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 POM 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

Mayumi Bowen
Senior Engineer, Genentech, Inc

Tina Rees
Associate Director—Human Factors, Ferring Pharmaceuticals

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:
Thursday, December 7, 2017

7:30  Complimentary Breakfast

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

8:00  Key Regulatory Changes Facing the Medical Device Industry

Natalie Kennel, President, NJK & Associates

The current regulatory environment for medical devices is an avalanche of regulatory changes. In the U.S., the FDA has embarked on several new programs along with increasing expectations in the pre and post market environment. Some of these new programs and guidances include the breakthrough device program, determining what changes need a new 510(k), UDI direct marking, applying ISO 10993 to biocompatibility requirements, pre-certification program for software, and regenerative medicine. These changes are in addition to FDA’s high emphasis on human factors, usability, and risk management. Beyond FDA, the European Union, and any company desiring to sell in the EU, is bracing for the sweeping changes to the regulatory framework for medical devices. Further FDA’s has embraced the Medical Device Single Audit Program (MDSAP). Health Canada has already decided to require MDSAP certification by 2019. Worldwide, medical device manufacturers need to revise and update their Quality Management System (QMS) to meet ISO 13485:2016. Nearly all of these regulatory changes in the medical device field impact combination products. This list is just a start—So what should you do? This talk will aim to provide attendees with an overview of these topics and with solid actions to help you and your companies prepare for and implement these changes.

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  Considerations for Selecting Drug Delivery Systems

Theresa Bankston, PhD, Director of Technical Services, 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.

11:10  A Cautionary Tale About Injection Pen Human Factors Research Gone Bad

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

Complimentary Lunch & Networking Hour

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.

1:40

Expert Elicitation of Use Error Probabilities for Combination Product Risk Analysis

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 these 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.

2:00

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.

Afternoon Coffee and Networking Break

3:00

A Framework For Extractable Leachable Considerations For Pre-Filled Syringes

Dr. Andrew Hall, Study Director, Toxikon

Combination products containing drug and novel delivery systems have exploded over the past decade. Evaluating combination systems for extractables and leachables is new territory for many end-users. Establishing a framework between extractables and leachables is necessary to interpret, and assess the interaction between a drug product and its container. Leachables can generate new compounds from the interaction between drug solutions and the packaging material. This presentation will focus on providing a framework regarding extractable and leachable testing of pre-filled syringes and the trials and tribulations associated with this testing with regard to analytical methodology.

3:25

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

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.

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.

Close of Program Day One

Friday, December 8, 2017
Complimentary Breakfast

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

8:00 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 Challenges and Opportunities for Development of Stability Program for Combination Products
Alireza Jahangir, PhD, Sr. Manager, Combination Products & Emerging Technologies 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.

COP Technical Data Update

Toshiro Katayama, Product Manager, Zeon Specialty Materials Inc.

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

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 root cause investigations and in combination product development programs.

Panel Discussion

1:05 What’s Next in the World of Pre-Filled Syringes? Re-imaging 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
Tina Rees, Ferring Pharmaceuticals

1:30 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.

Afternoon Networking and Coffee Break

2:15 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.
Many in the pharmaceutical community have struggled with the intense human factors requirements for pre-filled syringes. Given how ubiquitous these devices are, it is understandable to question the need for a full human factors program, culminating with a large validation effort. Indeed, the human factors requirements have both resulted in rejected applications and/or delayed the launch of many pre-filled syringe programs. Recently, the FDA has recognized this issue and has availed a new, simplified pathway for some combination drug products, covering both interchangeable generics (or biosimilars) and new drug applications (NDA). The pathway requires development of a “comparative” or “threshold” analysis to justify exclusion from human factors validation testing. During the presentation I will present the use cases for which the FDA allows this process, explain which analysis goes with which filing type, and walk the audience through the best approach to conducting and reporting the analysis.

This is an incredible opportunity for the pre-filled syringe community to streamline the approval process for devices that are already known to be generally safe, effective and easy to use.
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VENUE INFORMATION:

Dates: December 7–8, 2017
Venue: Sheraton La Jolla Venue
Venue Address: 3299 Holiday Court
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