PharmaED RESOURCES, Inc.

# 2017 Pre-Filled Syringes Forum:

## Strategic Development, Safety & Regulatory Compliance, and Commercialization of Pre-Filled Syringes

**December 7–8, 2017—West Coast, La Jolla, CA**

## *Featuring Lessons Learned and Case Studies From Industry Experts:*

**Jonathan Amaya-Hodges**
*Senior Manager Regulatory Affairs, Biogen*

**Alireza Jahangir, PhD.,**
*Sr. Manager, Combination Products & Emerging Technologies PQM The Janssen Pharmaceutical Companies of Johnson & Johnson*

**Natalie Kennel**
*President, Senior Quality/Regulatory Affairs, NJK & Associates*

**Nicholas Zampa**
*Senior Engineer, Technical Development Human Factors and Risk Management, Biogen*

**Tiffany K. McIntire**
*Sr. Human Factors Engineer, Eli Lilly*

**Bruno Reuter**
*Executive Director, Scandinavian Health Ltd.*

**With the Pre-Filled Syringes market expected to top $16 billion dollars by 2021, the industry is looking for next generation materials, technologies and production strategies to streamline commercialization and to adapt quickly to a changing regulatory environment. Pharma Ed Resources, an industry leader since 2004, in delivering market-driven research on PFS, is proud to announce its 2017 Pre-Filled Syringes Forum. Pharma Ed brings together top scientists, regulatory experts and innovators to share best practices and the latest research in this field, enabling you to maximize your organization's leverage in this dynamic and growing market.**

## *Including Special Coverage On:*

- Key Factors in Combination Product Development: Regulatory Hurdles in Receiving PFS and Pen Approvals for Human Factors Studies
- Patient Centric Designs For Pre-Filled Syringes
- Next Generation Materials & Design of Pre-Filled Syringes
- Improving Quality, Connectivity, and Cost Control in Combination Products & Autoinjectors
- Smart Devices: Their Emerging Role in Auto-Injector Systems
- Sterile Manufacturing of Injectables at CMO's
- Extractables case study of resins HDPE, TPU & PEBAX
- Managing the Materials used to Construct Pre-Filled Syringes—Selection and Supply Chain Control
- Latest Market Trends and Needs for PFS
- Overcoming Complex Requirements for Biologic Drug Delivery

## *Featuring Representation From:*

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## Thursday, December 7, 2017

**7:30** *Complimentary Breakfast*

**7:50** *Welcome and opening remarks by Chairperson: Michael Eakins, Principal Consultant, Eakins & Associates, Inc*

### *Critical Issues—Examining the Regulatory Environment for Pre-Filled Syringes & Combination Drug-Delivery Systems*

**8:00** **Key Regulatory Changes Facing the Medical Device Industry**

***Natalie Kennel, President, NJK & Associates***

Abstract coming soon

**8:40** **Quality and Regulatory Affairs Best Practices for External Partnerships in Combination Product Development**

***Jonathan Amaya-Hodges, Senior Manager, Regulatory Affairs, Biogen***

Combination products, particularly drug delivery systems, are becoming more prevalent with the increasing need for both product differentiation and ease of use for patients. These systems are often developed in partnerships between a biotechnology or pharmaceutical company and a device designer/manufacturer, and with the implementation of the combination product rule in the US (21CFR4), an effective working relationship between those parties becomes essential, particularly in Quality and Regulatory aspects. This presentation will highlight best practices in these areas including how companies can move beyond minimum compliance in order to establish and maintain an efficient, responsive, and mutually beneficial partnership for developing and supplying drug delivery combination products, including pre-filled syringes and auto-injectors.

**9:20** **Revision of USP's General Chapter <381> Elastomeric Closures for Injections as it Relates to Pre-Filled Syringes.**

***Michael N. Eakins, PhD., Principal Consultant, Eakins & Associates***

Primary packaging components for pre-filled syringes includes elastomers as well as both glass and plastic barrels. The USP published a major revision to General Chapter <381> in the Pharmacopeial Forum 43(3) on May 1, 2017 and is in the process of evaluating the comments received. Major changes have been made to chapter <381> in that functionality of elastomers has been moved to its own chapter <382>. The revised chapter <381> now titled "Elastomeric Components Used in Injectable Pharmaceutical Packaging/Delivery Systems", emphasizes the baseline requirements for the selection of thermoset and thermoplastic elastomeric components, expands the scope to include all elastomeric components used in an injection packaging system, and assesses extractable elements using modern methods. A new informational chapter <1381> "Elastomeric Evaluation of Elastomeric Components Used in Pharmaceutical Packaging/Delivery Systems" by describing elastomeric components and their materials of construction, providing a high-level introduction to elastomer chemistry and manufacturing technology, and explaining basic functional characteristics of components. Functionality tests now appear in chapter <382> "Elastomeric Closure Functionality in Injectable Pharmaceutical Packaging/Delivery Systems" and this chapter is supported by a new informational chapter, <1382> "Elastomeric Evaluation of Elastomeric Components Used in Pharmaceutical Packaging/Delivery Systems". These new chapters will be discussed in general and how they relate to components for pre-filled syringes.

**10:00** *Mid-Morning Coffee & Networking Break*

**10:25** **A Cautionary Tale About Injection Pen Human Factors Research Gone Bad**

CASE STUDY

***Joely Gardner, PhD, Usability Testing Expert, FDA Regulatory Consultant, Cal State Fullerton, Human Factors Research***

Not all human factors research is good research and applications have been denied because of "bad" research. This presentation will discuss a case study of injection pen human factors research and the elements that differentiate between well-designed and poorly-designed and executed studies.

This presentation will cover:

- A case study of an injection device usability trial that failed miserably
- Warning signs of an inadequate human factors study
- The practical differences between formative and summative usability research
- How to maximize the actionable data from formative studies
- How to prepare for usability trials to facilitate a successful outcome
- How to decide what must be tested
- Cautions about inclusion/exclusion criteria for recruiting participants

**11:10** **Expert Elicitation of Use Error Probabilities for Combination Product Risk Analysis**

CASE STUDY

***Nicholas Zampa, Senior Engineer, Technical Development Human Factors and Risk Management, Biogen***

Estimating use error probabilities for combination products is hindered by a lack of data. Lack of data results from complexities associated with simulating a realistic user environment for usability studies, unreliable post-market surveillance data, and significant cost associated with large-scale usability studies. Because of insufficient estimates of use error probabilities, management of top-level safety and efficacy risks are limited. As a result of the difficulties associated with estimating use error probabilities, the current industry and regulatory paradigm is to disregard probability estimates when characterizing risk. Instead, combination product manufacturers focus risk

management activities solely on the severity of harms. However, recommendations to ignore use error probabilities are not rooted in a belief that probability estimates inherently lack value. Rather, the status quo is based on the fact that historical probabilities were not rigorously estimated, resulting in poor risk management.

Expert judgment elicitation with human factors experts can serve to provide statistically valid estimates of use error probabilities for which data is unavailable, unreliable, or impractical to obtain. Improved quantitation of use error probabilities can improve the combination product design and development process through proactive risk management.

12:00 *Complimentary Lunch & Networking Hour*

## *Design Control and Risk Management*

1:00

### Applications of Design Control and Risk Management to Pre-Filled Syringe Development

***Ariel Waitz, CQE, Senior Engineer, US Device Development (PTDUD), Genentech, A Member of the Roche Group***

Design control and risk management are fundamental quality systems that apply to the development of pre-filled syringe combination products. This presentation will explore three specific examples of applying risk management in the context of design control to inform product development. First, the presentation will explore how design or system-based risk assessments can be used in conjunction with design tools (e.g., tolerance analysis) in order to assist in the design characterization and/or verification of your device. Second, the presentation will discuss how the risk management process can be used to map risk acceptability to design verification sampling plans. Finally, the presentation will discuss how user-centered risk analysis can be applied to identify safety-critical tasks in conducting summative validation studies.

## *Technology Spotlight—Considerations for Patient-Centric Designs*

1:45

### Human Factor implications of Novel Injection Paradigms

***Tina Rees, Associate Director-Human Factors, Ferring Pharmaceuticals***

Parenteral drug delivery has for a number of years relied heavily on pre-filled syringes for drug administration. While pre-filled syringes have a number of advantages, there are also other drug delivery systems which may be more appropriate for your specific molecule. Each delivery system has unique characteristics that need to be considered, particularly as you approach your human factors program. This presentation will give a short overview of alternatives to pre-filled syringes in parenteral drug delivery, with a special focus on the human factors implications of each.

2:30

### Identifying and Managing Use-Related Risk Through Human Factors

***Tiffany Kay McIntire, Human Factors Engineer, Eli Lilly & Co.***

When asked a question a Human Factors (HF) engineer will often tell you "it depends on your risk assessment." With a heavy reliance on industry guidance (e.g. IEC62366, ISO14971, HE75), this presentation will guide you through the process of how to begin forming that risk assessment. Often when people think about HF, they think about formative and Summative testing. While this is a way to evaluate the effectiveness of some of your design controls, that alone may not lead to safe design. Involving HF earlier in your process can reduce the use errors observed later in the product timeline, thus reducing interruptions and associated cost.

## *Safety Evaluation of Pre-Filled Syringes—Special In-Depth Coverage*

3:15

### Analytical Challenges and State of the Art Solutions Related to Chemical Safety Assessment of Pre-Filled Syringes

CASE STUDY

***Gyorgy Vas, PhD., Business-Technical Scientific Liaison, Intertek Pharmaceutical Services, (Contributing Authors: Louis Fleck, Jiun-Tang Huang)***

Pre-Filled Syringes (PFS), are finished pharmaceutical products, what are packaged into the special delivery device, over a period of the intended shelf-life. Both the formulation and the route of delivery present relatively high risk for toxicological risk assessment. To have the safety risk assessment performed properly chemical testing needs to be executed appropriately, based on high level analytical and quality standards. PFS finished products are often formulated and delivered in a complex matrix, as well as the low-level impurities leaching out from the delivery system adding an extra layer of complexity of the testing. To use complex and sophisticated analytical instrumentation been always required for providing reliable data for chemical safety assessment. New developments from the analytical instrument manufacturers re-shaped the testing industry. High performance extraction methods combined with various MS/MS and high resolution accurate mass (HRAM) detection, providing testing solutions for low level analytes in highly complex matrices, such as PFS finished products. This presentation will focus on a few case studies where high performance complex instrumentation was used on a routine basis for safety evaluation of PFS products.

4:00 CASE STUDY

## Challenges in Extractable and Leachable Studies of Pre-Filled Syringes

***Dujuan Lu, PhD, Technical Manager-Life Science Extractable and Leachable Testing, SGS North America Inc.***

Pre-filled syringes (PFS) are increasingly becoming a container of choice for storing and administering pharmaceutical products. PFS components and residues from processing tools may leach organic and inorganic chemicals into formulated drugs, as extractable and leachable compounds. As part of safety risk assessment, it is very important to identify and quantify those extractables and leachables as they may pose safety risks to patients and/or change the efficacy of the medical products.

This presentation will focus on a case study regarding the extractable and leachable testing of PFS for a drug formulation containing high content of castor oil. The choice of the extraction solvent systems and study design to bracket and mimic hydrophobicity and administration of drug formulation will be discussed. In order to obtain a comprehensive extractable profile, multiple analytical techniques were used to identify and quantify the extractables, including Headspace (HS)-GC-MS/FID analysis for volatile organic compounds, GC-MS/FID analysis for semi-volatile organic compounds, LC-MS/UV analysis for non-volatile organic compounds, and ICP-OES analysis for trace elements. This presentation will show that internal database and High Resolution Accurate Mass (HRAM) data facilitate confident compound identification and unknown compound structure elucidation. Analytical challenges associated with the drug formulation containing high amount of castor oil during the leachable testing will also be discussed.

## *Panel Discussion*

4:40

## What's Next in the World of Pre-Filled Syringes? Re-imagining an Industry Paradigm

Members of the audience will set the agenda in this open forum discussion of the current state and future of PFS and related injectable devices.

Moderator:

Michael Eakins, Eakins & Associates

Panelists:
Nicholas Zampa, Biogen
Alireza Jahangir, The Janssen Pharmaceutical Companies of Johnson & Johnson
Bruno Reuter, Scandinavian Health Ltd.

5:20 *Close of Program Day One*

# Friday, December 8, 2017

7:30 *Complimentary Breakfast*

7:50 *Chairperson Remarks: Michael Eakins, Principal Consultant, Eakins & Associates, Inc*

## *Technology Spotlight—Autoinjectors: Smart Device Interfacing & Systems Development Approaches*

8:00 CASE STUDY

## Challenges Associated with PFS Combination Product Development for Ophthalmic Applications

***Mayumi Bowen, Senior Engineer, Pharmaceutical Processing Technology Development, Genentech, Inc.***

There are stringent Health Authority guidance and ISO requirements for ophthalmic applications to prevent infection by eliminating pathogenic micro-organisms, considering eye safety, which are challenges to development of ophthalmic PFS combination products. This presentation will address guidance & requirements pertaining to particulate, endotoxin, silicone oil leachates, and external surface sterilization for ocular applications. In addition, points to consider, strategies, and case studies regarding material selections (e.g. PFS container closure, label, and sterile barrier system, etc) and sterilization process development to meet the stringent guidance and requirements.

8:45

## Trends in Self-Injection: Large Volume Autoinjectors, Wearable Devices, Connectivity in Self-Injection

***Jakob Lange, PhD, Director Delivery Systems, Ypsomed***

The pharmaceutical market is constantly changing and pharma companies around the world have to adjust to the pace of changes to be successful. The last decades have been characterized by the development of reusable pens as well as disposable pens and autoinjectors, all of them highly precise mechanical systems. Today the market is on the cusp of introducing next generation devices that are connected and to include complex electromechanical systems. This presentation will cover the latest developments of large volume autoinjectors, wearable devices as well as the completely new field of connected, smart devices.

9:30 *Mid-Morning Coffee & Networking Break*

9:55 CASE STUDY

## Challenges and Opportunities for Development of Stability Program for Combination Products

***Alireza Jahangir, PhD, Sr. Manager, Combination Products & EmergingTechnologies PQM, The Janssen Pharmaceutical Companies of Johnson & Johnson***

Combination products are unique therapeutics that combine two or more regulated constituent parts (i.e. drugs, devices and/or biological products), leading to products that provide ease of use, safer and more effective. While

the combination products have been developed and commercialized as a result of unprecedented collaboration between pharma and device industries to address patients' unmet therapeutic needs, they also have presented new regulatory, quality and development challenges. Unlike the stability program of pharmaceutical products, the combination product shelf life is not only determined by the effectiveness of a particular drug formulation, but also by device functionality as well as the sterile barrier system materials integrity during the product's entire supply chain from packaging to sterilization, transportation and storage. From a combination product perspective, while the individual shelf life data for each of the above-mentioned entities are critical, the complete stability testing plan should also include monitoring of the specific Stability Indicating Attributes/Parameters that demonstrate the interactions among these various constituent parts. Furthermore, in addition to following different international standards and guidelines (i.e. ICH, WHO, ASTM), governing the stability testing requirements for drugs, devices and/or their packaging systems, the manufacturers should also be aware of differing expectations by two review centers within FDA (i.e. CDER and CDRH) for approval of a drug/device combination product. Accordingly, by using case studies and industry best practices, this presentation will introduce a new end-to-end stability testing paradigm for different classes of combination products based on robust scientific, risk-based, holistic and proactive approach.

10:40 **Challenges of the Implementation for a "Standard Drug Container/Syringe" into a Modern Auto Injector**

***Bruno Reuter, Executive Director, Scandinavian Health Ltd.***

Modern types of auto injectors still using standard types of drug container as e.g. standard 1.0mL long and 2.25mL – staked needle syringes. The complexity of such a device and the tight specification in terms of injection time, injectable volume accuracy and other specified items leads at the end to a specific requirement profile for such a drug container which is not implemented in the pharmaceutical industry so far. The challenges for all parties; pharmaceutical end user, device manufacturer as well as primary container manufacturer, are not aligned so far and in most cases, the common understanding is still missing.

The presentation highlights some of these "imperfections" between device and drug container, at least no part of this "manufacturing triangle" can solve it alone, a common understanding and solution is necessary for an optimal solution at all.

## *Materials Selection in PFS for Biologics*

11:20 **Testing and characterization needs for combination products**

***Robert Schultheis, President, ZebraSci, Inc***

Complete characterization of primary packaging, formulation, and device is essential to launching combination products in a timely fashion. This presentation will show some of the variability that ZebraSci Labs has encountered in in root cause investigations and in combination product development programs.

12:00 *Complimentary Lunch & Networking Hour*

1:05 **Filling of High Concentration Monoclonal Antibody Formulations: Challenges in Filling Accuracy**

***Wendy Shieu, Engineer II, Genentech, Inc., Pharmaceutical Processing and Technology Development***

Filling of high-concentration/viscosity monoclonal antibody (mAb) formulations into vials or syringes by peristaltic pumps is an industrial standard. Control of the peristaltic pump on fill weight/volume accuracy/precision over time, however, has not been fully disclosed in the literature. This study systematically evaluated the impact of a broad range of system/pump parameters, from tubing set up to pump parameter settings to the filling nozzle, on filling precision using a bench-top system with fill weight readings from a high-precision balance. A low fill volume of 0.3 mL was targeted to fill liquids of various viscosities (including a high-concentration mAb formulation). Fill weight precision was reported via percent of fill weight data points (at least 100 consecutive points) falling within 3% of the target fill weight (e.g., within 0.009 g for a 0.3 g target fill weight). Experimental results suggested that the 3% precision target is challenging for filling high-viscosity liquids due to run-to-run and day-to-day variability. More importantly, none of the system/pump parameters seemed to directly correlate with fill weight precision.

1:50 **Considerations for Selecting Drug Delivery Systems**

***Justyna Dudaronek, PhD, Staff Engineer, BD Medical, Pharmaceutical Systems***

The requirements for biologic drug approval continue to grow, with an overall aim to improve patient safety, experience and health outcomes while managing cost. With increased competition, defining drug development strategies which properly consider the delivery system is critical to a program's success. This session will cover technical considerations and testing strategies to optimize the selection of delivery systems and prove their suitability, compatibility, and performance with the drug as a combination product.

## *Industry Spotlight—Examining Key Market Trends and Needs for Development of Next Generation PFS*

2:30 **Development Strategies for Prefilled Drugs Intended for Self-Injection**

***Tibor Hlobrik, Director, Global PFS Platform, West Pharmaceutical Services***

Many drugs in development are being targeted for self-administration using a prefilled syringe and cartridge in a custom device for increased compliance.

Selecting the right container and device combination is crucial to ensure high-quality treatments with better patient outcomes. This session will discuss strategies being applied by pharmaceutical companies for product selection with technical examples for a range of drug product applications, including high volume and through consideration of unique user requirements.

## *Materials Selection Part II*

3:15 CASE STUDY

### COP Technical Data Update

***Toshiro Katayama, Product Manager, Zeon Chemicals***

This presentation will provide an update and recent case study on COP, an innovative polymer widely used in the PFS industry. Topics to be covered include:

- Key properties and features of COP & its bene ts for pre-filled syringe applications
- Mechanical properties after exposure to gamma, steam, EOG and cryogenic temp
- JP, US, EU Pharmacopoeia and ISO 10993 status
- Extractable/leachable test data in COP syringes with various chemicals
- Protein adsorption/aggregation study data with actual protein drugs to COP vs. glass
- Delamination study data on glass syringe

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

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|---|---|
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| Venue: | Sheraton La Jolla Venue |
| Venue Address: | 3299 Holiday Court<br>La Jolla, CA 92037 |
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