People • Science • Regulation

PDA Letter

Volume LIV • Issue 2 www.pda.org/pdaletter February 2018

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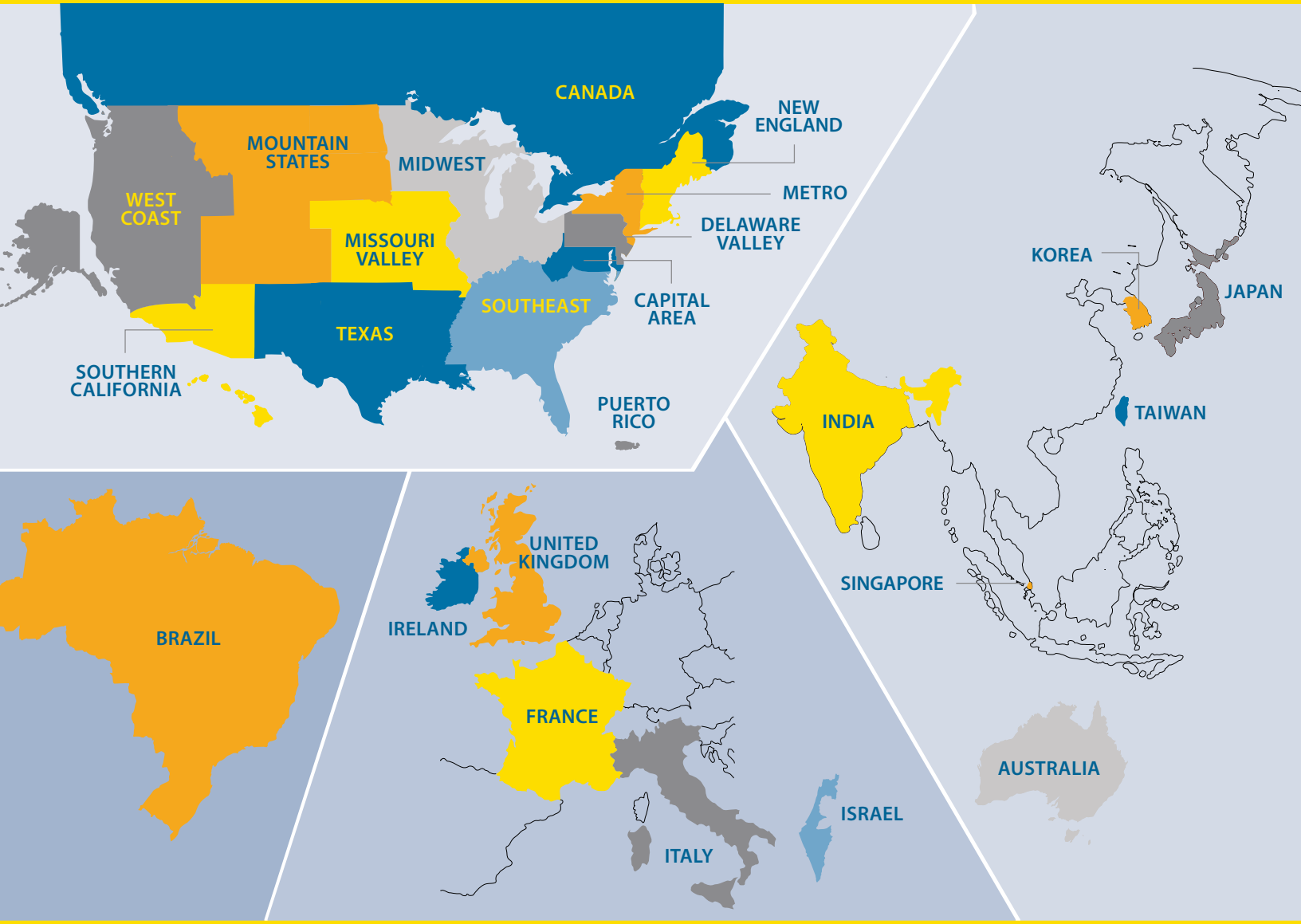
PDA Chapters

Your Local PDA Connection



Are you curious about the issues unique to your region?

Another layer of PDA leadership resides at the grassroots level in the Chapter organizations. Regional PDA Chapters provide local services to the membership, including translations of PDA publications, networking social events, student scholarship and annual regulatory and technical conferences. Each Chapter is managed by volunteer leaders.

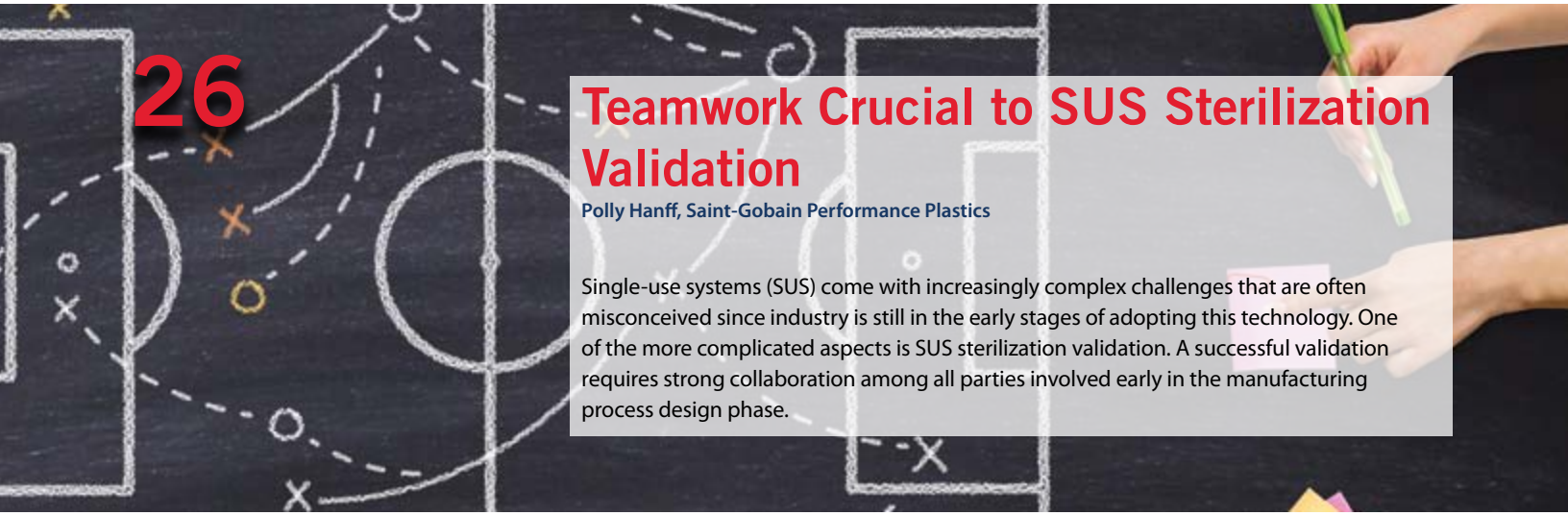
Learn more about your local Chapter at www.pda.org/Chapters.

February 2018 PDA Letter

2018 PDA Annual Meeting

Show Issue

This year's Annual Meeting takes place in Orlando, Fla. and will feature a new format and schedule. Thoughout this issue are a number of articles highlighting talks and other events at this signature PDA meeting.



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Teamwork Crucial to SUS Sterilization Validation

Polly Hanff, Saint-Gobain Performance Plastics

Single-use systems (SUS) come with increasingly complex challenges that are often misconceived since industry is still in the early stages of adopting this technology. One of the more complicated aspects is SUS sterilization validation. A successful validation requires strong collaboration among all parties involved early in the manufacturing process design phase.

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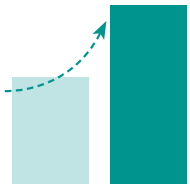

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CMOS and Single-Use Systems: Partnering Together for Flexibility

CMOs are adopting single-use systems for their operations, but why?

4 Capabilities to Operationalizing Resilience

Amy D. Wilson, PhD, Biogen

To ensure safety, quality and reliability while making such investments in productivity, there is another capacity that is needed. This is *resilience*.

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Digital Exclusives

> Quality: One Question, Many Answers
How can industry and the U.S. FDA adapt current quality standards to innovative therapies? Find out from DPS Engineering's **Stephanie Gaulding** who attended the *2017 PDA/FDA Joint Regulatory Conference.*

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For more information on all PDA podcasts and other interviews, please visit:

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To learn more about how PDA is promoting progress in aseptic manufacturing, visit pda.org

Wealth of Options for SUS Tech

Single-use systems (SUS) are a relatively new technology in pharmaceutical manufacturing, with roots in the early 1980s. Adoption of SUS has grown considerably since the 2000s ***(1).*** This was one of the reasons PDA published *Technical Report No. 66: Application of Single-Use Systems in Pharmaceutical Manufacturing* in 2014.

Considering the continuing adoption of SUS, I thought I would take a look at some of the advancements in these technologies by reviewing some recent articles found in the PDA *news uPDAte* newsfeed (http://www.pda.myindustrytracker.com/en/top).

SUS can be quite complex as they can require a lot of components, making the supply chain for SUS complex ***(2).*** Manufacturers using SUS often manage risk by performing additional tests or storing large amounts of safety stock ***(2).*** MilliporeSigma's Mobius® MyWay Portfolio, launched last January, offers customized SUS assemblies for manufacturers to reduce the lead time for implementing SUS. This portfolio offers flexible assembly design, reduced parts, decreased implementation time and improved stocking of components ***(2).*** Parker Hannifin also offers a design space solution for SUS assemblies, complete with validated parts ***(3).*** And when it comes to container closure integrity testing for SUS, French company Confarma offers an alternative to traditional dye tests using methylene blue and microbial challenges ***(4).***

As you can see, suppliers are continuing to improve the design and testing of SUS. Many of the exhibitors at the upcoming *2018 PDA Annual Meeting* offer SUS solutions/capabilities. If you plan to attend the meeting and either work directly with or are implementing SUS, I encourage you to talk to some of the exhibitors about the latest advancements in SUS technologies.

Finally, I wanted to get in a word about SUS and sustainability. Obviously, SUS are not reusable and from a green pharma perspective could present a challenge to sustainability efforts, especially considering that SUS components are generally made from plastic. Evidence suggests, however, that SUS may prove more sustainability friendly than traditional reusable stainless steel reactors due to lower energy and water requirements ***(5).*** So, if your facility, is not using SUS or just now considering it, this is one more thing to keep in mind.

I look forward to seeing some of you next month at the *2018 PDA Annual Meeting* in Orlando, Fla.

Rebecca Stauffer

References

1. "A Brief History of Single-Use Manufacturing." *BioPharm International* (Nov. 2, 2011) tinyurl.com/y9udulck
2. "Single-Use That's Ready When You Are." *The Medicine Maker* (November 2017) tinyurl.com/ycgsr4gx
3. "Design Solution for Single-Use Technology Applications." *BioPharm International* (Nov. 27, 2017) tinyurl.com/y9go3js4
4. Karcher, L. "Container Closure Integrity Tests (CCIT) for Single-Use Systems." *CONFARMA FRANCE SAS* (November 27, 2017) tinyurl.com/yad69x2v
5. Flanagan, B. "Single-Use Technology And Sustainability: GE Quantifies The Environmental Impact." *Biopharmaceutical Online* tinyurl.com/ydf4x5v3

Hit the Books at the 2018 PDA Annual Meeting

4 Academic Speakers to Address Innovation-Related Topics at Annual Meeting in March

This year's Annual Meeting will feature the following speakers representing academic institutions:

- **Steven Spear,** PhD, Senior Lecturer, System Dynamics, Massachusetts Institute of Technology will speak on company dynamics in the second plenary, Monday, March 19, 4 p.m.

- **Paul Stey,** PhD, Biomedical Data Scientist, will copresent on "New Approaches to Harnessing Data at a Portfolio Level" in "B3: Trends in Digital Information and Automated Technology," Tuesday, March 20, 4 p.m.

- **Suzanne Farid,** PhD, Codirector, Future Targeted Healthcare Manufacturing Hub, University College London, will present "Streamlining Biopharmaceutical Decision-Making," in "A3: Agile Bioprocessing," Tuesday, March 20, 4 p.m.

- **Matthias Gromeier,** MD, Professor, Department of Neurosurgery, Duke University Medical School, will close out the meeting with his talk, "Polio Virus Vaccine Trial," Wednesday, March 21, 2:15 p.m.

More information about these and other speakers can be found at www.pda.org/2018annual.

Global Regulators to Address Packaging Concerns

The following three regulators will offer regulatory perspectives on packaging issues at the PDA Europe *Parenteral Packaging* conference, Feb. 27, in the opening plenary session:

- **Andrew Hopkins,** MHRA, will speak on container closure integrity testing and Annex 1, 9:15 a.m.

- **Umit Kartoglu,** WHO, will speak on secondary packaging considerations, 9:45 a.m.

- **Charudharshini Srinivasan,** U.S. FDA, will speak on risk-based approaches to assessing pharmaceutical packaging for parenterals, 10:15 a.m.

For more information, visit www.pda.org/EU/parpack2018.

PDA Family Continues to Grow

PDA is excited to have some new folks join the PDA family, both in the United States and Europe.

Glenn Wright, has joined PDA effective Jan. 1 in the role of Business Development Fellow. Glenn has been a longtime PDA volunteer and was a member of the Board of Directors for many years.

Lindsey Navin, Senior Marketing Coordinator, joined PDA Oct. 23 and brings with her a broad background in marketing, having worked in a number of industries, including academia, communications and healthcare.

Annette Bacchus, Manager of Programs, joined PDA on January 22. Most recently she was Senior Manager of Industry Relations at the American Academy of Otolaryngology-Head and Neck Surgery.

Teresa Schubach, Manager Programs and Events, joined the PDA Europe office in Berlin on January 15. She has a degree from Johann Wolfgang Goethe University in Frankfurt where she majored in Biology.

PDA Remembers Edwin Rivera-Martinez

PDA was saddened to learn of the passing of longtime volunteer **Edwin Rivera-Martinez** on Dec. 28. Edwin was a major part of PDA's family. Many of us remember how he could spin a good yarn and capture an audience with his enthralling presentations. He was heavily involved in supporting efforts to ensure the supply chain around the world, including the Asia-Pacific region.

Edwin made many contributions as a PDA volunteer. From 2012–2017 he was part of the Regulatory Affairs and Quality

Advisory Board (RAQAB). As part of this role, he also served as the RAQAB liaison to the *PDA Letter* Editorial Committee. He also served on the program planning committees for PDA's supply chain conferences/workshops in 2010, 2011 and 2013 and was a speaker and instructor at a Japan Chapter Annual Meeting. Edwin also spoke at a 2009 PDA meeting in Europe on the supply chain of pharmaceutical ingredients. Additionally, he was an active contributor to the Quality Metrics Task Force. His significant contributions to PDA are part of his legacy that will remain with us.

His extensive industry experience served to benefit PDA and its members. He was proud of his many years of work at the U.S. FDA where he was an investigator. While at FDA, he was the driving force behind ICH Q7, *Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients.* As part of CDER, he was actively involved in many initiatives, training programs and conferences with PDA, where he contributed to communicating the Agency's expectations and industry practice on important technical and regulatory matters.

He left FDA in 2010 to join PAREXEL. Two years later he joined Sanofi-Aventis, working at an office down the street from PDA headquarters. In fact, it was not uncommon for him to drop by PDA and visit staff members.

While working at Sanofi over the past six years, Edwin was always fully dedicated to quality, compliance and patient safety and was a strong contributor to the company's quality culture journey. He was a true gentleman whose kindness was unanimously recognized by many Sanofi colleagues across the world.

Edwin will be sorely missed by PDA. His passion for ensuring safe medicines was infectious and the Association plans to carry on this legacy.

PDA Volunteer Spotlight

Borke Van Belle

- Senior Director Integrated Quality Solutions
- *Janssen, Pharmaceutical Companies of Johnson & Johnson*
- Member Since | **2009**
- Current City | **Schaffhausen, Switzerland**
- Originally From | **Ghent, Belgium**

Volunteering also helped me to grow my professional network

Why did you decide to volunteer for PDA?
Volunteering for PDA provides an excellent network for understanding, developing and sharing industry practices. It has allowed me to share some of the exciting technological and conceptual progress we have made at Janssen for the patients we serve. Volunteering also helped me to grow my professional network. Acting as a PDA program committee member, panelist, moderator and speaker has given me broad insight and perspective on where the industry is going.

You spoke at the *2nd PDA Europe Annual Meeting* last year. What was that like?
My presentation on the cost of quality was very well received; the audience really engaged in a dialogue on shifting from a pure "number of occurrences"-driven quality approach to an impact-driven quality approach. Speaking business language as a quality leader supports balanced priority-setting and decision-making, and is a key asset in driving proactive quality. This point of mine really resonated with the audience.

How has PDA contributed to your professional career?
PDA offers a broad network of technical, regulatory and scientific professionals. Through PDA's conferences and interest groups, I can stay on top of recent developments, and have opportunities to present, share and discuss progress within specific areas such as pharmaceutical freeze drying, visual inspection and cost of quality.

Who would you like to sit down with for a conversation?
I would enjoy sitting down with **Dr. Paul Janssen**, founder of Janssen Pharmaceutica, and discuss the latest innovations in transformational medicine. I think this would be very inspiring. With his phrase, "the patients are waiting," he summarized in only a few words why we do what we do!

What is on your reading list?
Since getting my Kindle, I always have a book at hand. The device makes me read a lot more books than previously. I recently enjoyed reading Nathan Hill's *The Nix,* and am now e-turning the pages of *Sprint* by Jack Knapp. This book looks at how to test new ideas in just five days.

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Where do leading experts turn to communicate with the PDA community?

The *PDA Letter* and *PDA Journal of Pharmaceutical Science and Technology*

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JAMES AGALLOCO
JAMES AKERS
DENNIS JENKE
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Chapter Learns About Future of Facility Design

Anthony Grilli, Focus Scientific

Is the industry ready to move from large biotech facilities to modular, predesigned and prefabricated facilities?

According to **Maik Jornitz** in his Oct. 17 PDA Metro Chapter presentation, "Future Facility and Process Needs – Where are We and What do We Need?", the answer is "yes."

Jornitz opened his talk by outlining the three trends driving biotechnology manufacturing to smaller flexible manufacturing: **1)** aging populations and a global rising middle class increases the need for manufacturing capacity, **2)** changing microbial diseases may require fast responses and **3)** personalized medicines require specific process systems on a very small scale.

The demand for increased speed, agility and efficiency points toward smaller container type manufacturing modules. Bioreactors have transitioned from 10,000 liter systems to 2,000 liter and smaller. Multiple products can be manufactured inside prefabricated containers housed in open ballroom-style manufacturing facilities, which allows for enhanced flexibility. Jornitz compared the development of these new manufacturing processes to the state of modern telephones—cordless phones and circular dials could be compared to brick-and-mortar facilities, mobile landlines (circa 1995) are analogous to modular facilities and cell phones can be compared to predesigned facilities.

Finally, Jornitz detailed how the return on investment can be significantly higher with prefabricated construction. He used examples from his own experiences, including transitioning from a 10,000 liter bioreactor to multiple 2,000 liter systems, a single-use technology implementation, migration from a single-product facility to multiproduct and Pfizer's use of prefabricated, modular pods at one of its facilities.

His conclusion featured the following takeaways:

- Facilities/processes are becoming too outdated to meet new requirements
- While there are many new tools available, legacy systems continue to prevail
- Cost-per-square foot is not the best cost measurement
- Multiproduct facilities are becoming prevalent
- New facility deployments require faster turnarounds

PDA Who's Who

Maik Jornitz, CEO, G-CON Manufacturing, Inc.

Student Chapter Shows Enthusiasm for Industry

Denyse Baker, PDA

In November, I had the great fortune to visit members of the PDA student chapter (part of the Southern California Chapter) at the Keck Graduate Institute in Claremont, Calif., the first higher education institution in the United States dedicated to the applied life sciences. This entrepreneurial approach to learning prepares these students to hit the ground running once they receive their degrees.

The group raised many great questions. Our discussion covered working for commercial companies as compared to the U.S. FDA and other opportunities for budding regulatory professionals. They impressed me with their knowledge of current regulatory issues. This group is much more aware of the landscape within the biopharma industry than I was at that point in my career. They are also great networkers and are building connections through PDA. Several will soon graduate; I am sure they will prove successful contributors to the industry.

(top l-r) Srinandhan Ramakrishnan, Ishan Billore, Justin Bown, Preet Marwaha, Jeremy Garibay, Sheba Zaman, Denyse Baker, Madelyn Low, Alexandra Kirby, Lyanna Jauregui, Nikita Malik, Barath Muralidharan, Edward Hong, Jasmine Tat
(bottom l-r) Swetha Prabhkaran, Joshua Sonico, Nicole Kohnen, Tiffany Smolinski, Indah Kusumawardhani

More Opportunities to Grow Your Network

This year's *PDA Annual Meeting* in Orlando, Fla., offers more opportunities for networking than in previous years. In addition, based on feedback from attendees of previous Annual Meetings, the meeting organizers have altered the schedule of networking events, which includes the following slate of activities.

Monday, March 19

Sunrise Yoga

Start the conference with some outdoor yoga exercise in Caiman Court. $40. Proceeds will go to charity.

Grand Opening Celebration

Join your colleagues to celebrate the grand opening of the Exhibit Hall. Meet with exhibitors to learn about the latest technologies and talk to poster presenters. Refreshments will be served. 5–6:30 p.m.

Tuesday, March 20

Happy Hour in the Exhibit Hall

After the first full day of sessions, take some time to network in the Exhibit Hall with fellow attendees. 5:30–6:30 p.m.

Wednesday, March 21

Havana Nights Closing Reception

The closing reception has been moved from Tuesday to Wednesday night. Grab your sundresses and sandals, guayabera shirt and fedora and celebrate the end of the meeting Cuban style! Join your fellow attendees for a Cuban-themed closing reception. Enjoy a night under the stars with live entertainment, specialty cocktails and Cuban-inspired bites. Attendees of the *2018 Manufacturing Intelligence Workshop* are also invited to join the festivities. 7–10 p.m.

In addition, attendees can take advantage of refreshment breaks and networking luncheons Tuesday and Wednesday for additional opportunities to reconnect with existing colleagues and make new contacts.

Conference Co-chair Hanns-Christian Mahler, Lonza

Dr. Florian Turk, Sandoz

Sudeshina Dutta Ray, Amgen

2017 PDA Europe Universe of Pre-filled Syringes & Injection Devices
November 7–8 | Vienna, Austria

At the close of the conference, former Senior Vice President Georg Rössling received a special thanks for his involvement in the *Universe of Pre-filled Syringes* meeting over the years

(l-r) Simon Wilson, Pfizer; Florian Turk, Sandoz; Sheldon Moberg, Amgen; Mathias Romacker, Pfizer

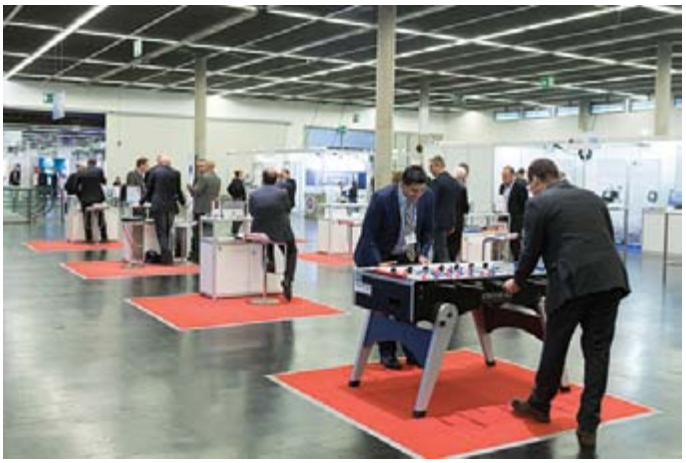
Manfred Maeder, PhD, Novartis, moderated the closing panel of the meeting

Michael W. Harrison, Eli Lilly, spoke in "Track A, Session 1: New Applications & Challenges"

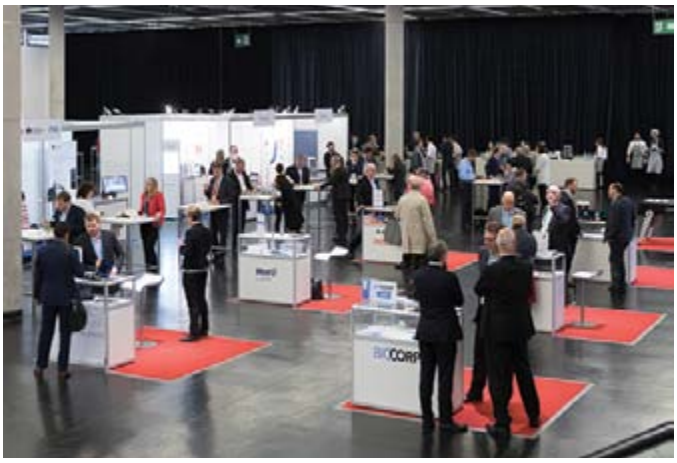
PDA Prefilled Syringes Exhibition Draws Crowd

Last year's *Universe of Pre-filled Syringes and Injection Devices* was PDA's most successful yet! One only had to experience the hustle and bustle of activity in the Exhibition Hall to see why this event flourished, making it one of the premier global events focused on prefilled syringes and injection devices. More than 100 companies exhibited products in the Exhibition Hall.

Held in the majestic city of Vienna, the organizers made a few changes to the exhibition based on experience from the 2015 meeting which was held in the same city. The layout of the booths was modified to allow more walking space (necessary due to the size of the crowds!). Additional coffee breaks were added, and lunch breaks were extended. Other enhancements included a live demonstration booth from Groninger of new techniques for decontaminating components, a communications corner where attendees could sit and catch up on emails and a few foosball tables for those who just wanted to let loose. And, for the first time ever, the exhibition featured an Innovation Gallery where companies could showcase their groundbreaking technologies in glass covered cases. The Innovation Gallery exhibitors included Vetter, Portal Instruments, Smart Skin, Altaviz, Biocorp and West.



All in all, the exhibition proved a large draw. The PDA Europe Exhibition Committee thanks the exhibitors, poster presenters and Innovation Gallery participants for helping make the whole event a huge success!



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Interest Group Tours Prefilled Exhibition Hall

Derek Duncan, PhD, Lighthouse Instruments, EU Packacing Science Interest Group Leader

During the *Universe of Pre-filled Syringes and Injection Devices* conference and exhibition in Vienna, the EU Packaging Science Interest Group met for a guided tour through the exhibition area before the start of the second day of the conference on Nov. 8. Starting in the Innovation Gallery, a new addition where key exhibitors could showcase innovative technologies, the group was given an interactive presentation and demo from Smart Skin Technologies on their novel pressure-sensitive skin technology. A lively discussion followed about the applications for monitoring and troubleshooting points in packaging and filling lines where containers experience excessive contact or pressure points using this solution.

The group was then hosted by representatives from Groninger who invited the group to view a demonstration of a new technique for decontaminating packaging components and transferring them into the sterile area. The next visit was to the poster area where experts from Oval Medical Technologies led a discussion about autoinjector design. Here, discussions covered the use of polymers for better user-centric device designs as well as the ability to handle administration of challenging formulations. The tour ended with a stop at the Atec Sterile Technology booth where representatives from the company provided a demonstration of a stopper processing system.

The purpose of the Packaging Science Interest Group is to bring packaging experts together to openly discuss current packaging topics. Thanks to all the people and companies who made the meeting in Vienna a success! The next meeting of the group will be the afternoon of Feb. 26 before PDA's *Parenteral Packaging* conference in Rome. Don't miss this opportunity!

IG *Corner*

New Format for PDA Interest Group Meetings at This Year's Annual Meeting

Change is in the air for PDA interest group meetings at this year's Annual Meeting! Instead of occurring after the final session of the first two days of the meeting, interest group meetings will be held concurrent with breakout sessions, starting the second day of the conference. This will give attendees more sessions from which to choose during the day and free up time in the evenings.

The new schedule for interest groups falling under the Science and Biopharmaceutical Advisory Boards is as follows:

Tuesday, March 20	Wednesday, March 21
10:45 a.m. – 12:15 p.m.	**10:45 a.m. – 12:15 p.m.**
Process Validation Interest Group Filtration Interest Group	Visual Inspection of Parenterals Interest Group Combination Products Interest Group
1:45 p.m. – 3:15 p.m.	
Biopharmaceutical Manufacturing Interest Group *(replacement for Biotechnology Interest Group)*	
4 :00 p.m.– 5:30 p.m.	
Cell and Gene Therapy Interest Group *(new interest group!)* Facilities and Engineering Interest Group	

The schedule for the Regulatory Affairs and Quality Advisory Board interest group meeting can be found on p. 37. For more information about interest group meetings, visit www.pda.org/2018annual.

Extractables Testing of Aluminosilicate and Borosilicate Glass Containers

Daniel Kramer, Robert Schaut, PhD, Ela Bakowska, Misty Riesbeck, Alex Thomas, Steven Tietje, Corning Incorporated

When it comes to required extraction studies ***(1)*** for new glass compositions that are starting to enter the parenteral packaging market, manufacturers naturally have questions about the suitability of these new products. One extraction study potentially answers these questions.

Extraction studies are necessary because glass containers, which are frequently considered inert, react with aqueous solutions at relatively low rates in most parenteral drug applications.

Extraction methods for glass assess the durability of the container surface to any number of solution chemistries, often accelerated using elevated temperatures. Solution analysis then quantifies the amount of glass constituents that have reacted or dissolved from the container into solution.

Compendial chapters offer methods to quantify the hydrolytic resistance of glass containers for pharmaceutical packaging ***(2–4).*** These methods involve an accelerated treatment (e.g., autoclave) of containers filled with pure water followed by titration of the reacted solution ***(5).*** A separate, quantitative analysis of the non-titrated, post-autoclave solution provides the concentrations of elements extracted from the interior of the glass container. While not an exhaustive representation of container extracts from all conditions ***(3),*** these are perhaps the most commonly referenced set of extraction conditions.

Although compendial chapters group results by nominal container volume and set numerous unique limits, glass corrosion literature has demonstrated that extracted solution concentrations are a result of glass surface area and true solution volume diluting the response ***(6).*** It is therefore helpful to compare extract concentrations from dissimilar container shapes by normalizing the results to the glass surface area-to-solution volume ratio (SA/V).

The chemical durability of glass containers (i.e., resistance to corrosion) depends on many factors, including bulk composition, changes in surface chemistry produced during manufacturing (e.g., converting), the solution chemistry of reaction and the time and temperature of exposure ***(3,7).*** For many years, glass vials used for parenteral packaging were mostly composed of borosilicate composition; durable, boron-free aluminosilicate containers have been introduced for use in parenteral packaging ***(8).*** Chemical strengthening with molten salt is used to improve the mechanical performance of borosilicate and aluminosilicate glass packaging components.

In this study, the aluminosilicate containers used were chemically strengthened. Regarding glass composition, hydrolytic resistance of silicate glasses generally depends on the relative amounts of oxides identified as network formers (e.g., SiO_2, B_2O_3), intermediates (e.g., Al_2O_3), and alkali/alkaline-earth modifiers (e.g., Na_2O, K_2O, CaO, MgO). In general, higher-silica glasses exhibit greater chemical durability, additions of alumina can improve durability in certain cases, and the addition of excess alkali oxides and boron ($R_2O + B_2O_3$) can have a negative effect on hydrolytic resistance ***(7).*** Other extractables may be a result of property modifiers (e.g., oxides of barium or iron) or fining agents (e.g., oxides of arsenic or tin) used in glass manufacturing, and from impurities in raw materials. The glass containers used in this study were commercially available borosilicate and aluminosilicate products designed specifically for use in primary pharmaceutical packaging. All three container types used in this study meet the Type I performance criteria (titration limit) for the surface hydrolytic test outlined in USP <660> Containers—Glass. The major components in each glass are outlined in **Table 1** below.

Although both glass tubing and/or formed containers may be used to characterize materials of construction, an extractables analysis of a primary packaging component must include testing of the final containers such as vials ready for drug fill. Containers that are molded or converted must be included in an extractables analysis in order to evaluate effects of the tube-to-vial converting process which can produce chemical heterogeneities across the container surface. These regions of variable chemical composition may lead to differences in chemical durability, which are undesirable, and these effects can only be evaluated in the final container.

Table 1 Oxide Components of Glasses Studied

Glass Type	SiO_2	Al_2O_3	B_2O_3	Na_2O	K_2O	CaO	MgO
Aluminosilicate A	✓	✓	×	✓	✓	✓	✓
Borosilicate B	✓	✓	✓	✓	×	✓	×
Borosilicate C	✓	✓	✓	✓	✓	✓	✓

✓ = present in bulk glass, × = not present

In certain cases, such chemical heterogeneities in borosilicate glass containers have been shown to produce delamination of silica-rich lamellae from the surface into the drug product ***(9,10).*** Often, these heterogeneities are caused by the volatilization of alkali and boron from the glass during the converting process and subsequent deposition resulting in a surface enriched in excess alkali and boron.

The vials used in this study were converted from size matched tubing and were converted to the same overall dimensions. The tubes were suitably closed with PTFE and silicone stoppers to hold liquid. Vials and tubes were filled with ultrapure water, and autoclaved with a hold of one hour at 121°C according to procedures outlined in USP chapter <660> and ISO 4802

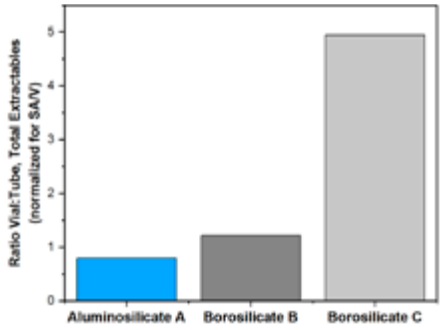

Figure 1 Ratio of Total Extractables for Vials and Tubes of Three Different Glasses *(The higher ratio for the borosilicate samples indicates a greater change in surface chemistry during the tube-to-vial converting process. Concentrations of extractables have been normalized for differences in SA/V.)*

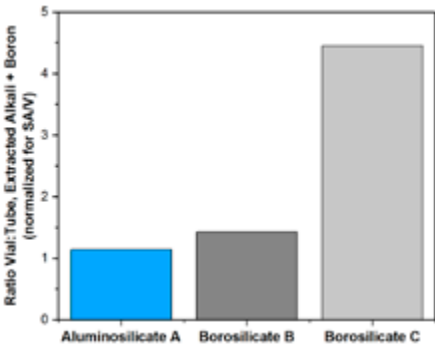

Figure 2 Ratio of Extracted Alkali+Boron for Vials and Tubes of Three Different Glasses

(2,4,6). The reacted solution samples were then analyzed quantitatively by ICP-MS. Concentrations were normalized for wetted surface area-to-fill volume to account for differences in container geometry.

To illustrate the effects of the converting process on chemical durability, extractables of formed vials and tubing are compared in **Figure 1** and **Figure 2.** For both borosilicate vials tested, the total concentration of extractables was greater than that of the parent glass tubing (even when normalized for differences in SA/V between the vials and tubing). This increase in total extractables after converting is due to changes in surface chemistry from the converting process. In **Figure 2,** only the relative concentrations of extracted alkali and boron are compared, and the vial-to-tube ratios of these extracted species were greater for the Borosilicate B and Borosilicate C containers/tubes than for the Aluminosilicate A containers/tubes.

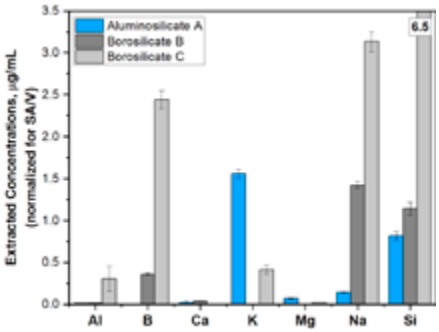

Figure 3 Extractables Profiles for Three Vial Types Measured by ICP-MS and Normalized by SA/V *(Concentrations greater than the chosen scale are labeled individually.)*

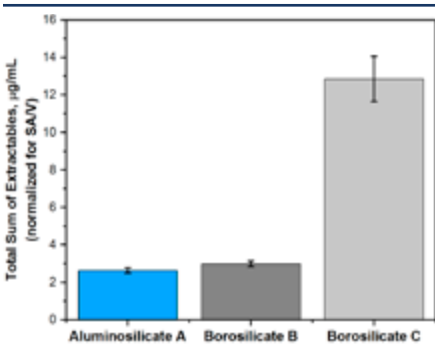

Figure 4 Total Sum of Extractables for Three Vial Types Measured by ICP-MS and Normalized for SA/V

The extractables profiles for size-matched vials are presented in **Figure 3** and include only extracted elements with a reported concentration greater than 0.01 ppm (µg/mL). A comparison of the total amount of extractables for each vial type is presented in **Figure 4**. The Aluminosilicate A containers exhibited lower concentrations of extracted aluminum and silicon than the (aluminum-containing) borosilicate containers. If the extracted amount of silicon, boron and aluminum is considered as a measure of breakdown of the glass network during corrosion, the extractables profile for Borosilicate C indicates it is the least chemically durable of the three container types tested. Alkali (Na, K) and boron components in glass have significantly higher dissolution rate in water compared to other glass components, so it is helpful to consider their extracted concentrations together rather than separately ***(7).*** The data in **Figure 3** shows that extracted Na+K+B is greater for both Borosilicate B and Borosilicate C than for Aluminosilicate A.

Despite a greater amount of extracted potassium for Aluminosilicate A, the comparison of total levels of extracted alkali+boron indicates that the Borosilicate B and Borosilicate C containers demonstrate a weaker resistance to corrosion in water compared to Aluminosilicate A. The Aluminosilicate A vials exhibited the lowest concentration of total extractables, overall.

In short, the extractables analysis shows Aluminosilicate A to have a high degree of chemical durability and more uniform surface chemistry after converting, further reinforcing its suitability for use in parenteral packaging applications.

[Editor's Note: The authors' company will be exhibiting at the *2018 PDA Annual Meeting*.**]**

References

1. Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics, May 1999, U.S. Food and Drug Administration.
2. Chapter <660> "Containers- Glass", Physical Tests, USP 40, United States Pharmacopeia.
3. Chapter <1660> "Evaluation of the Inner Surface Durability of Glass Containers", General Chapters, USP 40, United States Pharmacopeia.

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4. Chapter 3.2.1 "Glass Containers for Pharmaceutical Use", European Pharmacopeia.
5. ISO 4802:2016, "Glassware - Hydrolytic resistance of the interior surfaces of glass containers".
6. Ebert, W.L. "The Effects of the Glass Surface Area/Solution Volume Ratio on Glass Corrosion: A Critical Review," Argonne National Laboratory, March 1995.
7. Condradt, R. "Chemical Durability of Oxide Glasses in Aqueous Solutions: A Review." *Journal of the American Ceramic Society* 91 (2008): 728–735.
8. Schaut, R.A., et al. "A New Glass Option for Parenteral Packaging." *PDA Journal of Pharmaceutical Science and Technology* 68 (2014): 527–534
9. Schaut, R.A., and Weeks, W.P. "Historical Review of Glasses Used for Parenteral Packaging." *PDA Journal of Pharmaceutical Science and Technology* 71 (2017): 279–296.
10. Swift, R."Glass containers for parenteral products." In *Pharmaceutical Dosage Forms - Parenteral Medications, Third Edition,* edited by Sandeep Nema and John D. Ludwig, 287-304. Boca Raton, FL: CRC Press, 2012.

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Achieve True Manufacturing Reliability

Hal Baseman, ValSource, and Brett Duersch, Merck and Co.

2018 PDA Annual Meeting

Pharmaceutical manufacturing is changing. Perhaps better stated, the manufacturing of regulated healthcare products must change. We can no longer focus only on manufacturing products that are effective, safe and compliant. Today, we must also manufacture products that are affordable, available and a sound business proposition. This requires more complete knowledge.

The accessibility of information is leading to more complete knowledge. A few key questions reflect on how we can best use this data:

1. Not all data are created equal—some information is more important. What new approaches are required to help prioritize the most important information? How do we build in learning approaches that support priority of data over the lifecycle of a product/process?
2. How can these modern data approaches drive manufacturing improvements that lead to higher product quality and more reliable production?
3. How do we contextualize increasingly complex manufacturing datasets, and easily convert them to knowledge and action? Are there standard approaches that can lead to increased efficiencies within a firm and better sharing of information between companies?
4. What regulatory/quality challenges need to be considered as the quantity and complexity of data explodes? How do we partner with regulators so that everyone can take advantage of the modern data rich environment?
5. What are the barriers/risks of using new systems to gather this information? What are the benefits that make it worth confronting these challenges?

Next month, PDA will hold a groundbreaking workshop on manufacturing intelligence following the *2018 PDA Annual Meeting*, bringing together experts and interested parties in an interactive forum to learn about big data and how it can be used to achieve effective manufacturing. This is a very important meeting for those using, or considering using, aspects of big data to operate manufacturing systems. In other words, it is an essential meeting for anyone involved with manufacturing regulated healthcare products.

2018 PDA Manufacturing Intelligence Workshop

Orlando, Fla.

March 21–22

www.pda.org/2018mi

2018 PDA Upcoming Events

SAVE THE DATE for PDA's 2018 Events

FEBRUARY

25-28

NEW COURSE

Downstream Processing (DSP) – Purification of Biomolecules
Clausthal-Zellerfeld, Germany
pda.org/UC/DSP2018

26

Interest Group Meeting: Packaging Science
Rome, Italy
pda.org/EU/IDPackaing2018

26

Interest Group Meeting: Pre-filled Syringes
Rome, Italy
pda.org/EU/IGPrefilled2018

26-1

Fundamentals of Aseptic Processing – Option 1
Bethesda, MD
pda.org/2018FebFundAP

27-28

Parenteral Packaging Conference
Rome, Italy
pda.org/EU/ParPack2018

27-1

NEW COURSE

CBP – Continuous Bioprocessing of Biomolecules
Clausthal-Zellerfeld, Germany
pda.org/UC/CBP2018

28

PDA Southern California Chapter 7th Annual Industry Summit and Exhibitor Showcase
Yorba Linda, CA
pda.org/SoCal2018IS

28-2

Human Factors Course Series
Bethesda, MD
pda.org/2018HF

MARCH

1

Container Closure Development
Rome, Italy
pda.org/EU/CCD2018

1

Container Closure Integrity Testing
Rome, Italy
pda.org/EU/CCI2018

1-2

Extractables & Leachables
Rome, Italy
pda.org/EU/E-and-L2018

6-7

NEW COURSE

Strategies for Formulations Development: How to Get the Right Data in the Right Amount at the Right Time
Bethesda, MD
pda.org/2018SFD

12-16

PDA Aseptic Processing – Option 2
Week 2: Apr. 9-13
Bethesda, MD
pda.org/2018aseptic2

19-21

2018 PDA Annual Meeting
Orlando, FL
pda.org/2018Annual

21-22

2018 PDA Manufacturing Intelligence
Orlando, FL
pda.org/2018MI

22-23

2018 PDA Annual Meeting Course Series
Orlando, FL
pda.org/2018AnnualCourses

27-29

Airflow Visualization Techniques and Practices – Option 1
Bethesda, MD
pda.org/2018MarAir

27-29

Validation of Biotechnology-Related Cleaning Processes – Option 1
Bethesda, MD
pda.org/2018MarValBiotech

APRIL

4-5

NEW COURSE

Temperature Sensitive Packaging and Distribution for Biopharmaceuticals
Franklin, MA
pda.org/2018TempSensitive

10

Particle Identification in Parenterals
Berlin, Germany
pda.org/EU/TCParticleID2018

11-12

An Introduction to Visual Inspection
Berlin, Germany
pda.org/EU/tc-visual2018

11 -12

Mastering Automated Visual Inspection
Berlin, Germany
pda.org/EU/AutoVI2018

13

Interest Group Meeting Visual Inspection
Berlin, Germany
pda.org/EU/IGVisual2018

17-18

Quality Culture Transformation Resources
Mainz, Germany
pda.org/EU/AprTransform2018

19-20

SOLD OUT

PDA Quality Culture Transformation – ***Regulators Only***
London, UK
pda.org/2018AprTransform

20

NEW COURSE

Addressing Biofilm and Other Non-routine Microbial Events
Bethesda, MD
pda.org/2018Biofilm

Denotes laboratory courses taught in Europe. | This course is taught in PDA's U.S. manufacturing training facility.

For an updated PDA calendar of events, please visit:
pda.org/calendar

23-27
Freeze Drying in Practice
Osterode am Harz, Germany
pda.org/EU/fdp2018

23-27
PDA Visual Inspection Course Series – Option 1
Bethesda, MD
pda.org/2018AprVI

24
2018 PDA Lyophilization Interest Group Workshop
Bethesda, MD
pda.org/2018LyoIG

24-25
Vaccines Conference
Malaga, Spain
pda.org/EUVaccines2018

25
2018 PDA Visual Inspection Interest Group Workshop
Bethesda, MD
pda.org/2018VisualIG

MAY

1-4
Regulatory and Compliance Course Series
Bethesda, MD
pda.org/2018RCCS

7
Interest Group Meeting: Advanced Virus Detection Technologies
Florence, Italy
pda.org/EU/ADVT2018

7-11
PDA Aseptic Processing – Option 3
Week 2: Jun. 4-8
Bethesda, MD
pda.org/2018aseptic3

8-9
Virus Forum
Florence, Italy
pda.org/EU/Virus2018

14-15
2018 PDA Sterile Medicinal Products Manufacturing Conference
Bethesda, MD
pda.org/2018Sterile

15-17
Validation of Moist Heat Sterilization Processes – Option 1
Bethesda, MD
pda.org/2018MayVMH

21-24
Fundamentals of Aseptic Processing – Option 2
Bethesda, MD
pda.org/2018MayFundAP

29-30
Pharmacopoeia Conference
Vienna, Austria
pda.org/EU/pharma2018

ADDITIONAL SIGNATURE EVENTS IN 2018

JUNE

26-27 **3rd PDA Europe Annual Meeting**
Berlin, Germany | *pda.org/EU/Annual2018*

SEPTEMBER

26-27 **2018 PDA Biosimilars Workshop**
Washington, DC | *pda.org/2018biosimilars*

OCTOBER

8-9 **2018 PDA Universe of Pre-filled Syringes and Injection Devices**
Orlando, FL | *pda.org/2018PFS*

10 **2018 PDA Combination Products Workshop**
Orlando, FL | *pda.org/2018Combo*

15-16 **PDA Europe Pharmaceutical Microbiology**
Berlin, Germany | *pda.org/EU/PharmaMicro*
(Some sessions simulcast with PDA North America)

15-17 **13th Annual PDA Conference on Pharmaceutical Microbiology**
Bethesda, MD | *pda.org/2018Micro*
(Some sessions simulcast with PDA Europe)

17-18 **2018 PDA Endotoxins Workshop**
Bethesda, MD | *pda.org/2018Endotoxins*

NOVEMBER

6-7 **Outsourcing & Supply Chain: A 360° View**
Seville, Spain | *pda.org/EU/Outsourcing2018*

27-28 **11th Workshop on Monoclonal Antibodies**
Seville, Spain | *pda.org/EU/MABS2018*

27-28 **Pharmaceutical Freeze Drying Conference**
Seville, Spain | pda.org/EU/FreezeDrying2018

Teamwork Crucial to SUS Sterilization Validation

Polly Hanff, Saint-Gobain Performance Plastics

Single-use systems (SUS) come with increasingly complex challenges that are often misconceived since industry is still in the early stages of adopting this technology. One of the more complicated SUS aspects is sterilization validation. A successful validation requires strong collaboration early in the manufacturing process design phase among all parties involved.

The pharma firm, the SUS manufacturer, the contract sterilization vendor and the contract microbiology laboratory each play a part within the validation process. This partnership ensures shared understanding between all four players on the inherent complexity, uncertainty and resource demand in SUS design, validation and commercial manufacturing. Additionally, common misconceptions, false assumptions and veiled communication between the pharma firm and the SUS manufacturer must be highlighted, brought into the open and addressed. Such open collaboration cultivates invaluable knowledge transfer, greatly minimizing risk of SUS failures later on.

One of the most important outputs of this open collaboration can be found in an effective validation approach to the sterilization of SUS using gamma irradiation.

No Clear Guidance for Sterilization Validation

The complexity of SUS sterilization validation and associated process controls are commonly underestimated. Contributing to this is a lack of relevant regulation.

AAMI/ANSI/ISO 11137:2006 and ISO 11737:2006, *Sterilization of medical devices – Microbiological methods,* are the only two standards available today for sterilization of SUS in pharma manufacturing. The fact that these two standards (and, ostensibly, any other guidances published on irradiation validation) were developed solely for medical devices is the main factor that complicates applying them to SUS. Plus, these standards generally cover risk to patients from a device. In contrast, SUS sterilization validation is intended for decontamination and sterilization of *product/process solution equipment contact surfaces*—which do not come into direct contact with patients (i.e., the risk is different).

An SUS may be risk-assessed for lower sterility assurance levels (SALs) with lower lethality (e.g., 10–3 SAL) than the conventional 10–6 SAL. This risk-based determination can be made by assessing the specific step(s) in a bioprocess to determine if an SUS is used at a point in the process stream where there are downstream controls on sterility, such as sterilizing filtration. Process contact surfaces that have undergone the final 0.2 µm sterilizing filtration for drug product aseptic fill are the only ones that technically require 10–6 SAL. It is important for SUS end users to recognize that application of 10–6 SAL across all components of the bioprocess may not be appropriate from a unit operation contamination control strategy perspective and can lead to risks

> **End users are increasingly seeking a high degree of customization in designs, leading to complexity**

that are not so apparent. In reality, lower SALs, or statistical bioburden grouping strategies and controls for unit operations may prove a better risk-based approach.

There is additional benefit with this approach. Reduced gamma radiation dosages also lower SUS material effects that can impact drug product quality. There is a direct relationship between radiation dose levels/dose rate, and changes to SUS polymer chemical structure perspective. In order to achieve higher gamma irradiation dosing, a longer cycle time is required. Longer irradiation cycle times can foster increased gamma radiation-induced chemical modifications, and worsening of leachables/ extractables from the SUS. Ionization and accompanying molecular excitation of SUS materials differs across classes of polymers, with some exhibiting higher resistance to irradiation-induced modifications than others. All polymers are affected by gamma irradiation to some extent.

For SUS, the basis of a sterilization validation program is the development of a simulated product master (SPM)—commonly referred to as a "monster assembly." SPMs are designed to provide a model of worst-case materials, components, connections and processing used in the manufacture of all commercially-produced SUS assemblies at an SUS manufacturing plant. To fully simulate exposure to the same manufacturing conditions, these SPM "monsters" should be manufactured using the same processes as commercially produced SUS solutions.

Article at a Glance

- Lack of regulatory guidance hampers sterilization validation for SUS
- Teamwork approach can help prevent sterilization risks
- Pharma firms are demanding ever more complex SUS designs

The suggestion here is similar to process simulation media fills performed in the pharmaceutical industry. As the SUS manufacturer's portfolio of sterile SUS grows, the SPMs should routinely be evaluated to determine if they are still a good model of new products in the portfolio. If not, the SPMs must be modified or the sterilization validation program must be revised (i.e., with a new, more monstrous SPM, or a validation customized to the new SUS goods). This simulated master must be applied when establishing the minimum radiation dose specification, and for subsequent quarterly dose audits (revalidations). Assessing the attributes and criteria of devices for the purpose of creating a simulated master for validation that is feasible in application can be quite difficult when the customization and complexity demands grow.

Validation Requires Team Approach

As mentioned earlier, the pharmaceutical manufacturer, the SUS manufacturer, the contract sterilization vendor and the contract microbiology laboratory each own a piece of the activity within this sterilization validation process. The regulatory onus to ensure compliance and final product quality, however, remains the responsibility of the pharmaceutical firm. The perspectives and know-how of these four parties is based on their function within the supply chain.

This can become even more complex when distributors enter this mix between the SUS manufacturer and the end user, possibly resulting in less transparency and increased risk within the supply chain that is not understood. Among all these parties, there is often a lack of overall understanding on the necessary control scheme, the science, and the compliance needed to effectively maintain the validated state of the SUS. For example:

- The contract sterilization vendor is accustomed to decades-old processing to meet medical device manufacturers' needs, which are very different than SUS manufacturer needs. For example:
  - the variability of different product codes for medical devices is low
  - the volumes for a device manufacturer are relatively high compared to SUS
  - the variability of packaging configurations is relatively low in medical device
  - the density is relatively uniform for medical devices compared to SUS density nonuniformity—critical as variability of densities directly influences dose delivery and distribution variability

- Contract microbiology labs are commonly unaware of the significant risks the pharma industry faces in the event of sterility false positive (i.e., invalid sterility failure). They must have the infrastructure and technical capabilities to assess these large and multimaterial assemblies without contaminating them. Many test labs are unwilling to test very large systems when they understand the risk associated with the testing. They must have the capability to develop appropriate test methods and validate those test methods. The testing costs can become significant due to the time required to develop and validate test methods and perform routine testing of these "monstrous" assemblies. Thus, selection of a reputable, competent contract microbiology test lab is imperative.

- Too many SUS manufacturers do not understand the compliance requirements within the AAMI/ISO standards, and not all SUS manufacturers have knowledge on the material science or the necessary validation expertise. SUS manufacturers often do not understand fully how their SUS will be used in the biopharmaceutical process. SUS manufacturers commonly do not have technical experts capable of properly assessing the capabilities of the contract microbiology labs, without which it is difficult to recognize gaps that put the SUS manufacture and/or sterilization process at risk. ➤

- The pharmaceutical firm is often unfamiliar with the AAMI/ISO standard for sterilization of SUS, the significant lack of and/or gaps in the sterilization validation at many SUS manufacturers and the costs and time associated with maintaining a compliant sterilization validation program. The desire to choose the lowest cost vendor can often outweigh the value of choosing the most qualified supplier. This is short-sighted when considering the enormous risk associated with the product supplied via sterile SUS.

Playbook for Handling Complexity

The ever-increasing complexity of SUS designs presents another challenge. This scenario is on the rise due to manufacturers' desires to replace more of their fixed process equipment with disposable SUS. Large and unwieldy assemblies with dozens of feet of tubing, multiple filters, multiple connectors, needles and containers are becoming increasingly prevalent. End users are increasingly seeking a high degree of customization in designs, leading to complexity in the manufacturing, packaging, shipping and validation.

How does one assess an SAL on something like **Figure 1?** How does a testing lab even go about executing sterility testing on such a "monster?" What could the total bioburden look like on an assembly like this? Consider the following example. A biopharma company sought an SUS design to take product from final formulation to final fill. The company did not want any aseptic connections in their process suite and requested a design containing dozens of feet of tubing along with multiple connectors and filters, needles, containers, etc.

When the SUS manufacturer validated the SUS, the bioburden results were >3000 cfu on a total immersion of the system. These high bioburden levels were truly "monstrous." Naturally, the SUS provider was resistant to putting their entire customer-base at risk by revising their SPM to include all the elements of this new assembly.

This presented three options for the SUS provider and the biopharm firm: **1)** break up the assembly into three sections and add aseptic quick connectors; **2)** assess the risk within the biopharma process stream and determine if a specific section of the assembly is upstream of sterility controls (e.g., sterile filtration), thus, only the downstream section of the assembly may require 10^{-6} SAL; and, **3)** consider if a 10^{-6} SAL exclusively on the fluid path of the assembly is acceptable since there is typically significantly lower bioburden on the fluid path of SUS. The biopharma company ultimately determined that their process could allow for a sterile label claim only on the fluid path of the assembly.

There is also a time and cost factor that must be considered. The validation approach includes far more than just irradiation of the assembly. So what is the requirement within the current AAMI/ISO 11137:2006 guidance? The guidance covers the following areas with regard to a validated sterilization program:

- Determination of material radiation compatibility and resistance;
- Determination of the average bioburden for a specific product on a statistically representative number of parts;
- Exposure to a minimal radiation dose statistically calculated to deliver 10–2 SAL (termed a sublethal dose) on a representative number of parts;
- Bioburden evaluation and control on individual components within the SUS—often these can be purchased components which require robust supplier oversight;
- Validated test methods at the testing laboratory using representative samples of the SUS;
- Product dose levels validated as sterile are subject to routine "dose audits" involving bioburden testing, sublethal dose delivery and sterility testing:
- Control of the SUS manufacturing environment (e.g., cleanroom environment, viable/nonviable environmental monitoring, proper gowning); and,
- Evaluation of product density, product packaging shielding effects, and irradiator product load configuration.

When considering the risks as they exist today, consider the increased demand for SUS in the future. Industry groups including PDA (see PDA *Technical Report No. 66: Application of Single-Use Systems in Pharmaceutical Manufacturing*) are beginning a dialog on this topic. It will be increasingly important for there to be risk-based standards and guidance documents specific to SUS that address the needs and knowledge of both SUS providers and pharma. In the meantime, to ensure a sterile SUS, it is imperative the four types of partners discussed herein understand each other's needs and limitations to achieve the ultimate goal of ensuring supply of safe and effective products.

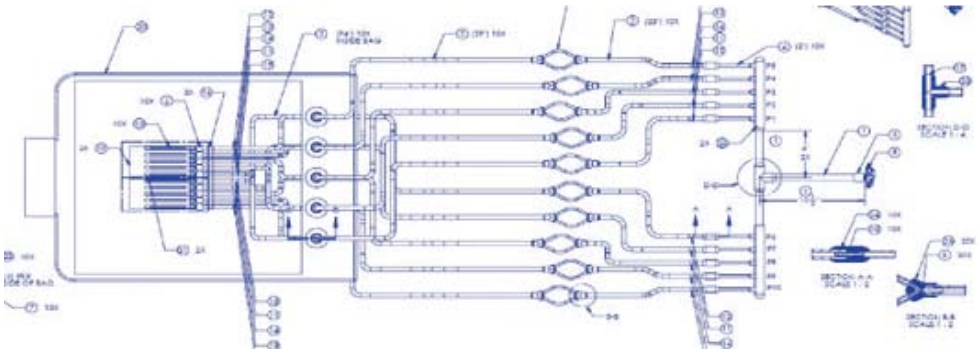

Figure 1 Example of a Complex SUS Assembly

About the Author

Polly Hanff is the Global Regulatory Affairs and Quality Director at Saint-Gobain Performance Plastics with overall responsibility to assure the quality and compliance of single-use systems manufactured for the pharma industry.

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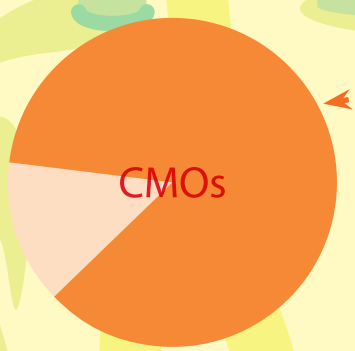
CMOS and Single-Use Systems: Partnering Together for Flexibility

It is forecast that adoption of single-use systems will grow by **34%** from 2014–2019. ***(1)***

Per a 2015 survey of manufacturers, more than **90%** of facilities use some type of single-use/disposable technology in their processes. Additionally, more than two-thirds of those surveyed reported improvements in biomanufacturing performance at their facilities due to the use of disposable devices. ***(2)***



86% of CMOs adopted or planned to adopt single-use technology, compared to **66%** of traditional drug manufacturers. ***(2)***

CMOs are more likely to adopt single-use technologies.

In 2013, a CMO opened a 100,000-square foot manufacturing facility based on single-use technology. ***(3)***

Why? Single-use systems provided flexibility for multiproduct production, such as quick changeover between products.

Sources

1. Technavio. Global Single-use Bioprocessing System Market 2015-2019. Press Release, July 29, 2015.
2. https://www.contractpharma.com/issues/2016-03-01/view_features/single-use-technology-integral-to-advancing-biomanufacturing/
3. https://www2.deloitte.com/content/dam/Deloitte/us/Documents/life-sciences-health-care/us-lshc-advanced-biopharmaceutical-manufacturing-white-paper-051515.pdf

Special thanks to Robert Repetto, Pfizer, for his assistance

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4 Capabilities to Operationalizing Resilience

Amy D. Wilson, PhD, Biogen

What is the capacity of your organization to succeed under varying conditions? How is that capacity impacted by changes in equipment, technology, personnel or operational expectations? These are questions you may not have asked about your operations before.

Generally, when considering operational performance improvement, the focus is on increasing batch and product yield, maximizing equipment utilization, creating efficiencies with new technology and automation and streamlining work processes. To ensure safety, quality and reliability while making such investments in productivity, there is another capacity that is needed. This is *resilience*—the ability of a system to adjust its functioning prior to, during, or following changes and disturbances, so that it can sustain required operations under both expected and unexpected conditions ***(1).*** Biogen has successfully integrated a focus on resilience as part of its operational practices, enhancing overall performance, safety and reliability.

Four Cornerstones of Resilience

Operationalizing resilience requires capabilities at all levels of the organization to *Anticipate*, *Monitor*, *Respond* and *Learn* ***(2).***

- *Anticipate* – know what to expect by looking ahead to potential threats and opportunities
- *Monitor* – know what is critical to pay attention to and look for while work is being performed
- *Respond* – know what to do when faced with disruptions and disturbances in real time
- *Learn* – know what has happened when this work has been done before, not just when it failed but also when it succeeded

Biogen's human performance efforts are focused on these organizational capabilities. Recognizing that people adapt to accomplish goals within complex systems, human performance ensures there are processes in place to learn about these adaptations and discover how to make systems more robust to the unexpected. These practices enhance risk management and set people up to be more successful in their work.

Real-Life Resilience in Action

Capacities to *anticipate, monitor* and *respond* have been built into Biogen's operations by identifying critical steps, performing prejob briefings before work is started and integrating practices known to reduce error likelihood during work execution. Critical steps are those points of action in the operation that if performed incorrectly, or if a preceding action was performed incorrectly, will result in immediate, irreversible and intolerable harm ***(2).***

At Biogen, critical steps were identified across all process areas and marked with a symbol in the relevant production instruction. This raises awareness during the normal flow of work to where significant undesired consequences could be realized.

Prejob briefings are performed prior to operations containing critical steps so that before work begins all personnel involved have discussed the following:

1. What equipment, supplies and instructions are needed and are they ready for use?
2. What is the status of completed tasks required for this activity to be successful?
3. What is our mitigation plan if an event occurs that challenges safety and/or other assets?
4. What conditions or events will require us to stop work?
5. What past experiences and lessons learned will help us complete this activity successfully?

In the first year of implementation, one Biogen manufacturing site realized a 50% reduction in unexpected outcomes during work preceded by a prejob briefing. These briefings proved a critical resilience practice that are owned and driven by the personnel performing the work across ➤

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all of Biogen's manufacturing locations. They have also been implemented in maintenance areas. Additional practices implemented to reduce error likelihood during work execution include disciplined communication practices and defined work stop criteria.

The capacity to *learn* has been improved at Biogen by implementing work observations to learn about the gap between "work-as-imagined" and "work-as-done," improving the company's investigation approach when faced with undesirable outcomes, and implementing postjob reviews and open reporting.

Work observations provide opportunities for leaders to gain a more accurate picture of how work is performed, and provide opportunity for positive interaction. Biogen's initiative is named "Work Observation and Risk Conversation (WORC)," which emphasizes its focus on going out and watching work where it is performed and having a dialog with workers about risks and their ideas to mitigate or eliminate those risks. Leaders are taught humble inquiry practices to facilitate a positive learning experience ***(3).*** One QC Manager stated after performing her first WORC, "By far, the best part of this observation was the humble inquiry conversation that followed the activity. This was where I learned. There was no judgment, there was no correcting, there was no advice giving. I was able to gather bits of information that loosely constructed, for me, the performer's perspective; a keyhole view of the foundation supporting the independent actions/decisions made by the performer."

Undesired outcomes that lead to investigations is another important opportunity to ensure organizational learning. Biogen is implementing nonlinear cause analysis approaches and applying human and organizational performance concepts to understand how things go wrong. There are multiple examples of events which, in the past, a conclusion of "human error" might have been reached; now these new approaches lead to CAPAs that address work process control deficiencies, ensuring sustained improvement.

Postjob reviews are performed following work activities for which a prejob briefing was performed, regardless of whether the outcome was a success or not. Postjob reviews capture what went well and why, as well as any surprises that occurred and recommendations for future improvement. Results from postjob reviews are recorded and reviewed during standing operations meetings to ensure broad sharing of the learning, and actions are taken, if needed, to improve future success.

Open reporting ensures no one has to wait to learn about how work is done until something goes wrong. Biogen's open reporting system captures variances not already captured in GMP quality/safety systems. These variances, which are both positive and negative, include work risks that have potential to impact successful performance, unexpected outcomes that do not meet the threshold of a quality deviation, positive experiences, and good catches. Since implementation in April 2017, the total reports received in this system are more than *four* times greater than the number of investigations conducted. This ratio demonstrates the significant value in expanding learning beyond only when things go wrong. From the reports received, over 100 actions have been identified and taken to proactively improve operational performance.

Adding Value Minus Major Costs

Biogen's focus on enhancing capabilities to anticipate, monitor, respond and learn have enhanced our ability to proactively address performance against safety, quality and reliability measures. The practices and processes put in place provide tangible evidence to employees that the company actively supports a learning culture and wants to support people in being successful in their work. These new practices require an investment in time, but the total time to conduct a prejob briefing, submit open reports and capture outcomes in a postjob review for a given work activity is less than 1% of the time it would take to complete a single deviation investigation.

Capturing new data, such as open reports and postjob reviews, enables Biogen to measure and monitor not just lagging indicators of what has gone wrong, but leading indicators that paint a different picture **(Figure 1).** A picture of how day-to-day, our people, processes and systems handle dynamic conditions. In other words, a picture of our capacity to be resilient.

[Editor's Note: The author will present this topic at the *2018 PDA Annual Meeting,* in session "P4: Increasing Capacity and Capability without Increasing Costs," Wednesday, March 21 at 9 a.m.**]**

References

1. Hollnagel, E. "Resilience Engineering – Building a Culture of Resilience." *PTIL.NO.* Petroleum Safety Authority Norway. tinyurl.com/y7xtuqya (Accessed Dec. 19, 2017)
2. Muschara, T. *Risk-Based Thinking: Managing the Uncertainty of Human Error in Operations.* Oxon, United Kingdom: Routledge, 2017.
3. Schein, E.H. *Humble Inquiry: The Gentle Art of Asking Instead of Telling.* Oakland, CA: Berrett-Koehler Publishers, 2013.

About the Author

Amy Wilson has been with Biogen since 2011 in Pharmaceutical Operations & Technology, responsible for operational performance improvement. Prior to joining Biogen, she worked for Wyeth/Pfizer for ten years.

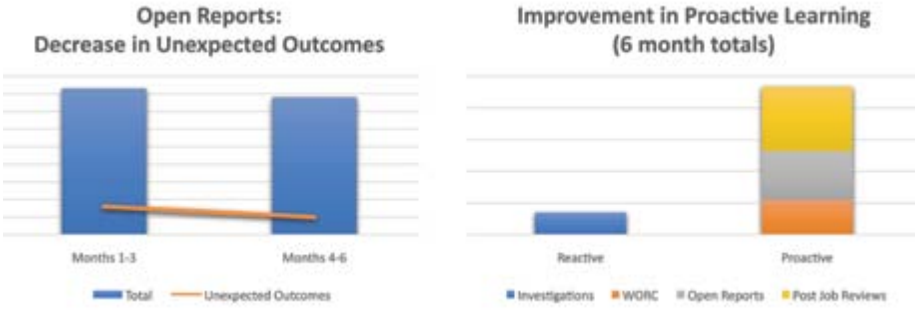

Figure 1 Leading Performance Improvement Indicators Shift Scales to Proactive Learning

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Joint PDA, IPEC Task Force to Work on Excipients TR

Michael Schousboe, Novo Nordisk, and Eva Urban, Celgene

Excipients serve a critical role in the production of final dosage forms for drug products and biologics as they help the product fulfil its purpose ***(1).*** Recognizing this critical role, recent EU regulations require manufacturers to ensure appropriate levels of GMP for excipients by using formalized risk assessments ***(2,3).*** As of March 21, 2016, excipient users/drug product manufacturers in the European Union are legally mandated to have performed the needed assessments of excipient use and function throughout the entire supply chain.

In 2016, following an initial webinar, a team under the PDA Quality Risk Management Interest Group exchanged their experiences on meeting this requirement. The group then surveyed other companies, finding that these companies have comparable questions. Different solutions have been found in different companies, but similar principles apply.

The group has joined forces with IPEC, who in 2016 published a guide for excipient users on the subject ***(4).*** Now, this group and IPEC will work together to produce a joint technical report. The group will form subteams for different specific topics. Volunteers working within these subgroups will consist of representatives from both PDA and IPEC, and reflect manufacturers and suppliers. Volunteers interested in sharing their company experience and working on the TR are welcome to join the group. Please contact PDA's Volunteer Coordinator (volunteer@pda.org).

The technical report will provide examples of industry practices, and propose a generic solution. The document will serve as practical guidance intended for use along with existing regulatory and industry standards. The technical report team expects that the document will enable manufacturers and CMOs to either set up or benchmark their systems, and further establish collaboration with excipient suppliers and distributers.

References

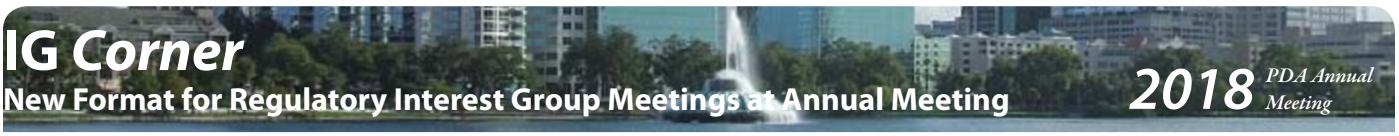
1. Holtz, F. "Establishing a Formalized Risk Assessment for Excipients." *PDA Letter* (January 2017) 53: 40–43.
2. "Directive 2011/62/EU." *Official Journal of the European Union* 54 (2011): 74-87.
3. Guidelines of 19 March 2015 on the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use (2015/C 95/02)
4. March 18 2016, IPEC Europe "How to" document related to Guidelines of 19 March 2015 on the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use (OJ 2015/C 95/02)

PDA Responds to Release of Annex 1 Draft

The European Commission published the long-awaited draft of Annex 1 "Manufacture of Sterile Medicinal Products" in December 2017. PDA is currently working with a team of 15 volunteers to comment on this document.

Hal Baseman, Chief Operations Officer, ValSource, and **Gabriele Gori,** Vice President Audit and Risk Management – Global Quality, GSK Vaccines, are leading this team. Both also served as co-chairs for five workshops on Annex 1 PDA sponsored in the United States and Europe in 2016 and 2017. **Jahanvi (Janie) Miller** can be contacted for any further details (miller@pda.org). A session at the *2018 PDA Sterile Medicinal Products Manufacturing Conference* will review PDA's comments. Register to attend at www.pda.org/2018aseptic.

PDA hopes the discussion around Annex 1 will lead to greater harmonization across the global industry.



The *2018 PDA Annual Meeting* features a new format for interest groups; instead of convening after the last session of the first two days, interest groups will convene at the same time as breakout sessions. Below is the schedule for the regulatory-focused interest group on the schedule at the *2018 PDA Annual Meeting:*

Tuesday, March 20
1:45–3:15 p.m.
The Quality Risk Management Interest Group

For more information about interest group meetings, visit www.pda.org/2018annual.

Quality and Innovation are Not Incompatible

A Report from the 2017 PDA/FDA Joint Regulatory Conference

Janmeet Anant, PhD, MilliporeSigma

Quality is essential no matter how revolutionary the drug product. That concept permeated the *2017 PDA/FDA Joint Regulatory Conference:* "Ensuring Product Quality in an Era of Innovative Therapies," Sept. 11–13, in Washington, D.C.

Three sessions in particular emphasized the spirit behind the theme of the meeting.

In the opening plenary, "FDA Perspective on Medical Product Innovation," **Peter W. Marks,** MD, PhD, Director, CBER, U.S. FDA, set the stage by reviewing the history of the FDA, including Agency initiatives to support product innovation. He focused on the recent chimeric antigen receptor (CAR)-T therapy approval, highlighting the fact that 76 INDs are now active for CAR-T therapeutics and more than 500 INDs have been introduced for gene therapy.

Overall, she sees the industry moving toward cell-based therapies and neuromodulation devices

Marks also pointed out that, by using it to disrupt HLA and other graft rejection factors, CRISPR/Cas9 gene editing technology will likely make allogeneic therapies possible. Currently, retroviral or lentiviral technology is generally used to deliver the CAR gene into the T-cells. With these viral methods, however, the CAR gene is often inserted into the genome of the recipient cells at random, which can result in unwanted genetic side effects. CRISPR technology, on the other hand, can deliver the CAR gene to a very specific location in the genome of the T-cell. This precise approach creates CAR-T cells with more stamina—they can kill tumor cells longer because they are less prone to exhaustion. This could lead to safer, more effective use of this powerful ➤

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- *Container Closure Systems and Integrity Testing* (**March 22-23**)
- *Sterile Pharmaceutical Dosage Forms: Basic Principles* (**March 22-23**)
- *Cleanroom Management* (**March 22-23**)
- *Process Simulation Testing for Aseptically Filled Products* (**March 23**)
- *Validation of Moist Heat Sterilization Processes: Cycle Design, Development, Validation and Ongoing Control* (**March 23**)

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form of immunotherapy in patients. In fact, the first clinical trials using CRISPR technology are currently being planned.

Next, **Rosemarie Hunziker,** PhD, Tissue Engineering/Regenerative Medicine Program Director at the National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health, reviewed the challenges and opportunities of regenerative medicine. Overall, she sees the industry moving toward cell-based therapies and neuromodulation devices, along with traditional small molecule and biologic protein therapies. Hunziker explained two approaches—autologous versus allogeneic—for engineering tissue or cell therapies. She also highlighted the development of various consortia with specific initiatives for regenerative medicine, such as the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), the Advanced Regenerative Medicine Institute (ARMI) and the National Cell Manufacturing Consortium. Another interesting topic Hunziker presented concerned tissue chips, which have the potential to be utilized not only for physiologically relevant toxicity studies, but also for the development of disease models and the evaluation of drug efficacy.

In addition to new therapies, the conference addressed innovative approaches to manufacturing. In his presentation, "Early Quality Assessment Interactions for New Technologies," **Sau (Larry) Lee,** FDA's Emerging Technology Director in the Office of Product Quality, answered the persistent industry question, "How is FDA encouraging innovation in manufacturing?" He said that one of FDA's main objectives is to "encourage development and adoption of emerging pharmaceutical technology." Lee chairs the Agency's Emerging Technologies Team, an FDA resource for companies considering implementing new manufacturing technologies.

Other sessions at the conference focused on managing partnerships with suppliers and CMOs, product lifecycle management, continuous processing, single-use pharmaceutical manufacturing systems and understanding FDA compliance policies. Each and every one of these sessions reinforced that while the need for novel drug therapies is strong, so is the need for quality in manufacturing and product development.

[Editor's Note: For another author's perspective on the *2017 PDA/FDA Joint Regulatory Conference,* visit the PDA Letter website**.]**

About the Author

Janmeet Anant, PhD, is a Board Member of the BioProcess Systems Alliance (BPSA). His role over the past few years has been to support products and services used in biopharmaceutical manufacturing, with a focus on aseptic processing and single-use technologies. He is a voting member of the ASTM and ASME-BPE standards-setting organizations and serves as a regulatory advocate for the Life Science division of MilliporeSigma. In addition, he promotes regulatory thought-leadership within various industry organizations.

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TUESDAY, APRIL 17, 2018

	INTERPHEX INNOVATION STAGE	MEETING ROOM 1 Optimizing Facilities through Innovation and Technology	MEETING ROOM 2 PDA, CRB Tech Tank and Continuous Manufacturing	MEETING ROOM 3 Manufacturing Efficiencies and Improvements	MEETING ROOM 4 Quality Metrics and Systems/Risk Management	MEETING ROOM 5 (Vendor Presentations)	FORMULATIONX	CMO/CDMO	INTERPHEX LIVE Crystal Palace
9:45am – 10:00am	Exhibit Hall Grand Opening & Exhibitor Awards								
10:00am – 5:00pm	Show Floor Open & IPX/BPI Poster Hall								
10:30am – 11:15am	**10:30am - 12:30pm** Pharmaceutical Technology Keynote Series	Integrating a Programmable Robotic Bioreactor System with a Biochemical Analyzer for Real-time Analysis	**10:30am - 11:30am PDA Roundtable** State of the Industry Practices for Pre-Use Post-Sterilization Integrity Testing	Accelerating Freeze-Drying: From Model to Production of a Semi-Continuous Aseptic Spray Freeze-Dryer	Bioprocess Simulations the means to decision making from Feasibility through Detailed Design	MasterControl Inc.	Coming Soon	A Molecules Journey is Breaking Down Roadblocks to Commercial Success - Navigating through the important considerations necessary to successfully bring a biologic molecule to market	**10:15am – 11:00am** Advantages of Continuous Manufacturing for Solid Dosage"
11:30am – 12:15pm		Data Integrity and Management in the Pharmaceutical Industry. Understanding and Complying with GMP & FDA requirements	Building the Foundation for Continued Process Verification with Industry 4.0 Manufacturing Analytics	Impact of Tank Cone Bottom Interior Angle on Agitator Design, Lowest Mixable Volume, and Process Results	Cleaning Validation Different approaches to limit setting for detergents	MilliporeSigma	Coming Soon	Coming Soon	**11:15am - 12:00pm** Formulation and Non-invasive Delivery of Biologics
12:15pm – 1:15pm LUNCH BREAK									
1:30pm – 2:15pm	**1:30pm – 3:00pm** Pharmaceutical Technology Keynote Series	Start-ups: Moving out of the Incubator into a New Pilot/Manufacturing Facility	**CRB TECH TANK** Solving the riddle of flexible facilities - biotech & fill/finish	Tablet Press and Encapsulating Machine Transactions	Remediation Challenges of Aging Facilities	**1:00pm** Rockwell Automation	Coming Soon	Coming Soon	**1:30pm – 2:15pm** Pharma Intelligence: 2018 Industry Outlook
2:30pm – 3:15pm		Optimized Manufacturing of mAb-based Products: Flexibility, Speed, and Efficiency can Co-exist	**CRB TECH TANK** Keep" em separated! Integrating segregation for gene vector production	Single use viable air monitoring in critical environments of a specialty multi-purpose contract manufacturing organization	On-dose identification for tablets and capsules dosage design and equipment innovation to mitigate risks in patient safety and brand protection	**2:00pm** LB Bohle LLC	Coming Soon	Coming Soon	**2:15pm – 3:00pm** Biosimilars 4.0
3:30pm – 4:15pm	Coming Soon	Case Study: Capacity Expansion and Conversion to Single-Use BioProcessing at an Existing cGMP CDMO Facility	**CRB TECH TANK** Solving demand allocation problem with modeling and simulations	A Case Study for an Improved Approach to Cleanroom Disinfection, Minimizing the Impact and Reducing Downtime	Risk analysis: Present state and industry's demand	**3:00pm** Sika Corp.	Coming Soon	Coming Soon	**3:00pm – 3:45pm** Vaccine Innovation
4:15pm – 5:00pm	Coming Soon	Process Economics: The Driving Force behind the Criteria for Cell Therapies Facility Design	Continuous OSD: Designing a Controls Model *(Continuous Manufacturing track)*	A Novel, Real Real Time Adaptive Process Control System for Optimizing Fedding in Bioreactors	Settling the Frontier of Fill-Finish Operations - High Tech Filling in a Proper Abode *(Optimizing Facilities track)*	**4:00pm** SP Scientific/PennTech	Coming Soon	Coming Soon	**3:45pm – 4:30pm** The Impact of Critical Utilities **4:30pm – 4:45pm** Show Wrap Up Day 1

WEDNESDAY, APRIL 18, 2018

	INTERPHEX INNOVATION STAGE	MEETING ROOM 1 Optimizing Facilities through Innovation and Technology	MEETING ROOM 2 PDA, CRB Tech Tank and Continuous Manufacturing	MEETING ROOM 3 Manufacturing Efficiencies and Improvements	MEETING ROOM 4 Quality Metrics and Systems/Risk Management	MEETING ROOM 5 (Vendor Presentations)	FORMULATIONX	CMO/CDMO	INTERPHEX LIVE Crystal Palace
10:00am - 12:00pm	IPS TECHNOLOGY TOUR *(Tour Registration Required)*								
10:00am – 5:00pm									
10:30am – 11:15am	**10:30am – 12:30pm** Pharmaceutical Technology Keynote Series	**10:30am – 11:30am FACILTY FOCUS 1:** Flexibility by Design: GMP Manufacturing for the Diverse Product Portfolio	Ensuring reliable, consistent production in pharmaceutical water systems	Making 'Spray and Pray' Obsolete with New Technologies	Cleaning Agent Screening: Key Aspects in Selecting a Suitable Cleaning agent for a GMP Cleaning Procedure	Rockwell Automation	Coming Soon	Coming Soon	**10:15am – 11:00am** New Regulations, Real Case Studies: ASME BPE Cabinet Washer Standards (SD-5.3.1)
11:30am – 12:15pm			Integrating IoT into your Life Sciences Packaging and Supply Chain Strategy - Best Practices to Take this Valuable Leap	The use of extractables data from Single Use components for risk assessment	Verifiable Containment Performance of Isolator Technologies	ADENTS	Coming Soon	Coming Soon	**11:15am – 12:00pm** Automation Trends Facing the Industry
12:15pm – 1:15pm LUNCH BREAK									
1:00pm - 3:00pm	IPS TECHNOLOGY TOUR *(Tour Registration Required)*								
1:15pm – 2:00pm	**1:30pm – 3:00pm** Pharmaceutical Technology Keynote Series	**1:00pm - 2:00pm FACILTY FOCUS 2:** Restrictive Access Barriers: Best industry practices for retrofitting a legacy filling lines with a RABS barrier	Global pharmaceutical packaging trends, beyond Serialization *(Optimizing Facilities track)*	Mass Spectrometry in Freeze Drying, Over 25 Years since the First Installation: How Far have we Come?	Harmonized Method for Cleanroom Hard Surface Disinfectant Efficacy Evaluations	**1:00pm** Eschbach GmbH	Coming Soon	Coming Soon	**1:30pm – 2:15pm** Utilizing AR/VR in Pharma Development and Manufacturing
2:15pm – 3:00pm		**2:15pm - 3:15pm FACILTY FOCUS 3:** Central Utilities for GMP Manufacturing: A Practical Dialog on Cost and Reliability	**2:00pm - 3:00pm PDA Roundtable** Technology and Process for Cell and Gene Therapy Manufacturing	Coming Soon	Data Driven Control Strategy for Critical Drug Container Closure Systems (CCS) Performance at Digital Age	**2:00pm** Bimba Manufacturing Company	Coming Soon	Coming Soon	**2:15pm – 3:00pm** Emerging and Transformational Technologies in Personalized Medicine – A Paradigm Shift
3:00pm – 5:00pm	IPS TOUR RECEPTION *(By Invite Only)*								
3:15pm – 4:00pm	**3:15pm – 5:00pm** Pharmaceutical Technology Keynote Series	Current trends & considerations for drug delivery device assembly of self-administered products	Single Use Applications in Continuous Biopharmaceutical Processing	Total Organic Carbon for Enhanced Verification of Bioprocess System Cleaning CQ	A Comprehensive Approach to Cleanroom Certification for Reduced Risk of Environmental Contamination and Improved Regulatory Compliance	**3:00pm** MilliporeSigma	Coming Soon	Coming Soon	**3:00pm – 3:45pm** Data Security/Data Lockdown
4:15pm – 5:00pm		Lessons learned from microbial contamination in pharmaceutical manufacturing; Benefit of end user and supplier collaboration	Facility Prefabrication – Coupling Flexibility, Mobility and Rapid Deployment into Turnkey Solutions *(Optimizing facilities track)*	Real-Time Analytics with Timeline View for Improved Analytics	Bridging the Gap Between Rinse Water Analysis and Surface Cleanliness	Vendor Presentation	Coming Soon	Coming Soon	**3:45pm - 4:30pm** FDA Inspection Preparations: What's New, What's Different **4:45pm - 5:00pm** Show Wrap Up Day 2

THURSDAY, APRIL 19, 2018

	INTERPHEX INNOVATION STAGE	MEETING ROOM 1 Optimizing Facilities through Innovation and Technology	MEETING ROOM 2 PDA, CRB Tech Tank and Continuous Manufacturing	MEETING ROOM 3 Manufacturing Efficiencies and Improvements	MEETING ROOM 4 Quality Metrics and Systems/Risk Management	MEETING ROOM 5 (Vendor Presentations)	FORMULATIONX	CMO/CDMO	INTERPHEX LIVE Crystal Palace
10:00am – 3:00pm	Show Floor Open & IPX/BPI Poster Hall								
10:30am – 11:15am	Life Cycle Cost for Multiple-Effect Water Stills	The Theory Behind Automatic Inspection Technologies for Subvisible-to-Visible Particle Detection and Container Closure Integrity	**10:30am - 11:30am PDA Roundtable** Use of Big Data for Predictive Process Control	Work smart: Risk based approach for cleaning validation	Endotoxin Remediation Strategies	**10:30am** Rockwell Automation	Coming Soon	Coming Soon	**10:15am – 11:00am** Regulatory Requirements Relating to Water
11:30am – 12:15pm	Coming Soon	Prescriptive Maintenance Leveraging IIoT Technology Can Become Your Competitive Advantage	How Understanding Loss in Weight Feeder Principles and Optimization of Feeder Refill and Overall Design can actually improve the Continuous Pharmaceutical Process	Achieving Manufacturing Efficiencies with Advanced Batch Management Technology	Case studies: Steam sterilization regulatory requirements, and end user impact analysis and common mistakes.	Vendor Presentation	Coming Soon	Coming Soon	**11:15am - 12:00pm** Process Control Interpretation within a Manufacturing Line **12:15pm - 12:30pm** Show Wrap-in Day 3

**As of January 16, 2018. Schedule subject to change.*

High Regulatory Expectations for Biosimilars

Stephan Krause, PhD, AstreZeneca Biologics, Emanuela Lacana, PhD, U.S. FDA, Jens Schletter, PhD, Sandoz, and Rebecca Stauffer, PDA

The development of biosimilar products continues to gain momentum across the world. The path forward, however, remains arduous, requiring protracted dialogue between the industry and global regulators. And nowhere was this more apparent than at the *2017 PDA/FDA Biosimilars Conference,* June 26–27, 2017 in Bethesda, Md.

The conference opened with a review of current international regulators' expectations for approval of biosimilars, featuring presentations from **Steven Kozlowski,** MD, Supervisory Medical Officer, CDER, U.S. FDA, and **Niklas Ekman,** PhD, Senior Researcher, Finnish Medicines Agency. Kozlowski provided an overview of FDA's involvement with biosimilars, pointing out that additional draft guidance documents will become available to assist biosimilar developers. The Agency's position on similarity is that analytical testing is the foundation.

Following Kozlowski's talk, Ekman covered the European experience with biosimilars. He explained that biosimilars have been able to gather considerable market share there (up to 50 or even 100%). Even in some cases, when only 1% market share was gained, this still helped drive down prices considerably. Biosimilars are increasing patient access to drugs and driving innovation.

European regulators have also conducted extensive research on the safety and efficacy of biosimilars. Since the first European biosimilar was approved, there have been no differences observed between a reference product and the corresponding biosimilar. A look at biosimilar reviews up to June 2017 shows that 59 biosimilar applications have been submitted. Of these, 48 have been reviewed with 36 receiving positive opinions from EU regulators. Ultimately, 28 have been approved. At this time, the European Union does not have regulatory advice concerning data accumulated during development; a pilot on tailored scientific advice launched in 2017. The European Union also does not require "a fingerprint-like biosimilarity." In the future, EU authorities may not request safety studies. For example, immunogenicity of insulin may be waived in specific circumstances.

Ekman pointed out that a new EMA concept paper on the use of statistical methodology for quality comparability is now available; the consultation period for this document ends March 2018. He further emphasized that analytical similarity tends to grow as uncertainty grows, i.e., less batches mean higher chances of passing the analytical similarity criteria.

With regard to statistical tools, Ekman mentioned that the minimum-maximum range represents the clinically qualified range of the reference product. In case equivalence testing is employed, a number of issues and assumptions need to be considered. Ideally, the equivalence margins used in analytical similarity studies should be the thresholds for what is acceptable (and not acceptable) in the clinic.

Analtyical Development: A Key Step

After the opening plenary talks by Kozlowski and Ekman, reverse engineering strategies served as the focus for the second plenary. **Laurent Chevalet,** Phd, Director, Head of Analytical and Pharmaceutical Development, Merck Biosimilars, presented "Analytical Implications of Reverse Engineering for Biosimilar Development." His talk covered the typical existing critical quality attributes (CQAs) for monoclonal antibodies (mAbs), highlighting a QC technology transfer process that uses multiple laboratories which can result in potential differences in test results.

Chevalet also provided some examples for the quality target product profile (QTPP) and method selection, calling out analytical method development as a critical step for developing a biosimilar product. He also made a point that a sponsor may need to balance the desire to use high throughput testing with the need for accurate test results, which use less throughput capability as high-resolution power is needed to look for analytical similarity.

Alla Polozova, PhD, Principal Scientist, Amgen, followed Chevalet's talk with further discussion on QTPP, specifically showing how it can be used for reverse engineering. She presented how QTPP can be established from both public knowledge about the reference product and reference product characterization. The process begins with the testing of the reference product and identification of attributes. Extensive characterization, including modifications and biological relevance all feed into defining the QTTP. Only after this exercise is the manufacturing process defined.

In her view, a quality-by-design n approach drives biosimilar development. The QTPP should be attribute-focused. ➤

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Ultimately, an end-to-end approach should be facilitated by the established QTPP.

while these biosimilar products are changing post-licensure, so too are the reference products

Case studies dominated the first afternoon session on Day 1. **Jens Schletter,** PhD, Head Regulatory CMC Group Biopharmaceuticals, Sandoz, presented a case study of a recently FDA-approved biosimilar providing an overview of what the sponsor learned from the development and approval process. The requirement to show statistical equivalence proved a particular challenge as the mean of the reference product batch values moved over time. This was solved by applying scientific structure-function relationship knowledge. Success in this case was achieved by interacting and working closely with regulators. A moving reference product mean, however, will result in the bar being higher or lower for different applicants developing biosimilars for the same molecule, depending on when they start/stop sourcing batches and how the mean of the reference product will move in this time.

Next, **Emily Shacter,** PhD, Independent Consultant, ThinkFDA, LLC, offered a case study on demonstrating analytical similarity. In her experience, demonstrating similarity requires meeting all the foundational elements of the similarity assessment. Additionally, consistent manufacturing and a control strategy that maintains biosimilarity is also critical.

She finds that one of the biggest analytical discrepancies that delays approval is ignoring what the data is saying. Other main issues are an inadequate number of lots or inadequate data, lack of comparability after the pivotal study and inadequate immunogenicity assays.

As far as statistical analysis, Shacter noted that what falls in Tier 1 are CQAs of high criticality. In Tier 2, quality range attributes are reviewed and in Tier 3 visual, graphical and absolute values are reviewed. The totality of evidence means that approval depends on integration of all submitted information that demonstrates a product is a biosimilar to the reference product. It all boils down to the need to use science to justify differences between the two products.

Shacter also reiterated the importance of communicating with FDA early in the process.

Jeff Yant, PhD, Biosimilars Operations Director, Amgen, then provided some case studies based on Amgen's experiences in biosimilar development. His company uses the QTPP to guide biosimilar development and takes a stepwise approach to demonstrating biosimilarity—each step reduces some level of uncertainty. These steps lead to continual refinement.

Comprehensive analytical similarity assessments are crucial to reducing uncertainty. In Yant's case study, he explained how Amgen included the need for a change in cell line due to potency issues, shifts due to technology transfer (i.e., back to the lab to address issues) and a high level of particles due to shear stress during drug product manufacture that led to changes in equipment.

Providing a regulatory perspective on analytical similarity, **Patrick J. Lynch,** PhD, Biologist, CDER, FDA, closed out the case studies. He explained that FDA looks at the totality of evidence and recommends a stepwise approach with analytical similarity as the foundation. In addition, the Agency also looks at primary structure, higher order structure, molecular weight, appearance and semi-quantitative assay results. Lynch further recommends that biosimilar sponsors ensure there are adequate numbers of independent lots for review. Different scales may be used if appropriately justified and supported by data. Reference product lots need to be collected over time and tested within expiry. It is important for reviewers to have information on the genealogy of lots of the biosimilar product.

After presenting these case studies, the speakers were joined by German regulator **Birgit Schmauser,** PhD, Quality Assessor, Pharmaceutical Biotechnology, Inspections Quality, Federal Institute for Drugs and Medical Devices, for a panel discussion on analytical similarity. Although statistical equivalence testing was not officially the subject of a dedicated presentation, it was nevertheless thoroughly discussed by the panelists. FDA wants a predefined approach common for all sponsors.

The panel also thoroughly discussed the number of batches required. Currently, ten is the default. The industry representatives expressed that production of additional batches will take time due to complexities in securing manufacturing. To achieve this number, pilot batches of reasonable size or technical batches can be taken as long as data shows that the batches taken are representative. FDA representatives were more cautious about this approach and recommended discussing it with the Agency before submission.

There was also discussion about statistical data. One way to avoid errors may be to use the median rather than the mean. And it remains very important for biosimilar sponsors to invest in analytics.

Day 2: PAC, Product Specs and Data

The Day 2 talks began with a look at post-approval changes (PACs) to biosimilar products. **Monika Lang-Salchner,** PhD, Head Regulatory CMC Oncology Products, Sandoz, presented a case study on how her company handled PACs to its Omnitrope biosimilar, the first biosimilar approved in Europe in 2006. According to her, all PACs for Omnitrope were handled according to ICH Q5E: *Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process.*

Lang-Salchner emphasized that the level of experience impacts the risks. She concluded her talk by pointing out that as of June 2016, 100,000,000 patient experience has been gathered for Omnitrope.

Despite a series of PACs, no unexpected or unique adverse event have been observed; in particular, there was also no difference in immunogenicity.

From a regulator's perspective, Schmauser offered her perspective of ten years of PACs to biosimilars in the European market. As of the conference, a total of 28 biosimilars have been approved in the European Union. More PACs to these products are also occurring. Yet while these biosimilar products are changing post-licensure, so too are the reference products. The same principles and risk ranking for PACs apply to both the reference product and the biosimilar. Schmauser concluded that since the launch of the first European biosimilar in 2006, very few changes have truly affected the quality profiles for biosimilars in the last ten years among the many changes submitted.

Following these two talks, the next session addressed control strategies for biosimilars. **Maria-Teresa Gutierrez Lugo,** PhD, Chemist, CDER, FDA, offered a regulatory perspective, beginning with an overview of the biosimilar development flow. Lugo explained that the control strategy should be in alignment with the QTPP. She used the example of a raw material qualification that was needed to reduce the level of a product-related impurity considered as a high risk CQA.

For an industry perspective, **Kyung-Ah Kim,** PhD, Vice President, Head of Bioanalysis, Samsung Bioepis, emphasized the role of quality in biosimilar development. She clarified that comprehensive analytical characterization is a fundamental development tool leading to product quality. Throughout the development process, tollgates exist for key development steps. During this process, stepwise risk assessments are conducted to further guide development. Kim ended her talk with the point that analytical characterization is key to assessing biosimilarity.

The first afternoon session covered product specifications. FDA representative **Leslie Rivera Rosado,** PhD, Director Regulatory Review Officer, CDER, spoke on the Agency's position on setting product specifications as they are part of the overall control strategy overview and support continued assurance for biosimilarity post-licensure. Specifications are based on ICH guidelines (e.g., ICH Q6B: *Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products* and Q5C: *Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products*) and should focus on quality attributes that are useful to ensure safety and efficacy. Not all CQAs need to be in the specifications. Specifications should also take into account knowledge of the reference product, including QTPP and for BLA specifications, manufacturing and assay variation, CQA assessments, development data and stability data.

Rosado then referred to a case study around a reference standard. In this instance, the reference standard was qualified for intended use. From this case study, it was apparent that it is key to establish the reference standard and maintenance/bridging to assure specifications can be set meaningfully and are acceptable to the Agency.

Sandoz's **Helmut Lerch**, PhD, Head Compliance Development Biopharma, then offered an industry perspective on specification. While in the pre-QbD era, specifications were a major control strategy element, nowadays, other control strategy elements have become important and can be used. But specifications in an enhanced QbD development program are only a final confirmation. Specifications should enable effective product/process lifecycle management (for all post-market changes).

The final session of the conference explored data expectations in biosimilar development. **Kate Hutterer,** Senior Scientist, Amgen, looked at points to consider for analytical similarity assessments. She suggested performing an age adjustment for the stability-indicating methods/data in the analytical similarity studies to provide a more accurate difference assessment for the biosimilar versus the reference product.

Joel T. Welch, PhD, Acting Review Chief, CDER, FDA, then focused on Agency expectations for data quality and quality data in biosimilar development. He focused his presentation on the current agency review experience and some common concerns from the existing gaps in the BLA submissions received. Reference standard bridging studies are critical from an agency perspective. The reference standard strategy should be established as early as possible. The earlier the reference standard can be locked in, the better for the sponsor and the Agency.

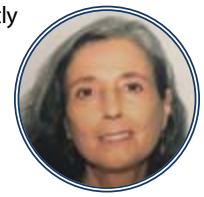
Outlier testing is to be consistent within usual GMP conditions. Data quality (OOT/OOS appropriately handled via written procedures) is absolutely necessary.

Welch spent last part of this presentation on preapproval inspection considerations. Biosimilar data review may take much longer with a focus on where each test result was generated, etc. Sponsor should consider what could happen to data quality if not tested in a GMP lab.

All the presentations generated strong discussion among attendees. Biosimilars will also be covered more in-depth at a PDA workshop in September following the *2018 PDA/FDA Joint Regulatory Conference.*

About the Authors

Stephan Krause, PhD, is AstraZeneca's Director of QA Technology. He manages the global biologics control strategy steering committee. He is also the coleader of PDA's Biosimilar Initiative and a member of the BioAB and Education Advisory Board (EAB).



Emanuela Lacana, PhD, is currently the Associate Director for Biosimilars and Biologics Policy in the Office of Biotechnology Products in CDER. Prior to her appointment at the FDA, she worked at Georgetown University and at NIH.

Jens Schletter, PhD, is currently working as Head Regulatory CMC Biopharmaceuticals of Sandoz' Regulatory Affairs Biopharmaceuticals department. As such he is responsible for all regulatory CMC aspects of Sandoz' biosimilar approved drugs as well as biosimilar development projects, on a global level.

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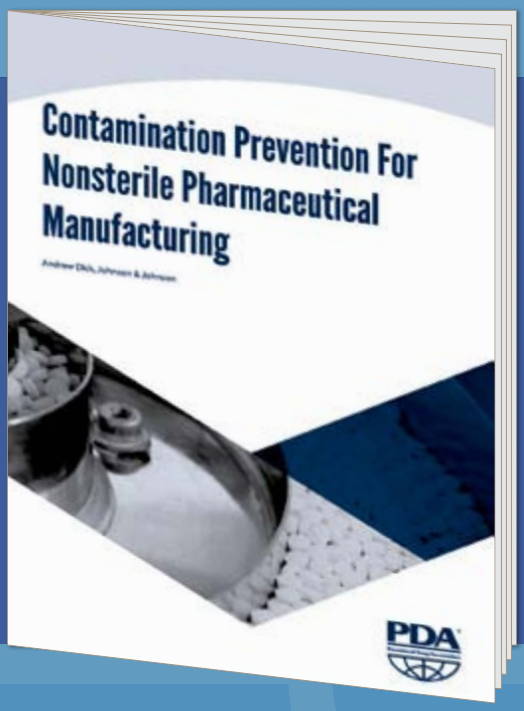

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