Wednesday - Thursday – April 18-19, 2018
USP Meeting Center: 12601 Twinbrook Parkway, Rockville, MD 20852

PQRI PODP Extractables and Leachables Workshop

Day 1 – Wednesday, April 18, 2018	
8:00 - 8:15 AM	**Registration and Continental Breakfast**
Session A Moderator: Desmond G. Hunt, Ph.D. *(United States Pharmacopeia (USP))*	
8:15 - 8:30 AM	**Welcome and Opening** *Desmond G. Hunt, Ph.D. (USP)*
8:30 - 9:00 AM	**I. Introduction to PODP Recommendation: Risk Based Concepts** *Diane Paskiet (West Pharmaceutical Services, Inc.)*
9:00 – 9:30 AM	**II. Derivation of Parenteral Safety Concern Thresholds (SCT)** *Douglas J. Ball, MS, DABT (Toxicology Consultant)*
9:30 – 10:00 AM	**III. Derivation and Validation of Parenteral Classification Strategy** *Tim J. McGovern, Ph.D. (US Food & Drug Administration)*
10:00 – 10:30 AM	**Q&A Panel**
10:30 – 11:00 AM	**Break**
Session B Moderator: James Castner Ph.D., *(Pharma Interface Analysis LLC)*	
11:00 – 11:30 AM	**IV. Best Practices Generating Extractable Profiles** *Dennis R. Jenke, Ph.D. (Triad Scientific Solutions, LLC)* *With the publication of its Best Demonstrated Practice Recommendations for Orally Inhaled and Nasal Drug Products (OINDP), the PQRI E&L team changed the scientific and regulatory landscape for establishing the suitability of use of packaging systems associated with these dosage forms. In extending the OINDP principles to other dosage forms, specifically parenteral and ophthalmic drug products (PODP), the E&L team addressed the considerable differences between the OINDP and the PODP dosage forms, their packaging systems and their clinical uses. On the chemistry side of E&L, such differences have a necessary and considerable effect on the setting and justification of proper experimental conditions for performing controlled extraction studies.* *In this presentation, the essential chemistry recommendations for PODP dosage forms, specifically considering controlled extraction studies, are enumerated and the best demonstrated practice recommendations for generating relevant, useful and scientifically valid extractables profile are discussed.*

11:30 AM – 12:00 PM	**V. Analytical Technologies and Compound Identification** *Daniel Norwood, Ph.D. (SCIO Analytical, LLC)* *The analytical technologies used for the discovery, identification and quantitation of extractables and leachables are the same as those used for any problem in trace organic and inorganic analysis. Since the late 1960s, mass spectrometry and techniques based on the combination of mass spectrometry and chromatography (i.e., GC/MS and LC/MS) have occupied a central role in trace organic analysis. The process of structural analysis (i.e., identification) of any trace organic analyte in a complex matrix has been systematized based on mass spectrometry. Identification criteria based primarily on mass spectrometry data elements have also been proposed and incorporated into USP general guidance chapters. This presentation will discuss these identification criteria and data elements, and give example case studies of extractables/leachables identifications based on them.*
12:00 – 12:30 PM	**Q&A Panel**
12:30 – 1:30 PM	**Lunch**
Session C Moderator: Alan Hendricker, Ph.D. *(Becton Dickinson)*	
1:30 – 2:00 PM	**VI. Component Characterization: Sources of Potential Leachables** Michael Ruberto, Ph.D. *(Material Needs Consulting)*
2:00 – 2:30 PM	**VII. The Analytical Evaluation Threshold: Derivation and Use** Thomas Feinberg, Ph.D. *(SCIO Analytical)*
2:30 – 3:00 PM	**Q&A Panel**
3:00 – 3:15 PM	**Break**
Session D Moderator: Christopher T. Houston, Ph.D. *(Bausch + Lomb / Valeant Pharmaceuticals)*	
3:15 – 3:45 PM	**VIII. The Simulation Study in Action – Establishing a Design Space for Terminally Sterilized Aqueous Drug Products in a Plastic Packaging System** *Dennis R. Jenke, Ph.D. (Triad Scientific Solutions, LLC)* *Screening a drug product for leachables down to levels as low as the AET is the most definitive and regulatorily acceptable way to address potential drug product quality issues related to interactions between the drug product and its packaging system. However, there may be complicating factors, both scientific and practical, which make such an undertaking an exercise in futility. This is especially true for certain parenteral products such as large volume parenterals (LVPs), where the complicating factors may include large daily dose volumes, complex drug product formulations, long shelf lives and clinical use involving chronic therapies. In such circumstances, extractables studies whose intent is to simulate the drug product and its clinical conditions of use may provide a means of adequately addressing the potential drug product quality issues associated with leachables.* *As the name suggests, a simulation study is a controlled extraction study in which the complicating factor experienced in leachables screening of the drug product is addressed by replacing the factor with a more expedient surrogate. For example, if a drug product cannot be screened for leachables down to the AET because of its complex formulation, a simulation study is performed by replacing the drug product with a simulating extraction solvent.* *The concept of the simulation study is introduced and discussed in the context of parenteral drug products and a case study describing the use and the outcome of such a study is presented.*

3:45 – 4:30 PM	**I. Biologic Quality and Compatibility Considerations** *Diane Paskiet (West Pharmaceutical Services, Inc.)*
4:30 – 5:00 PM	**Q&A Panel**
5:00 PM	**Close of Day 1**
5:30 – 7:30 PM	**Networking Reception** **Hilton Rockville – Potomac Foyer** 1750 Rockville Pike I Rockville MD 20852

Day 2 – Thursday, April 19, 2018	
8:00 - 8:15 AM	**Continental Breakfast**
Session E Moderator: Desmond G. Hunt, Ph.D. *(USP)*	
8:15 - 9:15 AM	**I. Experimental Design Considerations for Ophthalmic Drug Products (ODP)** **a. Chemistry** *Christopher T. Houston, Ph.D. (Bausch + Lomb / Valeant Pharmaceuticals)* **b. Toxicology** *Mary E. Richardson, Ph.D. (iuvo BioScience)* *All dosage forms are not created equally. Each has its own particular challenges and risks with respect to extractables and leachables (E&L). Ophthalmic solutions and suspensions are among those drug products classified as having a high level of concern with respect to leachables. These largely aqueous, topical products are typically delivered in small doses from polyolefin multiuse containers. Their formulations are not particularly aggressive and their primary container closure systems generally pose a low risk of generating significant extractables. However, these ophthalmic drug products (ODP) often pose a challenge in the study of E&L given the semipermeable character of the primary container closure system and the fact that secondary packaging components (e.g., labels, information inserts, unit cartons) can have a significant impact on drug product leachable/migrant profiles. Migration from these secondary versus primary components creates a number of challenges that must be managed carefully for a successful E&L study. Likewise, the qualification process of leachables for topical ODP presents challenges in that the focus is on local toxicity rather than the systemic effects more commonly evaluated for parenteral or inhalation products. The key toxicological endpoints that need to be considered for qualifying leachables for topical ophthalmic products include (i) ocular irritation and toxicity; (ii) sensitization (skin) and (iii) genotoxicity. However, there is currently not a sufficient database developed on all the toxicity endpoints relevant to ODP to recommend specific safety thresholds (i.e., sensitization, ocular irritation) for ODP at this time. Therefore, although the hypothesis that threshold principles could be extrapolated from OINDP to ophthalmic solutions and suspensions may be scientifically sound, sufficient scientific support is not available at this time. This presentation will explore the key challenges in characterizing and qualifying extractables and leachables in ODP and highlight good-science approaches used within the ophthalmic industry to mitigate them.*
9:15 – 9:30 AM	**Q&A Panel**

9:30 – 10:30 AM	**II. Application of Thresholds and Expectations: Regulatory Perspectives** **a. US Perspective**: Timothy W. Robison, Ph.D. *(US Food & Drug Administration)* **b. Japan Perspective:** Validation of the Toxicological Threshold for E&L from the Single Use System Akihiko Hirose, Ph.D. *(National Institute of Health Sciences (NIHS))*
10:30 – 11:00 AM	**Q&A Panel: Submission Information, Regulatory Perspectives** Moderator: Desmond G. Hunt, Ph.D. *(USP)* Akihiko Hirose, Ph.D. (*NIHS)* Tim Robison, Ph.D. (*FDA)*
11:00– 11:15 AM	**Break**
Session F Moderator: Tim J. McGovern, Ph.D. *(Food & Drug Administration)*	
11:15 – 11:45 AM	**III. Application of Thresholds Concept Applied to Container Closure System for a Parenteral Drug Products** **Leachable Evaluation of a Container Closure System - What to do When Above the Threshold** William (Bill) P. Beierschmitt, Ph.D. *(Pfizer Worldwide Research and Development)*
11:45 AM – 12:00 PM	**Q&A**
12:00 - 1:00 PM	**Lunch**
1:00 – 3:00 PM	**IV. Case Study Break outs** **a. Small Volume Parenterals:** R. Daniel Mellon, Ph.D. *(FDA),* Jim Castner, Ph.D. *(Pharma Interface Analysis LLC)* **b. Large Volume Parenterals:** Thomas Feinberg, Ph.D. *(SCIO Analytical),* Timothy W. Robison, Ph.D. *(FDA)* **c. Prefilled Syringes:** Tim J. McGovern, Ph.D. *(FDA),* Alan Hendricker, Ph.D. *(BD)* **d. Ophthalmic Drug Products:** Christopher T. Houston, Ph.D. *(Bausch + Lomb/Valeant Pharmaceuticals),* Desmond G. Hunt, Ph.D. *(USP)* **Breakout Sessions –** *there will be four concurrent rooms utilized to discuss the topics to facilitate small group discussion and problem solving.* *Participants will discuss case studies and will have the opportunity to interact with chemists, toxicologists and regulators to discuss problem solving in a regulatory submission context*
3:00 - 3:45 PM	**Break**
3:45 – 4:15 PM	***V.* Report out from Breakouts and Discussion** *Dan Mellon, Tom Feinberg, Tim McGovern and Chris Houston*
4:15 – 4:30 PM	**VI. Potential for New USP Chapter and Other Revisions** Desmond G. Hunt, Ph.D. *(USP)*
4:30 PM	**VII. Wrap Up and Close of Workshop**