PharmaED RESOURCES, Inc.

2019 Pre-Filled Syringes & Auto-Injectors Forum

February 27–28, 2019, Metro Meeting Center, Boston, MA

Pre-Filled syringes are known to be expanding at a stupendous rate among the other segments of the injectable drug delivery devices market. Numerous advantages such as ease of administration, enhanced safety, reduced risk of contamination, and accuracy of dosing, have made it more preferable over traditional delivery systems. These benefits lay the basic foundation on which the pre-filled syringe market expands. Incessant growth in the biologics market, rising preference for self-administrations which uses pre-filled syringes, pen injectors, and autoinjectors, are propelling the growth of the market. The value of the market is projected to hit US 7.9B by the end of 2024.

Steven W. Badelt, PhD

Chairperson, Managing Partner and Founder

Suttons Creek, Inc.

Rajiv Gupta, PhD, Director/Device Development Leader, Medical Devices, Shire

Fubin Wu, Co-Founder of GessNet, Solutions for Medical Device Safety, Cybersecurity and Regulatory Compliance

Gregory Manley, PhD, Product Manager at Unchained Labs

Suraj Ramachandran, RAC, CPM Director, Regulatory Affairs — Drug-Device Center of Excellence, Merck

Yuh-Fun Maa, PhD, Senior Principal Engineer at Genentech

Jakob Lange, PhD, Account Director, Ypsomed AG

Alireza (Alie) Jahangir, PhD, Sr. Manager, Combination Products & Emerging Technologies PQM, The Janssen Pharmaceutical Co.

Stephen Doherty, PhD, Associate Director, Analytical Chemistry at Toxikon Corporation

Howard Drake, Vice-President/ GM Ompi of America

Susan Dounce, Principal SME, Prefilled Syringes, Crystal Zenith, Combination Products, West Pharmaceutical Services

Akshay Kamdar, PhD, Associate Engineering Advisor,Group Leader, Parenteral Container Innovation & Development, Eli Lilly

Nicholas Zampa, Senior Engineer I — Human Factors and Risk Management, Biogen

Edmond Israelski, PhD, Co-Convener of ISO and IEC Medical Device Standards Committee, Former Director of Human Factors, Abbvie

Michael Song, PhD, Senior Manager, Drug Delivery and Device Development, MedImmune

Gyorgy Vas, PhD, Business Technical Scientific Liasion, Intertek Pharmaceutical Services

Julian Stauffer, COO, PTI, Packaging Technologies and Inspection

Klaus Ullherr, Senior Product Manager, Bosch

Toshiro Katayama, Product Manager, Zeon

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Wednesday February 27, 2019

8:00 *Complimentary Breakfast*

8:30 *Chairperson's Welcome and Opening Remarks*

Steven W. Badelt, PhD, Managing Partner and Founder Suttons Creek, Inc.

8:45 **Integrated Strategy and Approach to Combination Product Development for Biologics**

Rajiv Gupta, PhD, Device Program Leader, Medical Device, Shire

The pre-filled syringe and auto-injector presentations are injectable combination products that continue to be developed and commercialized for biologics. These product presentations provide patient-centric delivery options to patients in a home environment for self-administration and health care professionals in an office environment. The development of these drug-device combination products must be in accordance with regulations of the FDA and other regulatory authorities to support global launches.

This presentation discusses an integrated strategy and considerations around device platform approaches and how to potentially bridge between devices. It also discusses the high-level process and feasibility/development activities that are typically conducted in a cross-functional team structure to enable the start of clinical trials and regulatory submissions. Key technical considerations during the design development process are also discussed.

9:30 **Lessons on Platform Execution of Programs in Pharma**

Brian Intocca, Quality Consultant, Suttons Creek, Inc.

Abstract Pending

10:15 *Speed-Dating Networking*

11:00 **Challenges and Opportunities for Development of Stability Program for Combination Products**

Alie Jahangir, PhD, Sr. Manager, Combination Products & Emerging Technologies PQM, The Janssen Pharmaceutical Companies, 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.

11:45 **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, which are packaged into the special delivery device, over a period of the intended shelf life. PFS delivery systems are getting more and more popular to deliver both small molecule and biologics-based drugs. 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.

Complex and sophisticated analytical instrumentation has always been 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.

12:30 *Complimentary Lunch*

1:30 **Precision Capability of Peristaltic Pump for Filling High-Concentration Monoclonal Antibody Solutions at Low Fill Volumes?**

Yuh-Fun Maa, Senior Principal Engineer, Genentech

A common perception about the peristaltic pump is its inferiority in fill accuracy for low-fill volumes (< 0.5 mL) compared to other filling technologies, such as the piston pump and the time-pressure filler. This presentation will verify this perception and determine if peristaltic pump can precisely fill 0.3 mL of liquids of low viscosity (water) and more viscous high-concentration monoclonal antibody formulation (> 10 centipoise). This study aims to better understand the role of tubing. The performance of several different types of tubing (different brands of silicone as well as a unique silicone and Teflon composite) were assessed under a variety of filling conditions. Also, peristaltic pumps of different operation designs were assessed. Our findings suggest that while peristaltic pump, can achieve good low-fill-volume precision on water but is more challenging on higher viscosity liquids. The brand (or pump design) plays an important role in achieving high-fill precision for low-fill-volumes of viscous liquids. Surprisingly, tubing performance does not have as important an impact on fill accuracy as the design of the peristaltic pump. This study will look into what pump mechanisms, such as pump controls/designs, can differentiate pump performance.

2:15 **Combi Filling – Challenges and Solutions**

Klaus Ullherr, Senior Product Manager, Bosch

- Unique machines for processing pre-sterilized syringes, vials and cartridges
- 100% IPC
- Integrated capping
- Use of robotic systems
- Critical points regarding the filling and processing of the different containers
- Maximum product yield by using special start up and end of production filling processes
- State-of-the-art peristaltic pump technology together with a combi filling station
- State-of-the-art single use filling technology
- Mock up study for optimized use of barrier system
- Upstream processes for bringing the different containers to the point of fill

3:00 *Afternoon Networking Break*

3:30 **Platform-Based Drug Delivery Combination Product Risk Management: Challenges and Best Practices**

Fubin Wu, Co-founder, GessNet

A drug delivery combination product is composed of a drug and a delivery device. Risks for a drug delivery combination product include risks posed directly by a delivery device (e.g., cuts, bruises, biological infections) as well as risks due to interactions between the device and a drug (e.g., hypoglycemia due to insulin overdose). A traditional drug manufacturer tends to select an existing delivery platform from a vendor or outsource a vendor to develop a delivery device platform. It is becoming more and more common that one delivery device platform may end up being used for delivering multiple drugs, and a drug may end up being delivered through multiple delivery devices. There are a number of challenges faced by the drug manufacturers and delivery platform vendors on how to effectively and efficiently integrate risk analysis, generate risk-analysis documents supporting premarket submissions, and manage risk through the product life cycle. This session is to explore these challenges and associated best practices.

4:10 **Tools for Calculating the Return on Investment in Human Factors Engineering for Injection Systems**

Edmond Israelski, PhD, Consultant,Technical Advisor on Human Factors, Retired Director, Human Factors, Abbvie

This presentation will review tools that can be utilized to estimate the cost benefits of investing in solid Human Factors Engineering best practices such as Usability Testing in the development process for medical injection systems. Concepts such as Return on Investment, Payback period, and internal Rate of Return will be reviewed, and examples will be offered on applying these concepts to Human Factors investments during the development of medical products.

4:50 *End of Day One*

Thursday February 28, 2019

8:00 *Chairperson's Welcome and Opening Remarks*

Steven W. Badelt, PhD, Managing Partner and Founder Suttons Creek, Inc.

8:05 *Breakfast presentation by Toshiro Katayama, Product Manager, Zeon, Silver Sponsor*

ZEON

Biologics Formulation for COP Syringe Optimized to Eliminating Use of Surfactant

CASE STUDY

Key Properties of COP

- Case study: Biologics formulation for COP syringe optimized to eliminating use of surfactant

Most of biologic formulation contains surfactant such as Polysorbate 80 to reduce protein aggregation, but it is known to increase risk of hydrolysis/oxidation, causing a hypersensitivity issue. This new study shows the possible elimination of Polysorbate with use of COP syringe

- Case study: Study on Protein adsorption/aggregation – COP vs glass
- Case study: Study on delamination with glass syringe vs COP syringe

8:35 **Flexible Primary Container Closure Systems: Reimagining the Future of Parenteral Drug Delivery**

Akshay Kamdar, Associate Engineering Advisor / Group Leader — Parenteral Container Innovation and Development, Eli Lilly and Company

Abstract Pending

9:20 **Container Closure Integrity Assessment of PFS and Cartridges in Manufacturing and Transportation – Options, Approaches and Future Trends in Ensuring Product Safety**

Michael Song, Sr. Manager, Drug Delivery and Device Development, MedImmune

Available container closure integrity test methods and benefits and deficiencies.

Selecting the right CCIT method for your application.

How CCIT can be utilized to help establish a more robust manufacturing process and ensure product safety.

Optimizing and/or developing novel methods to meet new challenges.

Applying CCIT techniques to demonstrate container closure integrity during high altitude shipping.

10:00 ***Networking Break***

10:30 **Particles in Intravitreal Injections**

Susan M. Dounce, PhD, Principal SME, Pre-filled Syringes, Crystal Zenith and Combination Products, West Pharmaceutical Services, Inc.

The number of ophthalmic injections of anti-VEGF drugs to treat neovascular back-of-the-eye diseases such as wet Age-Related Macular Degeneration continues to grow. Patients with these indications may receive injections into the eye as often as once per month and although these therapies are preventing blindness, there are unique risks to intravitreal drug delivery that are exacerbated by the injection frequency. Introduction of particulate matter (including silicone oil, aggregated protein, biologic contaminants and other intrinsic / extrinsic particles) can lead to inflammation, infection, floaters in the vision or even, in extreme cases, vision loss. It is therefore critical to understand how the primary packaging / delivery device can impact the safety of the drug product and the ability to meet stringent USP<789> standards. Appropriate material selections are necessary to maximize patient safety.

11:15 **Pre-Filled Syringes Novel Approach & Technology: Increasing Safety and Performances in the Delivery of Demanding Biodrugs**

Howard Drake, Vice-President, Pharmaceutical System Division, Ompi of America, Stevanato Group

Today, biologics are fast becoming the driving force of the pharmaceutical industry. Because the primary route of administration for most biologics is still by injection, there is a demand for advanced drug-delivery systems that offer convenience and ease of administration. Pre- filled syringes have gained strong acceptance as delivery systems for injectable drugs, especially in the treatment of chronic conditions that require repeated administration of the medication. Nevertheless, it is well-known in the industry that Pre-filled syringes are not free of issues as they are complex systems where primary packaging components are challenged by large molecules such as MABS or sensitive drugs. This presentation will provide an overview of the latest Alba technology and the benefits for the Pharma industry to have a comprehensive solution under the same roof.

Items addressed are:

- **Particles reductions**
- **Injections performances related to viscosity — Delamination control**
- **DDS compatibility**
- **AI/Pen devices integration**

11:50 ***Complimentary Lunch***

12:50 **The Role of Human Factors in Evaluating Innovative Injectables**

Nick Zampa, D. Eng, Senior Engineer I, Technical Development, Biogen

In the (bio)pharmaceutical industry, (bio)pharma companies often rely on external developers to provide the device constituent part of a combination product. Prior to selecting a device for combination product development, (bio)pharmaceutical companies engage in landscaping, feasibility and/or other due-diligence activities. For sufficiently innovative devices, usability evaluations should be part of these initial assessments. However, extensive human factors data from the device developer is either absent, focused on non-target users or arrives as modified forms of market research (e.g., preference studies).

In these early pre-development stages, I propose a two-step approach for ensuring a sound human-factors-based evaluation of innovative products. First, a (bio)pharmaceutical company should evaluate and supplement the available data with sound human factors analysis, keeping in mind the specific combination product's intended use. Second, I propose merging human-factors evaluations with common, user-centered approaches to innovation management. Understanding the intended user's technology ecosystem, the role a new product would fill

in that ecosystem, and whether the combination product is competing with established products all play critical roles in assessing usability and adoptability. Further, understanding the current ecosystem into which a new and innovative product is to be launched can help predict potential usability problems, allowing the combination product owner to efficiently address usability risks during development.

1:30 **Framework For Evaluation of Pre-Filled Syringe Systems**
Dr. Stephen Doherty, Toxikon

Pre-filled syringes continue to become more common means for drug storage and delivery. The prolonged storage of the drug in the syringe creates its own challenges for the system. The syringe must protect the drug from environmental factors such as oxygenation, microbial ingress, and not introduce compounds such as leachable compounds from the syringe barrel, plunger and caps components. This study will examine challenges in the comprehensive evaluation of pre-filled-syringe stems. Given the complexities of many drug systems, it is often necessary to have comprehensive extractable studies which can be correlated to the leachable studies in drug product. Integration of the leachable program into the stability program can allow for an evaluation of the critical aspects of drug stability, maintenance of sterility and evaluation of leachable components. This presentation will examine strategies for the integration of comprehensive studies to examine critical aspects of the appropriateness of the pre-filled syringe systems.

2:10 **Tackle Pre-filled Syringe QC With Bouncer**
Gregory Manley, PhD, Product Manager, Unchained Labs

CASE STUDY

Syringe siliconization makes drug injections smoother and easier. Too little silicone, and the device can get jammed up, but too much and silicone can ooze into the drug causing aggregation. Bouncer measures silicone thickness and distribution in minutes so you can ensure the coating is just right. We will discuss how understanding silicone thickness and distribution can improve device manufacturing and the long-term stability of biologic formulations.

2:45 ***Afternoon Networking Break***

3:10 **What Is "New" In the Area of Autoinjectors, Pen Injectors, Patch Pumps and Wearables?**
Jakob Lange, Account Director, Ypsomed

CASE STUDY

Market overview and update: Recent innovations and trends on:

- Pens
- Auto-injectors
- Large-Volume Injectors
- Platforms

Case Study 1

- User acceptance of injection times >10s with handheld injectors

Case Study 2

- A new approach for HF usability validation of devices based on existing platform

3:50 **The Evolution in Vacuum Decay Leak Testing Technology**
Julian Stauffer, COO at PTI — Packaging Technologies & Inspection, SDA

This presentation will review vacuum decay technology, how it works and what has made it a lasting solution for the pharmaceutical industry for package leak detection and container closure integrity testing. Recent technology advances of the new evolution in vacuum decay will be discussed and how these new advancements will serve and benefit the pharmaceutical industry moving forward.

Vacuum decay is a test method that has been proven over decades and improved with new technology innovations. Vacuum decay has been verified that it is the most practical and sensitive vacuum-based leak test method. The test measurement creates a reliable and accurate quantitative result and a pass or fail determination. The standard vacuum decay leak test method (ASTM F2338), developed using PTI's VeriPac instruments, is recognized by the FDA as a consensus standard for container closure integrity (CCI) testing. The test method is listed in ISO 11607 and referenced in the United States Pharmacopeia Chapter on CCI (USP Chapter 1207).

Vacuum decay's acceptance as a regulatory tool is evident, and continued development optimizes the technology so that it can do more, do it better and perform it faster. PTI's next generation of improvements are not an incremental improvement, but rather foundational shifts in how the technology will serve the pharmaceutical industry. The PERMA-VAC technology is geared towards detecting leaks in the MALL range for parenteral packaging and can also be applied to flexible and semi flexible package formats.

4:30 ***Close of Program***

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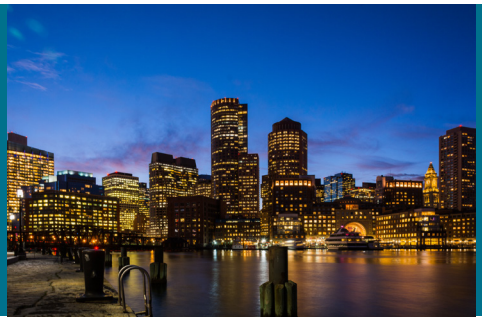

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