Morning

Session 7

8:00 AM–12:00 Noon

The Challenges of Safety Evaluation in Populations with Concurrent Disease

Co-Chairs: LuAnn McKinney, DVM, DACVP, FDA/CDER/OND/DNP, Silver Spring, MD; and John E. Sagartz, DVM, PhD, DACVP, Seventh Wave Laboratories, Chesterfield, MO

Comorbidities in patient populations include overt cardiovascular disease, obesity, or diabetes, singly or in combination with other, less prominent conditions. When xenobiotics are administered, drug-related adverse events in patients with concurrent disease may be detected during clinical trials. Often adverse responses are detected by post-marketing surveillance, by meta-analysis of clinical case reports, or through data mining by regulatory agencies. The challenge is to detect, predict, or ameliorate these adverse events in nonclinical studies before patients are adversely affected. This session will explore the current methodologies applied through the translational arc: the pharmacovigilance methodologies applied to clinical and post-marketing studies followed by discussion of the safety decisions in translation from normal animals to normal humans to patient populations to patients with concurrent disease. The session will also focus on the utility of studies in normal animals to predict adverse events in patient populations and review the efficacy of animal models of human disease to detect adverse safety signals. A panel discussion of these current challenges and how nonclinical studies may meet those challenges will follow.

8:00 AM–8:45 AM

The Evidentiary Basis of Safety Decisions from Normal Animal to Comorbid Patient

Ellis Unger, MD, FDA/CDER (Office of Drug Evaluation, I), Silver Spring, MD

8:45 AM–9:25 AM

Overview of Pharmacovigilance Methodologies to Detect Adverse Clinical Events in Comorbidities

Ajay Singh, MD, GlaxoSmithKline, Collegeville, PA

9:25 AM–10:05 AM

How the Early Preclinical Safety Assessment Can Identify Safety Issues and Minimize or Circumvent Adverse Safety Events

John E. Sagartz, DVM, PhD, DACVP, Seventh Wave Laboratories, Chesterfield, MO

10:05 AM–10:40 AM

Break

10:40 AM–11:20 AM

Animal Models of Human Disease for Nonclinical Safety Assessment of Novel Pharmaceuticals

Sherry J. Morgan, DVM, PhD, DACVP, AbbVie, Inc., North Chicago, IL

11:20 AM–12:00 Noon

Roundtable: What Can Preclinical Sciences Do to Meet This Clinical Challenge?

12:00 Noon

Meeting Adjourned