PharmaED RESOURCES, Inc.

Extractables, Leachables, & Elemental Impurities 2017

Ensuring Quality, Safety, and Regulatory Compliance for Drugs & Biologics

March 6–7, Racquet Club of Philadelphia

Featuring Lessons Learned and Case Studies from Industry Experts:

- **Updates & Case Studies on the Latest Compliance Implications of USP <232> and <233> and ICH Q3D Risk Assessment Filing Guidelines for Elemental Impurities**
  - **Andre Hermans, Principal Scientist, Merck**
  - **Timothy Shelbourn, Research Scientist, Eli Lilly & Co.**
  - **Cindy Qin, Principal Scientist, Boehringer-Ingelheim**
- **The Risk Assessment of Extractables—A Toxicological Window of Opportunity**
  - **William P. Beierschmitt, Research Fellow, Pfizer**
- **BPOG's Leachables Best Practice Guide: Study Design and Analytical Methods**
  - **Seamus O'Connor, Manager QC Chemistry Method Development, Regeneron**
- **Challenges & Consequences for the Medical Device Industry by the Revision of Three Major ISO 10993-Standards**
  - **Dr. Albrecht Poth, Scientific Director, Dr. Knoell Consult, GmbH**
- **Extractables Screening of Polyproylene Resins for the Identification of Suitability for Use Hazards**
  - **Dennis Jenke, Distinguished Scientist, Baxter**

And Comprehensive Coverage On:

- **Clearance of E&L from Single-Use Technologies through Ultrafiltration/Diafiltration**
- **Leachable Risk Assessment of Dosing Devices for Parenteral Applications**
- **Extractables & Leachables Studies on Single-Use Components in Biomanufacturing**
- **Addressing Challenges with Polysorbate 80**
- **E&L Test Methodologies for Lyophilized Drug Products**
- **Industry Working Group Updates: PQRI & BPOG**

With Representation From:

Boehringer Ingelheim · Pfizer · AMGEN · janssen Pharmaceutical Companies of Johnson & Johnson · MERCK Be well · Lilly · TRIAD · REGENERON science to medicine · SANOFI PASTEUR · Baxter · Allergan · eurofins Lancaster Laboratories · Genentech A Member of the Roche Group · NSF Health Sciences · ASPEN RESEARCH Our Vision is to Help You Realize Yours™ · Boston ANALYTICAL · West By your side for a healthier world™ · Material Needs CONSULTING Medical Device and Packaging Services · JordiLabs Material Solutions. Uncompromising Integrity. · Agilent Technologies

PharmaEd Resources, Inc. • 2810 Robeson Park Drive • Champaign, IL 61822
tel. 217.721.5774 • *web.* www.pharmaedresources.com

Monday, March 6

8:00 *Registration & Complimentary Breakfast & Chairperson's Welcome*

Critical Issues – Updates & Case Studies on the Latest Compliance Implications of USP <232> and <233> and ICH Q3D Guidelines for Elemental Impurities

8:30 **ICH Q3D Risk Assessment for New Filings – Examples and Regulatory Interactions**

Andre Hermans, Principal Scientist, Merck & Co., Inc.

Since the early implementation date of 01 June 2016 of the ICH Q3D guidance for new drug product filings in the United States and the European Union, Merck and Co. has conducted several elemental impurity risk assessment for a variety of drug products ranging from to small molecule solid oral dosage products to injectable biologics formulations. The risk assessment approaches for several of these products and their inclusion in filing dossier are being presented. Both drug product testing and component based approaches were successfully applied to demonstrate a low risk of elemental impurities in finished drug products. Further, early regulatory interactions experienced during filing review are being discussed.

9:00 **Control and Monitoring Strategies for Elemental Impurities in Active Pharmaceutical Ingredients**

Cindy Qin, Ph.D., Sr. Principal Scientist, Boehringer Ingelheim Pharmaceuticals Inc.

Control and monitoring of elemental impurities in drug substance and drug product have recently become a hot topic due to the new USP 232, 233 and ICH Q3D guidelines. The pharmaceutical industry has been diligently working with regulatory authorities to generate practical strategies for global implementation of these elemental impurity guidelines. Although the new guidelines only apply to the final drug products, control and monitoring of elemental impurities in active pharmaceutical ingredients (drug substances) play a major role in ensuring compliance of final drug products with regulatory requirements. This presentation will discuss strategies and practices for control and monitoring of elemental impurities in active pharmaceutical ingredients, including risk assessment strategies, analytical method development/validation approaches and challenges, analytical measurement considerations, and documentation of risk assessment and associated analytical testing results. The investigation of out-of-specification and/or suspect results will also be discussed. The practices and strategies used for drug substances can be adopted for the final drug products and excipients.

9:30 **ICP-OES and ICP-MS Method Development and Validation for the Quantification of Elemental Impurities in Large and Small Molecule Drug Substances and Products**

Timothy Shelbourn, Research Scientist, Eli Lilly and Company

Methodologies have been developed and validated for several small molecule and large molecule drug substances and drug products using ICP-OES and ICP-MS (with collision cell) for various elemental impurities. A variety of sample types and preparation schemes will be presented including direct organic solvent dissolution, aqueous dilution, and microwave digestion using nitric, hydrochloric and hydrofluoric acids. Elements and their associated toxicological limits were selected from USP <232> and ICH Q3D step 2b. The presentation will include some discussion of compliance strategy and the setting of internal specifications. Methods were validated per ICH Q2r2 and USP <233>. Acceptance criteria for accuracy, precision, linearity, and range were per USP <233>.

10:00 *Coffee & Networking Break*

10:25 **The Changing Regulatory Environment Concerning Elemental Impurities and Container / Closure Systems**

Diego Zurbriggen, Supervisor, Leachables/ Stability, West Pharmaceutical Services

Elemental impurities in drug products can arise from multiple sources such as raw materials, excipients, manufacturing equipment and container closure/delivery systems. The Permitted Daily Exposure (PDE) and controls will pose challenges to the industry due to the multiple contributing sources and unique drug product requirements. Risk based approaches for elemental impurities are outlined in ICH Q3D and USP <232> and <233> and include specific elements to be consider from any source. Current specifications for extractable elements from elastomers and plastics are defined by USP and EP but these do not encompass all elements of concern. In addition the limits do not translate to drug product dosing, so the question remains on how elements of concern can be incorporated into a meaningful drug product risk assessment. The USP is the process of revising chapters for elastomers and addressing these issues. It has been noted that limits for elements will no longer exist, instead low levels of elements will be reported as found to be incorporated into a drug product risk assessment. This presentation will provide an overview of a risk-based approach for testing elastomeric closures for this topic. Extraction conditions, method parameters, and results will be discussed.

Panel Discussion

10:55 **Is the Industry Ready for the New Elemental Impurities Requirements?**

Michael Eakins, Eakins & Associates
Andre Hermans, Merck
Cindy Qin, Boehringer Ingelheim
Timothy Shelbourn, Eli Lilly & Co
Diego Zurbriggen, West Pharmaceutical Services
Dennis Jenke, Triad Scientific Solutions

E&L Risk Assessment—Toxicological Perspectives

11:25 **The Risk Assessment of Extractables—A Toxicological Window of Opportunity**

William P. Beierschmitt, Ph.D., D.A.B.T., F.A.T.S., Research Fellow, Drug Safety Research and Development, Pfizer, Inc.

An essential, critical matter for the toxicologist to consider during the development of a parenteral product is the risk assessment of extractables and leachables originating from components of the container closure system. While performing a comprehensive risk assessment on the leachables (i.e. the chemicals that actually do migrate into the drug during storage) is intuitive, assessing the safety profile of the extractables (i.e. the chemicals that might migrate into the drug during storage) can provide valuable information. Towards this end, a preliminary qualitative/quantitative risk assessment paradigm for extractables focusing on a subset of crucial endpoints (i.e. genetic toxicology, carcinogenicity, reproductive toxicology, irritation, and sensitization) will be described, including actual case studies where this methodology was employed. Since in the subsequent migration studies the impurities identified will typically be a subset of the extractables, assessing the latter for safety issues is a "window of opportunity" for the toxicologist to identify a potential safety concern prior to proceeding with the final leachable work.

11:55 **Comparison of USP and BPOG Extractable Data for Autoclaved PES Filters**

Chien-Ju (Cherry) Shih, Ph.D. Senior Scientist, Regulatory and Validation Consulting, Pall Life Sciences

A primary concern limiting the rapid adoption and implementation of single-usetechnology has centered on standardizing single use component data packages to be used for end-user risk assessments.

In this presentation, we will share experimental findings from the execution of two standardized extractable protocols proposed by the Biophorum Operations Group (BPOG) and the USP <665> panel on an autoclaved Polyether sulfone (PES) sterilizing grade filter.

Specifically, filter capsules were extracted either in 6 suggested solvents for 30 min, 1 day and 7 days according to the BPOG protocol, or in solvents for 24 hrs per the USP protocol, with extract samples analyzed by headspace GC/MS, direct injection GC/MS, LC/UV/MS and ICP/MS.

The extractable results from GC/MS and LC/MS will be discussed in detail. Overall, the extractables observed in USP solvents (pH 3/salt, pH 10 buffer and 50% Ethanol) captured majority of extractable observed in other BPOG solvents (Water, 0.1M H_3PO_4, 0.5N NaOH, 5M NaCl and 1% PS80). Differences in 50% Ethanol and 1% PS80 profiles will also be shared, with the vast majority of compounds detected at the < 0.5 ppm level.

The experiences and lessons learned from this presentation are crucial to furthering the development of effective and practical standardized protocols for the use of single-use technologies. The aim is to help drive understanding and consensus approaches that serve the best interest of end-users, regulators, suppliers, and patients.

12:25 *Complimentary Lunch*

Regulatory Spotlight—Major Revisions to ISO 10993 – Implications for the Industry

1:45 **Challenges And Consequences for the Medical Device Industry by the Revision to the Three Major ISO 10993-Standards**

Dr. Albrecht Poth, Toxicologist
Dr. Knoell Consult, GmbH

Three major standards, ISO 10993-1, -17 and -18 are going to be revised. The revision of ISO 10993-1 "Evaluation and testing within a risk management process" will include additional requirements to be evaluated and only the chemical characterisation will be mandatory, while all other toxicological endpoints will be evaluated within a toxicological risk assessment.

A major revision will be made on ISO 10993-18 to incorporate the technical and scientific experience developed during the last 10 years since its publication, including a more detailed description of experimental requirements for the investigation of extractables and leachables and a revision of the stepwise chemical characterisation process, including the setting of the analytical evaluation thresholds (AETs) in alignment with the TTC-concept.

A major revision of ISO 10993-17 on allowable limits for leachable substances is in works. Risk assessment approaches to use the concept of Threshold of Toxicological Concern (TTC), already established and accepted for genotoxic pharmaceutic impurities, are in discussion. If it can be shown that an impurity is below the TTC, then it is assumed that the chemical substance is of no significant risk. Based on the proposed revisions it can be foreseen that in future the chemical characterization will be a key parameter in the risk management process of medical devices.

2:25 **Potential Leachable Risk Assessment of Dosing Devices for Parenteral Application**

Ping Wang, Ph.D., Sr. Manager, Janssen R&D
Dominick DeGrazio, Associate Scientist, DPD-LM , Janssen R&D

Dosing devices (such as iv bags, iv admin sets, etc) are the last product contact materials before the drugs are administrated to the patients. The potential leachable risks are of high safety and regulatory concern. The dosing devices are usually made of various polymeric materials, such as polyethylene, polypropylene, silicone, PVC, etc. Though it is impossible to test all dosing devices on the open market, some commonly used devices (20+) are tested for their potential leachables in this study. A generic biologics formulation is used to perform the in-use simulation. The leachables from these devices were measured using GC, HPLC, and ICP. The potential safety risk of these leachables from the dosing devices will be discussed.

3:05 *Coffee & Networking Break*

3:30 **Extractables and Leachables Assessments for Lower Risk Dosage Forms**

Michael A. Ruberto, Ph.D., Material Needs Consulting, LLC

Most of the newly published "best practices" for extractables and leachables testing for container closure systems and manufacturing equipment are focused on high risk dosage forms, such as inhalation, injectable, and ophthalmic drug products. But what are the regulatory expectations for lower risk dosage forms such as oral and topical? The best practices state that a "risk-based approach" may be applicable and that "low risk doesn't mean no risk." Selecting materials of construction for the container closure systems and manufacturing equipment that are regulated for food contact applications according to 21 CFR 174-186 is a requirement; however, demonstrating the actual compliance with the appropriate type of food products is no longer a "check box" activity. Should the testing requirements be different for aqueous formulations compared to those having high concentrations of organic co-solvents? This presentation will focus on pro-active approaches for determining the leachables risk for primary and secondary packaging used with solid and liquid oral dosage forms as well as topical drug products. A step-by-step approach for interpreting and utilizing the indirect food additive regulations will be provided. Examples of performing assessments in the form of "paper exercises" versus E&L testing will be discussed. Case studies will include:

- Effectively assessing the leachables risk of bottles constructed from various types of polymers
- The impact of closures and corresponding liners and/or induction seals on leachables
- How to efficiently determine the leachables risk of adhesive labels
- E&L study plans for plastic and metal tubes used to package topical drug products

4:10 **Evaluation of E&L Test Methodologies for Lyophilized Drug Products**

Ken Wong, Deputy Director, Sanofi Pasteur

In the current USP <1664>, the powder for injection formulation risk associated with its interaction with packaging component were downgraded from Medium (listed in FDA 1999 guidance document for industry on container closure systems for packaging human drugs and biologics) to Low. A case study will be presented to examine the appropriate level of analytical test methodologies for an injectable lyophilized drug product with low likelihood of interaction with packaging component. Lesson learnt was implemented in future E&L study plan for lyophilized formulation with significant test cost savings.

Industry Working Group Update—PQRI

4:40 **Points to Consider on Risks to Quality and Safety of Parenteral Drug Products (PDP) from the Product Quality Research Instituted (PQRI)" Leachables and Extractables Working Group.**

Diane Paskiet, Director of Scientific Affairs, West Pharmaceutical Services

Studies for qualifying pharmaceutical containment and delivery systems should be guided by risks to patient safety and final product quality. The degree of testing required for the materials of construction, finished components, as well as complete packaging systems should be justified. Evaluations for extractables/leachables on PDP, ophthalmic drug products, large volume parenteral and biologics will have unique considerations. The chemistry of the materials individually and together with the final systems will provide the basis for understanding compatibility for various applications. This presentation will provide case examples related to compatibility of components and systems associated with aspects of safety and quality. Chemical characterization and simulation data acquired by the PQRI Leachables and Extractables Working Group will be referenced.

Tuesday, March 7

8:00 *Complimentary Breakfast*

Research Spotlight—Extractables Studies on Polymers and Resins

8:30 **Extractables Screening of Polypropylene Resins for the Identification of Suitability for Use Hazards**

Dennis Jenke, Distinguished Scientist, Baxter

Pharmaceutical products are packaged in containers so that they can be manufactured, distributed and used. Because extractables from such containers are precursors of leachable impurities in the product, extractables represent potential hazards to user safety.

Polypropylene resins are frequently used as materials of construction for packaging of liquid parenteral drug products. Thus extractables profiling of polypropylene resins may be an effective means of hazard identification associated with the resin's safe use.

Twenty-one PP resins were extracted using aqueous and organic extraction solvents and the resulting extracts were screened for extractables using appropriate general chemistry, chromatographic and spectroscopic methodologies. The resulting extractables profiles were toxicologically reviewed by a defined process to identify potential hazards given a specified therapeutic application involving chronic use of a large volume aqueous parenteral drug product (LVP).

The organic extractables profiles of individual PP resins were variable in terms of the individual extractable identified and their extracted levels, consistent with high variability in PP resin formulations and PP manufacturing. However, the profiles were similar in terms of the groups of extractable measured. Thus, for example, all the resins had extractables associated with antioxidants as all the resins contained antioxidants but the specific extractables for a given resin depended on the specific antioxidants present in that resin. Few of the targeted extractable elements were present in the extracts at measurable levels although most resins had measurable levels of extracted aluminum, silicon and alkali and alkaline earths.

A worst case extractables profile (all the extractables measured in individual resins at their highest levels) was toxicologically reviewed considering an aqueous large volume parenteral (LVP) drug product. This review established certain extractables as potential hazards whose actual toxicological safety risk assessment would require more rigorous data and a more rigorous process than those used for hazard identification.

9:10

The Effect of Solvent Polarity Modifiers on the Extractables from HDPE, TPU, and PEBA Resins

Roger Pearson, Ph.D., President Analytical Services, Aspen Research Corporation, Maple Grove, MN, USA

Extractables studies have become an integral part of product development in pharmaceutical products and also in medical devices. In the pharmaceutical arena extractables testing of container/closures is used to set the stage for leachables studies where leachables in the drug product is the measured endpoint for risk evaluation. In the medical device area the extractables information become the end product for risk evaluation as they are not normally analyzed for in the body. Guidance for medical device suggests sequential extractions of the device of interest until a compound of interest in the extraction solvent falls to 10% of it's initial extraction concentration. In the single use world, concentrations occurring over time and over different time periods have been considered.

In all cases, when designing extractable studies the questions always arise as to what solvent, what temperature and for what durations. This presentation will show findings from a study of extractables from resins of HDPE, TPU, and PEBA. The study employed ethanol and isopropanol (IPA) as polarity modifiers and hexane as the most non polar solvent. Resins were extracted (2 grams per 10mL, ISO 10993-12) for 24 hour time periods at 50°C. Sequential extractions were decanted at the end of each 24 hour period and replaced with fresh solvent. One extraction was carried out without replacing the solvent for 7 days. Modifier concentrations used were 10%, 50%, 75%, 95% ethanol, 100% IPA and hexane. Extracts were analyzed by HPLC-DAD-TOFMS and selected extracts by GC/MS and ICP/MS. The study provides a unique data set to compare effects of modifier type (ethanol and IPA), modifier concentration (10%, 50%, 75%, and 100%), and extraction duration (1 day, 7day) on detected extractables and their concentrations from three widely used polymers.

9:50 *Coffee & Networking Break*

Industry Working Group Update—BPOG

10:15

Biophorum Operations Group (BPOG) Leachables Best Practice Guide: A Focus on the Study Design and Analytical Methods

Seamus O'Connor, Manager QC Chemistry Method Development, Regeneron

The BPOG leachable working group has authored a comprehensive best practice guide for use in assessing single use systems from a leachable perspective. This guide provides a framework from which to generate a thorough and comprehensive leachable study from beginning to end including study and sampling design and analytical methods. A model for assessing the risk potential for leachables entering product streams is presented to provide a tool for practitioners to reference throughout the leachable study process.

10:55

SUS Leaching Propensity Assessment

Laszlo Litauszki, Ph.D., Associate Director, Engineering Systems Validation Lead, Shire

A risk based qualification approach requires a robust risk assessment methodology. The risk assessment must be science based, comprehensive, flexible and pragmatic. BPOG has developed a risk assessment guideline for the Biotechnology industry based on how Single Used Systems (SUS) are typically used. The guidance provides the framework and includes technical elements to be considered in assessing Leaching Propensity, i.e. the likelihood of unknown leachables entering the process stream and remaining in the Final Drug Product (FDP) at a concentration of concern. The guidance provides a level of flexibility and can be adjusted to individual companies risk mitigation practices while still keeping a comprehensive approach. The guideline is also intended to support regulators as a harmonized platform to assess

the FDP Quality Risk originating from SUSs in Biopharmaceutical manufacturing, as it harmonizes the currently varying approaches into a uniform, structured model.

The model considers leaching kinetics and thermodynamics. A rating system is used to assess Leaching Propensity based on SUS material of construction and exposure conditions. The Leaching Propensity Assessment ranks the Single Use Systems and provides a scientific rationale when an Extractables & Leachables study is needed and where it may not provide added value. An example of the Leaching Propensity Assessment will be applied to a typical manufacturing process using SUS.

11:35 **Extractables Studies on Single-Use Components in Biomanufacturing – Collaborative Efforts from End User and Supplier**

Weibing Ding, Ph.D., Principal Scientist, Process Development, Amgen
Sara Ullsten, Ph.D., R&D Section Manager, GE Healthcare

The use of disposable equipment in the biopharmaceutical industry is rapidly increasing as it offers advantages in terms of flexibility, no batch-to-batch cross contamination, and reduced capital expenditure.

The materials used to fabricate single-use systems (SUS) are primarily polymeric and extractables data is a key element of SUS implementation to ensure patient safety. While biopharmaceutical companies are responsible for safe use of SUS and for performing comprehensive leachables evaluation, providing extractables data is supplier's responsibility. In the absence of an industry standard or specific regulatory requirements for generating extractables data, a wide range of extractables study protocols are being used in the industry.

An extractables case study will be presented addressing the user requirements for extractables data, approaches and challenges to standardization and its benefits to the industry from a supplier and end-user perspective.

12:05 ***Complimentary Lunch***

Critical Issues—E&L Clearance Through Ultrafiltration/Diafiltration Operations in Biopharmaceutical Manufacturing

1:15 **Clearance of Extractables and Leachables from Single-Use Technologies Through Ultrafiltration/Diafiltration Process in Various Chemical Environments**

Kate Lee, Process Development Engineer, Genentech

Single-use technologies are increasingly adopted in the clinical and commercial manufacturing for their reduced risk of cross-contamination, increased process flexibility, and elimination of cleaning validation. However, implementation of single-use technologies have been restricted due to a number of concerns, with the most commonly cited being the presence of extractables and leachables (E/L) impacting patient safety and product quality. Due to a lack of data on clearance of E/L, overly conservative estimates of E/L are often used in the risk assessment by applying the assumption of total carryover of initial E/L to the final product. This results in a time-consuming, costly, and extensive E/L assessment for single-use technology.

Here, we provide a scientific approach to quantify and confirm the clearance of E/L through Ultrafiltration/Diafiltration operations in biopharmaceutical manufacturing. Results from the study indicated clearance of defined E/L in protein solutions. In particular, the study will focus on the E/L clearance trends seen in various chemical environments such as protein concentrations and protein drug types. The results from this study will contribute to the simplification of the E/L risk assessments and allow increased speed and greater flexibility when implementing single-use technologies in biopharmaceutical manufacturing.

1:55 **Extractables and Leachables: Challenges with Polysorbate 80**

Michelle J. Kolodziejski, Principal Chemist for the Extractables/Leachables Testing Department at Eurofins Lancaster Laboratories

According to J.T.Baker, "Polysorbate 80 (PS 80) is a mixture of oleate esters of sorbitol and sorbitol anhydrides, predominantly consisting of the monoester, condensed with approximately 20 moles of ethylene oxide." PS80 is used to stabilize protein therapeutics in many pharmaceutical formulations including parenteral, ophthalmic, oral and topical preparations. Because PS80 is an integral part of the formulation for many pharmaceutical products it has become one of the most requested solvents for evaluating extractables profiles. As PS80 is a mixture of molecules of varying size, rather than a single uniform compound it presents many challenges for the laboratories that have to analyze it chromatographically and spectroscopically. In this presentation we will elucidate the complexities of PS80 and present data showing the mass spectral identification of the major breakdown products of the molecule, its accelerated degradation in glass when incubated at elevated temperatures for more than 7 days and its extraction power compared to other common extraction solvents.

2:35 ***Coffee & Networking Break***

2:50 **Characterization of IV Bag for Extractables**

Eric Hill, Director, Boston Analytical

Polymeric materials used for pharmaceutical packaging must be thoroughly characterized and evaluated for their suitability of use. The USP's recent revision to monograph <661> includes monographs <661.1> *Plastic Materials of Construction* and <661.2> *Plastic Packaging Systems for Pharmaceutical Use*, and references

to <1663> *Assessment of Extractables Associated with Pharmaceutical Packaging/Delivery Systems* and <1664> *Assessment of Drug Leachables Associated with Pharmaceutical Packaging/Delivery Systems*. These monographs provide a holistic approach to characterization of drug product packaging materials from resin to final package system – ensuring patient safety. A case study is presented for an extractables evaluation of an IV bag used to store aqueous solutions used for treatment of blood plasma. This case study includes testing according to USP monographs <661.2> and <1663>. A summary of the initial risk assessment and study design will be discussed. Data for the materials characterization study and simulation study are provided, including Headspace GC-MS, liquid injection GC-MS, LC-MS, and ICP-MS data. Tables of compounds identified using Boston Analytical's extractables compound database are presented.

3:30

Qualitative Assessment of Extractables from Single-Use Components Employed in the Storage or Manufacture of Biopharmaceuticals

Mark Jordi, President, Jordi Labs;
Smriti Khera, Global Marketing Manager, Agilent Technologies

Recent emphasis by the FDA as well as several high profile incidents have raised awareness as to the importance of the analysis of extractable and leachable compounds (E&L) from components employed in the storage or manufacture of biopharmaceuticals. The advent of single use bioprocess systems has introduced a new potential source for E&L's as these systems are often comprised of polymeric materials. Several working groups (BPOG, BPSA), the FDA and USP have issued guidance on methodologies for performing E&L analyses for systems in contact with pharmaceuticals. These documents typically indicate that mass spectroscopy methods should be applied for discovery of E&L's but provide little guidance as to the exact process which should be applied. In this talk, we will present an example analysis on a single use bioprocess system and use this case study to demonstrate an LC/MS and GC/MS software workflow for analysis of E&L's. This workflow allows for the fast identification of E&L's as well as rapid comparisons between samples. A new high-resolution LC/MS database consisting of over 1000 common E&L compounds and MS/MS spectra will be shown in order to quickly identify knowns from component extracts and perform early risk assessment using the references in the database. We will also describe differential analysis workflows for mining both LC/MS and GC/MS data and providing a convenient way of visualizing the large volume of data arising from these experiments and to facilitate presentation of results. Suggestions regarding method design with an emphasis on optimum standard selection will also be discussed.

4:00 ***Close of Program***

Extractables, Leachables, & Elemental Impurities 2017 is Sponsored By:

PharmaED RESOURCES, Inc.

PharmaEd Resources, Inc. • 2810 Robeson Park Drive • Champaign, IL 61822

About your conference destination:

The Racquet Club of Philadelphia is located in the heart of downtown Philadelphia, adjacent to beautiful Rittenhouse Square. From the conference venue, you can access many points of interest in Philadelphia including Independence Hall, the Kimmel Center, the Avenue of the Arts, numerous shops, and excellent restaurants!

Registration Information

Register for the conference using one of three options:
Online: www.pharmaedresources.com **Phone:** (217) 721-5774
Mail: 2810 Robeson Park Drive, Champaign, IL 61822

Please Complete the Following

FIRST NAME: _____

LAST NAME: _____

TITLE: _____

COMPANY: _____

ADDRESS: _____

ADDRESS: _____

CITY: _____ STATE: _____

ZIP: _____ COUNTRY CODE: _____

OFFICE PHONE: _____

MOBILE PHONE: _____

FAX: _____

E-MAIL: _____

VENUE INFORMATION:

Dates:	March 6–7, 2017
Venue:	The Racquet Club of Philadelphia
Venue Address:	215 South 16th Street Philadelphia, PA 19102
Venue Phone:	(215) 735-1525
Hotel Room Block:	The Warwick Hotel
Hotel Address:	220 South 17th Street Philadelphia, PA 19103
Hotel Telephone:	(215) 735-6000

Please register me for:

Extractables, Leachables & Elemental Impurities 2017

Standard Registration: $1,595
Early Bird Special: Register by Jan. 27th and save $200!
Call for government or academic discount

PAYMENT METHOD

CREDIT CARD REGISTRATION:

☐ CREDIT CARD ☐ VISA ☐ MASTERCARD ☐ AMEX

NAME: _____

CARD #: _____

EXPIRATION: _____ / _____

SIGNATURE: _____

BILLING ADDRESS: _____

CHECK REGISTRATION:

To pay by check, please provide a purchase order below. Please note that all payments must be received five (5) days prior to the conference to ensure space. Attendees will not be admitted to the conference without full payment.

PURCHASE ORDER #:

PLEASE NOTE:

PharmaEd Resources does not offer refunds. However, if you cannot attend after registering, we are happy to apply your registration fee to another PharmaEd Resources event, or transfer your registration to a colleague. Notice of cancellation must be received at least 5 days prior to the event.