The objective 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 will then vote using wireless keypads and the results will be displayed on the screen. Time is allowed for discussion after each voting session.

Career Development Session (Sunday AM)
8:00 AM–12:00 Noon

Looking Forward: Cutting-Edge Technologies and Skills for Pathologists in the Future

**Co-Chairs:** Kyathanahalli Janardhan, BVSc, MVSc, PhD, DACVP, Integrated Laboratory Systems, Research Triangle Park, NC; and Rebecca Kohnken, DVM, PhD, DACVP, AbbVie, North Chicago, IL

Toxicologic Pathology is one of the most valuable fields contributing to the advancement of animal and human health. With the ever-changing technological and economic environment, the basic skill set pathologists are equipped with may not be sufficient to address the current and future needs. Periodically, pathologists must add relevant, new skills to their toolbox. This session provides a comprehensive review of some of the skills that will be handy for the current time and the near future.

CE1 (Sunday AM)
8:00 AM–12:00 Noon

Data Interpretation, Visualization, and Statistics for Nonclinical Toxicity Studies

**Co-Chairs:** Michael Logan, DVM, PhD, DACVP, AbbVie, Highland Park, IL; and Susan G. Emeigh Hart, VMD, PhD, DACVP, DABT, ERT, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT

Analysis of anatomic and clinical pathology data is central to the safety assessment of new molecules. Technologic advancement and the push for additional measures for both toxicity and risk prediction have expanded the pathologist’s toolbox for data presentation and analysis. This course will explore the application of new data visualization tools and their application to toxicologic pathology with examples that are applicable to both anatomic and clinical pathology. In addition, the more traditional statistical analysis tools for data analysis will be scrutinized. The appropriate (and sometimes inappropriate) use of these techniques will be presented in a user friendly and toxicologic pathology focused manner.

Medical Device Safety Assessment: The Frontiers of Safety Assessment Pathology

**Co-Chairs:** Maureen T. O’Brien, DVM, MS, DACVP, Charles River Laboratories, Frederick, MD; and Serge D. Rousselle, DVM, DACVP, Alizée Pathology, Thurmont, MD

Pathology of medical devices poses unique, ever-evolving challenges and considerations that often cannot be answered by employing traditional toxicologic pathology methods. Furthermore, medical device specimens may be limited and/or expensive; therefore, having a structured approach to pathology is particularly essential for study success. Medical device regulation
differs from that of drugs, and knowledge of the regulatory pathways is an asset when providing pathologic evaluation of medical devices. This course provides an introduction to basic medical device pathology, including specialized methods for pathology such as plastic embedding, unique considerations for the pathologic evaluation, topical discussion of pathology, and an overview of the regulatory path to market for medical devices.

8:00 AM–9:00 AM
Basic Techniques in Medical Device Pathology
Nicolette D. Jackson, DVM, DACVP, Accelab, Boisbriand, QC, Canada

9:00 AM–9:30 AM
Overview of the Regulatory Approval Process for Medical Devices in the United States
Karen Manhart, VMD, MA, DACVP, US FDA, CDRH, Laurel, MD

9:30 AM–10:00 AM
Break

10:00 AM–10:30 AM
Biocompatibility: Key Concepts for Medical Device Safety Assessment
William C. Stoffregen, DVM, PhD, DACVP, Northstar Preclinical and Pathology Services, LLC, Lake Elmo, MN

10:30 AM–11:00 AM
A Primer of Common Medical Device Biomaterials
Michael N. Helmus, PhD, Consultant, Worcester, MA

11:00 AM–11:30 AM
Medical Device Bioabsorption
Serge D. Rousselle, DVM, DACVP, Alizée Pathology, Thurmont, MD

11:30 AM–12:00 Noon
Hernia Mesh Implants
John H. Keating, DVM, DACVP, CBSET, Inc., Lexington, MA

CE3 (Sunday PM)
1:30 PM–5:30 PM
Cardiac Effects Commonly Encountered in Drug Development: Mechanisms and Clinical Relevance
Sponsored by American College of Toxicology (ACT)

Co-Chairs: Matthew M. Abernathy, PhD, DSP, Eli Lilly & Company, Indianapolis, IN; and Donald N. Jensen, DVM, MS, US FDA/CDER, Silver Spring, MD

The cardiovascular system is an intricate meshwork of organ structures regulated by multiple feedback loops to maintain organ perfusion, deliver fuel, and remove cellular waste. Due to the range of CV targets that are dispersed throughout our many tissues, it should be of no surprise that a high percentage of drug attrition falls at the feet of cardiovascular findings both preclinically and clinically. Given the high exposures achieved and techniques used to assess CV safety in preclinical models, the number of preclinical observations of CV effects generally exceeds the prevalence of effects observed clinically. Findings may range from cardiomyopathy to arrhythmia, and not all CV safety signals carry the same weight when deciding to continue to develop a compound. Thus, safety margin and target patient population heavily influence judgment-based development decisions beginning early on in compound discovery. This course will focus on mechanisms for both histological and functional cardiac effects encountered during drug development. Additionally, decision-making strategies for unexpected CV effects and use of in silico models to predict the mechanism and translation of cardiac effects to the clinic will be covered in depth.

1:30 PM–2:10 PM
Cardiac Toxicity: Options from a Regulatory Perspective
Donald N. Jensen, DVM, MS, US FDA/CDER, Silver Spring, MD

2:10 PM–2:50 PM
Integrative Cardiovascular Toxicologic Pathology—Building Translational Bridges
Brian Berridge, DVM, PhD, DACVP, NIEHS/NTP, Research Triangle Park, NC

2:50 PM–3:20 PM
Break

3:20 PM–4:00 PM
Measuring, Interpreting, and Decision Making Based on Drug-Induced Hemodynamic Effects, Case Studies in Diabetes and Oncology
Derek J. Leishman, PhD, DSP, Eli Lilly & Company, Indianapolis, IN

4:00 PM–4:40 PM
Safe QTc Prolongation? How the Comprehensive In Vitro Proarrhythmia Assessment Will Spare Nontorsadogenic Molecules that Prolong Cardiac Repolarization (QTc Interval)
Wendy Wu, PhD, US FDA/CDER, Silver Spring, MD

4:40 PM–5:20 PM
In Silico Modeling in Cardiorenal Safety Assessment
K. Melissa Hallow, PhD, University of Georgia, Athens, GA

5:20 PM–5:30 PM
Panel Discussion

CE4 (Sunday PM)
1:30 PM–5:30 PM
Otic Toxicologic Pathology

Co-Chairs: Kenneth A. Schafer, DVM, PhD, DACVP, Vet Path Services, Inc., Greenfield, IN; and Bradley L. Njaa, BSc (Hons), DVM, MVSc, DACVP, Kansas State University, Manhattan, KS

The ear is infrequently evaluated in toxicologic pathology, and only so when there are very specific drivers to evaluate it. These include known compound classes where otic toxicity may be anticipated or when the intended therapeutic is applied directly to the ear. This session will cover an overview of otic anatomy, otic physiology, techniques in otic toxicology, otic pathology, and regulatory considerations for otic toxicology studies.
polluted air may directly or indirectly foster the development of or exacerbate a wide-range of respiratory, cardiovascular, metabolic, autoimmune and neurological diseases. Research to identify why certain sub-populations (e.g., children, the elderly, diabetics) appear more susceptible to the health effects of air pollution, as well as studies to identify effective interventions to prevent or treat air-pollutant-triggered illnesses will also be presented. The session will foster discussions on data gaps and future research that are needed to address this global environmental health problem.

9:00 AM–9:10 AM
**Introduction to Topic and Speakers**
Mark Cesta, DVM, PhD, DACVP, NIEHS, Research Triangle Park, NC

9:10 AM–9:45 AM
**Cardiopulmonary Health Effects of Air Pollution**
Kent E. Pinkerton, PhD, University of California Davis, Davis, CA

9:45 AM–10:20 AM
**Susceptibility Variations in Air Pollution Health Effects**
Urmila P. Kodavanti, PhD, DABT, US EPA, Research Triangle Park, NC

10:20 AM–10:50 AM
**Break**

10:50 AM–11:25 AM
**Exposure to Ambient Ultrafine Particles as a Risk Factor for Neurodevelopmental Disorders**
Deborah A. Cory-Slechta, PhD, University of Rochester School of Medicine, Rochester, NY

11:25 AM–12:00 PM
**New Onset Asthma, Ozone, and Innate Lymphoid Cells: A New Pathogenesis Paradigm**
Jack R. Harkema, DVM, PhD, DACVP, ATSF, Michigan State University, East Lansing, MI

**Career Development Lunchtime Series**

12:30 PM–1:30 PM
**Global Perspective on Careers in Environmental Toxicologic Pathology**
Chair: Wanda Haschek-Hock, BVSc, PhD, DACVP, DABT, FIATP, University of Illinois, Urbana, IL

A wide range of career options are available globally in the environmental toxicologic pathology (ETP) arena including academia, government, contract research organizations and the agrichemical industry. This small and specialized subset of toxicologic pathologists addresses the effects of contaminants and pollutants on human, animal and ecological health (One Health). Veterinary students and pathology trainees are primarily exposed to diagnostic pathology and often have limited exposure to toxicologic pathology and even less so to the issues and opportunities in environmental toxicology. The speakers will provide a brief overview of global opportunities in their work sector and personal perspectives of their careers in environmental toxicologic pathology. The goal of the panel discussion is to engage the audience and provide an opportunity to explore careers in this specialty.
Session 2

1:30 PM–5:00 PM

Toxicologic Pathology of Workplace Agents

Co-Chairs: Ann Hubbs, DVM, PhD, DACVP, NIOSH, CDC, Morgantown, WV; and Peter Spencer, PhD, FANA, FRCPATH, Oregon Health & Science University, Portland, OR

The workplace environment often produces a different spectrum of exposures than those received by the general public. This session focuses on the pathology and pathogenesis of diseases associated with workplace environments. The talks emphasize the toxicologic pathology of occupational diseases that challenge workplaces today. Significant organic solvent exposure continues to occur in global workplaces, and the session begins with an update on mechanisms of y-diketone solvent neurotoxicity. Emerging and re-emerging occupational diseases and associated pathologies are addressed in talks on flavorings-related lung disease and on the ongoing outbreak of rapidly progressive pneumoconiosis in Appalachian coal miners. Lifestyle factors may interact with workplace exposures to influence the pathology of occupational disease, as will be discussed in a talk on the effect of dietary omega-3 fatty acids in silica-exposed lupus-prone NZBWF1 mice. The session will end with a panel discussion addressing a very important question: Can we predict/prevent occupational disease before workers get sick?

1:30 PM–1:35 PM
Introduction to Topic and Speakers
Ann Hubbs, DVM, PhD, DACVP, NIOSH, CDC, Morgantown, WV

1:35 PM–2:10 PM
Organic Solvent Neurotoxicity
Peter Spencer, PhD, FANA, FRCPATH, Oregon Health & Science University, Portland, OR

2:10 PM–2:45 PM
Rapidly Progressive Pneumoconiosis in Appalachian Coal Miners: Clinical and Pathology Findings
Robert Cohen, MD, FCCP, University of Illinois Chicago, Chicago, IL

2:45 PM–3:15 PM
Break

3:15 PM–3:50 PM
Silica, Lupus, and Dietary Omega-3 Fatty Acid Interventions
Kathryn Wierenga, BA, Michigan State University, East Lansing, MI

3:50 PM–4:25 PM
Flavorings-Related Lung Disease
Ann Hubbs, DVM, PhD, DACVP, NIOSH, CDC, Morgantown, WV

4:25 PM–5:00 PM
Panel Discussion

Town Hall
5:30 PM–6:30 PM

Session 3

8:00 AM–12:00 Noon

Toxicity Assessment Paradigms in Regulatory Pathology

Co-Chairs: Deepa B. Rao, BVSc, MS, PhD, DABT, DACVP, US FDA, CDER, Silver Spring, MD; and John C. Lipscomb, PhD, DABT, ATS, US EPA, Cincinnati, OH

Toxicologic pathologists are routinely engaged in the histopathologic evaluation of tissues from toxicity studies. Toxicology studies encompass a wide spectrum of agents that include drugs and biologics, chemicals (industrial, environmental and occupational), food additives, cosmetic ingredients, tobacco products, medical devices, and even physical agents such as radiation and noise. Toxicity assessments differ between such diverse agents depending on exposure settings, target populations, and safety assessment by the appropriate regulatory authorities. The objective of this session is to provide an overview of safety assessments in toxicology studies through examples where the safety decision has hinged on pathology end-points. This session is designed to maximize the cross-talk and collaboration between toxicologists/risk assessors and toxicologic pathologists, so that the differences in toxicity and risk assessments between diverse example agents are highlighted. Each example includes perspectives from a toxicologist and a pathologist; and the examples in this symposium session include a physical agent (cell phone radiation), environmental chemicals (hydrogen sulfide, acetaldehyde), polymer conjugated biologics (polyethylene glycol), and a food additive (myrcene) to provide an overview of the role of various regulatory agencies in the risk assessment of toxic agents.

8:00 AM–8:05 AM
Introduction
Deepa B. Rao, BVSc, MS, PhD, DABT, DACVP, US FDA, CDER, Silver Spring, MD

8:05 AM–8:30 AM
Purpose-Specific Toxicity and Risk Assessments
John C. Lipscomb, PhD, DABT, ATS, US EPA, Cincinnati, OH

8:30 AM–9:05 AM
Toxicity Assessment of Food Additives: Myrcene, a Synthetic Flavoring Agent
Steve Mog, DVM, DACVP, US FDA, CFSAN, Silver Spring, MD; and Yu Janet Zang, PhD, DABT, US FDA, CFSAN, Silver Spring, MD

9:05 AM–9:35 AM
Cell Phone Radiation: Toxicity Assessment of a Physical Agent
Mark Cesta, DVM, PhD, DACVP, NTP, NIEHS, Research Triangle Park, NC; and Michael Wyde, PhD, NTP, NIEHS, Research Triangle Park, NC

9:35 AM–10:05 AM
Break

10:05 AM–10:20 AM
Student Speaker
During the past twenty years, investigations involving endocrine active substances (EAS) and reproductive toxicity have dominated the landscape of ecotoxicological research. This has occurred in concert with heightened awareness in the scientific community, general public, and governmental entities of the potential consequences of chemical perturbation in humans and wildlife. The exponential growth of experimentation in this field is fueled by the expanding knowledge into the complex nature of endocrine systems and the intricacy of their interactions with xenobiotic agents. Complicating factors include the ever-increasing number of novel receptors and alternate mechanistic pathways that have come to light, effects of chemical mixtures in the environment versus those of single EAS laboratory exposures, the challenge of differentiating endocrine disruption from direct cytotoxicity, and the potential for transgenerational effects. Although initially concerned with EAS effects chiefly in the thyroid glands and reproductive organs, it is now recognized that anthropomorphic substances may also adversely affect the nervous and immune systems via hormonal mechanisms, and play substantial roles in metabolic diseases such as type 2 diabetes and obesity.

The six expert presenters and one highly motivated student in this session will cover a diverse variety of topics that are intended to provide an overview of the field as it currently stands, in addition to the latest cutting-edge research. At minimum, discussions will encompass known and potential effects of EAS in humans, non-human primates, rodents, and fish. Categories of EAS to be discussed will include agonists and antagonists of estrogenic and androgenic pathways, among others. In addition to histomorphology, presentations will demonstrate a variety of diagnostic approaches for investigating EAS effects, and developmental effects of EAS will be highlighted. Regulatory implications for chemicals suspected of having endocrine activity will be mentioned, and controversial aspects of EAS research will be briefly explored. It is hoped that attendees will leave this session with an enhanced understanding and appreciation for endocrine and reproductive toxicity and the associated pathological consequences.
STP 38th Annual Symposium

Update on Intersex and Endocrine-Induced Reproductive Abnormalities in Fish
Mac Law, DVM, PhD, DACVP, North Carolina State College of Veterinary Medicine, Raleigh, NC

11:15 AM–11:45 AM

IATP/STP Lunchtime Workshop
12:30 PM–1:30 PM

Bridging the Gap between Toxicologic Pathologists and the Medical Device Industry
Co-Chairs: Darlene Dixon, DVM, PhD, DACVP, FiATP, NTP/NIEHS, Research Triangle Park, NC; and Robert R. Maronpot, DVM, MS, MPH, DABT, FiATP, Maronpot Consulting LLC, Raleigh, NC
Speaker: JoAnn C. L. Schuh, DVM, PhD, DACVP, DABT, JCL Schuh PLLC, Bainbridge Island, WA

This lunchtime workshop will explore the existing gap between the field of toxicologic pathology and the medical device industry and the need for toxicologic pathologists to improve this relationship.

Introduction to Topic and Speakers
11:45 AM–12:00 PM

Student Speaker

Pathology in Ecological Research with Implications for One Health
Co-Chairs: Wanda Haschek-Hock, BVSc, PhD, DACVP, DABT, FiATP, University of Illinois, Urbana, IL; and Mac Law, DVM, PhD, DACVP, North Carolina State College of Veterinary Medicine, Raleigh, NC

Ecological toxicologic pathology is a relatively new field that builds on the science of environmental toxicologic pathology to study the effects of toxic substances and physical agents, especially pollutants, at the population, community, and ecosystem levels. The objective of this session is to illustrate the wide-ranging aspects of this field and the potential contributions of toxicologic pathology. This session explores the effects of pollutants on One Health beginning at the ecosystem level, including microbes, insects, fish, and humans. Presentations will explore the interaction of pesticides, pathogens, phytochemicals and xenobiotic biotransformation in bee colony losses critical for food security (honey bees have been proposed as models for gut microbiota research and recently listed under the 2017 US FDA veterinary feed directive); the role of pathology in identifying the effects of pollutants on fish as sentinels for human health; the effects climate and nutrients on harmful algal blooms and toxin production leading to animal and human disease; the processing of environmental carcinogens by intestinal microbiota; and the clinical pathology of per- and polyfluoroalkyl substances (PFAS) that can persist in the environment and contaminate drinking water.

1:30 PM–5:00 PM

Biochemical and Hematologic Changes in 28-Day Rat Biochemical and Hematologic Changes in 28-Day Rat
Mac Law, DVM, PhD, DACVP

2:45 PM–3:10 PM

Studies of Seven Per- and Polyfluoroalkyl Substances (PFAS)—Beyond PFOA and PFOS
Aadra Bhatt, PhD, University of North Carolina at Chapel Hill, Chapel Hill, NC

3:35 PM–4:20 PM

Cyanobacterial Toxins
Neil Chernoff, PhD, US EPA, Research Triangle Park, NC; and Gregory S. Travlos, DVM, DACVP, NIEHS, Research Triangle Park, NC

4:20 PM–5:00 PM

The Occurrence and Toxicological Effects of Freshwater Cyanobacterial Toxins
Aadra Bhatt, PhD, University of North Carolina at Chapel Hill, Chapel Hill, NC

THURSDAY, JUNE 27

Session 6
8:00 AM–12:00 Noon

Integration of Big Data Technologies with Toxicologic Pathology
Co-Chairs: Charles E. Wood, DVM, PhD, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT; and Matt Martin, PhD, Pfizer, Inc., Groton, CT

Large-scale bioinformatic tools play an increasingly important role in environmental health, as well as translational and regulatory science. The Thursday morning session will address emerging concepts and drivers related to the integration of these new technologies in current toxicologic pathology practice. Talks will explore how big data analytics can be used to guide nonclinical testing strategies, streamline diagnostics, enhance target discovery, and inform interpretation of pathology outcomes. Topics will range from alternative toxicological models to use of digital pathology and machine learning. Speakers will also discuss issues, challenges, and future directions related to translation and use of molecular information in pathology.

1:30 PM–1:35 PM

Introduction to Topic and Speakers
Matt Martin, PhD, Pfizer, Inc., Groton, CT
8:10 AM–8:45 AM  
**Use of Alternative Methods/Technologies/Data Types in Hazard Characterization**  
Warren Casey, PhD, NTP, NIEHS, Durham, NC

8:45 AM–9:20 AM  
**Diagnostic Applications of Artificial Intelligence and Machine Learning in Pathology**  
Ilan Wapinski, PhD, PathAI, Boston, MA

9:20 AM–9:45 AM  
**Bridging the Gap between Data Sciences and Toxicologic Pathology: Chemical Screening and Prioritization**  
Sean Watford, PhD, US EPA, Durham, NC

9:45 AM–10:15 AM  
**Break**

10:15 AM–10:50 AM  
**Regulatory Perspective of Whole Slide Imaging and Digital Pathology in Nonclinical Safety Assessment**  
LuAnn McKinney, DVM, DACVP, US FDA, CDER, Silver Spring, MD

10:50 AM–11:25 AM  
**Molecular Applications for Target Identification in Archival FFPE Tissue Samples**  
Charles E. Wood, DVM, PhD, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT

11:25 AM–12:00 PM  
**Panel Discussion**

12:00 Noon  
**Meeting Adjourned**