People • Science • Regulation

PDA Letter

Volume LIV • Issue 1 www.pda.org/pdaletter January 2018

Collaboration Through Mutual Reliance Brings FDA and EMA to the Table 26

CORNING

Pharmaceutical Technologies

Corning is a global supplier of pharmaceutical glass products. With a continuous commitment to innovation, Corning designed Valor™ Glass, a glass composition engineered for pharmaceutical packaging that has improved chemical durability and **eliminates** delamination.

The interior drug-contacting surface of Corning Valor™ Glass containers are never predisposed to delaminate and have low extractable concentrations, making Valor Glass ideally-suited to protect drug products. In addition, Valor Glass containers reduce the probability of contamination or loss of sterility due to glass particles.

Learn more at: corning.com/valor

Corning is one of the world's leading innovators in materials science, with a 166-year track record of life-changing inventions. Corning applies its unparalleled expertise in glass science, ceramics science, and optical physics, along with its deep manufacturing and engineering capabilities, to develop category-defining products that transform industries and enhance people's lives.

January 2018 PDA Letter

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Collaboration Through Mutual Reliance Brings FDA and EMA to the Table

Rebecca Stauffer, PDA

In the past ten years, the number of U.S. FDA-regulated shipments at 300 U.S. ports have doubled. These products originate from more than 150 countries, 130,000 importers and 300,000 foreign facilities. These numbers illustrate the level to which foreign production of FDA-regulated goods and materials has exploded over the last decade.

Cover Art Illustrated by Kagenmi

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Regulators Tackle Tough Micro Questions on Panel

The *12th Annual PDA Global Conference on Pharmaceutical Microbiology* concluded with an "Ask the Regulators" panel. Find out what some of the interesting questions that arose during this panel in a transcript of a portion of the session.

AIDC is a Sign of Things to Come: Part II

Napoleon Monroe, New Directions Consulting

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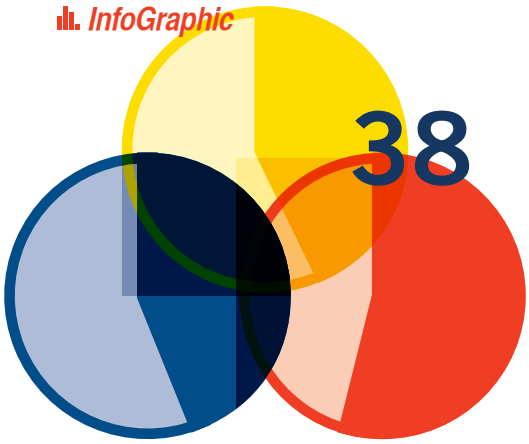
In order to save overall payer costs, ensure access to products when needed and improve compliance with protocols, combination products are often designed to be administered by patients or nonprofessional caregivers.

InfoGraphic



38

Mad for RABS

PDA recently conducted a survey of both members and nonmembers regarding current aseptic processing trends within the industry. Over 300 responded, providing insights into the current state of aseptic processing. Some of these insights pertain to the state of restricted access barrier systems (RABS).

PDA Letter

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Articles published in the PDA Letter do not represent the official positions of PDA, Inc., but are the opinions of the authors submitting the articles.

Subscriptions are not available.

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Departments

Digital Exclusives

> **On the Issue** | Contamination Recovery Rates in Low-bioburden Facilities
Bristol-Myers Squibb's **Paula Peacos** discusses how to use contamination recovery rates for environmental monitoring trending in the latest On the Issue video.

> Cracking the Challenges of Glass Packaging
In the early 2010s there was a spike in drug recalls related to glass packaging. What has changed since then?

pda.org/letter

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PDA Europe Conference, Exhibition, Education

The Parenteral Drug Association presents:

Virus Forum

Register by 17 March 2018 and SAVE!

8-9 May 2018

Hilton Florence Metropole

Florence | Italy

pda.org/EU/Virus2018

2018 PDA Glass Quality Conference

Improving Primary Packaging of Parenterals

After nearly five years, PDA is bringing back the *Glass Quality Conference*!

At the *2018 Glass Quality Conference*, discover the latest advancements, discuss current challenges, and brainstorm possible improvements to pursue in glass manufacturing, characterization, handling, and packaging.

Informative plenary and breakout sessions will feature the following topics:

- Best practices for glass handling
- Current expectations for incoming glass and pharmaceutical product packaging
- Issues of glass-drug interactions, glass breakage, and glass particulate
- Challenges of regulatory acceptance of innovation and modernization of pharmacopoeias
- Key insights from the 2017 PDA Glass Survey
- And more!

Registration includes:

- Two days of exploration into the world of pharmaceutical glass packaging
- Access to an exhibition featuring vendors showcasing some of the most advanced glass packaging solutions available
- Admission to the networking reception where you can mix and mingle with friends and colleagues old and new

Take advantage of this opportunity to enhance your knowledge and connect with other professionals with an interest and experience in pharmaceutical glass packaging.

To learn more and register, please visit pda.org/2018Glass

PDA Parenteral Drug Association

January 23-24, 2018 | Washington, DC
Exhibition: January 23-24
#PDAGLASS

CONNECTING PEOPLE SCIENCE+ REGULATION®

Another Year for Good Storytelling

Recently, an anthroplogy team studying the Agta, a society of hunter-gathers in the Philippines, asked which members of the society they would most want to live with ***(1).*** The researchers were using the question to determine which qualities the Agta most valued among their peers. Interestingly, the majority of the Agta valued one particular group's skills the most. Not the best hunters and fishers. Not the best foragers. Not the best healers.

Above all, the Agta valued most the best *storytellers* within their society. In fact, great storytellers were valued twice as much as great hunters ***(1).***

I share this because I am proud to begin a new year of sharing the stories that are important to our industry. We may not be sitting around a nighttime fire hearing about the exploits of hunts past and present but we are sharing lessons learned from past experiences, case studies, analysis of recent regulations, etc. And we are trying to pass these "stories" down to the next generation of pharmaceutical manufacturers.

The *PDA Letter* editors have ambitious plans to further our storytelling in 2018. You can expect more videos and online-only articles this year. We also plan to do a better job of linking our multimedia content to text articles, expanding the reader experience.

We could not do all of this alone. The *PDA Letter* Editorial Committee (PLEC) helps us identify the most pertinent themes for our issues and assists in reviewing article submissions. These subject matter experts allow us to provide you with high-quality storytelling in each issue. With this in mind, I want to thank those who are departing the PLEC this year: **Maria Brown, Winston Brown, Robert Darius, Robert Lechich, Pritesh Patel, Praveen Prasanna, Lan Zhang** and **Ilana Zigelman.** Your service on the Letter has proved beneficial over the previous two years and helped keep the publication strong.

Along these lines, I want to welcome **Joanne Beck, Andrew Dick, Walid El Azab, Stephanie Gaulding, Richard Hameister, Tamer Helmy** and **Wendy Zwolenski Lambert** to the PLEC. I look forward to working with all of you on continuing to produce a strong product for PDA members.

Working with the PLEC is always a pleasure and I enjoy all the different perspectives each Committee member brings to the table. Their assistance is truly invaluable to the Letter. We are always looking for new folks to join at the end of each year to replace those coming off the Committee, so if you would like to be considered for 2019, feel free to contact me over the course of the year with your interest.

Speaking of cooperation, I want to return to the Agta. Apparently, the majority of their stories emphasize the importance of cooperation ***(1).*** Interestingly, I have noticed that many of our articles/videos emphasize cooperation, whether it is between industry and regulators, those on the shop floor and in the lab, contract giver and contract receiver, or supplier and client. Here is hoping this spirt of cooperation and collaboration continues in 2018!

Rebecca Stauffer

References

1. Yong, E. "The Desirability of Storytellers." *The Atlantic* (December 5, 2017). https://www.theatlantic.com/science/archive/2017/12/the-origins-of-storytelling/547502/

2018 Board of Directors

PDA is pleased to announce the results of the 2018 Board of Directors and Officers election.

Executive Committee

The following candidates have been elected to serve as officers on the PDA Board of Directors:

Chair: **Rebecca Devine,** PhD, Biopharmaceutical Consultant

Chair-Elect: **Jette Christensen,** Scientific Director, Compliance, Novo Nordisk A/S

Treasurer: **Michael Sadowski,** Director, Research, Baxter

Secretary: **Steven Lynn,** Global Head, Group/Corporate Compliance and Audit, Novartis

Immediate Past Chair: **Martin VanTrieste**

PDA also thanks **Hal Baseman,** COO, ValSource, who ends his term as Immediate Past-Chair.

Directors

PDA congratulates the following new and returning directors to the Board:

Masahiro Akimoto, Senior Manager, Research and Development and Quality Assurance Division, Otsuka

Kerry Ingalls, Vice President, Site Operations Amgen

Mary Oates, Vice President of Innovative Operations and Network Excellence, Pfizer

Emma Ramnarine, Senior Director Global Biologics, Genentech/Roche

Ursula Busse

PDA also thanks outgoing directors **Ursula Busse,** PhD, Head Quality Intelligence and External Relations, Novartis, and **Deborah Autor,** Senior Vice President, Strategic Global Quality and Regulatory Policy, Mylan for their service on the Board.

Deborah Autor

You Spoke, PDA Listened

2018 Annual Meeting to Feature New Format Based on Attendee Feedback from Past Meetings

In response to feedback from attendees at previous Annual Meetings, we are trying a new format for the *2018 PDA Annual Meeting*. This event will deliver the same high-quality content you have come to expect, but in a new lineup designed to better meet your needs.

Here are the changes:

- The meeting will now begin with the Opening Plenary at **1 p.m. on Monday, March 19**
- A Grand Opening Celebration will kick off in the Exhibit Hall at **5 p.m. on Monday, March 19—this is your first opportunity to meet with exhibitors and learn about the latest products and services**
- Interest group sessions will be held at the same time as break-out sessions, giving attendees more sessions from which to choose during the day and allowing for more free time in the evening
- The Closing Reception will be the final event of the meeting and takes place after the close of the meeting on **Wednesday, March 21, at 7 p.m.**—be sure to stay and celebrate with us!

Learn more about the *2018 PDA Annual Meeting* at www.pda.org/2018annual.

PDA Volunteer Spotlight

Renee Morley

- Cleanroom Consultant
- Member Since | 2010
- Originally From | Eastlake, Ohio

Anything worth doing, is worth putting forth 110% effort

Why did you decide to volunteer for PDA?
When I moved to Raleigh, N.C., from Eastlake, Ohio, I also transitioned from being an internal employee to a field employee. This meant I could not meet people in a traditional office environment. My manager at the time—a volunteer for PDA's Southeast Chapter—suggested I join PDA. She always spoke very highly of the organization and how it helped her grow professionally due to her involvement with the chapter.

Of your PDA volunteer experiences, which have you enjoyed the most?
In the Southeast Chapter, we host a "Meet the Professionals" night where various professionals within the industry provide advice for students studying for science degrees. These professionals range from those starting out in their careers to those at the vice president level. The chapter also tries to include representatives from a range of disciplines within pharmaceutical manufacturing.

Although everyone's background is different, each experience provides the same insights: work hard, always take risks and focus on what you enjoy. They also discuss what being a PDA member has done for them. The evening ends with pizza and networking, allowing students one-on-one time with the professionals.

How has PDA contributed to your professional career?
After being a member for almost eight years, PDA has been a big contributor to my professional career in many ways. I have had opportunities to network with the top leaders in pharmaceutical manufacturing and learn how they are overcoming challenges to provide safe drugs for patients. I have strengthened my technical knowledge by attending conferences, interest group meetings and networking events. And I have been able to give back by helping provide programs and scholarships for students. PDA has helped shape me into a well-rounded technical professional.

Tell us about a personal hero you would like to meet.
I think I would want to meet someone who made a great impact on the world, but did not live to see it. **Christa McAuliffe** is an example of a person that I admire. She was selected from more than 11,000 applications to participate in the NASA Teacher in Space Project and was scheduled to become the first teacher in space.

2018 PDA Annual Meeting

Agile Manufacturing Strategies:
Driving Change to Meet Evolving Needs

Register by January 8, 2018 and save!

The *2018 Annual Meeting* will address industry "hot topics," including the end users' patient perspective, innovative manufacturing strategies, disruptive technologies, and product value chain logistics. Attend to find out about the latest trends in Big Data, Artificial Intelligence, and robotics!

NEW FORMAT FOR 2018:

Same high-quality content in an ALL NEW meeting format!

In response to attendee feedback, PDA is debuting a NEW meeting format at the *2018 PDA Annual Meeting*, designed to better meet the needs of attendees.

Please note these important changes to the 2018 PDA Annual Meeting Schedule:

- The Conference will now begin with the Opening Plenary at **1:00 p.m. on Monday, March 19**
- The Grand Opening Celebration will kick off in the Exhibit Hall at **5:00 p.m. on Monday, March 19** – take advantage of your first opportunity to see the latest products and services and meet with exhibitors!
- Interest Group sessions will be held at the same time as the breakout sessions, giving attendees more sessions from which to choose during the day and allowing for more free time in the evening
- The Closing Reception will take place on **Wednesday, March 21 at 7:00 p.m.** – Be sure to stay and celebrate with us!

Discover how the industry is using novel approaches to stay agile in the face of development and commercialization of innovative therapies. Sessions will focus on exciting topics such as continuous biomanufacturing, serialization, advances in analytical sciences and quality control strategies, patient-centered precision medicine, and next-generation manufacturing.

Don't miss the Exhibit Hall where vendors and suppliers will showcase their latest technologies and offer solutions to current and future pharmaceutical manufacturing challenges.

Be a part of one of the most exciting events of 2018!

Learn more and register at pda.org/2018Annual

And, on **March 22-23, 2018**, PDA Education will host a choice of seven courses as part of the *2018 PDA Annual Meeting Course Series* to help you further advance your knowledge. ***Learn more and register at pda.org/2018AnnualCourses***

PDA Parenteral Drug Association

March 19-21, 2018 | Orlando, FL
Exhibition: March 19-21
Post-Meeting Workshop: March 21-22
Courses: March 22-23
#PDAANNUAL

CONNECTING PEOPLE SCIENCE+ REGULATION®

Aseptic Processing Proves a Hot Topic in Brazil

Wolfgang Harry Löscher Filho, Libbs Farmacêutica, Brazil Chapter Secretary

Imagine having the opportunity to participate in hands-on activities around the latest aseptic processing techniques.

For 50 members of PDA's newest chapter, Brazil, this was an opportunity realized.

On Sept. 18–22, the Brazil Chapter held the *Workshop on Aseptic Processing Techniques*, in São Paulo. Lectures were located at the Regional Council of Chemistry (CRQ), and hands-on activities were offered at a Eurofarma manufacturing facility on the outskirts of São Paulo. Eurofarma is one of the biggest pharmaceutical companies in Brazil; the chapter thanks the company for granting access to the site for the event.

Workshop attendees pose for a group photo along with speakers

The workshop proved to be a success. It was limited to 50 people in order to provide high-quality, hands-on activities, and several names had to be added to a waiting list due to the strong interest in this topic.

The workshop had the support of key suppliers within the Brazilian pharmaceutical industry: Pall, Elis, Bausch + Ströbel, West, PMS, Merck, Ompi, Alsco, Eurofarma, Steris and Biomérieux. These suppliers exhibited their products in a beautiful showroom next to CRQ's auditorium, which was open to everyone in the pharmaceutical community Sept. 19–20 during the workshop. Over 200 representatives of the local pharmaceutical industry attended the exhibition.

David Matsuhiro, one of the regular instructors for the PDA Education's "Fundamentals of Aseptic Processing" course at

the PDA Training and Research Institute, was the main speaker for the workshop. Regulator **Tathiane Oliveira** also spoke, sharing her experiences with the audience. Oliveira also spoke at the chapter's inaugural symposium held in March.

Chapter members and attendees also had the opportunity to gather with friends and area professionals at a networking happy hour on Sept. 21 at CRQ. Refreshments were served on behalf of chapter board members, some of whom joined the celebration to hear firsthand feedback about the workshop.

This event was extremely important for the Brazilian pharma industry. The chapter thanks Eurofarma's CEO **Maurizio Billi** for use of the company's facility.

Presentations and photos of the event will be available soon on the chapter website: www.pda.org/brazil. We invite the PDA community to participate in chapter meetings and events in 2018. We are also open to suggestions, which can be e-mailed to us at eventos@pdabrazil.org. Additionally, the aseptic processing workshop will be repeated in the region some time in 2018.

The PDA Brazil Chapter was approved in September 2016 and has already executed events on data integrity, visual inspection and risk management. Within the chapter, an interest group on environmental monitoring is led by **Izabel Silva** and **Alexandre Terada** and one on visual inspection is led by **Samara Mateiro**.

PDA Who's Who

Maurizio Billi, CEO, Eurofarma

Samara Mateiro, Sanofi

David Matsuhiro, Senior Consultant, Cleanroom Compliance Inc.

Tathiane Oliveira, COVISA (City of São Paulo health authority)

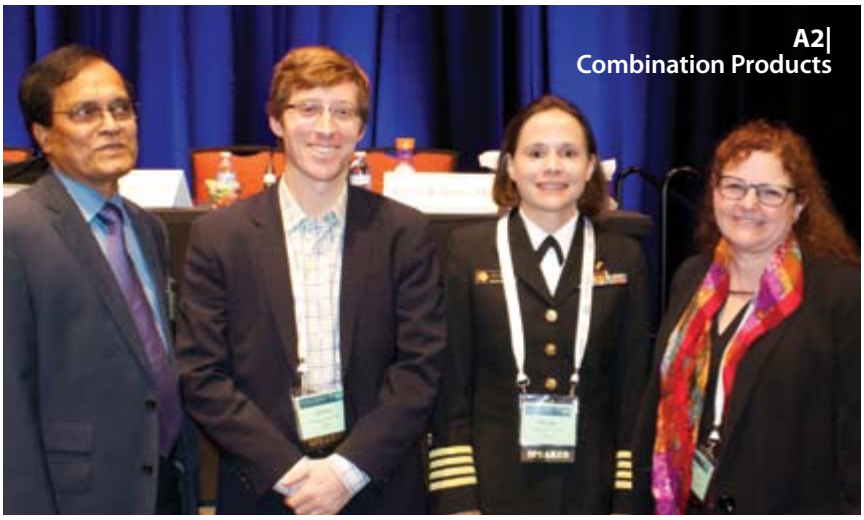
Izabel Silva, Allergan

Alexandre Terada, Allergan

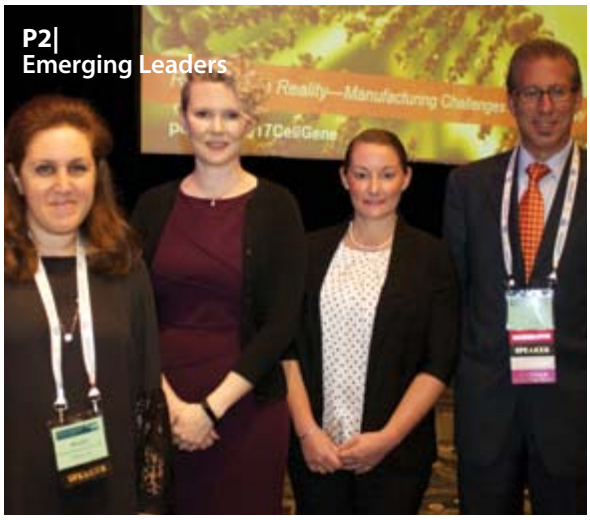
Speakers Tathiane Oliveira (second from left) and David Matsuhiro (second from right) pose with two workshop attendees

12th Annual PDA Global Conference on Pharmaceutical Microbiology
October 16–18 |Bethesda, Md.

(l-r) Edward Tidswell, PhD, Merck & Co.; Leslie Falco, Pfizer; Walid El Azab, STERIS; James Polarine, Jr., STERIS



(l-r) Vinayak Pawar, PhD, U.S. FDA; Steven Hertz, FDA; Melissa Burns, FDA; Susan Neadle, Johnson & Johnson, Janssen Pharmaceutical Companies



(l-r) Melissa Gulmezian-Sefer, PhD, Allergan; Sarah Weiser, Pfizer; Carly Krystopik, Bristol-Myers Squibb; Michael Miller, PhD, Microbiology Consultants

(l-r) Marsha Steed (Hardiman), ValSource; Kim Sobien, PETNET Solutions

(l-r) Dona Reber, Pfizer; Paula Peacos, Bristol-Myers Squibb; Marsha Steed (Hardiman), ValSource; Laure Singer, Pfizer

(l-r) Jennifer Gogley, FDA; MaryEllen Usarzewicz, Bristol-Myers Squibb; Amanda Bishop McFarland, ValSource; Lisa Sykes-Winstead, Merck & Co.

(l-r) Amy McDaniel, PhD, FDA; Anthony Cundell, PhD, Microbiological Consulting; Michael Miller, PhD, Microbiology Consultants; Bryan Riley, PhD, FDA

Passport Drawing

Pharmaceutical Cold & Supply Chain Logistics
October 10–11 |Prague

Gert-Jan van Diest (left center) holds his raffle prize while conference co-chair Rafik Bishara (right, holding microphone) looks on

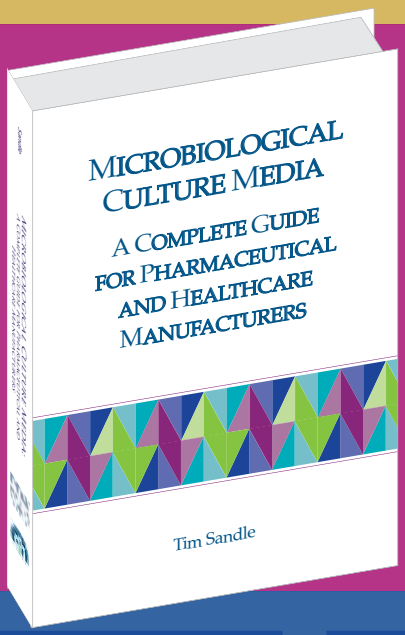
Eric Stener, Sanofi Pasteur, presented on truck shipping qualification

2018 PDA/FDA Joint Regulatory Conference
Program Planning Committee Face-to-Face Meeting
December 12, Bethesda, Md.

(back l-r) Jason Brown, PDA; David Chesney, DL Chesney Consulting; Paul Perdue, Office of Regulatory Affairs, U.S. FDA; Rick Friedman, CDER, FDA; Jackie Kunzler, Baxter; Douglas Campbell, InterPro QRA; Reyes Candau-Chacon, CDER, FDA; Kenneth Nolan, FDA; David Doleski, Sanofi; Molly Moir, PDA

(front l-r) Clarice Hutchens, Pfizer; Rebecca Devine, Biopharmaceutical Consultant; Mai Huynh, CVM; FDA; Laurie Norwood, CBER, FDA; Myriam Sosa, Merck; Valerie Whelan, Amgen; Carol Rehkopf, CBER, FDA; Tara Gooen Bizjak, CDER, FDA; Denyse Baker, PDA

PDA Bookstore New Release



Microbiological Culture Media: A Complete Guide for Pharmaceutical and Healthcare Manufacturers

By: Tim Sandle

PDA MEMBER PRICE: $240

PDA NON-MEMBER PRICE: $299

HARDCOVER: ITEM NO. 17345

DIGITAL: ITEM NO. 18041

Taking into account that 90 percent of quality control microbiology remains reliant upon culture based methods, this unique text focuses on microbiological culture media as applied to pharmaceutical microbiology. This book takes into consideration that innovations continue to arise with new media recipes that are formulated for the selection of new strains for the application of media in conjunction with rapid microbiological methods. In 23 chapters, the book covers how media is used in the modern pharmaceutical microbiology setting and recaps the past, signals the future, and helps interpret the present.

go.pda.org/MBCM

About the Author:

Dr. Tim Sandle is the Head of Microbiology at Bio Products Laboratory, UK and visiting tutor with the School of Pharmacy and Pharmaceutical Sciences, University of Manchester. He serves on several national and international committees related to pharmaceutical microbiology and cleanroom contamination control, including Pharmig and PDA technical working groups. He is a member of several editorial boards. He is the author of over 500 book chapters, peer-reviewed technical articles, and several published books including *Aseptic and Sterile Processing*; which he co-edited with Edward C. Tidswell and is co-published by PDA and DHI Publishing.

SNAPShot

PDA Welcomes New Standards Manager

PDA is pleased to welcome **Christine Alston-Roberts** who joins PDA as its Senior Standards Manager. Christine will manage various workgroups to develop consensus standards and oversee the American National Standards Institute (ANSI) standards process. PDA was approved by ANSI as a standards development organization (SDO) in 2016.

Christine comes to PDA after spending 15 years at the American Type Culture Collection (ATCC) where she worked as a Standards Specialist. There, she was responsible for ensuring the effective operation of the ATCC SDO and any standards or certification initiatives undertaken by ATCC. Her responsibilities included coordinating workgroups, performing administrative, operational and compliance functions of the company's standard program, communicating as required with the Steering Committee, the membership, standard development workgroups and ANSI, ensuring that records of the ATCC SDO were maintained in compliance with ANSI requirements and serving as the content administrator for the SDO website.

In addition to the SDO duties, she effectively maintained the ATCC Proficiency Standard program and product line, led cross-functional project plans and teams that involved planning, production, and launch of company certified reference materials (CRM) to satisfy ISO Guide 34 requirements and ensured that information was accurate on the company's Web-based Standards Resource site.

Christine graduated with a bachelor's degree from Virginia Tech. She is excited to join the Scientific and Regulatory Affairs department at PDA.

Journal *Preview*

Pharmaceutical Microbiology Analyzed in Three Papers

This edition offers three papers on pharma microbiologys: Tidswell & Sandle on Micro Data Integrity; Menezes, et al, on QRM and micro contamination for non-sterile drug products; and Jimenez, et al, on real-time PCR for low-level contamination.

Review

Edward C. Tidswell, Tim Sandle, "Microbiological Test Data – Assuring Data Integrity"

Fran L. DeGrazio, "Holistic considerations in optimizing a sterile product package to ensure container closure integrity"

Research

Matthew V. Tirrell, et al., "Inhibiting sterilization-induced oxidation of large molecule therapeutics packaged in plastic parenteral vials"

Bruna Filipa Ribeiro Berardo, Ana Teresa Machado Reis, Rui Loureiro, "Quality of medicines in Portugal: a retrospective review of medicine recalls (2000–2015)"

Natarajan Rajagopalan, et al., "Impact of Drug Formulation Variables on Silicone Oil Structure and Functionality of Prefilled Syringe System"

Case Study

José C. Menezes, et al., "A QRM Discussion of Microbial Contamination of Non-Sterile Drug Products, using FDA's and EMA's Warning-Letters Recorded Between 2008 and 2016"

Technology/Application

Luis Jimenez, et al., "Real-Time PCR Detection of Burkholderia cepacia in Pharmaceutical Products Contaminated with Low Levels of Bacterial Contamination"

Commentary

Derek Willison-Parry, et al., "Elastomer Change Out—Justification for Minimizing the Removal of Elastomers to Prevent Cross-Contamination in a Multiproduct Facility"

Derek Willison-Parry, et al., "Guidelines for Risk-Based Changeover of Biopharma Multi-Product Facilities"

Letter/Erratum

John Mattila, et al., "Erratum to "Retrospective Evaluation of Low-pH Viral Inactivation and Viral Filtration Data from a Multiple Company Collaboration""

Monitor Viable Air with Single-Use, Real-Time Tech

Recent Advancements Address Regulatory Requirements for Monitoring of Cleanrooms

Frank Panofen, PhD, Particle Measuring Systems

Viable air monitoring is a crucial part of an environmental monitoring program. Because common viable air monitoring methodologies have not been introduced in many years, monitoring in critical manufacturing areas like Grade A, RABS and isolators creates a dilemma for the industry.

Traditional methods lack the necessary sensitivity. Singular results only provide an indicator of cleanroom status; often there is no direct correlation between number of organisms and product contamination risks ***(1).***

A defensible monitoring program should be based on the following criteria:

1. **Frequency of testing:** Frequent/continuous
2. **Location:** Close to critical points
3. **Performance:** Without adding any contamination risk to the product

With most traditional methods, it is virtually impossible to achieve a defensible monitoring program. Manufacturers frequently disregard the fact that handheld instrumentation contributes to particle load of an area and causes flow turbulences close to manufacturing. Mobile devices cannot be properly sterilized for use in Grade A environments.

For process security, viable air monitoring devices that can sample remotely into ISO Grade 5 areas must be installed. In the near future, international inspectors will not accept any handheld devices in critical areas.

When remotely sampling very close to critical control points, a risk assessment can determine whether the manipulation and cleaning procedures for the remote atriums used impose a risk to the patient or the product. Knowing that, in many cases, the risk cannot be correctly assessed, as traditional viable air sampling techniques do not produce realistic views of the environment, manufacturers may consider the use of single-use air sampling atriums to drastically reduce operator handling close to the critical zone. A risk-based approach includes the use of real-time viable air testing during media fill (process validation) exercises, enabling the manufacturer to map the full critical process in real-time operation.

There are two options to ensure the full manufacturing process is continuously monitored with data generated: single-use and real-time technologies.

Single-use technologies have been validated for long-term, two-hour sampling in critical environments at 25 LPM. In an eight-hour process model, this relates to only four sampling units covering the full manufacturing process for viable air sampling, limiting the need to frequently interfere with the process.

Continuous viable air sampling can also be managed by a real-time monitoring device instrument. Data accumulated by this instrument better equips manufacturers with a full understanding of the manufacturing environment and allows for immediate action when critical concentrations of biological counts are reached. Lines can be stopped, material waste avoided, and quality assurance dramatically increased with a perceptible decrease in production loss and cost.

Real-time viable measuring tools not only capture culturable microorganisms, but also viable, nonculturable microorganisms, well known in the pharmaceutical industry to be a risk not controlled by current sampling technologies. As a result, counts of those technologies are generally higher in contaminated areas, but zero counts are also possible in critical environments. When moving to these technologies, it is possible for manufacturers to detect some biological counts where previously zero CFU with traditional methods would be common. Regulators indicate that the primary advantage of better process control could be attained by occasionally finding a biological count in areas where it is not expected. Incidents of biological counts in critical areas are detected almost regularly, but strong deviations from this trend and frequency indicate in real time whether the process is out of control and needs to be readjusted.

As with particle monitoring, a correct selection of alert and action limits must be based on a risk assessment and a consistent amount of trending data. ISO 14644-2 recommends the selection of a reasonable alarm notification strategy, not based on a single-event triggering alarm, but on a combination of multiple out-of-specification counts over a period of time. The main goal of selecting the appropriate alert/action alarm strategy is essential to avoid nuisance alarm events that could be ignored by operators ***(2).***

A disadvantage of real-time viable monitors is the fact that identification of contaminants is not possible due to the nature of the detected microorganisms. Therefore, pharmaceutical manufacturers are advised to combine real-time viable testing with a continuous viable monitoring approach. With this combination, the safety of the drug and process will be moved to a higher standard, protecting patients from microbial contaminations.

Regulatory Concerns Justify New Tech

With the introduction of modern manufacturing concepts and an increasing number of industry standards, there is a need to adopt viable air monitoring in conjunction with the most recent regulatory trends ***(3).*** Regulations provide specifications for the selection of a viable air monitoring strategy.

ISO standards are becoming more important as a reference for the pharmaceutical industry. The EU GMP Annex 1 explains that ISO/EN norms should be considered as reference documents when it comes to detailing methods for the determination of

microbiological and particulate cleanliness of air, surfaces, etc. ***(4).***

The ISO 14698 standard states that "a sampling device shall be selected according to the area being monitored" ***5).*** Looking at the expected concentration of viable particles in different clean zones, in critical areas like Grade A/ ISO 5 with expected low to zero counts of microorganisms, high sampling volumes or continuous sampling is preferable ***(1,4,6).*** the EU GMP Guide supports this: "Where aseptic operations are performed monitoring should be frequent using methods such as settle plates, volumetric air and surface sampling" ***(4).*** Also, U.S. regulations state "sample sizes should be sufficient to optimize detection of environmental contaminants at levels that might be expected in a given clean area" ***(7)*** and "routine microbial monitoring should provide sufficient information to demonstrate that the aseptic processing environment is operating in an adequate state of control" ***(8).***

Under European guidelines, "for Grade A zones, particle monitoring should be undertaken for the full duration of critical processing" ***(4).*** Particulate matter not only consists of inert, nonviable particles, but also viable particles. Continuous monitoring of viable particles should be undertaken for ISO 5/Grade A cleanroom settings.

When considering risk zones, manufacturers typically focus on Grade A/ISO 5 areas, and not the overall cleanroom concept, which includes Grade B, C and ISO 7 zones. Contaminations in areas surrounding ISO 5 can significantly contribute to product/patient contamination risk; thus, similar monitoring plans should be considered when selecting the instrumentation for those environments.

A Grade A/B cleanroom

Both U.S. and European regulatory guidelines and ISO standards outline the need for routine monitoring of cleanrooms. Using single-use and real-time technologies in conjunction offers a way to address these requirements by bringing manufacturing processes to a greater level of quality.

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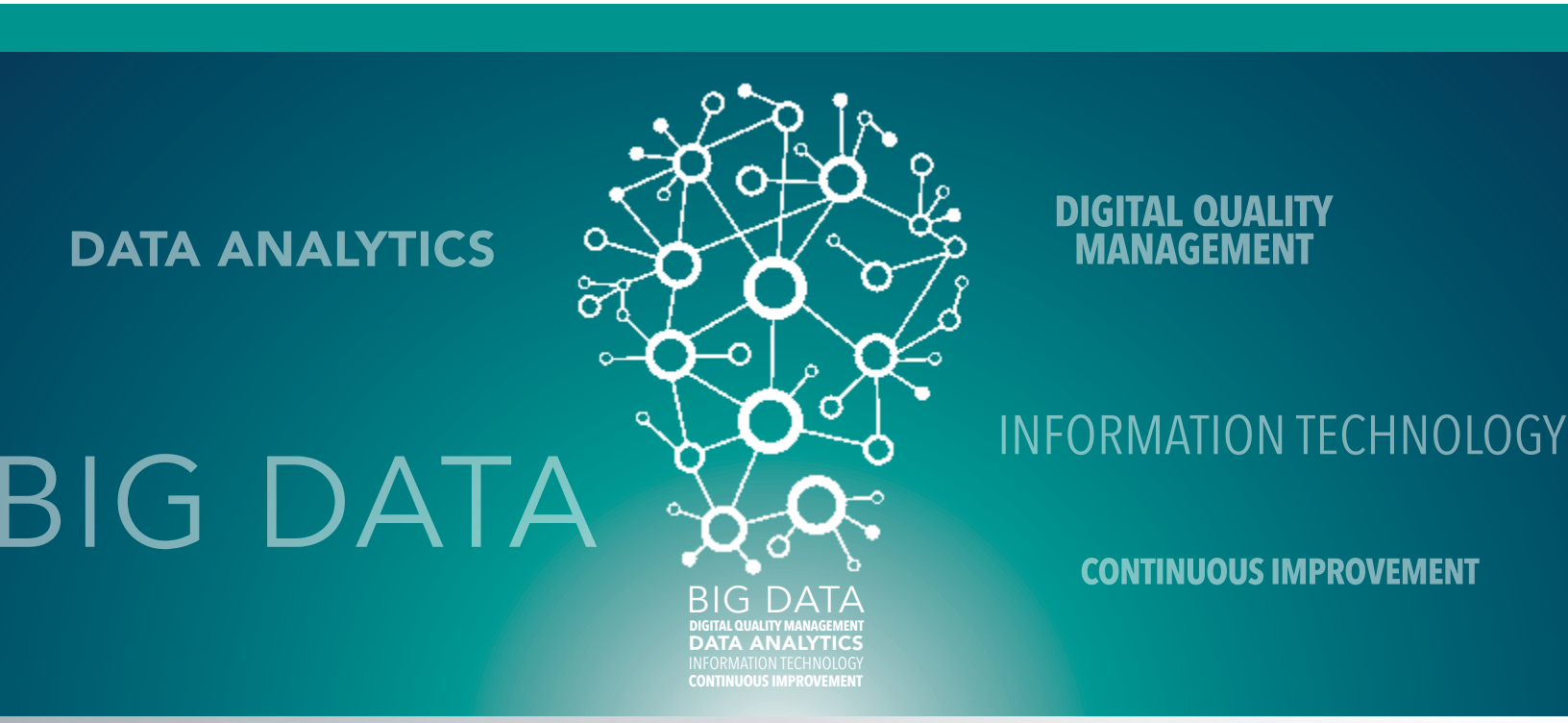
About the Author

Frank Panofen, PhD, has expansive experience in the field of applied pharmaceutical microbiology and serves as the Sterility Assurance/Microbiology Product Line Manager at Particle Measuring Systems.

2018 PDA Manufacturing Intelligence Workshop



It has become increasingly clear that maintaining a competitive edge will require the effective understanding and use of manufacturing-related data.

Help ensure that you raise your organization's performance, across the board, by attending the *2018 PDA Manufacturing Intelligence Workshop*. Take advantage of the opportunity to find out how the Pharma industry is developing its capacity to better employ and advance the use of big data in manufacturing and supply chain management.

Sessions will focus on:

- Big data fundamentals
- Real-world case studies
- Manufacturing information models
- Digital quality management
- Top risks/challenges surrounding big data
- Challenges with big data in a highly regulated industry

Come discuss the needs and challenges of managing manufacturing-related data and see how the holistic use of data and corresponding insights gained can help effectively meet these challenges. Acquiring an understanding of the development and implementation of big data strategies will also be a key take away!

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PDA Parenteral Drug Association

March 21-22, 2018 | Orlando, FL
Exhibition: March 21-22
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Disruptive Change is on the Horizon

2018 PDA Annual Meeting

Tia Bush, Amgen

Have you created the tools to respond quickly to customer needs and market changes while still controlling costs and quality? Do you know which technology and digital trends are shaping the future of healthcare? Is your company proactively solving complex problems in a time of hyper change and increased competition? Are you and your teams taking action based on the vast amounts of data that you have collected on your products and manufacturing processes?

In a time of transformational scientific and technical advancement, leaders in the healthcare industry are striving to be the first to answer "yes" to all these questions. Technology-driven change is accelerating at an exponential rate and those companies that act upon the enormous opportunities that exist are driving innovation that will lead to personalized approaches to medicine. For example, genomic profiling is being used to target specific treatments for individual patients with specific molecular markers.

Furthermore, increased competition, societal pressure on access of medicines and limited patent protection are pushing companies to faster development cycle times, creative clinical trial designs and new manufacturing platforms. Massive datasets are being generated that require new capabilities in machine learning, visualization and process modeling. With these capabilities, meaningful conclusions can be drawn for more cost-effective manufacturing solutions.

You can be part of the transformation! Join us for the *2018 PDA Annual Meeting* where we will explore topics focused on innovation, agility and technology and how they are changing the world of healthcare as we know it. You will hear from industry experts who will share their experiences on a variety of topics, including the future of patient therapies, insights from the manufacturing floor, strategies in digital information and transformations in manufacturing facility design and process technology. Regulators will also share their perspectives on innovation and technology, offering suggestions on how best to navigate the complex regulatory environment to bring these exciting advancements to patients. **[Editor's Note:** See p. 9 to learn how this Annual Meeting will be different from previous ones.**]**

2018 PDA Annual Meeting and PDA Education Courses

Orlando, Fla.

March 19–23

www.pda.org/2018annual

New PDA Task Force Targets Big Data

Michele D'Alessandro, Merck & Co., Inc., and Aaron Goerke, F. Hoffmann-La Roche Ltd.

Manufacturing is undergoing massive change due to increasing reliance on digital connectivity. Referred to as Industry 4.0 or the Internet of Things, this change is also impacting our segment of manufacturing as well.

At the same time, the information age has created mountains of data in every field. More data has been created in the past two years than in the entire history of the human race—and in our experience, manufacturing generates more data than any other sector. That being said, the proliferation of data itself is not the disruption. The disruption is the way the data is processed, made available, and ultimately, used to drive outcomes. This includes the ability to combine structured and unstructured data using modern data warehousing technology and advanced statistical modeling. Enhanced by a multitude of technology advances such as software robotics and machine learning, pharma manufacturers can leverage insights from data to optimize product development, quality control, process analytics and more.

To further the opportunities in this area, PDA and its Manufacturing Science and Operations Program℠ (MSOP), an advisory body, formed a special task force to assist pharma manufacturers with the use of big data to improve regulated product manufacturing and supply chain management. This task force held its first ideation session on Oct. 19 at the Sanofi-Genzyme Research and Development facility in Cambridge, Mass. An ideation session is a specialized gathering where participants outline a problem and brainstorm potential solutions.

With more than 20 industry colleagues attending from a variety of leading bio/pharmaceutical companies, this ideation session provided an opportunity to share ideas, challenges and solutions for the development and implementation of big data strategies for managing manufacturing-related data. Three areas, in particular, were identified as critical to transforming the current state of manufacturing:

Manufacturing Information Model: Defining standards and structure to promote the ease of interoperability and exchange of information

Process Robustness: Efficient and effective validation approaches across unit operations, equipment and raw materials

Inexactitude versus Precision: Using data throughout its lifecycle for enhanced computerized system controls

Each of these areas will have its own work team comprised of industry stakeholders who will collaborate on developing documents on how success can be achieved in these areas. The ultimate goal of these collaboration efforts is to help ensure that the industry achieves levels of excellence in the area of manufacturing reliability leading to high levels of quality and compliance. While we are at the start of our task force efforts, much has already been done in individual areas. By sharing these practices and further capitalizing on common initiatives, we can drive the industry to significantly greater levels of product success. The task force is also looking for volunteers to assist in these three areas. If this interests you, please contact PDA's Volunteer Coordinator (volunteer@pda.org).

These areas of focus will be further explored and advanced during a dedicated *2018 PDA Manufacturing Intelligence Workshop* in March following the *2018 PDA Annual Meeting*. This workshop will combine a broader introduction on topics such as big data, digital quality management, machine learning and information security with the latest information on the three areas specified above. This workshop will combine a broader introduction on topics such as big data, digital quality management, machine learning and information security with the latest information on the three areas specified above. This workshop, as well as the task force, is a great opportunity to be part of the industry's efforts to advance the use of big data in manufacturing and supply chain management. Please join us by volunteering for one of the three task force topics above, participating in the workshop, or both!

2018 PDA Manufacturing Intelligence

Orlando, Fla.

March 21–22

www.pda.org/2018MI

(l-r) Christopher Darrel, Jack Prior, Leo Xu, Abdel Zamamiri, John Moehnke, Rodney Rietze , Patrick Hyett, Ned Winslow, Brett Duersch, Olav Lyngberg, Michele C D'Alessandro, Daniel Wasser, Gerald Leister, Susanne Stocker, Arne Zilian, Lori Pfahler, Paul Kolosick, Aaron Goerke, Thomas Amirault, Hal Baseman, George Skillin and Josh Eaton

2018 PDA Upcoming Events

SAVE THE DATE for PDA's 2018 Events

JANUARY

22-26
■ **PDA Aseptic Processing – Option 1**
Week 2: Feb. 19-23
Bethesda, MD
pda.org/2018Aseptic1

23-24
2018 PDA Glass Quality Conference
Bethesda, MD
pda.org/2018Glass

30-31
PDA Quality Culture Transformation
Thousand Oaks, CA
pda.org/2018Transform

FEBRUARY

25-28
NEW COURSE
Downstream Processing (DSP) – Purification of Biomolecules
Clausthal-Zellerfeld, Germany
pda.org/UC/DSP2018

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

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

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

PDA
Parenteral Drug Association

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

APRIL

20
NEW COURSE
Addressing Biofilm and Other Non-routine Microbial Events
Bethesda, MD
pda.org/2018Biofilm

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

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

MAY

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

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

15-16
Virus Forum
Florence, Italy
pda.org/EU/Virus2018

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

24-26
2018 PDA/FDA Joint Regulatory Conference
Washington, DC | *pda.org/2018PDAFDA*

OCTOBER

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

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)

NOVEMBER

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

COLLABORATION THROUGH MUTUAL RELIANCE BRINGS FDA AND EMA TO THE TABLE

Rebecca Stauffer, PDA

> **We need to work with our foreign regulators. We need to share inspectional resources.**

In the past ten years, the number of U.S. FDA-regulated shipments moving through 300 U.S. ports has doubled. These products originate from more than 150 countries, 130,000 importers and 300,000 foreign facilities. These numbers illustrate the level to which foreign production of FDA-regulated goods and materials has exploded over the last decade.

Susan Laska, Senior Advisor for Medical Products and Tobacco Operations, Office of Regulatory Affairs, FDA, shared these figures in the opening slides of her Oct. 18 presentation, "FDA's Mutual Reliance Initiative," at the *12th Annual PDA Global Conference on Pharmaceutical Microbiology*. Her talk offered a look at the new Mutual Reliance Agreement between FDA and the European Union. In March, both agencies signed an agreement to allow U.S. and EU regulators to use the other agency's GMP inspections of pharmaceutical manufacturing facilities, a culmination of three years of hard work between the two agencies ***(1).*** The Agreement comes at a time when globalization of the pharmaceutical industry is changing the Agency's approach to inspections, necessitating greater collaboration with other regulatory agencies.

"This rise of global markets and supply chains has been remarkable," Laska said. "Emerging markets and developing economies are gaining prominence. Import volume has grown exponentially and inspecting products at ports of entry is no longer adequate to ensure our consumers have safe products."

She then pointed out that currently 35% of the medical devices used by U.S. patients are made overseas, and approximately 80% of API manufacturers are located outside the United States.

"Globalization is not just a vague term, it is an overwhelming force," Laska concluded. "As this distinction between foreign and domestic products continues to blur and supply chains become more complex, the job of ensuring the safety and efficacy of food, drugs and medical devices has become more challenging."

At present, opportunities abound throughout the complex global supply chain, from raw materials to intermediates to manufacturing and distribution, for product to be improperly formulated, incorrectly packaged, contaminated and even counterfeited or adulterated. Many (but not all) of these issues occur in emerging markets. With so many areas to focus on, according to Laska, this taxes the Agency's "precious inspectional resources."

"Prevention of problems before they reach our borders requires strengthening the quality and safety oversight in countries from which we import products," she said.

And FDA has certainly not been resting on its laurels. In fiscal year 2016, the Agency conducted over 16,000 domestic inspections of all commodities. That is almost 1,345 inspections a month, or 60 inspections each day. Additionally, FDA conducted more foreign inspections in 2016 than previously—3,512 to be precise. The Agency's labs are also busy. In fiscal year 2015, FDA labs reviewed over 33,000 samples. That same year, the Office of Criminal Investigations pursued cases that led to 348 arrests, 305 convictions and more than $1.2 billion in fines, restitutions, asset seizures and civil forfeitures.

"But we cannot do it all," Laska emphasized. "We need to work with our foreign regulators. We need to share inspectional resources."

Recent legislation, notably the Food and Drug Administration Safety and Innovation Act (FDASIA) has been the "spark" behind the Mutual Reliance Initiative, she explained. FDASIA gave FDA the authority to enter into agreements to recognize drug inspections conducted by foreign regulators if the Agency determined those regulators are capable of meeting U.S. requirements for inspections ***(1).*** FDA began taking the first steps in this area in 2014 when both the Agency and EMA began collaborating on a potential agreement, which became the Mutual Reliance Agreement. As part of this process, EMA invited FDA to observe the EU Joint Audit Programme. Under this program, two EU countries audit the regulatory body of another EU country. FDA's first observation was of the Swedish inspectorate by auditors from the United Kingdom and Norway; since then, the Agency has observed 13 more audits of EU regulatory agencies ***(1).***

The need to share inspectional resources between the two regions is great. Laska cited the "remarkable" five-year growth in FDA-registered facilities around the world. Between 2011 and 2016, there was a 16% growth in registered facilities in Europe, a 55% growth in India and a 63% growth in China.

Mutual Reliance a Step Forward

"We are very excited about the Mutual Reliance [Agreement] that was signed in March of this year," Laska emphasized. "The Mutual Reliance Agreement will allow the FDA and EU inspectorates to use inspection reports and other related GMP information obtained during drug manufacturing facility inspections whether conducted by an EU inspectorate or by the FDA to help determine whether a facility is making high-quality drugs."

Article at a Glance

- Pharma supply chain has grown increasingly complex
- FDA and EMA to share inspection data through collaboration
- Brexit not expected to impact Mutual Reliance Agreement

Implementation of the Agreement began in November 2017. While the Agreement is with the European Union as a whole, FDA continues to assess individual EU member states' inspectorates. The Agency is using these assessments to determine if these member states' inspection reports are consistent with high-quality inspections.

The first step in this assessment process is determining if these inspectorates have a satisfactory Conflict of Interest policy. Next, FDA experts observe an EU audit of a member state as part of the Joint Assessment Program, including a pharmaceutical inspection conducted by the inspectorate being audited. FDA then conducts a primary assessment where FDA experts from various offices review the final EU audit report, the observers' reports, the inspection reports, and other supporting documentation. The final step is a secondary assessment. Here, FDA's senior leadership assesses the primary team's conclusions and determines if the inspection data meets their expectations.

The Mutual Reliance Agreement covers routine GMP surveillance inspections, i.e., post-approval inspections. She stressed, however, that "under certain conditions, preapproval inspections may be considered." During the Q&A following her talk, Laska affirmed that inspectors from both Agencies should strive to focus on risk-based inspections.

> **"The FDA hopes to complete its assessment of all 28 EU member states by July 2019"**

While the Agreement does cover a wide range of drug products, it excludes veterinary drugs, vaccines and plasma-derived biological products. These are being evaluated for possible inclusion in the future.

Laska listed the key points within the Agreement:

- All EU member states are included
- EMA will conduct its Joint Assessment Program audits as usual every 5–6 years and FDA will observe
- Both parties (FDA and EMA) will retain the ability to make their own enforcement decisions
- All parties involved can request that an inspectorate inspect a facility within their domain
- EU and FDA will reserve the right to perform GMP inspections in one another's domain as needed

"Certainly, the benefits of the Mutual Reliance extend not just to the European Union pharmaceutical inspectorates and the FDA but to the regulated industry as well," Laska said. "I think it is fairly obvious the Mutual Reliance will allow our regulatory systems to operate more efficiently; however, we also note that decreasing duplicate inspections benefits the pharmaceutical industry in terms of both time and money."

Today EMA, Tomorrow the World

The FDA hopes to complete its assessment of all 28 EU member states by July 2019. In October, FDA already announced that the Agency will recognized the following eight European regulatory bodies as capable of meeting FDA inspection requirements: Austria, Croatia, France, Italy, Malta, Spain, Sweden and the United Kingdom ***(2).***

As the United Kingdom moves ahead with withdrawing from the European Union,

Laska said that FDA has continued to assess the UK MHRA, noting that the Mutual Reliance Agreement work began in 2014, two years prior the 2016 Brexit referendum. Since then, FDA has operated as if MHRA is still part of the European Union. Once the United Kingdom finalizes its departure from the European Union, FDA and MHRA will, if needed, renegotiate any existing agreements around sharing inspectional data ***(3).*** She stressed that this illustrates the Agency's commitment to potential agreements with agencies beyond the European Union.

"We know that with Mutual Reliance, we're not done with just Europe," she said. "There are other authorities out there, for instance, Switzerland, that we have had long-established relationships with as far as sharing information. And there are other authorities that are not part of the European Union. So, this is just the beginning. "FDASIA has enabled us to do this and the European Union was the first…I think this is the first of a long line," Laska added.

She further reiterated that the Agency views the Agreement as a means of reallocating its inspection resources to other, more high-priority regions of the world.

"We recognize that mutual reliance is all about a shift in our inspectional resources going from EU-capable authorities to other parts of the world."

References

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About the Expert

Susan Laska started her career with FDA in the Philadelphia District in 1989. She has been very involved from the onset with the EU Mutual Reliance Agreement and the international Pharmaceutical Inspectorate Convention Scheme.

Regulators Tackle Tough Micro Questions on Panel

The 12th Annual PDA Global Conference on Pharmaceutical Microbiology *concluded with an "Ask the Regulators" panel. Throughout the conference, attendees could submit their questions on cards that were later collected and distributed to a panel of U.S. FDA regulators specializing in microbiology. Attendees could also ask questions at the microphone during the session.*

The panel consisted of: ***Lynn Ensor,*** *PhD, Division Director, Division of Microbiology Assessment, CDER;* ***Julie Dohm,*** *PhD, JD, Agency Lead on Compounding, CDER;* ***Sharon Thoma,*** *Office of Medical and Tobacco Products Operations, ORA;* ***Laurie Norwood,*** *Deputy Division Director, Manufacturing Product Quality, Office of Compliance and Biologics Quality, CBER;* ***Ramesh Kapil Panguluri,*** *PhD, Microbiologist, CDRH; and CAPT* ***Elizabeth Claverie,*** *Branch Chief, Infection Control Devices Branch, CDRH.* ***John Metcalfe,*** *PhD, Master Microbiology Reviewer, CDER, and* ***Kim Sobien,*** *Principal Sterility Assurance Engineer, PETNET Solutions, moderated the panel.*

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Below is a portion of a blinded transcript of the session. The full transcript can be found at the PDA Letter *website.*

Q: What is FDA's opinion on the use of reduced incubation time biological indicators (BIs) in the pharmaceutical industry?

Ensor: As far as for manufacturing drug products our group would be reviewing, we do not support the use of reduced incubation time BIs. Please note that the guidance that references [reduced incubation time BIs] was not a CDER-based guidance and it was intended more for things that were being sterilized in a hospital setting direct for immediate use, and was not intended to be used for drug manufacturing facilities.

(l-r) John Metcalfe, Sharon Thoma, Elizabeth Claverie, Laurie Norwood, Kim Sobien, Ramesh Kapil Panguluri, Lynn Ensor, Julie Dohm

Q: What is the thinking on the pharmacist's role in 503B facilities?

Dohm: The statute, as everyone knows, is that a drug is compounded by or under the direct supervision of a licensed pharmacy and facility…and we received a number of questions about what that means and what is the role of the pharmacist that provides either the compounding itself or the direct supervision…we intend to issue guidance on this issue; we have not done that to date. But we have been collecting information about how the various outsourcing facilities use pharmacists in their operations and whether or not they are part of or separate from the quality control unit and the like. When we get that information, we will use it to inform our policies. We will issue a draft guidance and then it will be available for notice and comment.

Q: FDA and EMA are collaborating, but what about collaboration with ANVISA [Brazilian regulatory authority], China FDA, Korean agencies, Turkish agencies, etc.? Will that be possible?

Thoma: I think **Susan [Laska]** with the Mutual Reliance just said we are currently working with the European community but that is going to extend further out. Now, whether all of these are going to become a collaborative group within FDA, only time will tell. And I don't think we have an answer to that at this point.

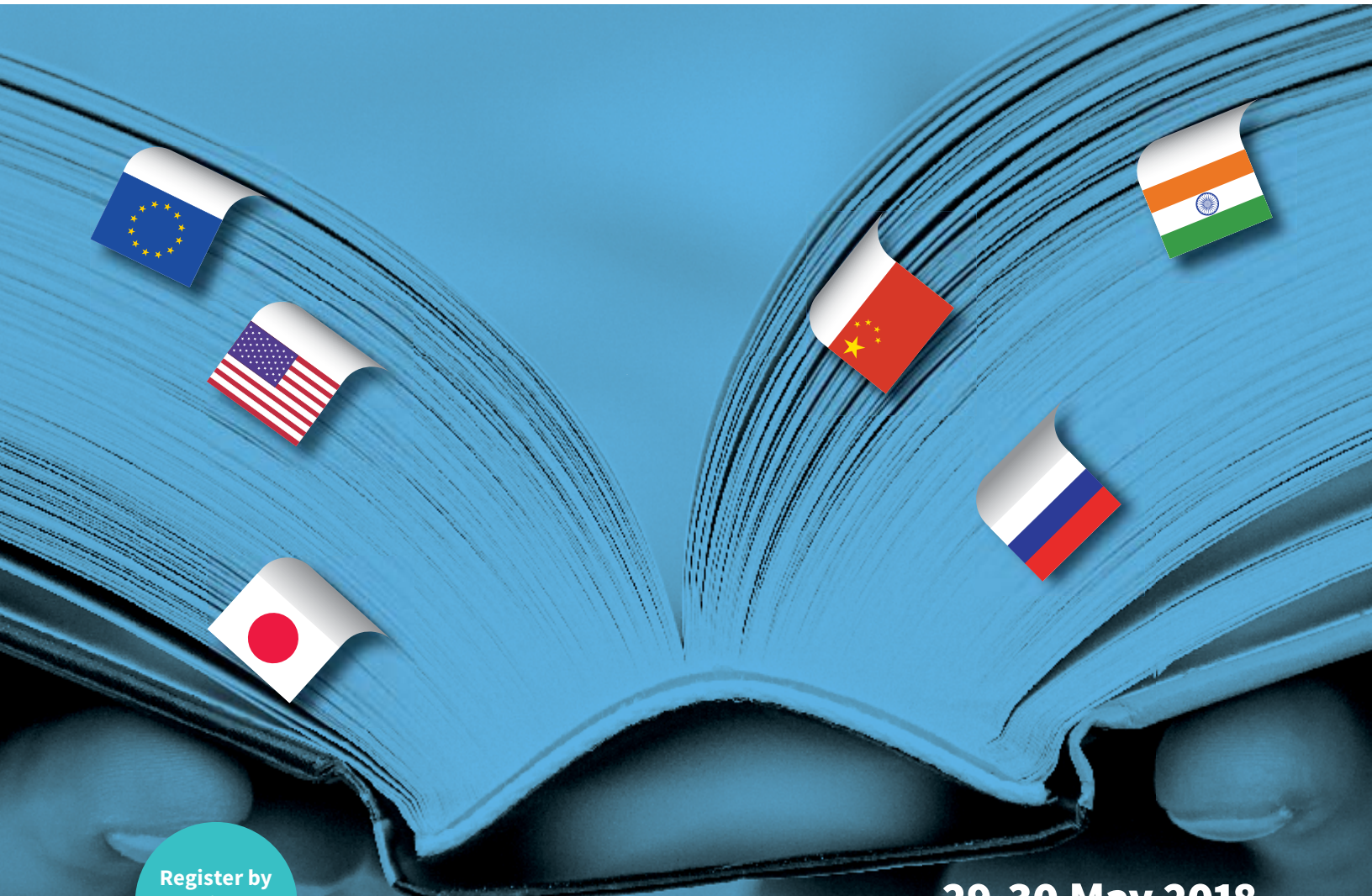
I would definitely, if you are looking at if you want to collaborate, check with your authorities in those countries and [see] what you need to do to become part of PIC/S and become part of these other areas where you can get more involved. **[Editor's Note:** For more on the Mutual Reliance Initiative, see the cover story on p. 26**.]**

PDA Europe Conference, Exhibition, Education

The Parenteral Drug Association presents:

Pharmacopoeia Conference

Convergence, Harmonization & The Future Direction of Pharmacopoeias



Register by 8 April 2018 and SAVE!

29-30 May 2018

Hotel Renaissance Vienna

Vienna | Austria

pda.org/EU/pharma2018

Q: Companies are being cited on 483 observations for inadequacies of their in-process monitoring programs. Issues include not justifying the sample holding time, inaccurate method validation, not justifying alert/action limits, inadequate investigation of out-of-level bioburden results, etc. What are the Agency expectations in this area?

Norwood: I think part of [this] conference has demonstrated the importance of hold times and the importance of bioburden control, so my short answer is: there is an expectation that you [will] have all that established because, if you do not have control of your process, then you do not know what is being introduced to your process based on the equipment you are using, [and] you do not know what the outcome is going to be. And so that is why FDA asks if you have evaluated all of these. With regard to bioburden, this is very critical. If you have a method that is not validated—and granted there are going to be some bulk materials where it might interfere with the bioburden or endotoxin test if that is what you are going to have done—and so you need to be able to investigate that and determine what test can help you with the control in your process…it is expected.

Q: If any additional item has to be added during use, should validation be conducted prior to sterilization and/or assessment, or would assessment be sufficient?

Ensor: I would have it [be] part of the validation and also, when you are trying to claim the validation studies, try and bracket any possible load types that need to be part of that validation. So, try [to] be a little bit more proactive when you go about it and not just adding pieces to it as you go during your manufacturing.

Q: If a 503B outsourcing facility has validated a dozen products using the same filtration parameters for sterile injectable drugs, and they have a new drug with a combination of two previously validated drugs but at lower concentrations, can the retention study be skipped since the product may be bracketed by the higher concentration single products?

Dohm: So, unfortunately, I am not a technical expert and cannot answer this question but [what] I can say is that we have a draft guidance on the cGMP for outsourcing facilities available, and I do not know if this is covered or not in there...but there is a draft guidance out there and we are avidly working on revising it based on the comments we have received. Does anyone else on the panel have thoughts?

Norwood: Unless you have demonstrated that the combination of those two in the diluted state are not going to have an impact on the ability for the microbial retention to affect the efficiency of that filter, unless you know that, I would think you have to demonstrate it.

Thoma: Yes, I would say I totally agree because they mentioned using the bracketed approach but yet we do not know what the bracket is; you only know the upper limit, you do not know the bottom limit.

Metcalfe: To follow on, FDA is not, in terms of sterilization validation strategies for 503B, we are not lowering the bar in terms of that piece. So, I agree with the two responses.

Norwood: Well, and then the other response on that is that you always should qualify your filter to show the loss upon drug filtration with the different product or formulation of that product with what you are filtering as well.

Q: When you conduct an inspection, are there specific sanitization frequencies for each ISO class you expect to see?

Thoma: That is going to be based on *your* cleaning procedure, your sanitization procedures, your location, how you do your risk assessment, how you validated your sanitization processes, when you validated your cleaning procedures and your disinfectants. Are people actually mixing them the way they are supposed to be mixing them? The way it was validated to be mixed? Are they allowing the contact time? Are they looking at the hold times of both disinfectants that are sitting there open, closed, open, closed? Or are they concentrated and diluted out? So, I would expect you to have procedures in place for all of that that tells me what you are going to do and then you have the data that supports and shows that you do not have a problem within the ISO 5 or ISO 7 areas, then that is probably going to be sufficient. But at the same time, I am going to look at your environmental monitoring as well. And I am going to look at any potential problems with cross-contamination, how you eliminate cross-contamination. You know, some people will do cleaning frequencies, sanitization between campaigns of products; some people are going to have to do it with changeover products. If you go from a lower-strength product to a higher strength product that is identical, you may have minor cleans-in-place and you may not sanitization. So it all depends on what you are doing with that. I cannot just answer that 'yes' or 'no.'

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AIDC is a Sign of Things to Come: Part II

Combo Products Can Benefit Most from Serialization

Napoleon Monroe, New Directions Consulting

In order to save overall payer costs, ensure access to products when needed and improve compliance with protocols, combination products are often designed to be administered by patients or nonprofessional caregivers.

This moves combination products into relatively untrained and unregulated hands. Oral dosage is rather simple. Injection, inhalation and other parenteral dosages, however, are more complex, and because they require special handling, these often fragile and costly combination products are designated "specialty products." In spite of their challenges, these products provide the greatest hopes for improved patient outcomes. Specialty products represent the majority of products currently moving through the U.S. FDA approval process.

Many of these specialty products require injections which can create potential biohazards demanding some level of product control before, during and after use. These facts make informing and gathering information from users ever more important.

This all comes back to serialization. In Part I ("AIDC is a Sign of Things to Come: Part I," November/December 2017), I covered how serialization allows stakeholders better ways to gather information about a product. Combination products represent a segment of the industry that could benefit most from serialization, in my opinion.

When it comes to the information embedded within a product's serialized code, there is a wealth of information that can be stored and referenced in databases. Certain manufacturing changes may not normally occasion a lot or batch number change. This is especially important for combination products since they have more mechanical and electronic components from an array of suppliers than simpler dosage forms. More components and more vendors can result in failure to report potentially meaningful changes.

Experience has shown that the use of thousands of dose administrations in field conditions may be necessary to really learn product performance. There are many changes that can occur in component manufacture and in the field. Examples include mold repair issues, component processing, changes in resin lots, vendor, software or firmware changes and other changes thought by a vendor to be innocuous. Also, the combination product itself may change while in patient hands. Information about abuse, loss, damage, residual shelf and battery life can be important.

We all know that consumer appliances often include an insert detailing minor product changes made to a model. This complicates instructions. Neither retail consumers, nor patients or other stakeholders follow printed instructions anyway. All are very unlikely to sort through model numbers. Printed information is fixed. When it comes to combination products, these facts together make serialization essential differentiated from consumer appliances. Serialization allows information to be sent to individual stakeholders about their specific combination product, facilitating product-specific communication and reducing confusion.

Reducing confusion about your combination product is more important than confusion about your dishwasher.

Fortunately, many—even most—patients already have a tool, i.e., their smartphones, to capture serial numbers. Patients can also monitor and provide information on use and nonuse, and information from companion products, such as diagnostic devices, personal health monitoring devices, etc. In addition, patients can submit personal observations. They might even provide information about products from competitors.

Combo Products Meet the Real World

Combination product failures are sometimes obvious to users. Patients, caregivers and other stakeholders now inform each other via social media about their real-world experiences. Facebook posts and Tweets are becoming part of real-world evidence (RWE) or real-world data (RWD). More regulators and payers now demand RWE/D.

The National Evaluation System for health Technologies (NEST) incorporates initiatives to mine social media as RWE. On Aug. 31, FDA issued *Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices* for comment ***(1).*** The FDA's stated intent is to "collect the needed data to address the public health questions."

Competitors and litigators also mine the Internet, including social media. An important question is: Who will have the data first and who is best able to interpret and use the information? Arguably, the answer is the combination pharmaceutical product marketer.

How much credence RWE/D will assume in both prospective (approval) and retrospective (post-market) situations is still unclear. There is a lot to learn from adherence and behavioral data, but it can be difficult to collect meaningful day-to-day statistics. ➤

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The challenges of combination product approval and reimbursement are already complicated. If RWE/D simply becomes yet another gate to get through on the way to drug approval, it will seriously hamper digital health innovation.

The combination product industry stakeholder community is fragmented. No one company has all the resources required to do everything. Therefore, pharma needs to be able to collect and analyze information related to causes, effects and perceptions of their products from other stakeholders (e.g., patients, payers, distributors, pharmacies, regulators, prescribers, programmers, device suppliers and device component suppliers). Knowledge of real-world product performance and patient outcomes is essential.

Medication telemanagement enabled by serialization presents opportunities to provide better care *and* to avoid risks. Product management, including adherence and compliance, is essential to safety and efficacy.

Human factors issues compound combination product challenges. Product instructions might be poorly provided, misunderstood, forgotten or ignored. The use of combination products by untrained, unlicensed individuals with varying levels of education, mechanical ability and language facility opens questions of what human factors will come to bear on use. It is not possible to have algorithms built into systems covering every possible situation. Concerns about human factors often delay product launch. The very real win with serialization is the ability to respond to the effects of human factors that arise in the real world.

Serialization can enable information to assist in intelligent responses. If pharma has access to necessary information close to real time, this can be used to better help end users manage their products. Just as Apple's Geniuses (Apple's trademark) help customers understand and use Apple products (most of which are serialized and have cataloged experiential data to allow assisted intelligence), pharma can enhance product value by providing expert service. Satisfying service is now often provided by mediated communication (e.g., prompting a patient to find a serial number before the Genius engages) and assisted intelligence (using known prior experience with a specific patient or serialized product to assist a "Genius" in finding the answer for a patient's current question).

> **"Knowledge of real-world product performance and patient outcomes is essential"**

Serialization allows pharma to make situational changes to protocols for a group of products, a class of users or even a specific user. Some examples are immediate product corrective actions, refresher training in the protocol and techniques and rotating administration sites.

For combination products, a revised version of the GS-1 Q&A about UDI serialization for all products in Part I may be instructive. The italicized content below is added to this section in the companion article.

How much control of my products in the supply chain should I have *when the supply chain extends to patient self-use and involves patient human factors?*

How expensive are my products? Does tracking the products afford me better control of these expensive assets? *Combination products are often quite expensive.*

How much risk can we assume if something goes wrong? With lot/batch, I will have one level of risk; with serialization, I will have significantly less risk since I will be able to bound the issue in smaller groups and not an entire batch/lot. *The number of contractors and components involved in combination products and the possibilities for patient misuse multiply the risks.*

How do I want to handle a recall? With lot/batch, how many products will be impacted vs. serialization controls where a company can be bound by serial number? *These issues should be considered in light of the human factors and contractor/component complexities. Can serialization help me avoid recalls, post-marketing costs and reputational damage?*

Many stakeholders lay claim to "owning" the patient relationship; pharma needs to be able to access and correlate certain information to serve its role in the drug/patient relationship. Pharma can be well served by having access to information enabled through serialization and then applying their expertise in cooperation with other stakeholders for the benefit of patients, as well as their own and others' interests. Serialization helps achieve these benefits.

Please consider these words from **Bill Gates:** "Your most unhappy customers are your greatest source of learning." Remember that even if you are not learning about your combination product performance, others are. It is better to know your situation than be blindsided by information in the hands of third parties. And, as always, ignorance is a poor defense.

This article contains opinions and is not regulatory guidance. The author and his clients have interests in the use of AIDC in healthcare.

Reference

1. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices, U.S. Food and Drug Administration, Aug. 31, 2017. tinyurl.com/y7kwxwln

About the Author

Napoleon Monroe's expertise includes product development, licensing, regulatory processes, risk management and international marketing, with experience managing business relationships in more than 30 countries.

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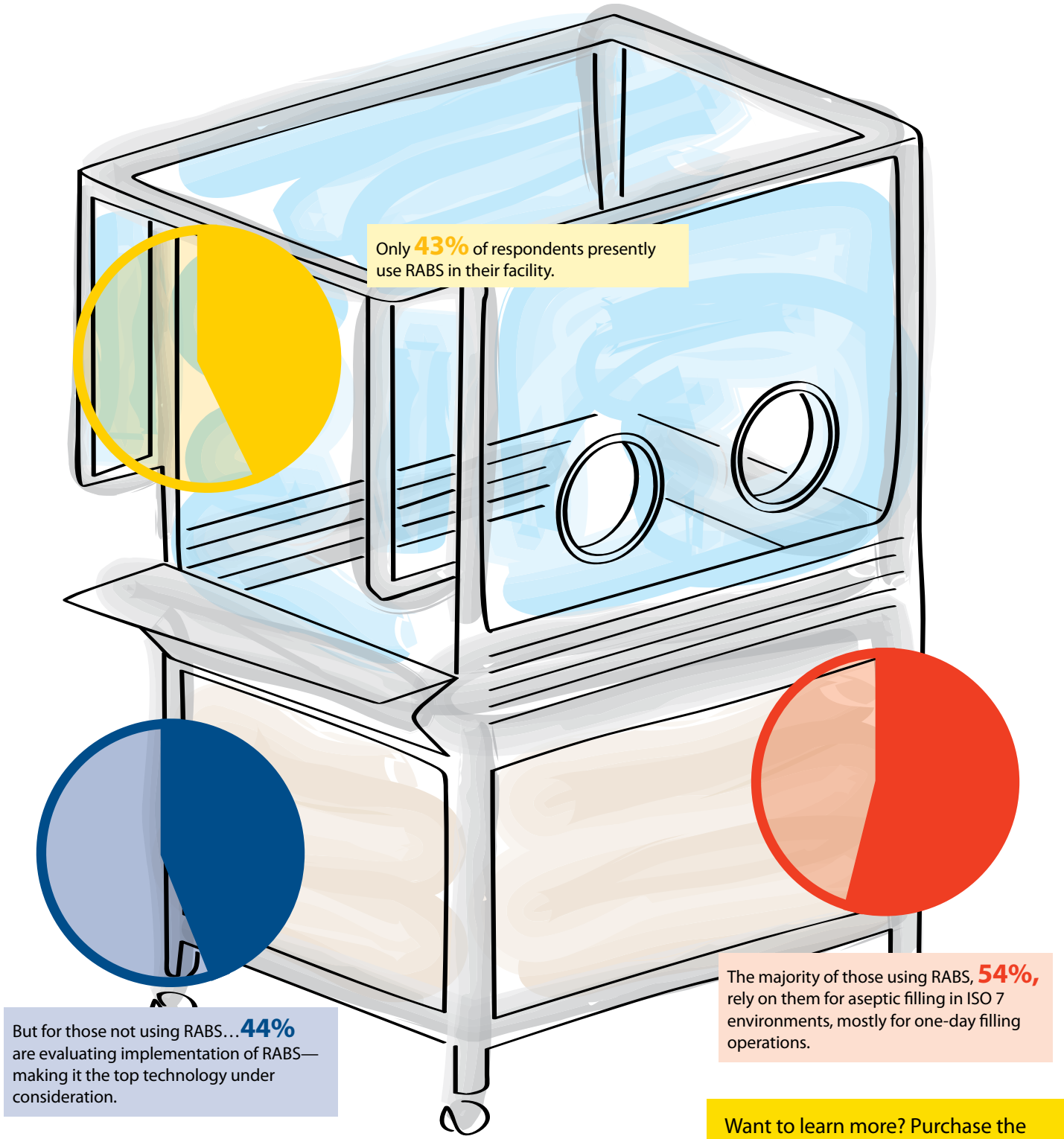
Mad for RABS

PDA recently conducted a survey of both members and nonmembers regarding current aseptic processing trends within the industry. Over 300 responded, providing insights into the current state of aseptic processing. Some of these insights pertain to the state of restricted access barrier systems (RABS).



Only **43%** of respondents presently use RABS in their facility.

But for those not using RABS…**44%** are evaluating implementation of RABS—making it the top technology under consideration.

The majority of those using RABS, **54%,** rely on them for aseptic filling in ISO 7 environments, mostly for one-day filling operations.

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PDA Data Integrity Code of Conduct Impacts Industry

Anil Sawant, PhD, Merck/Merck Sharp & Dohme; Ronald Tetzlaff, PAREXEL, and Denyse Baker, PDA

How has PDA's *Elements of a Code of Conduct for Data Integrity in the Pharmaceutical Industry* impacted the companies of those who downloaded it?

The Code is a collection of recommended best practices for employee and management conduct related to data integrity, presented in a ready-to-use format. It was published on the PDA website in March 2016, available free for download (www.pda.org/codeofconduct). PDA's Data Integrity Task Force, under the leadership of **Anil Sawant,** PhD, Vice President, Quality Management Systems and External Affairs, MSD, and **Ronald Tetzlaff,** Corporate Vice President, PAREXEL, developed the Code with the goal of sharing it with the industry at large. It was written to apply to employees, corporate officers, third-party suppliers and others acting on behalf of, or at the behest of, a company. This includes individuals that develop, test, manufacture or submit marketing authorizations for pharmaceutical and biological products. The Code was designed so that it could be tailored for each individual company's needs. A company could implement the elements within the Code in their entirety or only certain elements identified as pertinent for establishing their own customized policies, standards, procedures, or other quality system elements to define data integrity requirements.

The task force aimed to distribute the Code of Conduct as broadly as possible, thinking it would be especially useful for smaller manufacturing firms, or those that supply raw materials, components or testing services who may not yet have taken this step toward quality system and culture maturity. It was developed to be used directly by smaller firms to shore up existing quality systems. Additionally, larger firms or contract givers could use elements of the Code to assess their current internal codes or use it to when drafting or revising supply and quality agreements. As of October 2017, more than 3800 copies of the Code have been downloaded. Most of the copies were downloaded in North America, Western Europe and Japan, which is consistent with PDA's large membership in these regions. Analysis of website data shows the downloads have also occurred in regions representing areas of emerging pharmaceutical manufacturing as Africa, Eastern Europe, India and China **(Figure 1.)** This is encouraging as it supports one of the task force's goals of expanding education and tools to identify and rectify data integrity gaps.

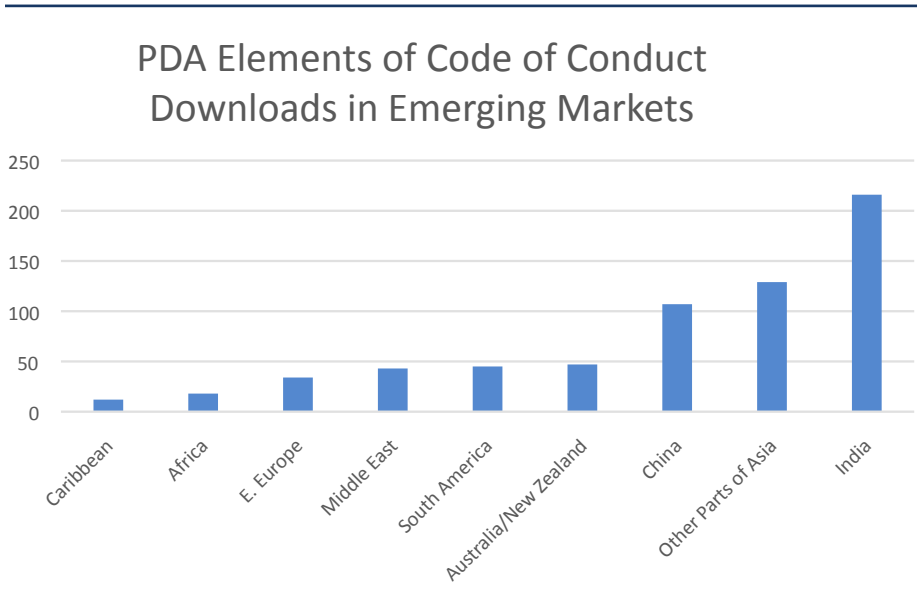

Figure 1 Number of Downloads by Region Outside of United States, Western Europe and Japan

One year after publication, PDA sent a follow-up survey to those who had downloaded the document to learn about the outcomes of implementing the Code, collecting a total of 95 anonymous responses. Approximately 40% self-identified as a quality leader or member of quality staff and 20% as compliance leaders or compliance staff. Another 30% identified themselves as consultants. The remainder self-identified as members of manufacturing production, legal counsel, validation, development and marketing.

There was an almost even distribution in the size of the respondents' companies as shown in **Figure 2.**

Responses to the question regarding the location of manufacturing sites indicated survey respondents represent manufacturing sites from all regions of the world **(Figure 3).**

The survey also asked how the Code was used after being downloaded. More than half indicated they used the Code as a guide on good data integrity practices, while 33% used it as a benchmark to evaluate internal practices and 14% used the Code in developing agreements with outsourcing partners or suppliers. Almost 20% of the respondents adopted the Code in whole or in part into their internal business processes and practice. More than 90% of the survey respondents rated the Code as useful. A quarter also found it practical for their company or clients to adopt or follow.

More than 90% of respondents also indicated they believe it will help reinforce a culture of quality and trust within the pharmaceutical industry. This aligns with ➤

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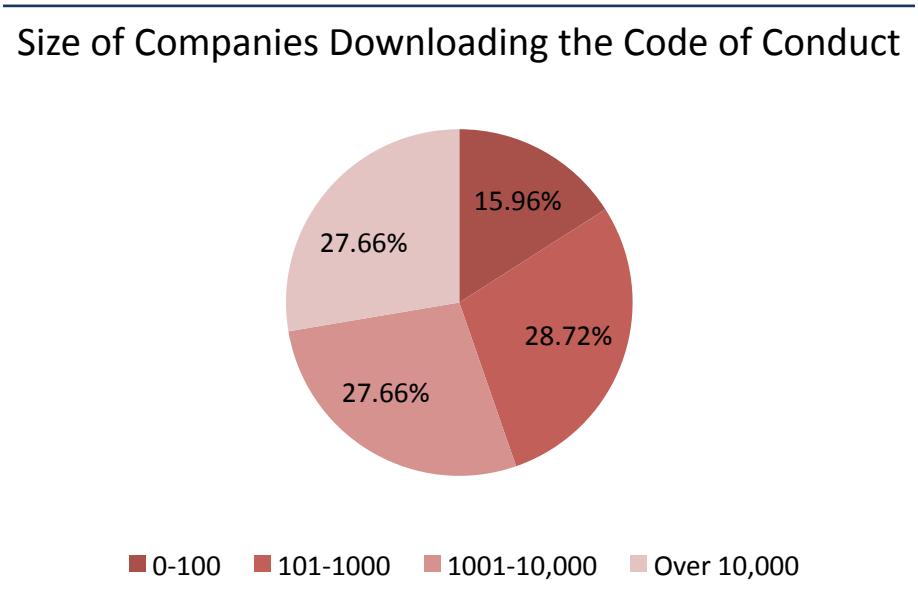

Figure 2 What is the Number of Employees in Your Company/Average in your Client's Company?

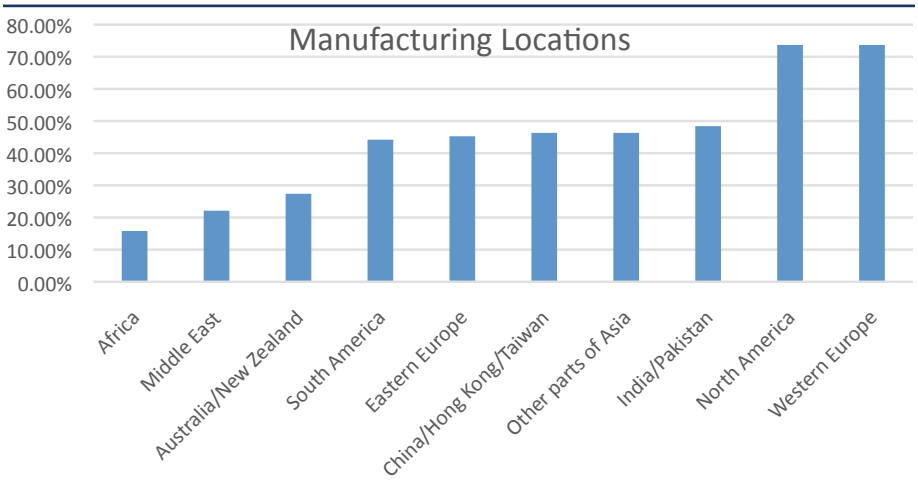

Figure 3 Where Does Your Company (or Client) Manufacture Products?

the original goal of the task force to raise awareness and provide useful tools within the pharmaceutical industry.

The survey included a question for open-ended responses. Here are some of the positive comments received about the Code:

- *"I believe that your take on data integrity was accurate, because it is basically awareness of existing regulations. What I fear (and what you have thankfully not done) is over-engineering what regulatory agencies have already expected…similar to what happened with the term 'risk-based.' I applaud your paper because it was fundamental and basically summarized what was already expected in regs and guidances. I also liked that in reality it didn't require a CSV group to create more templates (which I have already seen organizations do!) but instead incorporate these concepts into existing gxp processes (e.g., SOPs, CSV UR templates)."*
- *"CoC helps a lot about thinking policy in good GMP documentation practices. Thanx for that. This kind of guidance should be mandatory for equipment vendors as well."*

Some respondents expressed concerns about the structure of the document and others noted perceived redundancies. Additionally, there were suggestions to include practical examples within the document. Several respondents mentioned that a code of conduct alone cannot create data integrity; instead, there must be a culture of integrity. PDA is already moving to address many of the suggestions. Another task force is focused on culture within pharmaceutical manufacturing and has previously published the results of a survey ***(1).*** Building on these initial results, this Quality Culture Task Force has completed a pilot program to measure quality culture at more than 40 participating companies and expects to publish these results in 2018. The PDA Data Integrity Task Force also expects to publish technical reports on data integrity in 2018, one for laboratory systems and another for manufacturing systems.

Conclusion

Based on the positive results of this survey, the PDA Data Integrity Task Force will continue its work to develop additional tools and resources for the pharmaceutical industry. The Code of Conduct remains available for download at www.pda.org/dataintegrity.

Reference

1. Patel, P., et al. "Quality Culture Survey Report." *PDA Journal of Pharmaceutical Science and Technology* 69 (2015) 631–642.

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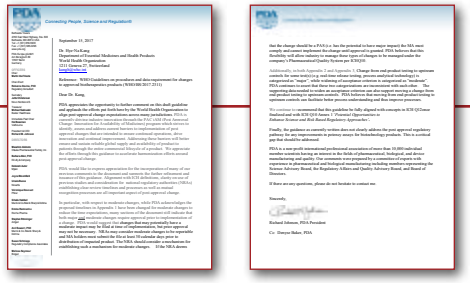

September 15, 2017

Dr. Hye-Na Kang
Department of Essential Medicines and Health Products
World Health Organization
1211 Geneva 27, Switzerland
kangh@who.int

Reference: WHO Guidelines on procedures and data requirement for changes to approved biotherapeutics products (WHO/BS/2017.2311)

Dear Dr. Kang,

PDA appreciates the opportunity to further comment on this draft guideline and applauds the efforts put forth here by the World Health Organization to align post-approval change expectations across many jurisdictions. PDA is currently driving industry innovation through the PAC iAM (Post Approval Change: Innovation for Availability of Medicines) program which strives to identify, assess and address current barriers to implementation of post approval changes that are intended to ensure continued operations, drive innovation and continual improvement. Addressing these barriers will better ensure and sustain reliable global supply and availability of product to patients through the entire commercial lifecycle of a product. We appreciate the efforts through this guidance to accelerate harmonization efforts around post-approval change.

PDA would like to express appreciation for the incorporation of many of our previous comments to the document and supports the further refinement and issuance of this guidance. Alignment with ICH definitions, clarity on use of previous studies and consideration for national regulatory authorities (NRAs) establishing clear review timelines and processes as well as mutual recognition processes are all important aspect of post-approval change.

In particular, with respect to moderate changes, while PDA acknowledges the proposed timelines in Appendix 1 have been changed for moderate changes to reduce the time expectations, many sections of the document still indicate that both major and moderate changes require approval prior to implementation of a change. PDA would suggest that changes that may potentially have a moderate impact may be filed at time of implementation, but prior approval may not be necessary. NRAs may consider moderate changes to be reportable and MA holders must submit the file at least 30 calendar days prior to distribution of impacted product. The NRA should consider a mechanism for establishing such a mechanism for moderate changes. If the NRA deems that the change should be a PAS (i.e., has the potential to have major impact) the MA must comply and cannot implement the change until approval is granted. PDA believes that this flexibility will allow industry to manage these types of changes to be managed under the company's Pharmaceutical Quality System per ICHQ10.

Additionally, in both Appendix 2 and Appendix 3, Change from end-product testing to upstream controls for some test(s) (e.g. real-time release testing, process analytical technology) is categorized as "major", while widening of acceptance criterion is categorized as "moderate". PDA continues to assert that these two categorizations are inconsistent with each other. The supporting data needed to widen an acceptance criterion can also support moving a change from end-product testing to upstream controls. PDA believes that moving from end-product testing to upstream controls can facilitate better process understanding and thus improve processes.

We continue to recommend that this guideline be fully aligned with concepts in ICH Q12once finalized and with ICH Q10 Annex 1 *'Potential Opportunities to Enhance Science and Risk Based Regulatory Approaches'.*

Finally, the guidance as currently written does not clearly address the post approval regulatory pathway for any improvements in potency assays for biotechnology products. This is a critical gap that should be addressed.

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our comments were prepared by a committee of experts with experience in pharmaceutical and biological manufacturing including members representing the Science Advisory Board, the Regulatory Affairs and Quality Advisory Board, and Board of Directors.

If there are any questions, please do not hesitate to contact me.

Sincerely,
Richard Johnson
President and CEO, PDA
Cc: Denyse Baker, PDA; Richard Levy, PDA

PDA Commenting Task Force

Melissa Seymour, Biogen (lead)

Karolyn Gale, Emergent BioSolutions

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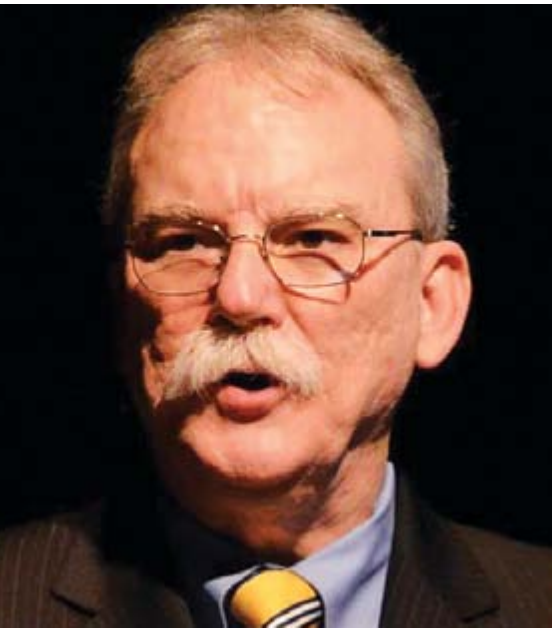

Richard Johnson

As PDA begins our 72nd year, it is a good time to reflect on where we have been and where we are going. In 1946, PDA began as a U.S.-based organization with fewer than 50 members. In 2018, we are now a global, 10,000+ strong scientific association with a mission to advance pharmaceutical/biopharmaceutical manufacturing science and regulation so members can better serve patients.

Like the pharmaceutical industry, PDA is increasingly global, nearing 50% of members outside of the United States **(Figure 1).** In addition to our individual members from the industry, we have many members who are from government, as well as a growing academic and student cadre **(Figure 2).**

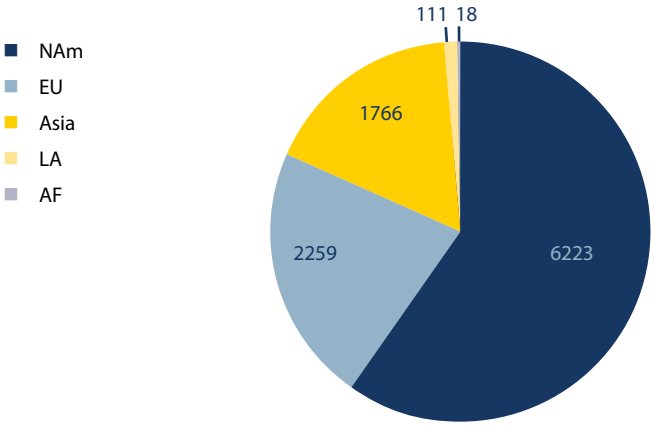

Figure 1 Members by Region

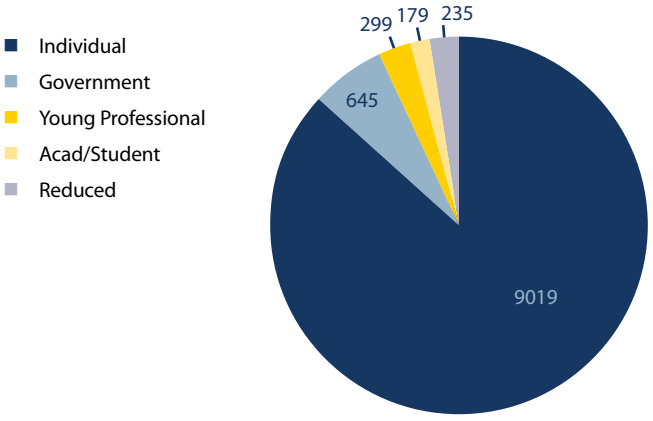

Figure 2 Members by Type

PDA continues to offer an unbiased place for interaction and education for people from across this diverse community. We offered 36 conferences and workshops in 2017 **(Figure 3),** and more than 110 training courses in locations around the world **(Figure 4).**

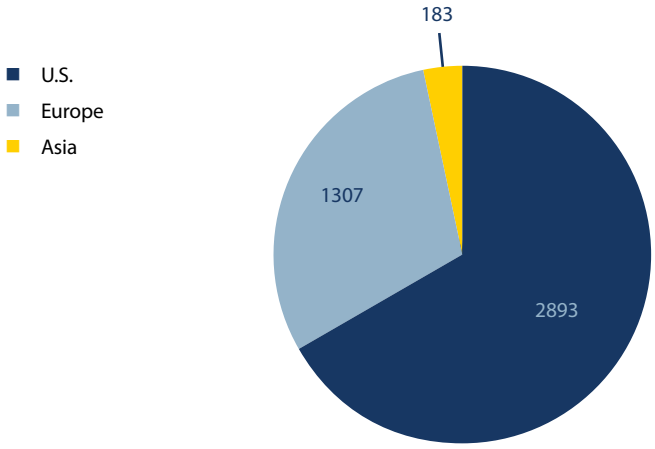

Figure 3 Total Number of Conference and Workshop Attendees

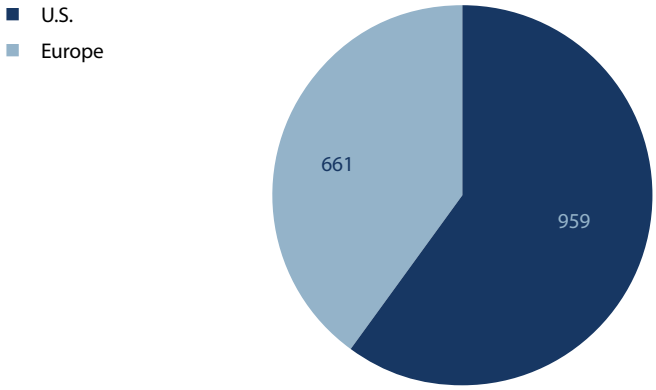

Figure 4 Total Training Course Attendees

PDA continues our long tradition of leadership in scientific approaches to pharmaceutical manufacturing with a robust publication program of technical reports, position papers, peer-reviewed scientific articles and research/surveys, all of which we provide to our members without charge. Of the 96 nonretired technical publications we have, 57% have been published in the last five years**.** In addition, PDA is embarking into new territory by becoming a standards-developing organization **[Editor's Note:** Learn more about our new Senior Standards Manager on p. 18**].**

PDA continues to have a high level of interaction with regulators around the world. Continuing global initiatives focus on drug shortages, data integrity, post-approval changes and others. We interacted with many regulatory agencies in 2017, including the U.S. FDA, ICH, Japanese PMDA, UK MHRA, EMA, WHO, Mexico's COFEPRIS and others, and provided training to 153 health authority members. We also continued to provide constructive feedback on numerous draft regulatory documents to regulatory agencies worldwide in 2017.

All of this has been accomplished through the work of our many volunteers on committees and task forces, collaborating with colleagues around the world to advance PDA's important mission. I also want to thank our tireless staff who have maintained a level of excellence in support of a wide spectrum of activities. These efforts have made our accomplishments possible, and we look forward to your integral role in maintaining PDA's position as an industry leader. We will continue to value and appreciate your contributions!

Looking Ahead at 2018

Rebecca Devine, PhD, Biopharmaceutical Consultant

As a PDA member for more than 20 years and a member of the Board of Directors for 13 years, I am pleased to be taking on the role of Chair in 2018. There are many interesting challenges awaiting PDA and our industry as we move into 2018. PDA has achieved many accomplishments in 2017 that have served our membership as we connect People, Science, and Regulation® to assure high-quality medicines for patients, and we will continue to address emerging scientific, manufacturing, compliance and quality topics in 2018.

I am also very excited to be co-chairing the *2018 PDA/FDA Joint Regulatory Conference* in September 2018 along with **Rick Friedman** of the U.S. FDA. This year marks the tenth anniversary of the Heparin contamination crisis that led to a critical drug shortage. Since then, the industry has come a long way in addressing many of the complex supply chain issues that led to the crisis. In addition, many other emerging topics will be addressed at the conference; the committee is already actively working on the agenda. I know this will be another fantastic meeting. I look forward to seeing you there.

Looking ahead to some of our activities in 2018, PDA has been making great strides in addressing the complex issues faced by manufacturers of emerging technologies such as cell and gene therapy products. These exciting new products entered the realm of commercialization with the approval of the CAR-T cell therapies KYMRIAH® and Yescarta®. There are many complex challenges facing this sector of the industry; PDA is poised to assure that technical reports, conferences/workshops and other training and resources are available to assist those involved in manufacturing cell and gene therapy products. These revolutionary new products will change the landscape of patient therapy for many serious diseases and, as an industry, we need to be sure we are able to adequately manufacture and deliver these products for waiting patients. To serve this sector of our membership, the Biopharmaceutical Advisory Board has plans for a new interest group on cell and gene therapy products. A technical report on the topic is also being drafted. PDA also hosted a conference on cell and gene therapies in December. I look forward to what these efforts can accomplish.

Biosimilars is another emerging area, and PDA plans to create another new interest group focused on these products. There are unique challenges associated with the development of biosimilars; PDA is well positioned to provide an avenue for working through them. Following a successful meeting co-sponsored with the FDA in June, PDA plans to hold a third conference on this topic with the help of our many active volunteers in this space.

As we move forward into 2018, I want to say a few words about PDA's volunteers. I believe PDA has the most dedicated, talented and leading subject matter expert volunteers. Your contributions allow PDA to succeed in its mission. Having volunteered for many years myself, I understand the commitment of your time made as a volunteer—giving of your free time (after working a regular day job) to contribute your knowledge to PDA's efforts so they can be shared by the membership and industry as a whole. I would like to thank all PDA volunteers for your time and effort. I hope that you feel rewarded by your contributions because they make a big difference in the lives of the people who use the products made by our industry. I look forward to seeing the great work that PDA's dedicated staff and valued volunteers have in store for 2018!

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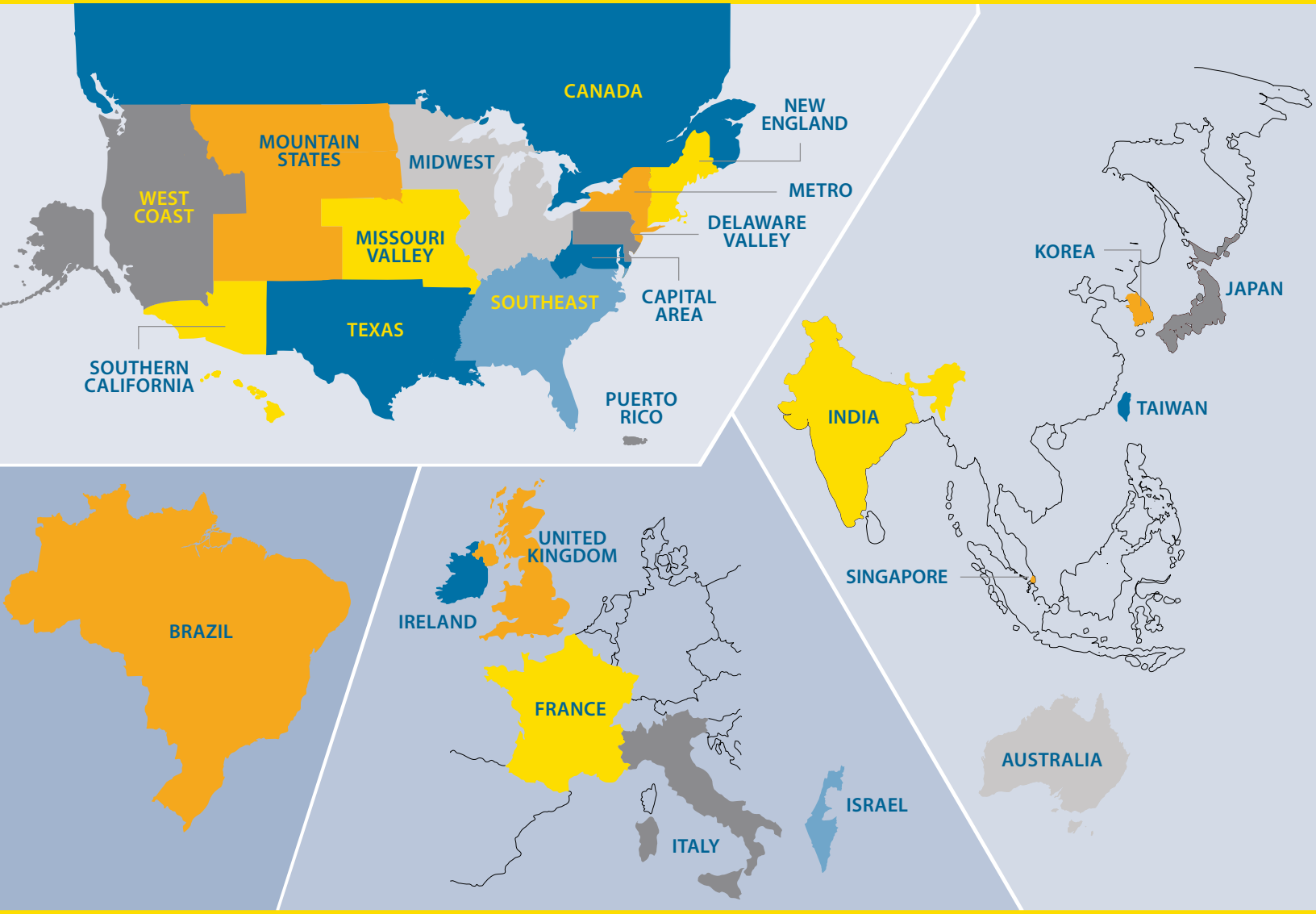

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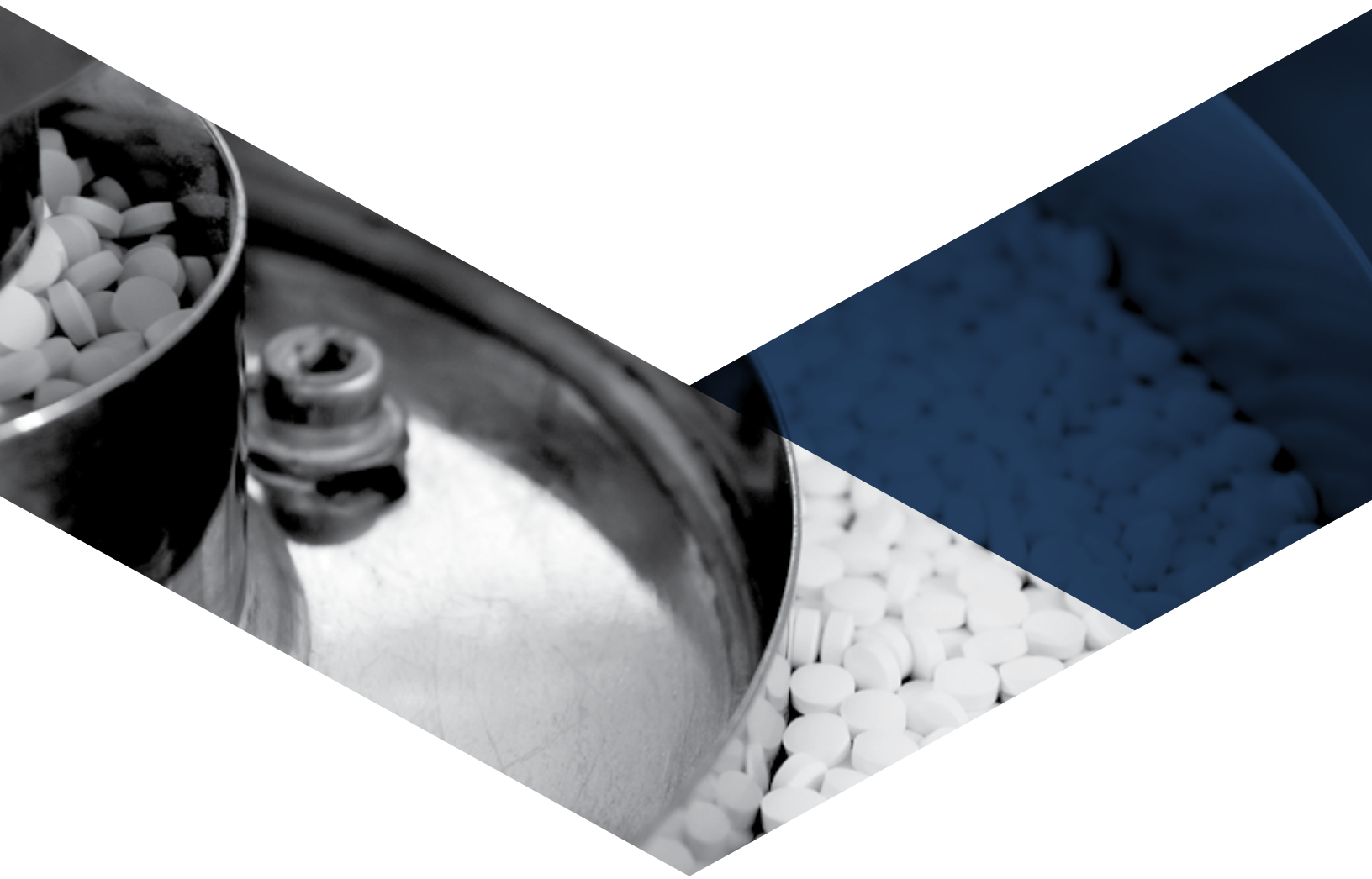

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