Material Biocompatibility and Standard for Plastic Manufacturing Systems/Components Workshop

Speaker Biographies & Abstracts
(listed alphabetically)

Douglas Ball, M.S.
USP Biocompatibility of Materials Used in Packaging Systems, Medical Devices and Implants Expert Panel Member
DABT Research Fellow, Regulatory Strategy and Compliance
Pfizer
Groton, CT

Doug obtained his BS and MS in Biology from St. John's University, Jamaica, NY in 1977 and 1980, respectively and became board certified in general toxicology (DABT) in 2003. Doug is a full member of the American College of Toxicology (ACT), Society of Toxicology (SOT) and has served as President, Vice President and Secretary/Treasurer for the Northeast Chapter of SOT (NESOT). Prior to joining Pfizer, Doug was employed as a toxicologist at Sandoz (now Novartis) and Boehringer Ingelheim. Over the years, Doug has assumed various project and regulatory strategy roles and is currently a Research Fellow in Regulatory Strategy and Compliance at Pfizer.

Doug is a recognized expert in the evaluation and qualification of leachables and extractables (L&E) in drug products. He co-chaired a Product Quality Research Institute (PQRI) L&E work group and co-authored the PQRI Best Practices Recommendations for Evaluation of L&E in Orally Inhaled and Nasal Drug Products (OINDP, 2006). Currently, Doug serves as a co-chair for the PQRI work team for L&E evaluation in parenteral and ophthalmic drug products (PODP), the Co-Topic Lead for the International Conference on Harmonisation (ICH) Expert Working Group (EWG) and Implementation Working Group (IWG) for Elemental Impurities (Q3D), an Expert Panel member for USP <381> Elastomeric Closures for Injection and Biocompatibility <87> and <88>, and is past Chair and current Board member of the Extractables and Leachables Safety Information Exchange (ELSIE).

Presentation Abstract
Revision of USP's Biocompatibility Requirements for Materials of Construction: What are the Key Issues?
Monday, June 20, 2016, 9:00 a.m. – 9:30 a.m.

The concern over the biocompatibility of materials started around 1960 when USP and NF began discussions on developing standards for plastics used in connection with pharmaceuticals. USP and NF recognized that the use of plastics in pharmaceuticals presented certain risk factors that could impact patient health. By 1965, USP XVII introduced Biological Tests—Plastics Containers section was added and made official in the Compendium. Plastics were assigned Class I-VI based on the biological in vivo testing (systemic injection, intra-cutaneous, and implantation tests). In 1988, in vitro tests were explored, and USP concluded that in vitro assay(s) could serve as a decision point as to whether or not a sample would be tested in animals. In 1990, USP XXII added <87> Biological Reactivity Tests, to the Compendia. The Biocompatibility Expert Panel is currently evaluating strategies to REDUCE the amount of redundant testing of existing materials and limit the testing

of new materials to in vitro biocompatibility testing, REFINE the type of testing performed to align with the potential risk, and REPLACE in vivo testing with a risk based quality by design approach based on the knowledge of the material. The Expert Panel believes that the implementation of the 3R strategy (reduce, refine, and replace) for biological reactivity will lead to conduct of in vivo testing only when deemed necessary by the risk assessment and potentially eliminate the need for I-VI classification of plastics.

William P. Beierschmitt, Ph.D., D.A.B.T., F.A.T.S.
USP Biocompatibility of Materials Used in Packaging Systems, Medical Devices and Implants Expert Panel Member
Research Fellow, Worldwide Research and Development
Drug Safety Research & Development
Groton, CT

Bill received his B.S. in Biology from Mount Saint Mary's University, and his Ph.D. in Toxicology from the University of Maryland. After completing post-doctoral work at the University of Connecticut, he joined Pfizer's Drug Safety Research and Development department in Groton, Connecticut. Bill is a Diplomate of the American Board of Toxicology, and a Fellow of the Academy of Toxicological Sciences. In his 28 years of experience in the pharmaceutical industry, Bill has been involved in a wide range of toxicology issues associated with impurities in drugs, including the development of strategies to risk assess extractables and leachables.

Presentation Abstract
Safety Evaluation and the Risk Assessment Process
Monday, June 20, 2016, 2:45 p.m. – 3:15 p.m.

Biocompatibility testing (USP <87>/<88>) has been an integral part of establishing the safety and acceptability of materials and components of a container closure system (CCS) for many years. Importantly, however, the USP <87> in vitro biocompatibility test uses an endpoint that is not particularly robust (i.e., cytotoxicity), while the USP <88> in vivo biocompatibility test uses acute endpoints that may not be toxicologically relevant and are difficult to translate into predictable clinical outcomes. Thus, as the science and experience surrounding packaging issues has evolved, a more contemporary approach in choosing appropriate CCS components is worthy of consideration. In this regard, knowing the actual chemical composition of CCS components can improve the ability to identify and assess potential toxicological concerns and how to mitigate them. Towards this end, the initial use of a risk-based quality by design approach provides significant chemical information to conduct a thorough and meaningful safety qualification, leading to improved decision making and an elimination and/or decrease in biocompatibility testing. Two specific examples will be provided to illustrate the potential benefit of a risk based approach to establish the safety and acceptability of CCS components.

Piet Christiaens, Ph.D.
Scientific Director
Toxikon Europe NV
Heverlee, Belgium

Piet Christiaens received his Ph.D. from the Analytical Chemistry Department of the University of Leuven (Belgium) in 1991. From 1992 to 1997, he was Lab Manager in two Analytical Contract Laboratories.

From 1997 to 2000, he worked as an independent consultant with Shell Chemical Company in Houston, TX (US) where he conducted research on a new hydrogenation catalyst system for Hydrogenated Triblock Co-polymers (Kraton Polymers).

From 2001 onwards, Mr. Christiaens holds the position of Scientific Director at Toxikon Europe where he develops analytical methods and protocols for both extractables and leachables studies for the Medical and Pharmaceutical Industries. Mr. Christiaens oversees all laboratory operations at Toxikon Europe and is also giving support to the European business development.

Presentation Abstract
The USP Protocol for the Comparison of Extraction Conditions for Plastic Manufacturing Components – Applied to Bioreactor Bags
Tuesday, June 21, 2016, 3:30 p.m. – 4:45 p.m.

The USP <661.3> Expert Panel wrote a draft chapter that includes a proposal for the extracting solutions to be used and the extracting conditions, e.g. temperature, time frame and stoichiometry. The USP Extraction protocol is partially aligned with the proposal put forward by the Biophorum Operations Group (BPOG).
In the Current Study, the 3 Extraction conditions of the USP protocol (**C1**: *Acidic Salt KCl pH3*; **C2**: *Phosphate buffer pH 10* and **C3**: *50% Ethanol*) were used to perform the extractions. In addition, the 5 BPOG Extraction Solutions were also investigated (**S1**: *0.1M Phosphoric Acid*; **S2**: *0.5N NaOH*; **S3**: *50% Ethanol*; **S4**: *WFI* and **S5:** *High Salt 5M NaCl*).

The Bioreactor Bags were filled to their nominal volume with the extraction solutions and were extracted for 21 days at a temperature of 40°C with shaking incubation at 50 rpm. Tests were performed in duplicate, where possible.
The analytical methods, used to characterize and analyse all extracts and to establish a detailed organic extractable profile, were TOC for the aqueous solutions (as indicated in the USP Draft Protocol), Headspace GC/MS (for the analysis of volatile compounds), GC/MS (for the analysis of semi-volatile compounds) and UPLC-HRAM (High resolution Accurate Mass) LC/MS (for the analysis of the non-volatile compounds). The UPLC-HRAM was run in 4 different modes: APCI+, APCI-, ESI+ and ESI-. For all chromatographic analyses, our internal TOX-RAY database was used for identifying the detected compounds, based upon retention time and

mass spectrum.

In addition, ICP was used to further characterize the aqueous extracts for the presence of any metals.

The presentation will give an overview of all obtained results. In addition, an overview of the most important observations will be given in view of the differences in Protocol between the USP approach and the BPOG protocol.

Raymond Colton, MBA, MS
President
VR Analytical
Bend, OR

Raymond Colton is the founder and president of VR Analytical, a CRO that specializes in extractables and leachables testing (E/L).

After 15 years in the E/L field, Colton is a leading expert in extractables and leachables science. He is the author of a book chapter, numerous presentations, and published papers. He was also the lead author of the first two papers about extractables and leachables published by the Bio-Process Systems Alliance in Bio-Process International.

As science and regulatory expectations continue to evolve, he is actively contributing to the development of best practices and understanding regulatory expectations. Currently, he is a member of the ASTM E55 subgroup that is writing a test standard for extractables testing, and advises the BPSA with regard to the best practices science of extractables testing. His experience has helped biopharmaceutical end users and suppliers around the world understand the need to mitigate the potential risk of extractables and leachables from reaching patients, and helped them prepare for regulatory submissions

Colton earned his Bachelor of Science degree in Chemical Engineering from Clarkson University in New York, and a Master of Science in Chemical Engineering from the University of Washington. He also obtained a Masters of Business Administration from New York University. He is a member of the Parenteral Drug Association, the BioProcess Systems Alliance and the Oregon Bioscience Association.

Presentation Abstract
Comparison of BPOG and USP Test Matrixes for a Hydrophilic PES Capsule Filter
Tuesday, June 21, 2016, 3:30 p.m. – 4:45 p.m.

Hydrophilic polyethersulfone pleated filters encapsulated in a capsule made of polypropylene with polypropylene internal supports were extracted after gamma irradiation. The extraction media consisted the three USP solvents, KCl at pH 3, Phosphate Buffer at pH 10 and 50% ethanol/water along with the BPOG solvents including 0.1 M H_3PO_4, DI Water and 0.5 N NaOH. 1% Polysorbate 80 was not tested. The extractions were ended after 1 day and 7 days. The extracts and controls were analyzed by Headspace GC-MS/FID, GC-MS/FID, LC-UV-MS and ICP-MS. General chemistry tests including Total Organic Carbon, UV-vis and pH change were also performed on selected media. Results and comparisons will be reported.

Weibing Ding, Ph.D.
USP <661.3> Plastic Systems Used for Manufacturing Pharmaceutical Products Expert Panel Member
Principal Scientist, Process Development
Amgen Inc.
Thousand Oaks, CA

Weibing Ding is a Principal Scientist in Process Development at Amgen Inc. where he is the subject matter expert in single-use systems (SUS) and extractables & leachables in the Materials Science Group. He is responsible for evaluation and facilitating implementation of single-use technologies in upstream, downstream and fill & finish of biomanufacturing. He contributes to Next Generation Manufacturing by performing risk assessments of raw materials, deep understanding of both supplier's and end user's manufacturing processes, and minimizing impact of raw materials on bioprocesses, drug substance, and drug product. He is an active member of BPOG's Disposables work stream and USP <661.3> expert panel. Mr. Ding obtained his Ph.D. in Chemical Engineering from the University of Utah in 1997.

Presentation Abstract
User Expectation: What is the problem to be solved?
Tuesday, June 21, 2016, 9:35 a.m. – 9:55 a.m.

An overview of end-users perspective on extractables and leachables (E/L) and several key end-users challenges from the survey (end users and CROs) will be discussed. These challenges include alignment of extractables protocols, risk assessment methods, and lack of regulatory inputs on how the proposed standard fit into the overall E/L qualification of Single-Use Systems (SUS).

Michael Eakins, Ph.D.
Vice Chair, USP Packaging & Distribution Expert Committee
Principal Consultant
Eakins & Associates
East Windsor, NJ

Dr. Michael Eakins is the Founder and Principal Consultant of Eakins & Associates with over 35 years' experience in pharmaceutical research and development. At Eakins and Associates, Michael provides experience and advice on parenteral primary packaging, especially on glass delamination and glass defects, the selection and product development in glass and plastic pre-filled syringes, and on extractables and leachables for parenteral packaging components. He regularly lectures on these topics worldwide for the USP.

Michael was responsible for the pharmaceutical development of diagnostic radiology products at E. R. Squibb and Bristol-Myers Squibb and for global packaging initiatives for contrast media at Bracco SpA.

Michael was the Vice-Chair of the USP Packaging, Storage and Distribution Expert Committee in the 2005-2010 and 2010-2015 cycles and is currently Vice-Chair of the USP Packaging and Distribution Expert Committee for the 2015-2020 cycle. He is an active member of the Parenteral Drug Association, being the co-chair of the Glass Defects Task Force that revised Technical Report 43 and is a member of the Elastomers and Seals Defects Task Force. He obtained his Ph.D. from London University and has contributed to over 60 publications and 8 USA patents.

Presentation Abstract
Overview of USP's Approach to Assessing Extractables and Leachables
Tuesday, June 21, 2016, 8:30 a.m. – 8:50 a.m.

USP General Information Chapter <1663> *Assessment of Extractables Associated with Pharmaceutical Packaging/Delivery Systems* describes a framework for considering the issues associated with the proper design and justification of the extraction process used to assess the potential impact of contact between a packaging material and a drug product. This chapter together with chapter <1664> *Assessment of Drug Product Leachables Associated with Pharmaceutical Packaging/Delivery Systems*, provide a scientific basis for the approach to revise three USP General Chapters covering elastomers, glass and plastic materials of construction both for pharmaceutical packaging/delivery systems and for pharmaceutical manufacturing components.

Chapter <661> covering plastic materials has undergone a major revision in 2015 and is now split into two parts <661.1> *Plastic Materials of Construction* and <661.2> *Plastic Packaging Systems for Pharmaceutical Use*. A further revision is planned to be published in the Pharmacopeial Forum (PF) in July 2016. A new chapter <661.3> *Plastic Components and Systems used in Pharmaceutical Manufacturing* has been published in the PF in May 2016. The presentation will review the current status of

<661.1> and the background and the development of <661.3> as an introduction to the Workshop.

Jennifer Goode, BS
Scientific Reviewer, Office of Device Evaluation
FDA, Center for Devices and Radiologic Health (CDRH)
Silver Spring, MD

Jennifer L. Goode, BS, Biomedical Engineer is currently on detail to the Office of Device Evaluation at FDA where she is responsible for biocompatibility issues associated with guidance development and training. Ms. Goode has been a premarket reviewer for over 22 years, with experience reviewing devices and combination products for surgical and interventional treatment of the peripheral vasculature, as well as cardiac monitoring, pacing, neurology and obstetrics and gynecology devices. For the past ten years, Ms. Goode has served as an FDA primary liaison to several ISO Working Groups responsible for the development of international standards for the biocompatibility evaluation of medical devices, including ISO 10993-1 and ISO 10993-4. Since 2008, Ms. Goode has been one of two Office of Device Evaluation representatives to the Biocompatibility Standards Task Group (STG) at the Center for Devices and Radiologic Health. This Biocompatibility STG is responsible for coordinating FDA input to, and scientific review and recognition of all biocompatibility standards used by CDRH.

Presentation Abstract
Regulatory Expectations for Biocompatibility Testing for Medical Devices
Monday, June 20, 2016, 11:15 a.m. – 11:45 a.m.

Medical device biocompatibility evaluations may include leveraging of previously conducted biocompatibility testing, new endpoint-specific testing, or rationales for why particular biocompatibility endpoints do not require additional assessment. This presentation will provide an overview of how risk assessment and testing can be used to support a medical device biocompatibility evaluation for submissions to the Office of Device Evaluation (ODE) in the Center for Devices and Radiological Health (CDRH). In addition, Ms. Goode will discuss how information from USP <87> and <88> testing can be used within the context of a medical device regulatory submission.

James Hathcock, Ph.D.
USP <661.3> Plastic Systems Used for Manufacturing Pharmaceutical Products Expert Panel Member
Senior Director
Pall Life Sciences
Port Washington, NY

Dr. James Hathcock is Senior Director of The Regulatory and Validation Consulting Team at Pall Life Sciences, which includes responsibility for the extractables and leachables characterization strategy to support the safe and successful end-user implementation of technologies enabling pharmaceutical manufacturing. Since joining Pall in 2008, James has been actively involved in chemical and performance characterization of Medical and Biopharmaceutical products, as well as relevant technical packages supporting regulatory filings. Prior to joining Pall, James was an assistant professor of hematology at the Mt. Sinai School of Medicine in New York City, where he served as director of a protein production and purification core laboratory. He is a member of the PDA, ASTM, ISPE, and BPSA organizations.

Presentation Abstract
Vendor Expectation: What is the problem to be solved?
Tuesday, June 21, 2016, 9:55 a.m. – 10:15 a.m.

The accelerated drive toward lean pharmaceutical manufacturing, single use technology adoption, and continuous manufacturing for the on-demand production of low cost, universally-accessible therapeutics, has led to an increased quality-management responsibility on suppliers to provide reasonable, relevant, state-of-the-art characterization profiles for polymeric materials intended for use in pharmaceutical processing. Some level of scientifically-reasoned standardization of these characterization profiles that properly align with end user expectations as well as regulatory requirements can serve as a tremendous beacon to both simplify and align the supplier community while providing added value to end users. Starting with understanding the central purpose a standard or consensus end-user requirement is intended to achieve, we share experiences, challenges and lessons learned in trying to achieve and align to a tractable, meaningful, industry-consistent standard.

Desmond G. Hunt, Ph.D.
Sr. Scientific Liaison, Global Science and Standards Division
U.S. Pharmacopeial Convention
Rockville, MD

Dr. Desmond G. Hunt is a Sr. Scientific Liaison in the Global Science and Standards Division at the United States Pharmacopeial Convention. For the 2010-2015 revision cycle, he is responsible for assisting USP Expert Committees, Packaging and Distribution, and Dosage Forms, in the development and revision of USP Standards. Dr. Hunt has over 15 years of research experience and prior to joining USP, in 2005, was a Research Fellow at the National Institutes of Health, Bethesda, MD, USA. Dr. Hunt has conducted a number of studies relating to the development and establishment of public standards for materials used for pharmaceutical packaging and has developed Pharmacopeial Education Courses on pharmaceutical packaging, the determination of particulate matter in parenterals and ophthalmic products and good storage and shipping practices. He is a member the Product Quality Research Institute Container-Closure and Extractable and Leachable Working Groups.

He obtained his Master of Science and Doctoral Degree from the University of Texas at Austin, USA.

John Iannone
USP Biocompatibility of Materials Used in Packaging Systems, Medical Devices and Implants Expert Panel Member
Director, Extractables & Leachables
Albany Molecular Research Inc. (AMRI)
Waltham, MA

John Iannone has a background in Biomedical Engineering from Boston University, where he later became a research engineer. Since entering the Biotech Industry 13 years ago, John has assisted many drug & medical device companies with the development of their product safety evaluation strategies. His areas of expertise include Material Qualification/ Biocompatibity, Extractables & Leachables/ Chemical Characterization, and attainment of either Biological or Toxicological risk assessments for medical devices, pharmaceutical container systems, bioprocessing systems, and combination products. John has given numerous technical presentations and has led several workshops on Extractable & Leachable Considerations, Biocompatiblity, Microbiology, and Regulatory Testing Requirements. John participates in the development of both industry groups' recommendations and regulatory guidelines. Additional responsibilities have included providing technical consultation to clients regarding unique testing requirements in an effort for them to meet global regulatory expectations.

Presentation Abstract
USP Proposal: Biological Activity/Biocompatibility
Monday, June 20, 2016, 1:45 p.m. – 2:15 p.m.

Biocompatibility has a history of being utilized to measure container/packaging compatibility, material suitability for medical product production, and overall qualification. The industry knowledge pertaining to the material science (including Extractables & Leachables), biological assay sensitivity, and relevant evaluation has progressed substantially in the last decade. This presentation will outline a proposal to better align the USP standards with industry expectations for the proper use of biological reactivity tests and assessments, as well as those regulations set forth in other related applications like medical devices (ISO 10993). Further, aspects that drive the necessity for the proposed revision will be outlined and discussed. Along with the other complementing presentations given in today's workshop, this presentation aims to move the way biocompatibility is viewed within the USP into the 21st century (or at least closer than it is now).

Edwin Jao, Ph.D.
Acting Quality Assessment lead (QAL)
U.S. FDA
Silver Spring, MD

Edwin Jao is an acting Quality Assessment lead (QAL) in the Office of process and Facilities (OPF), which is part of the office of Pharmaceutical Quality (OPQ). Edwin has been working with FDA for 13 years, covering various phases of drug product approval process, ranging from IND, NDA, ANDA, post approval supplement, and recently, manufacturing process and facilities. Edwin's expertise includes evaluation of drug substance and complex drug product dosage forms including MDI, DPI, and nasal spray. Prior to joining FDA, Edwin worked in major pharmaceutical companies for 18 years with increasing responsibilities. Edwin holds a PhD in medicinal chemistry from Rutgers University.

Presentation Abstract

FDA's Expectations for Equipment Compatibility Studies for Manufacturing of Liquid Dosage Forms
Tuesday, June 21, 2016, 8:50 a.m. – 9:35 a.m.

Both cGMP compliance and application approval require satisfactory compatibility data for manufacturing equipment. Currently there is no specific law, compendial chapter, guidance, MAPP, and policy to clearly address this issue. The key points to be discussed in the presentation will be:

- Why are equipment compatibility studies needed?
- Review issue or GMP issues?
- What compatibility data should be provided?
- Similarities and differences between equipment and container/closure system in terms of compatability
- Compendial chapters and guidances for container/closure system the principles of which can be referenced
- Proposal for risk-based approach
- Case studies for consideration

The goal will be a recommendation for a OPQ wide policy in this regard from a risk based approach perspective, clearly delineating the regulatory expectation to the industry and harmonizing the internal review process

Dennis Jenke, Ph.D., MBA
Chair, USP <661.3> Plastic Systems Used for Manufacturing Pharmaceutical Products Expert Panel
Baxter Distinguished Scientist
Baxter International, Inc.
Round Lake, IL

Dr. Dennis Jenke is a Baxter Distinguished Scientist at Baxter Healthcare Corporation where he works with a team whose primary responsibility includes the assessment of material/product compatibility, specifically with respect to establishing the suitability for use of packaging systems, manufacturing systems and administration devices for pharmaceutical products (for example, leachables/extractables and product ingredient binding). He has published extensively in the areas of analytical chemistry, environmental science and material/solution compatibility and serves as an expert reviewer for numerous pharmaceutical and analytical journals, He is the author of the book Compatibility of Pharmaceutical Solutions and Contact Materials; Safety Considerations Associated with Extractables and Leachables and a contributing author to the Leachables and Extractables Handbook. Dr. Jenke is a member of industry groups whose charter is to establish best demonstrated practices in the area of material/solution compatibility including:

- Past Chair, Board of Directors, for the Extractables and Leachables Safety Information Exchange (ELSIE) Consortium;
- Member United States Pharmacopeia (USP) Packaging, Storage and Distribution Expert Committee;
- Chair, USP Expert Panel for Revision of Chapter <661>;
- Member, USP Expert Panels for Generation of USP Chapters on Extractables and Leachables (<1663> and <1664>),
- Chair, USP Expert Panel for Generation of Chapter <661.3> Plastic Manufacturing Systems;
- Chair, Chemistry Team, Product Quality Research Institute (PQRI) Extractables/Leachables in Parenteral and Ophthalmic Drug Products (PODP);
- Member, Association for the Advancement of medical Instrumentation (AAMI) ISO/TC194 Task Force, including Working Groups BE/WG11 (Allowable Limits for Leachable Substances), BE/WG12 (Sample Preparation and Reference Materials), BE WG`4 (Materials Characterization).

Dr. Jenke was recently included in The Medicine Maker magazine's Power List 2015 of the 100 most influential medicine makers.

Presentation Abstracts

USP General Chapter <661.3>: Plastic Components and Systems Used to Manufacture Pharmaceutical Drug Products
Tuesday, June 21, 2016, 11:00 a.m. – 11:40 a.m.

USP General Chapter <661.3> contains tests, test methods and specifications for characterizing materials used to construct manufacturing components and for components used in manufacturing systems. In this presentation the philosophy behind the form and contents of <661.3> is discussed, specifically focusing on similarities and differences between packaging (addressed in <661>1> and <661.2>) and manufacturing. The essential aspects of <661.3>, including the Initial Assessment, the Risk Evaluation Matrix, and the Standard Extraction Protocol, are introduced. Finally, the difference between characterization (to drive selection) and qualification (to secure regulatory approval) is considered, specifically in the context of how <661.3> assessment, designed to support selection, could fulfil certain of the requirements for qualification.

Rationale for the Standard Extraction Protocol (SEP) used in <661.3>
Tuesday, June 21, 2016, 2:10 p.m. – 2:40 p.m.

The Standard Extraction Protocol (SEP) is applied in those high risk circumstances where extractables profiling of components is necessary. In this presentation the rationale behind the SEP is explained and the major features of the Protocol (extraction solvents, times and durations) are justified. Additionally, practical considerations in terms of generating extracts for different manufacturing components (e.g., bags, tubing, filters etc) are discussed.

David Jones, BSc, MSc, EurBiol, CBiol, MRSB, MTOPRA, European Registered Toxicologist
Expert Pharmaco-Toxicologist
Medicines and Healthcare Products Regulatory Agency (MHRA)
London, UK

After spending 8 years in Contract Toxicology and 11 years as a Toxicologist in the Pharmaceutical Industry, David currently work as an Expert Pharmaco-Toxicologist within the Licensing Division of the Medicines and Healthcare products Regulatory Agency (MHRA) in London, whom he joined in 1996.

His current role principally involves assessing nonclinical data for Clinical Trial Applications, both non-biological and biological. A further aspect of his job is to offer regulatory advice to companies on behalf of the MHRA or the EU's Committee for Human Medicinal Products (CHMP). He is one of the UK's accredited non-clinical experts to support the CHMP and the UK representative on the EU's Safety Working Party (SWP). David represented the EU in the ICH revision of the M3 Guideline and on the new ICH S10 Guideline.

David is now EU Rapporteur on the new ICH S11 (Juvenile Animal Studies) guideline and the Q&A document for ICH S3 (Toxicokinetics).

He works closely with the NC3Rs and represents the MHRA on a Governmental body dealing with animal welfare.

David is also a guest lecturer at the University of Surrey, the University of Wales, and the University of Leicester and a frequent presenter at conferences around the world.

Presentation Abstract
Advancing Biocompatibility Evaluation into the 21st Century
Monday, June 20, 2016, 9:30 a.m. – 10:15 a.m.

This presentation will briefly cover the existing paradigm for assessing biocompatibility and then indicate possible areas that need improvement or change. The talk will also briefly cover the revision of the medical device Directive in the EU.

Douglas Kiehl, MS
USP Biocompatibility of Materials Used in Packaging Systems, Medical Devices and Implants Expert Panel Member
Principal Research Scientist
Eli Lilly & Company
Fortville, IN

Douglas Kiehl is a Principal Research Scientist at Eli Lilly & Company, and currently leads the corporate Spectroscopy, Raw Materials and Extractables/Leachables team. His group's responsibilities include performing structural characterization of process impurities, related substances, degradation products and contaminants across the small and large molecule portfolios as well as acquisition and qualification of raw materials for both small and large molecule process streams. Additionally, his team characterizes chemical entities associated with extractable and leachable studies involving materials utilized in pharmaceutical processing, container/closure and drug delivery systems. Mr. Kiehl received B.S. and M.S. degrees from New Mexico State University and has over 34 years' experience with the application of mass spectrometry in the structural characterization of small molecules, 22 years of which are in the Pharmaceutical Industry. His research interests include the application of mass mapping and visualization techniques for the rapid characterization of highly diverse and complex molecular mixtures.

Presentation
USP Proposal: The Role of Chemical Characterization in Biocompatibility Testing
Monday, June 20, 2016, 2:15 p.m. – 2:45 p.m.

Biocompatibility describes the interaction of a living system or a specific tissue with components or materials comprising a finished medical device. Biocompatibility testing comprises a suite of *in vitro* and *in vivo* tests which are performed to determine the potential toxicity resulting from any bodily contact with a material or medical device. Biocompatibility testing is not trivial, and a meaningful assessment of biological effects includes consideration of multiple, interrelated factors. Chemical characterization plays an important role in biocompatibility testing. Particularly, chemical characterization can (1) provide an understanding of materials, (2) assist with failure mode analysis by providing a clear and scientifically sound rationale for a biocompatibility test failure, and (3) play an important role in reducing unnecessary use of live animals and *in vivo* testing. Furthermore, chemical characterization can provide information permitting the toxicological assessment of chemical entities that may predictably elicit irritation, sensitization or acute toxicity effects, and thereby inform appropriate and meaningful biocompatibility testing. Correlating chemical characterization with both *in vitro* and *in vivo* biocompatibility testing poses some significant challenges in that biocompatibility testing solvent and media are not necessarily compatible with analytical techniques required to permit

comprehensive chemical characterization of complex mixtures of diverse organic and inorganic chemical entities. Ideally, sample preparation and solvent selection should be analytically expedient while appropriately representing the extraction characteristics of the solvents employed in biocompatibility testing; particularly with failure mode analysis. This presentation will discuss the proposed role of chemical characterization as an important tool in implementation of a risk-based approach to biocompatibility testing, as well as challenges that must be addressed with applying chemical characterization in a comprehensive and meaningful manner.

Timothy J. McGovern, Ph.D.
Office Associate Director for Pharmacology/Toxicology
Office of New Drugs, CDER, US FDA
Silver Spring, MD

Dr. McGovern is currently an Office Associate Director for Pharmacology/Toxicology in FDA CDER's Office of New Drugs where he interacts with nonclinical review teams in the review of IND, NDA, and BLA submissions, advises Office Directors on nonclinical issues, and is involved in development of policy and guidances related to nonclinical and regulatory issues.

Prior to returning to FDA in 2013, he spent 5 years as a nonclinical/regulatory consultant where he assisted pharmaceutical companies in designing and conducting nonclinical programs including the safety evaluation of container closure systems. In a previous tenure at FDA, Tim was a primary nonclinical reviewer and then supervisor in the Divisions of Pulmonary and Allergy Products and Anesthetic, Critical Care and Addiction Products. He participated as a member of a PQRI working group that developed recommendations on the safety evaluation of leachables and extractables for Orally Inhaled and Nasal Drug Products.

Presentation Abstract

Regulatory Expectations for Biocompatibility Testing for Pharmaceutical Packaging Systems
Monday, June 20, 2016, 10:45 a.m. – 11:15 a.m.

The recommendations for and roles of biocompatibility testing for pharmaceutical packaging systems are described in numerous FDA guidances. The need for biocompatibility testing can depend on the type of packaging used as well as the product formulation. This testing can provide an initial screen for the compatibility of materials but in most cases does not adequately address potential safety issues associated with leachables derived from the materials. This talk will provide an overview of the recommendations and describe the role biocompatibility testing plays in the overall safety evaluation of packaging systems.

Daniel Norwood, M.S.H.P., Ph.D.
Co-Chair, USP Biocompatibility of Materials Used in Packaging Systems, Medical Devices and Implants Expert Panel
Executive Partner
SCIO Analytical
New Milford, CT

Dr. Daniel Norwood joined SCIO Analytical as Executive Partner in June 2015. Prior to SCIO Analytical, Dr. Norwood was a key technical employee at Boehringer Ingelheim Pharmaceuticals where he was successful in various pharmaceutical development roles, including Director Physical and Chemical Analysis. In June 2015, Dr. Norwood retired with the title of Distinguished Research Fellow in Analytical Development. Prior to joining Boehringer Ingelheim, Dr. Norwood, with Dr. Feinberg, founded the Structural Chemistry Group at Magellan Laboratories, later Catalent Pharma Solutions, which became widely recognized for its work in pharmaceutical impurity structure elucidation, and in leachables and extractables characterization. Prior to Magellan, he was a pharmaceutical development scientist at the Glaxo Research Institute.

Dr. Norwood is an internationally recognized expert in the field of leachables and extractables assessment in pharmaceutical development and manufacturing. He served as chair of the widely-quoted Product Quality Research Institute (PQRI) Working Group on leachables and extractables in inhalation drug products. He is also a member of the PQRI Working Group on leachables and extractables in parenteral and ophthalmic drug products (PODP), and has served on various technical teams of the International Pharmaceutical Aerosol Consortium on Regulations and Science (IPAC-RS). Since 2010, he has served as a member of the USP Expert Committee on Packaging, Storage and Distribution where he chairs the subcommittee on extractables and leachables. Dr. Norwood has received several industry awards, including the CEO's Award from Glaxo (1994), the President's Award from Boehringer Ingelheim (2007), the Excellence in Research Award from PQRI (2009), and the Award for an Innovative Response to Public Health Challenges from USP (2013). Dr. Norwood completed his bachelor's degree in Biochemistry at Virginia Tech and his doctorate degree in Environmental Chemistry at the University of North Carolina at Chapel Hill, School of Public Health.

Presentation Abstract
Expectation and Goals for the <87> and <88> Workshop
Monday, June 20, 2016, 8:30 a.m. – 9:00 a.m.

In 2014, the USP General Chapters - Packaging and Distribution Expert Committee took on the task of revising several USP chapters related to the concept of biocompatibility. At its essence, biocompatibility related to pharmaceutical packaging systems, components, raw materials and medical devices is the ability to be in contact with a living system without producing an adverse effect. The general

chapters being considered for revision include <87> and <88> which include, respectively, *in vitro* and *in vivo* tests and standards for biological reactivity, and <1031> which is an informational chapter related to biocompatibility. In 2015, the USP PDEC formed an Expert Panel to consider and revise these general chapters.

This presentation will discuss the reasons for considering revision of these chapters, the process of revision, the guiding principles of the revision process, and questions being considered during the process. The presentation will act as a general introduction to the Workshop and implore the audience participants to provide critical and constructive feedback and opinions to the process.

Cheryl L.M. Stults, Ph.D.
Co-Chair, USP Biocompatibility of Materials Used in Packaging Systems, Medical Devices and Implants Expert Panel
Principal
C&M Technical Consulting, LLC
San Mateo, CA

Dr. Stults is Principal at C & M Technical Consulting, LLC, working with various local and global companies to advance the development of parenteral and inhalation products. Her primary area of focus is on device and packaging materials analysis and characterization for purposes of selection, qualification and control. She holds a Ph.D. in Analytical Chemistry from Michigan State University and a Masters in Management from Aquinas College. Prior positions include: Senior Fellow at Novartis Pharmaceuticals Corporation, Assistant Research Professor at San Francisco State University and Quality Associate at a Johnson & Johnson owned company. She was co-editor of the Leachables and Extractables Handbook (Wiley 2012) and has been a member of the Board of Directors for two consortia: Extractables and Leachables Safety Information Exchange (ELSIE) and International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS). She has led industry initiatives focused on pharmaceutical packaging and device materials and has continued involvement as an IPAC-RS Science Advisor participating in global outreach and materials related initiatives. Dr. Stults is currently a USP Packaging and Distribution Expert Committee member contributing to development and revision of materials-related chapters.

Presentation
USP Proposal: Process Flow for Determining Biocompatibility Testing—A risk-based approach
Monday, June 20, 2016, 1:15 p.m. – 1:45 p.m.

For many years biological reactivity testing has played a key role in assessing the safety of packaging, delivery, manufacturing systems and medical devices. The current USP <1031> chapter provides guidance regarding the selection of tests through the use of a decision tree. The USP modernization of the approach to biocompatibility testing seeks to incorporate a risk-based approach that is aligned with ISO 10993 and involves consideration of multiple sources of information in addition to testing. A general process for biocompatibility risk analysis, evaluation and control will be described and discussed. The utilization of a comprehensive risk-based, product specific approach is anticipated to streamline testing and provide a foundation that will appropriately support development and lifecycle management of biocompatible products.

Ken Wong, Ph.D.
USP <661.3> Plastic Systems Used for Manufacturing Pharmaceutical Products Expert Panel Member
Deputy Director
Sanofi Pasteur
Nazareth, PA

Ken Wong leads Sanofi Pasteur E&L program for all vaccine and biologic development projects and in-line supports at Swiftwater site. He is responsible overall E&L evaluation and qualification processes, risk ranking model design, material change strategy development, and E&L study design for both single-use systems and container closure systems qualifications with over 16 years of Biopharma industry experiences.

Mr. Wong is currently representing Sanofi on

1) ELSIE material working group
2) ASTM extractable subcommittee and
3) E&L subteams within the Biophorum Operations Groups (BPOG).

He is honored to be serving this USP <661.3> as an expert panel member.

Presentation Abstract
User Expectation: What is the problem to be solved?
Tuesday, June 21, 2016, 9:35 a.m. – 9:55 a.m.

An overview of end-users perspective on extractables and leachables (E/L) and several key end-users challenges from the survey (end users and CROs) will be discussed. These challenges include alignment of extractables protocols, risk assessment methods, and lack of regulatory inputs on how the proposed standard fit into the overall E/L qualification of Single-Use Systems (SUS).