

2019 Pre-Filled Syringes & Auto-Injectors Forum

September 4–5, 2019, Sheraton La Jolla, La Jolla, CA



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.



Carolyn Dorgan
Senior Team Lead
FDA



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



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



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



Carl Dabruzzo, Director, Product Management, Self-Injection Systems, West Pharma



Jakob Lange, PhD, Account Director, Ypsomed AG



Toshiro Katayama, Product Manager, Zeon



Michele Arduini, Manager, Ima Life



Jonathan Amaya Hodges, Associate Director, Regulatory Affairs, ASQ CMQ/OE CQE, Biogen



Christian Lavarreda, Product Manager, Pharmaceutical Operations, Bosch Packaging Technology



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



Douglas Cusato, Director, Sumitomo Rubber



Howard Drake, Vice-President/GM Ompi of America



Ellie Younger, Device Project Lead — Human Factors and Risk Management, Biogen



Robin Sweeney, PhD, Unchained Labs Product Manager



Alireza (Alie) Jahangir, PhD, Sr. Manager, Design to-Value (DtV)/ Quality Engineering (QE), Johnson & Johnson



Wenliang Chen, Technical Director, Asia Market, PTI



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



Patrick Gallagher, Polymer Solutions, SCHOTT North America Inc.



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

With Representation From:



Wednesday September 4, 2019**8:00** *Complimentary Breakfast and Registration***8:25** *Chairperson's Welcome and Opening Remarks***Steven W. Badelt, PhD, Managing Partner and Founder Suttons Creek, Inc.****8:30** **Combination Product Topics of Interest: EPRs, Control Strategies, Lifecycle Management and Platforming****Carolyn Dorgan, Senior Team Lead, FDA**

Combination Products are no longer niche products in the world and it is time to engage in a collaborative dialogue to explore best practices in combination product development including device essential performance requirements, lifecycle management and considerations for when design of platform devices are appropriate. Combination Product development requires a unique strategy beyond the established drug and device siloed development processes. By breaking down these traditional barriers, industry can create opportunities to leverage these concepts across multiple product lines and streamline development.

9:15 **Integrated Strategy and Approach to Combination Product Development for Biologics****Rajiv Gupta, PhD, Device Program Leader, Medical Device, Takeda**

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.

9:55 *Mid-morning coffee break — Exhibitor Room***10:20** **Combination Product Development – Collaborations without Complexity****Carl Dabruzzo, Director, Product Management, Self-Injection Systems, West Pharma**

Pharmaceutical companies are rethinking their approach to drug delivery, especially as it relates to biologics. The historical pressures to concentrate injection formulation volumes to 1mL or less are going away as the availability of large volume handheld and wearable delivery systems become more prevalent. As this transition to large volume combination products moves ahead, compa-

nies are faced with the challenge of identifying injection technologies that represent the best opportunity for success in the market while minimizing the amount additional regulatory and commercialization risk being assumed.

11:00 **Post-marketing Safety Reporting for Combination Products****Jonathan Amaya Hodges, Associate Director, Regulatory Affairs, ASQ CMQ/OE CQE, Biogen**

With FDA's publication and implementation of the Post-marketing Safety Reporting (PMSR) rule for Combination Products, the management of safety reporting for such products has received increasing interest and regulatory scrutiny. We will explore the effects of this rule on pre-filled drug delivery system, including syringes and auto-injectors, and remaining challenges faced by industry. This information will inform organizations with established combination products, and those with products in development that need to plan for coming launches. Finally, we will see how this aligns with global safety reporting schemes.

11:40 **Challenges and Opportunities for Development of Stability Program for Combination Products****Alireza (Alie) Jahangir, PhD. Sr. Manager, Design to- Value (DtV)/ Quality Engineering (QE), 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.

12:20 *Complimentary Lunch***Combination Products Q & A—
Ask the Experts**1:20 **Panel Discussion: Exploring Challenges & Opportunities in the Combination Product Market**
Moderator: Steven Badelt, Suttons Creek, Inc.

Panelists:

- Carolyn Dorgan, FDA
- Rajiv Gupta, Takeda
- Carl Dabruzzo, West Pharma
- Jonathan Amaya Hodges, Biogen
- Alireza Jahangir, Johnson & Johnson

Discussants: The Audience

1:50 **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.

2:25

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

Yuh-Fun Maa, PhD, 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.

3:00

Afternoon Networking Break

3:25

Combi Filling — Challenges and Solutions

Christian Lavarreda, Product Manager, Pharmaceutical Operations, Bosch Packaging Technology

Advances in container and filling technology are expanding the toolset for optimizing aseptic filling processes for parenteral containers, in particular when combination filling is involved. New nest and tray-based packaging material options are enabling more robust aseptic filling processes through more advanced automation. This presentation will explore and provide:

- The tradeoff between output and flexibility as a parenteral product moves through the pre-clinical, to clinical, and commercial manufacturing phases
- Concrete examples of how combined processing has been implemented for a variety of container type combinations in the various manufacturing phases
- Considerations in the design and implementation of single use filling systems in combination fillers
- An overview of the latest technology and features found in flexible fillers

4:00

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.

4:35

Design the Container Around the Device — Benefits of Primary Container Customization for Large Volume Injectors

Patrick Gallagher, Polymer Solutions, SCHOTT North America Inc.



As high volume delivery of biologic drugs continues to be an area of industry focus, pharmaceutical companies and device manufacturers have developed a number of wearable devices and large volume bolus injectors for in-home self-administration. Some of these devices rely on existing syringe and cartridge configurations as accepted market standards while others utilize novel designs that require customized primary containers. While glass is an established material in the market, high performance polymers such as cyclic olefin copolymers (COCs) have now cleared the high barriers of entry and are approved as primary containers in all major markets. COC polymers have particular benefits for wearable devices, allowing for unique customization options and superior break resistance to withstand the high forces required for viscous drug delivery while maintaining consistent functionality. Newer technologies such as additive prototyping provide considerable development flexibility and a highly iterative approach during the early stages of development, saving time and reducing costs and project risk. Overall this allows the pharmaceutical industry to develop the primary container around the device, not the device around the primary container. This presentation will discuss the wearable device landscape and highlight some of the benefits of primary container customization in combination with large volume injectors.

5:10

End of Day One

CASE
STUDY

Thursday September 5, 2019

8:00

Chairperson's Welcome and Complimentary Breakfast

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

8:15

Pre-Filled Syringes Novel Approach & Technology: Increasing Safety and Performances in the Delivery of Demanding Biologics

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

8:55

Case Studies Launching Platforms for Big and Small Pharma

Steven Badelt, Ph.D., Managing Partner, Suttons Creek



The term platform has been promoted within the drug delivery marketplace with multiple interpretations and implications for both pharmaceutical companies and their suppliers. The nuances for execution with "platform" are different for well-established pharma with large device teams and for small pharma who have never launched a combination product. In this presentation, we will discuss the circumstances and lessons learned in case studies across large and small pharma, with both internal and external development projects. The materials presented will provide common challenges in project execution, on getting approvals from the agencies, and solution pathways.

- Challenges, case studies from over 50 combination products.
- Governance considerations
- What we've learned and implemented into our internal IP.
- The common challenges seen in execution.
- Integration of concepts from some recent FDA presentations.

9:35 *Mid-morning coffee break — Exhibitor Room*

10:00 **What Is “New” In the Area of Autoinjectors, Pen Injectors, Patch Pumps and Wearables?**
Jakob Lange, Account Director, Ypsomed



Market overview and update: Recent innovations and trends on:

CASE STUDY

- 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

10:40 **Biologics Formulation for COP Syringe Optimized to Eliminating Use of Surfactant**

Toshiro Katayama, Product Manager, Zeon

ZEON



Key Properties of COP

CASE STUDY

- 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

11:20 **The Role of Human Factors in Evaluating Innovative Injectables**

Ellie Younger, Device Project Lead, Human Factors and Risk Management, Biogen (Co-Author, Nick Zampa, D. Eng, Senior Engineer I, Technical Development)



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.

12:00 *Complimentary Lunch Sponsored By:*



1:00 **Lunch Sponsor Presentation: Robotic Revolution and Annex 1 implications**

Michele Arduini, Manager, IMA LIFE



In 2018 the FDA approved 25 new “personalized medicines” (42% of all new drug approvals in year 2018). These products are manufactured with smaller volumes for medium-to-low production batches. The increasing complexity of these new high-value drugs requires the adoption of new methods and technologies to process high-mix batches into multiple formats or sizes (such as vials, cartridges and syringes for parenteral use) so as to ensure a flexible and repeatable process, in a controlled, safe environment.

INJECTA's intensive use of robots not only provides precise, consistent handling activities, but also offers a high level of flexibility while improving product quality, manufacturing efficiency and data management with Industry 4.0 capability.

1:20 **Particles in Intravitreal Injections**

Susan M. Dounce, PhD, TCS Director, Technology, 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.

2:00

Future Manufacturing Networks and Process Technology Strategies to Support the Next Generation of Elastomeric Components for PFS Drug Delivery Devices

Douglas Cusato, Director, Sumitomo Rubber

PFS drug delivery devices continue to evolve to support new regulatory expectations, personalized patient needs and the broader pharmaceutical industry strategy. As this device progression moves forward, there will be a continued demand for primary container technology innovation. The demand and related innovations will certainly include improved manufacturing technologies and process capabilities and flexible manufacturing networks. Some of these architectural changes will be opportunistic and some of the changes will be foundational for organizations to succeed in the future.

This presentation will focus on future manufacturing networks and process technology strategies to support the next generation of elastomeric components for PFS drug delivery devices and the broader pharmaceutical industry strategy.

2:30

Afternoon Networking Break

2:50

The Evolution in Vacuum Decay Leak Testing Technology

Dr. Wenliang Chen, Technical Director, Asia Market, PTI

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



3:20

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.



3:50

Tackle Pre-filled Syringe QC With Bouncer

Robin Sweeney, PhD, Unchained Labs Product Manager

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.



CASE STUDY

4:20

Chairperson's closing remarks

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