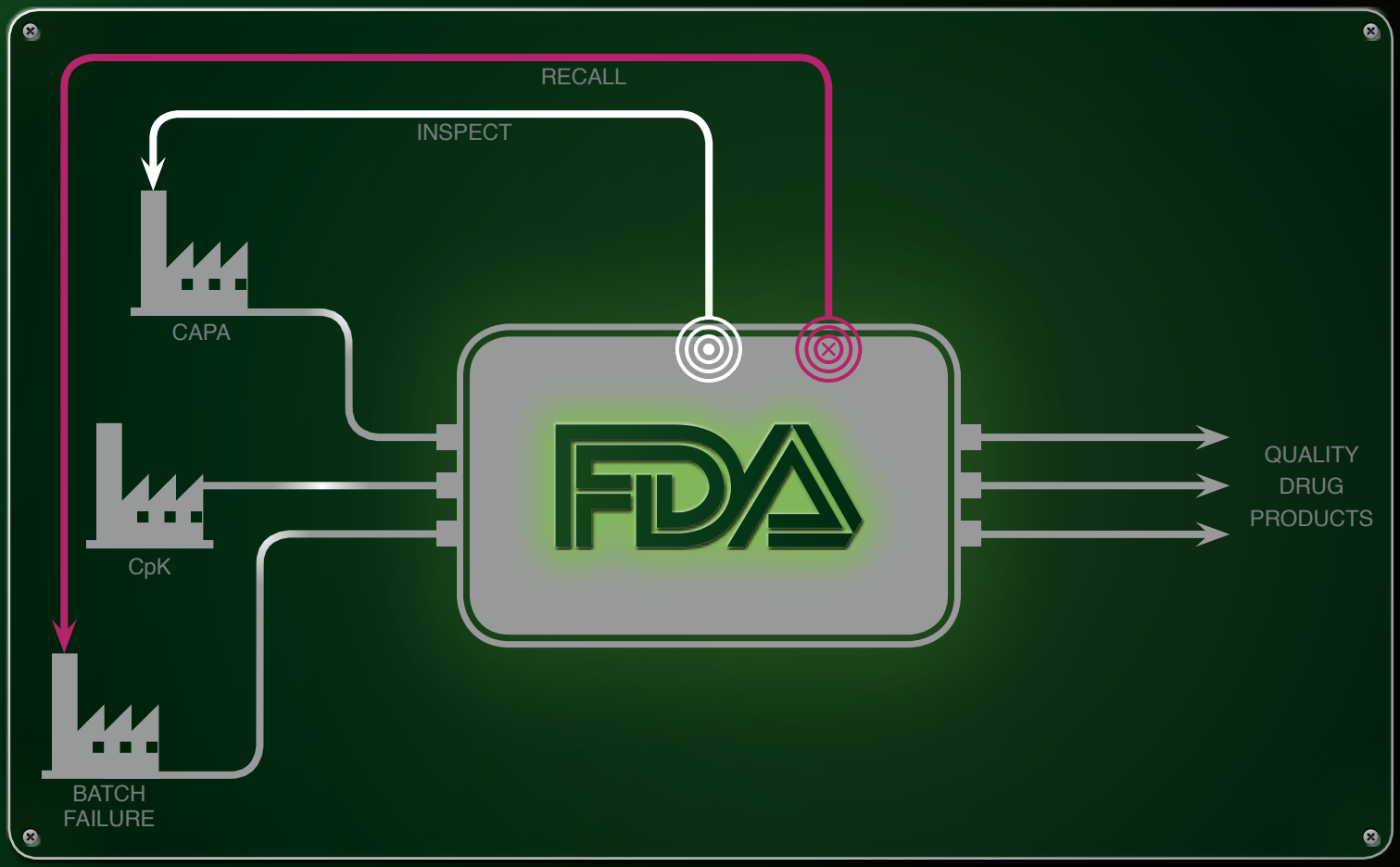
People • Science • Regulation

PDA Letter

Volume L • Issue 2 www.pda.org/pdaletter February 2014



PDA RESPONDS TO FDA'S CALL FOR QUALITY METRICS RECOMMENDATIONS

22

UPCOMING LABORATORY AND CLASSROOM TRAINING FOR PHARMACEUTICAL AND BIOPHARMACEUTICAL PROFESSIONALS

APRIL 2014

2014 PDA Annual Meeting Course Series
April 10-11 | San Antonio, Texas
www.pdaannualmeeting.org/courses

- Risk-Based Product Development Basics for Combination Products: Harmonizing Design Controls and Quality-by-Design in Product Development and Market Authorization Documents – *New Course* (April 10)
- Biosimilars: Understanding the CMC Challenges of Meeting 'Similarity' – *New Course* (April 10)
- Implementation of Quality Risk Management for Commercial Pharmaceutical and Biotechnology Manufacturing Operations (April 10-11)
- Process Validation and Verification: A Lifecycle Approach (April 10-11)
- Validation of Moist Heat Sterilization Processes: Cycle Design, Development, Validation and Ongoing Control (April 11)
- Quality Control and Quality Assurance of Cell-Based Therapeutic Products (April 11)

Validation of Moist Heat Sterilization Processes
April 15-17 | Bethesda, Maryland
www.pda.org/moistheat

PDA Biotechnology Week
April 21-25 | Bethesda, Maryland
www.pda.org/biotechweek2014

- Biopharmaceutical Manufacturing under Regulatory Compliance: Process Strategies, CGMP Considerations and Facility Requirements (April 21-22)
- Biosimilars – Understanding the CMC Challenges of Meeting 'Similarity' (April 23)
- CMC Regulatory Compliance of Biopharmaceuticals (April 24-25)

Management of Aseptic Processing – *New Course*
April 28-30 | Bethesda, Maryland
www.pda.org/apmanagement2014

MAY 2014

2014 PDA Knowledge Management Workshop – Enabler for ICH Q8 – Q11, QRM and Continued Process Verification Course Series
May 21-22 | Bethesda, Maryland
www.pda.org/kmcourses2014

- Integration of Risk Management into Quality Systems (May 21)
- Learning and Training as Contributors to Knowledge Management (May 21-22)
- Technology Transfer – *New Course* (May 22)

2014 PDA Packaging Conference Course Series
May 22-23 | Washington, D.C.
www.pda.org/packagingcourses2014

- Implementing Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations: Case Studies in the Packaging and Labeling of Drug Products (May 22)
- Identification and Classification of Nonconformities in Elastomeric Closures and Aluminum Seals for Parenteral Packaging: Covering Vial Closures, Prefilled Syringe and Cartridge Components – *New Course* (May 23)

For more information on these and other upcoming PDA TRI courses, please visit www.pda.org/courses

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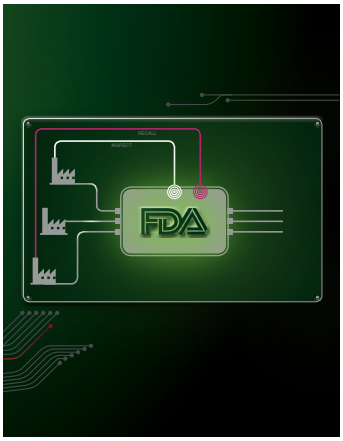
PDA Letter

Volume L • Issue 2 www.pda.org/pdaletter

Cover



Cover Art Illustrated by Katja Yount

Departments

News & Notes

People

Science

Regulation

Voices of PDA

Contents

Features

"Universe" Speakers, PDA Europe Rally to Help Children

On behalf of all the speakers at the *Universe of Pre-filled Syringes and Injection Devices* conference held last November, PDA Europe donated 1,000€ to a Berlin children's hospice, the Björn Schulz Stiftung. In lieu of the usual speaker gift, all speakers enthusiastically supported this cause which PDA Europe plans to keep up with in 2014.

PDA Europe Sr. VP, Georg Roessling, PhD, (far left) hands the check to Marita Trojan, Fundraiser at Björn Schulz Stiftung, with Melanie Decker, Director, Events and Exhibition, PDA Europe (far right).

PDA Volunteer Leaders Speaking on cGMPs at INTERPHEX

PDA conferences usually feature the latest scientific and regulatory developments in the cGMP arena, usually in partnership with regulatory authorities. PDA now brings this expertise to the pharmaceutical industries largest trade shows, INTERPHEX. PDA has reached a first-of-its-kind agreement to serve as a Premier Sponsor at INTERPHEX. As part of the sponsorship, PDA will offer cGMP programming at upcoming INTERPHEX events.

INTERPHEX is an annual trade event focused on pharma and biotech. The next INTERPHEX event will be held March 18–20 in New York City. The cGMP track has been developed by PDA and will feature plenary talks on industry and regulatory trends, biopharmaceutical and sterile manufacturing, prefilled syringes and drug delivery, supply chain management, packaging and aging facilities.

PDA President **Richard Johnson** opens the proceedings, which includes expert talks by the following PDA volunteers:

- **Hal Baseman,** COO, ValSource (Board of Directors Chair, Science Advisory Board, program committees, speaker, author, task forces, PDA Letter Editorial Committee)
- **E.J. Brandreth,** Althea (Chair of PDA's Biotech Advisory Board)
- (invited) **Rick Friedman,** CDER, U.S. FDA (program committees, speaker, author, task forces)
- **Igor Gorsky,** ValSource (PDA Interest Group Leader)
- **Maik Jornitz,** COO, G-Con (BoD Past Chair, PDA Letter Editorial Committee, program planning, author, speaker)
- **Christopher Smalley,** PhD, Merck (PDA Board member, Interest Group Leader, task forces, program committees, speaker, author)
- **Glenn Wright,** Eli Lilly (PDA Board member, Science Advisory Board, task forces, program committees, speaker)
- **Steven Wolfgang,** PhD, CDER, U.S. FDA (program committees, speaker)

In addition, PDA's Facilities/Engineering and Pharmaceutical Water Interest Groups will meet as well. To learn more and to register, please visit www.interphex.com/pdaeducation.

PDA Volunteer Spotlight

Don Elinski, RPh

- Senior Associate
- *Lachman Consultants*
- Member Since | **1984**
- Current City | **Cape Coral, Florida**
- Originally From | **Warren, Pennsylvania**

Starting something is easy, but it takes perseverance to finally succeed

During a visit to a plant that made substantial changes for the better, Don found that in honor of one supervisor, staff let her paint a reactor her favorite color: hot pink!

Which PDA conference is your favorite?

The Annual Meeting. Its focus is usually on innovation. The only way we move ahead as an industry is to focus technology on the manufacture and quality assessment of medication. This is especially true with parenteral manufacturing where the error margin is so low.

What are some topics you would like to see covered at future events?

CAPA (Corrective and Preventative Action). I still see a universal lack of understanding of the basic concepts. In many instances, I see a paper system with little focus on improvement. Discussion of CAPA plans and Effectiveness Measures would be a helpful topic for industry.

What has been the most memorable moment of your long PDA tenure?

Seeing my name as a contributor on a technical report. For me, it was recognition that I had accumulated enough knowledge and expertise to be able to pass it on to others and complete the circle.

What is the most challenging part of your job?

Learning to deal with different people and different cultures, sometimes in difficult surroundings. Probably 50% or more of my assignments are dealing with an outcome of a bad U.S. FDA inspection.

Who do you admire most within your field?

I would say **Jim Agalloco**. To be able to solve problems is great, but to be able to teach others those skills is a different level. He has never lost his passion for the field.

Tell us something surprising about you.

I once tried to get my pilots license. I was very adept at takeoffs, but terrible with landings, especially crosswind situations, which was most of the time in Colorado. It did teach me that starting something is easy, but it takes perseverance to finally succeed. That, and natural talent!

What's launching March 18?

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chapter update

India Chapter Hones in on Quality, Sterility Assurance

PDA India Chapter

Aseptic processing presents many inherent risks for parenteral production. Yet conducting thorough investigations and implementing preventive controls can potentially alleviate many of these risks.

These were the thoughts of the leaders of the PDA India Chapter as they hosted *The Quality Edifice and Sterility Assurance of Parenterals* meeting Nov. 11–12 in Mumbai. More than 70 participants, including prominent leaders in the Indian parenteral manufacturing industry, attended the event which also featured exhibitors IMA Life and Sartorius Stedim. Chapter leaders **Sanjay Singh,** President; **Vishal Sharma,** Secretary; and **Ivy Louis,** Treasurer, were also present

Rich Levy, PhD, PDA, and **Kenneth Muhvich,** PhD, Micro-Reliance, each presented case studies on specific topics and then led discussion of the case studies with distinguished panelists from across the Indian pharmaceutical industry.

The first case study, "Investigation – The ABC of Expectations," outlined the processes involved in correctly investigating procedures that are seemingly simple and straightforward, focusing primarily on common issues in aseptic processing, such as glass particles, sterilization and media fills. The case study also included a summary of the *2013 PDA/FDA Improving Investigations Workshop* held in September.

The next case study explored environmental monitoring, particularly the need for preventive controls and verification possibilities, and offered a U.S. FDA perspective on current issues in this area along with an example of a microbiologist unable to detect organisms on the monitoring plate.

Following lunch, panelists discussed "Understanding Risks for Predictive Controls," and explored PDA's perspective on quality metrics in addition to how one might turn around a crucial internal audit. After this session, there was a brief refreshment break followed by an open house.

Front row (l-r): Krishna Chandran, Sartorius; Sumitra Pillai, Dr. Reddy's Laboratories; Sunil Mahajan, Eisai India; Ivy Louis, Vienni Training and Consulting; Davinder Singh, CIPLA; Rich Levy, PhD, PDA; Sanjay Singh, Aurobindo; Shirish Belapure, Cadila Healthcare; Vishal Sharma, Vienni Training and Consulting

Second row (l-r): Shista Domadia, Zydus Cadila; Shishir Kumar Ojha, USV; Nandan Chandavarkar, FDC Limited; Ranjit Menon, Zydus Hospira; Vikram Shukla, Zydus Hospira; Nandu Kagvate, Xellia; Suryanarayana D, Dr. Reddyís Laboratories

The second day opened with a recap of the previous day's sessions before delving into a case study exploring the nuances of PDA's response to the FDA's draft guidance on circumstances constituting delaying, denying, limiting or refusing an inspection. Next, a case study offered a look at the crossroads of manual aseptic processing, honing in on critical behavior requirements when processing under open/semiclosed filling machines.

And finally, Muhvich presented the last case study, "Sterility Assurance Packages – Essentials and Expectations," which looked at the ease of validation versus the reliance on people skills in relation to the development of sterility assurance strategies, which are required for establishing consistency in parenteral products.

Future activities of the India Chapter will include a one-day meeting, *Tricks and Traps in Preparing and Handling FDA Inspections,* in Goa on March 1, a two-day workshop on visual inspections in Hyderabad on July 2, a one-day meeting on environmental monitoring in Ahmedabad on Sept. 3, and a two-day workshop on lyophilization and prefilled syringes in Bangalore on Nov. 4.

PDA Who's Who Box

Rich Levy, PhD, Sr. VP, Scientific and Regulatory Affairs, PDA

Kenneth Muhvich, PhD, Principal Consultant, Micro-Reliance

Sanjay Singh, SVP, Operations, Aurobindo Pharma

Vishal Sharma, Director, Vienni Training and Consulting

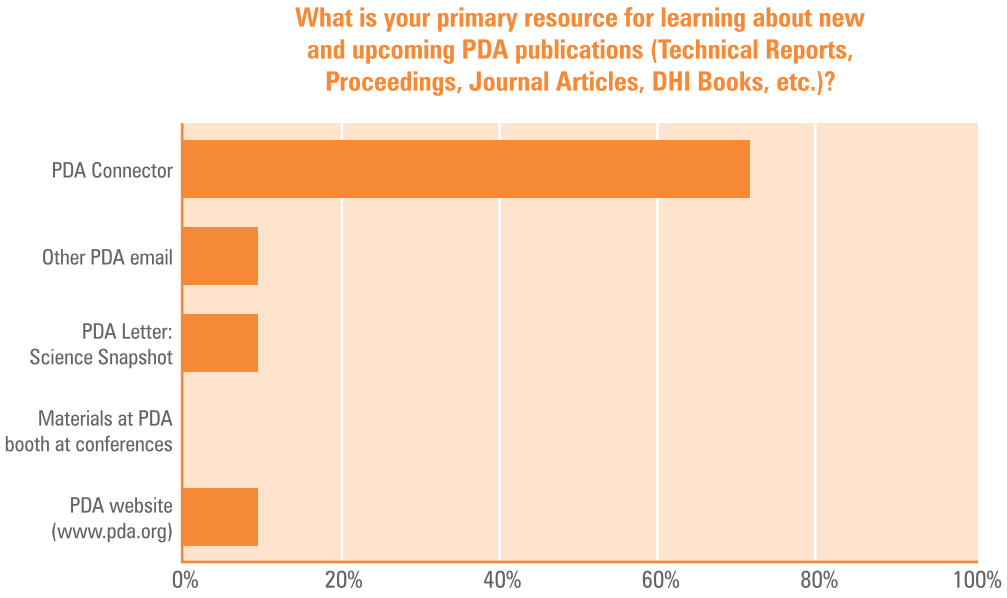
Ivy Louis, Director, Vienni Training and Consulting

PDA Pulse

PDA Connector a Top Resource for New Publications Info

The weekly *PDA Connector* beats all other forms of PDA communication in educating members about new publications, according to the latest PDA *Pulse*. Over 60% of respondents said the weekly email was their "primary source" for PDA new releases. Other emails, www.pda.org, and the *PDA Letter* were considered primary by less than 20%.

We want to hear from you. Keep an eye on upcoming *PDA Connector* emails and Membership emails for more PDA *Pulse* surveys. To manage your email notifications, go to "email preferences" near the login section of www.pda.org.



TOOLS FOR SUCCESS

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5 Reasons Your Resume May Not Be Generating Interviews

Perry Newman

A RESUME can cost you job interviews and keep you unemployed for a prolonged period of time if it conveys the wrong message. Here are five ways a resume can harm your chances for success.

1 The resume is too short to tell a compelling story. Many people take the adages "a resume must be one page" or "a resume can't be more than two pages" too seriously. In doing this, they omit vital information to make a two-page resume fit onto one page and a three-page resume onto two pages. This is especially true for senior level and executive resumes where a three page resume will paint a better picture of value and worth. There's no set rule on how many pages a resume should be if it covers all the bases. Professional editing should cut down the length of most resumes but there is a difference between editing a document and omitting information to make it smaller.

2 The resume lacks continuity. This is something I see all the time. Most resumes are chock full of facts and figures that can sell a candidate to an employer, however, they failed to sequence them so when the reader reads them they do not make sense, they can't be found or are overlooked and, worse yet, they come across as being trivial.

3 The resume reads more like a job description than a marketing document. This happens a lot when people take whole sentences from a job description and this is the bulk of the final product.

4 The resume tells people how good you are but has nothing in it to back up your claims.

5 The resume is sloppily written with numerous grammar and spelling mistakes.

About the Author

Perry Newman, CPC/CSMS, is a nationally-recognized career services professional; an executive resume writer and career transition coach, certified social media strategist, AIPC-certified recruiter and a straight-shooting blogger on how to conduct a successful job search.

Your Local PDA Connection

Are you curious about the issues unique to your region?

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

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

snapshot

Biotechnology Advisory Board Pushes Robust Agenda

E.J. Brandreth, Althea, and Barbara Potts, PhD, Potts and Nelson Consultants

PDA's Biotechnology Advisory Board (BioAB) has been at the forefront of the latest trends in the biotech industry, and for 2014 shows no signs of stopping, as evidenced by ongoing initiatives.

One of the most significant efforts under the BioAB is the creation of the technical reports, *Emerging Methods for Virus Detection,* led by **Kathryn King,** PhD, and *Virus Contamination in Biomanufacturing: Risk Mitigation, Preparedness and Response,* led by **Mike Weibe,** PhD. Both of these teams will be providing the most current technical direction for viral safety to the biotech industry.

In early December, the BioAB reviewed a proposal for developing an interest group centered on the topic of emerging trends for virus detection. The advisory board is also looking for greater international involvement in this area from EU and World Health Organization regulators.

In other BioAB news:

- During the first week in February, the final version of the technical report on single-use systems was sent to the advisory board for review.
- The *Gene and Cell-based Therapies* technical report team is reviewing an outline for a technical report.
- The *Analytical Methods Development* technical report is being prepped for review by the BioAB.
- The *Bioburden and Biofilm Management in Pharmaceutical Drug Substance Manufacturing* technical report team is also attempting to fast-track that technical report for publication prior to the Annual Meeting.
- The team behind the technical report on biopharmaceutical reprocessing convened in December and will meet in a face-to-face meeting in March to finalize the draft for peer review.

Continued at top left of page 16

Journal *Preview*

Special January–February Issue Features Viral Clearance Conference Proceedings

This special issue of the *PDA Journal of Pharmaceutical Science and Technology* features conference proceedings from the *Viral Clearance Symposium 2011,* an invitation-only meeting featuring presentations from industry and regulatory experts on viral clearance and related contamination control issues. Many of the presenters are also involved with PDA's *Virus and TSE Safety Conference* (see page 20 for more information about this conference) as well as PDA's technical reports on viral filtration and virus spikes used for virus clearance studies.

Editorial

Kurt Brorson, Rich Levy, "Proceedings of the 2011 Viral Clearance Symposium"

Introductions

Kurt Brorson, "Overview of 2009 Indianapolis conference white paper: The goal of an integrated viral clearance strategy"

Lixin Xu, et al., "Role of Risk Assessments in Viral Safety: an FDA perspective"

Johannes Blümel, "Viral Safety Perspective from the Paul-Ehrlich-Institut in Europe"

Articles

Brian Hubbard, "Viral clearance by traditional Operations With Significant Knowledge Gaps (SESSION II): Protein A Chromatography"

Qi Chen, "Viral clearance using traditional, well-understood unit operations (session I): Low pH Inactivation"

David Roush, "Viral clearance using traditional, well-understood unit operations (session I): Anion Exchange Chromatography (AEX)"

George Miesegaes, "Viral clearance by traditional Operations With Significant Knowledge Gaps (SESSION II): Cation exchange chromatography (CEX) and detergent inactivation"

Dayue Chen, "Viral clearance using traditional, well-understood unit operations (Session I): Virus Retentive Filtration"

Brian Hubbard, David Roush, "Emerging unit operations (Session III): Hydroxyapatite-, mixed mode-, and adsorptive membrane chromatography; UV-C inactivation; chemical precipitation"

Hannelore Willkommen, "Viral clearance integration (Session IV): General trends, bracketing, QbD, virus preparation quality attributes"

K. Brorson, et al., "Conference summary: Gaps, "Lessons Learned" and Areas for Improvement"

Appendix

Dominick Vacante , Lisa Connell-Crowley, "Protocol for evaluation of virus inactivation using low pH treatment"

Tech *Trend*

Thermal Validation, Mapping Deliver More with Less

Sorin Haias, Lives International

Use of heat is essential for pharmaceutical and biopharmaceutical processes and impacts the critical quality attributes (CQAs) of pharmaceutical products. Heat is used for cleaning, sterilization and specific unit operations involving a large variety of equipment that must be maintained in a state of validation throughout the product lifecycle (development, transfer, commercial manufacturing, etc.).

Current temperature validation practice is based on proven, stable and safe technologies that are, however, time consuming and not user friendly. Wired systems require thermocouples, which present one big inconvenience: it is like a permanent umbilical cord to the acquisition system, as if the "baby" required its mother's care for its entire life!

Thermocouples need to be passed inside a vessel through a special device—therefore integrity tests are needed in order to protect against damages during installation and moisture ingress during the study process, and require full recalibration after retrieval. Along with the never-ending untangling required, this makes the job very time consuming and the operator's work challenging.

Historically, the best advantage of thermocouple systems over data loggers was availability of real-time data.

With the arrival of real-time data loggers, this is no longer the case. These data loggers do everything thermocouples do and much more—they represent a significant change and advancement in thermal validation.

Real-time data loggers eliminate integrity break of the equipment to validate, replacing precalibrations with verifications due to highly accurate four wire PT100 temperature sensors, thus minimizing the validation time in half.

Wireless data loggers do not require pre/postcalibrations, although some data logging software allows for close-loop calibrations and verifications in order to comply with regulations. Operating data loggers is easy and efficient: simply program

Continued at bottom left of page 16

Task Force *Corner*

Glass Handling Task Force Identifies Best Practices

Rebecca Stauffer, PDA

Glass use as a whole may be over 5,000 years old but the material remains notoriously prone to breakage. Not surprisingly, incidents involving glass breakage are common in pharma, resulting in a need for better, proactive measures to ensure safe handling, as indicated in PDA's *Technical Report No. 43: Identification and Classification of Nonconformities in Molded and Tubular Glass Containers for Pharmaceutical Manufacturing.*

Now, Technical Report No. 43 has spurred the creation of a task force focused on exploring methods to prevent glass breakage during the product lifecycle, according to **Bill Bogle,** Chairman, Genesis Packaging Technologies, and chair of the glass handling task force. His group is currently working on a technical report on the topic. This team will initially publish a study of glass vials, followed by a similar study of cartridges and syringes.

Roger Asselta, Vice President, Technical Affairs, Genesis Packaging Technologies, and task force member, explained that the technical report will offer best practices gained from other pharma companies' experiences.

"There's a need to have some kind of document that guides them through this process, but at the same time we're taking advantage of what's been done by others to share this information," he said.

The document will also take a lifecycle approach to glass handling. Asselta pointed out that the team found that breakage incidents were evenly distributed throughout the manufacturing process.

"Certainly, we see some problems at the initial handling, and even at the receipt and storage of the glass sometimes there are problems…so, it really is important to address the entire process," he said. "And look not so much at the point in the process, but the common practices such as glass-to-glass contact, impact areas, glass to metal abrasions, and these can occur anywhere in the process."

Bogle responded, "I would also add to that...there are places in the operation where glass is more vulnerable than in other

Continued at right of page 16

Rate the *PDA Letter* Science Snapshot!

According to the 2013 *PDA Letter* Readership Survey, the Science section of the Letter was designated as one of the most informative sections of the publication. Now, the editors would like to hear what you think specifically about the Science Snapshot. Do you enjoy learning about the latest innovations in the field in our Tech Trends? Or do you like learning more about the activities of our Science-related interest groups and task forces? Perhaps the Journal Preview reminds you to check out the latest manuscripts?

To rate which sections of the Snapshot you enjoy the most, complete the online survey here: www.surveymonkey.com/s/ScienceSnapshot.

Biotechnology Advisory Board Pushes Robust Agenda continued from page 14

Mycoplasma also remains a hot topic, and the advisory board is developing a very positive program in this area, led by **Barbara Potts,** PhD, focusing on best practices using state-of-the-art technology with involvement from the European Union and WHO in developing reference standards. In 2012, a subsection of the mycoplasma task force submitted an article on the topic that has been accepted by the *PDA Journal of Pharmaceutical Science and Technology* and will appear in the May-June 2014 issue of the Journal. Additionally, the team is working on a technical report on the topic.

As always, the BioAB encourages anyone interested in biotechnology to consider joining one of the biotech-focused interest groups. To learn more about these interest groups and how to volunteer, please contact PDA's Volunteer Coordinator at volunteer@pda.org.

Tech Trend continued from page 15

the loggers and place them inside the equipment to validate, regardless if it's an autoclave, freeze dryer or refrigerator.

Once starting the cycle, the signal from data loggers passes through the walls of the equipment and data can now be visualized in real time on the remote computer under U.S. FDA 21 CFR part 11 compliant environment regulations.

The final reports generate automatically, eliminating the need for data treatment outside of the software.

The software automatically performs calculations based on existing regulations or users' custom-made templates.

Manufacturers of advanced wireless data loggers eliminate thermal inertia (some using ketron as the body material). The conception of their loggers allows the signal to pass through the autoclave's or freeze dryer's walls in any circumstance.

Once the change from thermocouples to wireless data loggers has been undertaken, potential results include time savings, comfort during use, user security and increased productivity. The methods currently used in thermal mapping and validation were developed in the 1970s and have changed little since. Advances in data logging technology now enable companies to do more with less.

About the Author

Sorin Haias, President, Lives International, has 17 years in the pharmaceutical industry specializing in manufacturing of thermal validation and mapping systems

Task Force Corner continued from page 15

portions of the operation. For example, when it first comes out of depyrogenation it's very dry. If it contacts another vial it can cause damage more easily than it would if it, for example, just came out of the warehouse."

He also explained that "what happens in the operation is, in many cases, you inflict the flaw in one part of the operation so you don't see the damage but then stress is exerted in a different part of the organization."

The technical report, Asselta said, will also look at what happens to glass upon its receipt by the manufacturer but not the handling that occurs by the supplier. In addition, the report will provide technical information on the nature of glass, including why it breaks and what has to happen for events to occur.

In developing best practices based on other companies' experiences, the task force relied mainly on information from large pharma companies as the "handling lines tend to be fully automated lines rather than manually operated lines."

In fact, representatives from pharmaceutical firms are part of the task force as well as glass manufacturers and equipment suppliers. Team members hail from North America and Europe—a key point as the team found that some U.S. pharmaceutical companies' only experiences with suppliers involved European glass suppliers.

"It really is a wide cross section from producers to users and even a few consultants that have experience in the industry," Asselta said.

In addition, Bogle said, "Because we have members on the task force from pharmaceutical companies, from equipment companies and from glass manufacturers, we have been able to do some experimentation. And we have actually been able to do some experimentation at a glass factory where we were using extremely raw vials."

Ultimately, "I think the results will be very well received," Bogle concluded.

About the Experts

Roger Asselta joined Genesis Packaging Technologies in 2006 as Vice President of Technical Affairs, continuing nearly twenty years of working in pharmaceutical packaging. At Genesis, he is involved with parenteral vial sealing, developing methods for evaluating seals using Residual Seal Force and elastomer compression measurements.

Bill Bogle is Chairman of Genesis Packaging Technologies, a leading manufacturer of capping equipment and related testing equipment for pharmaceutical companies that are manufacturing injectable drugs.

"Remember the Science" at PDA's Annual Meeting

Jeffrey Hartman, Merck, and Program Committee Member

2014 PDA Annual Meeting • San Antonio, Texas • April 7–11 • www.pdaannualmeeting.org

Today, many of the new drug products being developed are biopharmaceuticals and sterile formulations that promise to have a significant health impact and benefit to patients. To make these medicines affordable and accessible, innovative drug development approaches as well as a focus on the value added to patient health are a must. Gaining the knowledge to develop and utilize new technologies to bring these products to the market is critical to your company or organization. Knowledge is power—dissemination of that knowledge will better drive world class science and technology into your organization.

With this in mind, the Program Planning Committee has selected "Biopharmaceutical and Sterile Manufacturing – Embracing Innovation to Meet Global Challenges" as the theme for this year's upcoming *PDA Annual Meeting,* held in historic San Antonio, Texas.

This is PDA's "flagship" event, serving as a wellspring of scientific discussion and collaboration. Previous Annual Meetings provided in-depth overviews of leading scientific trends in industry, including biofilm myths, cytotoxic facility regulations, the Knowledge Management Function Model, low endotoxin recovery and more. And this year's Annual Meeting is no different.

For the opening plenary session, the committee is pleased to present **Rahul Singhvi,** Sr. VP/COO, Takeda Vaccines, who will share with us the impact of technology on vaccine manufacturing and its impact on human health. On Day Two, **David Shanahan,** President, Mary Crowley Cancer Research Centers, will return to provide another inspiring lecture on new developments in cancer research and treatment. Joining him will be **Wilfried Dalemans,** CTO, TiGenix, to provide an update on new cell and gene therapies coming to the market. For the closing plenary, **J. Christopher Love,** PhD, Associate Professor of Chemical Engineering, The David H. Koch Institute for Integrative Cancer Research Institute, MIT, will provide his vision on the treatments of tomorrow,

Continued at bottom of page 19

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2014 PDA ANNUAL MEETING

Biopharmaceutical and Sterile Manufacturing – Embracing Innovation to Meet Global Challenges

April 7-9, 2014 | JW MARRIOTT SAN ANTONIO HILL COUNTRY | SAN ANTONIO, TEXAS

> "This meeting was a great opportunity to meet and reconnect with the 'movers and shapers' of the pharmaceutical and bio-pharmaceutical world, but more than that, it is an opportunity to hear many of those 'movers and shapers' speak from podiums, at Interest Group sessions and the other exciting venues offered by the meeting."
>
> **CHRIS SMALLEY,** *Merck, Sharp & Dohme*

Today, many of the new drug products being developed are biopharmaceuticals and sterile formulations that promise to have a significant health impact and benefit to patients. To make these medicines affordable and accessible, innovative drug development approaches is a must.

Do not miss the opportunity to leverage and learn from leading subject matter experts at PDA's premier event, the *2014 PDA Annual Meeting*. Knowledge is power and dissemination of that knowledge will better drive world class science and technology into your organization.

Leading the discussions:

- **Ali Afnan,** *Step Change Pharma, Inc.*
- **Wilfried Dalemans,** *TiGenix*
- **Katherine Eban,** *Fortune Magazine*
- **J. Christopher Love,** *MIT Koch Institute*
- **David Shanahan,** *Gradalis*
- **Kalavati Suvarna,** *CDER, FDA*
- **Karen Takahashi,** *CDER, FDA*
- **Martin VanTrieste,** *Amgen, Inc.*

Following the conference, there will be a post-conference workshop, ***PDA Biofilm and Bioburden Workshop*** on April 9-10.

Want to learn more? From April 10-11, six in-depth training courses will be held. These courses for professionals involved in developing and manufacturing quality pharmaceutical products will cover a range of topics from implementation of quality risk management to process validation and verification.

EXHIBITION: APRIL 7-8
POST-CONFERENCE WORKSHOP: APRIL 9-10
COURSES: APRIL 10-11

www.pdaannualmeeting.org

Contamination Control Science Targeting Sessile Biofilms

Program Planning Committee, PDA Bioburden and Biofilm Workshop

PDA Bioburden & Biofilm Workshop • San Antonio, Texas • April 9–10 • www.pda.org/bioburden2014

Can your company identify all the areas of your manufacturing processes that invite the formation of microcolonies?

In recent years, there has been a fundamental shift in the understanding of microbial growth, and it is now widely recognized that the preferred form of microbial growth in nearly all environments is as attached microcolonies, or sessile biofilms. Manufacturers of sterile products, in particular, must understand both the biology of these sessile biofilms and the evolving engineering principles of the environments that support them in order to properly control this source of process/product contamination.

These issues are important to understand, whether designing a new manufacturing process or operating a legacy process.

The organizers of the *PDA Bioburden and Biofilm Workshop*, which follows the *2014 PDA Annual Meeting*, have placed this evolving science front and center. The opening plenary session features two industry experts who will discuss both the biology and engineering aspects of sessile biofilms.

Industry and regulatory perspectives presented throughout the workshop will focus on defining effective microbial control program for processes, as well as facility, equipment, utilities and personnel controls. The workshop will present practical approaches to the prevention, detection, and remediation of microbial contaminations that attendees can use in daily production and laboratory operations. The workshop will also provide attendees with a first look at the outcome of the PDA survey on bioburden and biofilm management along with an update on the status of the *Bioburden and Biofilm Management* technical report. The workshop will conclude with case studies of successful contamination remediation efforts.

If you are responsible for or concerned about the sources of contamination in your manufacturing processes, this workshop will help you understand the latest bioburden/biofilm science.

"Remember the Science" at PDA's Annual Meeting continued from page 17

leveraging the innovative technology we have today. To close the meeting, we are delighted to have **Martin VanTrieste,** Sr. Vice President, Quality, Amgen, and PDA board member. His presentation will focus on the future of pharmaceutical growth as companies expand to emerging markets.

A variety of presentations are being offered, covering many of the critical issues the industry faces, such as:

- Biosimilar development, analytical methods, and hurdles in manufacturing
- Challenges in sterile manufacturing, including facility maintenance, particulates, counterfeiting and novel sterilization technologies
- Reengineering Quality Systems to drive world class performance for CAPA effectiveness, regulatory inspection readiness, statistical process control and new PAT applications

Additionally, advances in manufacturing/process science, supply chain management and technical transfers will be addressed.

The Program Planning Committee for the *2014 PDA Annual Meeting* is committed to making this meeting a valued, informative, and knowledge building experience. So please, "Remember the Annual Meeting" and join us this April in San Antonio, Texas.

Viral and TSE Safety Remains Key Goal

Program Planning Committee Co-chairs Kurt Brorson PhD, CDER, U.S. FDA, and Hannelore Willkommen, PhD, RBS Consulting

2014 PDA/FDA Virus & TSE Safety Conference • Bethesda, Md. • June 9–13 • www.pda.org/virus2014

The risk of viral contamination in biological products is significant as these products are manufactured using materials of human or animal origin. The multistep manufacturing process involves significant contamination risks from source materials, cell culture components, human involvement and cell banks, but at the same time the purification process can remove/inactivate viruses. For this reason, global regulatory agencies require that manufacturers demonstrate viral safety of the products, generally through spike/removal studies as described in ICH Q5A.

Transmissible Spongiform Encephalopathy agents also pose a danger, via contamination from bovine-derived raw materials and plasma containing Creutzfeldt-Jakob disease agents.

Because viral and TSE safety relies on both assessing the pathogen threat landscape for new agents, and a comprehensive understanding of potential safety gaps in manufacturing, risk management in this area depends on the careful analysis of new information, including emerging infectious agents and subtle changes during the production lifecycle.

The *2014 PDA/FDA Virus & TSE Safety Conference* will explore these issues this June. The conference will feature an exciting agenda covering the forefront of this critical area of biopharmaceutical safety and quality.

The meeting will start with a regulatory update from agencies in Europe, North America and Asia. Following this, there will be sessions devoted to specific topic areas, including testing for emerging viruses, risk considerations related to new cell substrates, viral safety risks of reagents used for cell cloning and viral contamination risk mitigation. This will be followed by sessions covering viral clearance by filtration, chromatography, inactivation methods and other unit operations. Finally, the meeting will be rounded out by two sessions on TSE safety, including updates on global risks in this critical area.

The threat of TSE and viral contamination remains a rapidly evolving issue. The planners of the 2014 conference believe that additional discussion will generate new ideas and spur additional approaches, strategies and procedures to mitigating these threats.

Packaging Innovations Continue to Flourish

Program Co-chair Ronald G. Iacocca, PhD, Eli Lilly

2014 PDA Packaging Conference • Washington, D.C. • May 20–23 • www.pda.org/packaging2014

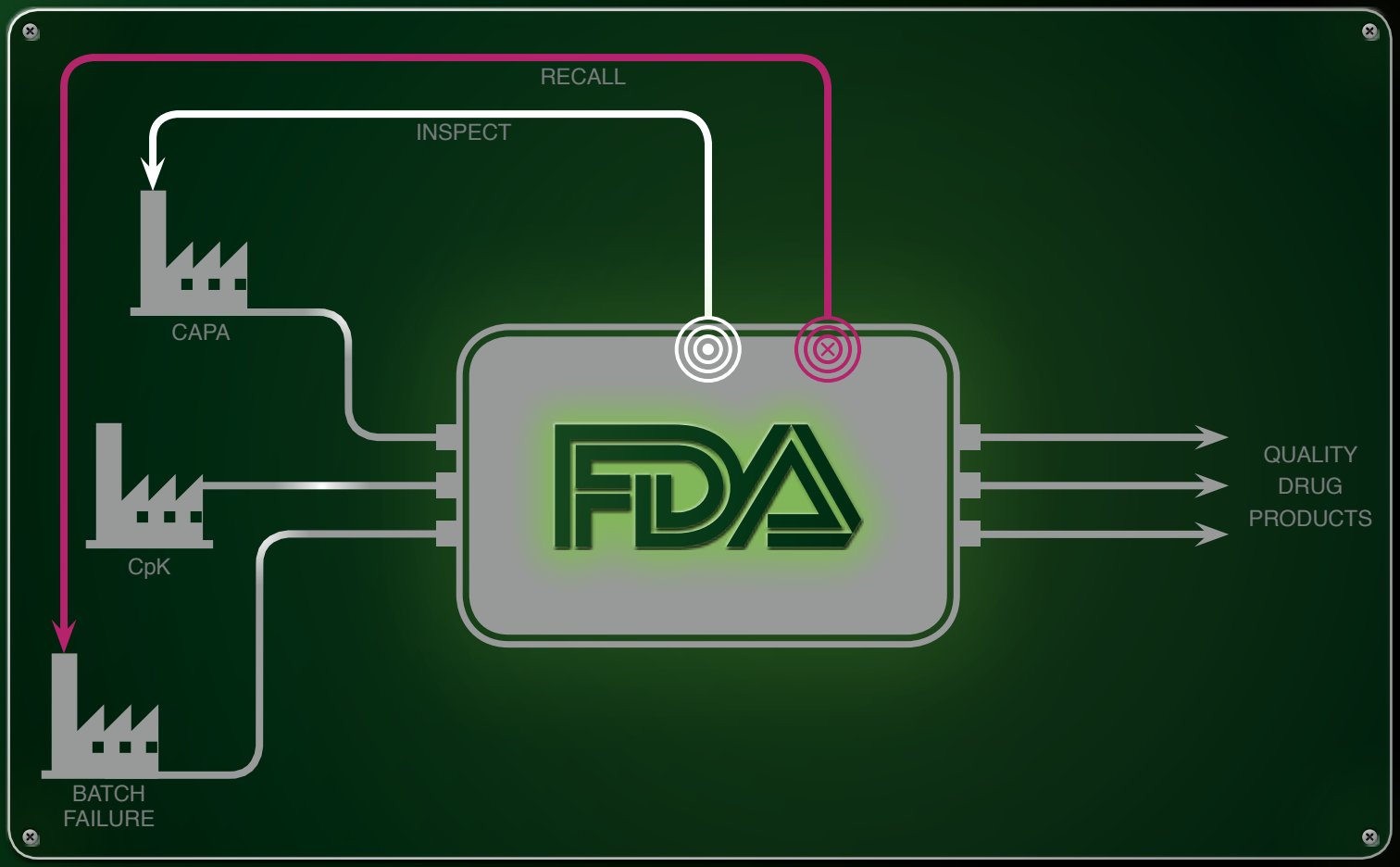
As new and innovative medicines are developed, it is crucial to understand all aspects of primary packaging components. No longer can packaging be viewed as a "black-box" container. In many instances it is an integral part of a sophisticated and carefully designed drug delivery system.

The *2014 PDA Packaging Conference* will continue offer a forward look into the world of parenteral packaging and will include presentations on topics such as current and future regulatory trends, the responsibility of pharmaceutical companies and suppliers in evaluating changes in primary container closure components, and future trends in packaging development. Speakers have been selected from pharmaceutical companies, packaging manufacturing companies, and regulatory agencies, thereby ensuring that a balanced and holistic perspective will be given on these important topics.

The first session will provide attendees with an update from the U.S. FDA on expectations for parenteral packaging. Because of the deliberate selection of Washington, D.C. for this conference, there will be significant involvement of members of the FDA. The second session will contain presentations that provide the scientific foundation for pharmaceutical companies to understand the fundamental scientific impact of the chemical and physical properties of packaging on product quality and patient safety. Subsequent sessions will build on these topics and provide the ideal venue for discussion and collaboration. We also hope you'll take full advantage of the exhibit hall and discover what new packaging solutions are available in the market place.

PDA RESPONDS TO FDA'S CALL FOR QUALITY METRICS RECOMMENDATIONS

Walter Morris, PDA



Article at a Glance

- Over 300 industry representatives collaborated on identifying appropriate metrics
- This collaboration resulted in a Points to Consider document
- PDA will work with other industry groups to define some of the metrics

PDA answered the U.S. FDA's Center for Drug Evaluation and Research (CDER) call for help in identifying quality metrics that can be used for the Center's new drug quality enforcement initiative by connecting people, science, and regulation.

That call came in a February 2013 *Federal Register* announcement in which FDA explained how it intends to implement Sec. 1003 of the Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012 ***(1).*** Sec. 1003 of the new law amends the Federal Food, Drug, and Cosmetic Act by requiring the Agency to form a task force to develop and implement a strategic plan for enhancing its response to preventing and mitigating drug shortages.

As part of this strategy, FDA explained its intention to address the major underlying causes of drug and biological product shortages, which over the last several years have largely resulted from quality-related manufacturing shutdowns.

FDA, therefore, is seeking new ideas to encourage high-quality manufacturing and to facilitate expansion of manufacturing capacity (see the sidebar for more details from the *Federal Register* announcement). To help with the former, FDA requested input on how drug companies currently employ manufacturing quality metrics.

In response to that *Federal Register* announcement, PDA formed an 11-member volunteer task force. This group issued comments to FDA on March 13 that included a discussion of 15 quality metrics commonly used by manufacturers, as well as answers to other questions posed in the announcement ***(2).***

Most importantly, the comments team informed FDA that it would be willing to facilitate dialogue between the Agency and industry on the subject of manufacturing and product quality metrics. Over the next several months, the PDA Pharmaceutical Quality Metrics Committee worked with CDER officials to develop an interactive conference and to summarize the dialogue in a Points to Consider (PtC) document.

On Dec. 9–10, 2013, over 300 industry experts on drug product quality and manufacturing, representing 150 companies, assembled to participate in the *2013 PDA Pharmaceutical Quality Metrics Conference* in Bethesda, Md. The attendees covered a wide range of functional responsibilities such as quality, engineering, manufacturing, technical services and regulatory affairs. Virtually every sector of the industry, both domestic and overseas, was present, including generics, OTC, CMOs, and pharmaceutical and biotech companies that manufacture large and small molecule APIs and drug products.

The committee outlined many important factors that "must be balanced" for FDA to achieve its objectives

This strong showing of support for the FDA initiative was well-received by CDER Director **Janet Woodcock,** who took the podium in the closing session to thank PDA and discuss the need to press forward with the metrics initiative.

"This is really important," Woodcock said. "We are having an ongoing dialogue about this issue of metrics. I was able to come and listen to the report-out from the polls and breakout sessions. I was very intrigued by both the engagement and what people actually said about what is going on. It gave me a lot of hope that we can really make this happen."

Feedback gained during the interactive workshop, which afforded attendees the opportunity to vote on metrics categories they deemed useful and suggest metrics not presented in advance by the PDA Pharmaceutical Quality Metrics Committee, assisted the in the completion of the PtC document, which PDA submitted to the FDA on Dec. 19, 2013 ***(3).***

In closing the conference, PDA President **Richard Johnson** assured participants that the feedback received greatly helped the committee refine the PtC. "Whatever the team was thinking before the meeting, I can assure you it is different today," he said. "If it was easy, we wouldn't need a meeting."

The PtC expresses PDA's overall support of FDA's effort to use quality metrics as important tools:

> *PDA recognizes FDA's intent is to establish metrics with clinical relevance to patients which will also move towards a more proactive quality assessment model for companies. PDA also understands the objective is to move organizations from assessing primarily against compliance standards to assessment based on quality performance against established clinically relevant specifications and driving continual improvement.*

Drawing from the discussions at the metrics workshop, the committee outlined many important factors that "must be balanced" for FDA to achieve its objectives. For instance, identifying and defining "leading metrics" (harder to define but more useful) versus "lagging metrics" (more commonly used today). The committee envisions a time in the future when industry would more widely adopt leading indicators, demonstrating a commitment to the ICH Q10 principle of continuous improvement. Use of leading indicators *is necessary to improve prediction and mitigation of potential drug shortages especially in increasingly complex manufacturing process and supply chain environments,* the committee wrote.

The committee recommends specific metrics for FDA collection, broken down as trend metrics per product and trend metrics per site. The former includes confirmed product quality ➤

2014 PDA UPCOMING EVENTS

FEBRUARY EVENTS

3-7
2014 Aseptic Processing Training Program – Session 1
Bethesda, Maryland
www.pda.org/2014aseptic1

17
Pre-Conference Workshop on Bacterial and Endotoxin Testing
Berlin, Germany
https://europe.pda.org/PWSBACT2014

18-19
Pharmaceutical Microbiology
Berlin, Germany
https://europe.pda.org/Microbio2014

20
Rapid Microbiological Methods & An Overview of the New Technical Report 33
Berlin, Germany
https://europe.pda.org/TCRMM2014

20
Microbial Contamination Control in the Pharmaceutical Industry
Berlin, Germany
https://europe.pda.org/Contamin2014

20-21
The A to Zs of Biofilm Control, Monitoring, Validation, and Excursion Investigations of Pharmaceutical Water Systems
Berlin, Germany
https://europe.pda.org/Biofilm2014

20-21
2014 PDA – PIC/S Q7 Training
Bethesda, Maryland
http://www.pda.org/GlobalEventCalendarandRegistration/2014-PDA-PICS-Q7-Training.aspx

20-21
An Introduction to Visual Inspection – Session 1
Bethesda, Maryland
www.pda.org/visual1

3-7
2014 Aseptic Processing Training Program – Session 1
Bethesda, Maryland
www.pda.org/2014aseptic1

10
Pre-Conference Workshop on Elastomeric Closures
Brussels, Belgium
https://europe.pda.org/PWSElasto2014

11-14
Parenteral Packaging
Brussels, Belgium
https://europe.pda.org/ParPack2014

13
Container Closure Integrity – Regulations, Theory, Test Methods, Application
Brussels, Belgium
https://europe.pda.org/ContainerInteg2014

13
Interest Group Meeting Pre-filled Syringes
Brussels, Belgium
https://europe.pda.org/IGPrefilled2014

www.pda.org

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

Save these dates!

MARCH EVENTS

13
Identification and Classification of Glass Defects – PDA Technical Report 43
Brussels, Belgium
https://europe.pda.org/TR432014

13-14
Post-Conference Workshop on Extractables & Leachables
Brussels, Belgium
https://europe.pda.org/WSE&L2014

14
Container Closure Systems
Brussels, Belgium
https://europe.pda.org/CCS2014

17-21
Fundamentals of Aseptic Processing – Session 1
Bethesda, Maryland
www.pda.org/apfundamentals1

18-19
PDA/PICs API Training Course
Johannesburg, South Africa
https://europe.pda.org/API2014

18-20
2014 Interphex – PDA Premier Sponsor
New York, New York
http://www.pda.org/GlobalEventCalendarandRegistration/2014-INTERPHEX.aspx

25-26
Modern Biopharmaceutical Manufacturing
Lyon, France
https://europe.pda.org/Biopharm2014

March 31 April 9
2014 Aseptic Processing Training Program – Session 2
Bethesda, Maryland
www.pda.org/2014aseptic2

APRIL EVENTS

1
Interest Group Meeting on Freeze Drying
Basel, Switzerland
https://europe.pda.org/IGFreezeDrying2014

7-9
2014 PDA Annual Meeting
San Antonio, Texas
www.pdaannualmeeting.org

9-10
PDA Bioburden and Biofilm Workshop
San Antonio, Texas
www.pdaannualmeeting.org/bioburden2014

10-11
2014 PDA Annual Meeting Course Series
San Antonio, Texas
http://www.pdaannualmeeting.org/courses

21
2014 PDA Biotechnology Week
Bethesda, Maryland
www.pda.org/biotechweek2014

28-30
Management of Aseptic Processing
Bethesda, Maryland
www.pda.org/apmanagement

29-30
Vaccines & Beyond Workshop Brussels, Belgium
https://europe.pda.org/Vaccines2014

FDA's Looking for New Quality Ideas

The following is from the February 2013 *Federal Register* announcement which prompted PDA to form the Pharmaceutical Quality Metrics Committee.

1. In an effort to address the major underlying causes of drug and biological product shortages, FDA is seeking new ideas to encourage high-quality manufacturing and to facilitate expansion of manufacturing capacity.

a. To assist in the evaluation of product manufacturing quality, FDA is exploring the broader use of manufacturing quality metrics. With that in mind, FDA would like input on the following issues: What metrics do manufacturers currently use to monitor production quality? To what extent do purchasers and prescribers use information about manufacturing quality when deciding how to purchase or utilize products? What kinds of manufacturing quality metrics might be valuable for purchasers and prescribers when determining which manufacturers to purchase from or which manufacturers' products to prescribe? What kinds of manufacturing quality metrics might be valuable for manufacturers when choosing a contract manufacturer? How frequently would such metrics need to be updated to be meaningful?

b. The use of a qualified manufacturing partner program similar to one used under the Biomedical Advanced Research and Development Authority (BARDA) has been suggested as a potentially useful approach to expanding manufacturing capacity and preventing shortages. FDA recognizes that there are important potential differences between the BARDA program and the use of a parallel program to address shortages. For example, the BARDA program covers a relatively stable and limited number of products, but drugs at risk of shortage are many, may change rapidly over time, and are difficult to predict in advance. In addition, FDA does not have funding to pay manufacturers to participate in a drug shortages qualified manufacturing partner program or to guarantee purchase of the end product. With these differences in mind, is it possible to design a qualified manufacturing partner program that would have a positive impact on shortages?

c. Are there incentives that FDA can provide to encourage manufacturers to establish and maintain high-quality manufacturing practices, to develop redundancy in manufacturing operations, to expand capacity, and/or to create other conditions to prevent or mitigate shortages?

2013 PDA Pharmaceutical Quality Metrics Committee

Steven Mendivil, Chair, Amgen
Ian Elvins, Consultant
Anil Sawant, Johnson & Johnson
Anders Vinther, Genentech
Glenn Wright, Eli Lilly
Marty Nealey, Hospira
Sue Schniepp, Allergy Labs
Gabriele Gori, Novartis
Joyce Bloomfield, Merck
Bob Kieffer, Consultant
Vince Anicetti, Boehringer Ingelheim
Denyse Baker, PDA

complaint rate by product and batch reject rate by product. The latter includes confirmed OOS rate (drug substance and drug product) by site.

The document also highlights useful site and product-specific metrics identified at the conference as *important, but difficult to compare.* Process capability and CAPA effectiveness rate are examples of these.

The PtC includes advice on comparing metrics. Data trends of metrics are *more reliable predictors of potential risk than single values*, the team wrote. They provided examples to support their claim.

The document also includes a section on "direct comparison metrics"—in acknowledgement of FDA's request for absolute value and trends of metrics appropriate for direct comparison between products and manufacturing sites. If the Agency takes that approach, the team recommends limiting it to two product metrics and one site metric reported annually.

In the conclusion, the team warns against *just comparing numbers in order to achieve FDA's goal of objective measures of product quality, site operations quality, and site systems performance.* The conclusion also warns against unintended consequences of metrics collections.

The committee also suggests in the PtC document possible additional activities PDA could pursue in 2014 to help FDA develop the pharmaceutical quality metrics program. They also suggest that FDA could consider offering companies that demonstrate a commitment to quality performance "preferred opportunities," such as "preferred handling" of postapproval changes to submissions that enhance system/process capabilities and less frequent inspections.

Johnson pledged that PDA "will invite and try to work with other organizations in the coming year to harmonize specifically some definitions of some of these metrics so as we move forward at least that is not a barrier."

Finally, Johnson indicated that PDA is considering a follow-up *Pharmaceutical Quality Metrics Conference* in 2014.

References

1. Department of Health and Human Services, Food and Drug Administration. Food and Drug Administration Drug Shortages Task Force and Strategic Plan; Request for Comments; *Federal Register,* 2013, 78(29), 9928-9929. www.gpo.gov (accessed January 6, 2014)
2. PDA Comments on FDA Drug Shortages Strategic Plan Docket No. FDA-2013-N-0124; Parenteral Drug Association, Inc.: March 13, 2013. www.pda.org/Science-and-Regulatory-Affairs/RAQAB/Regulatory-Comments-Resources/2013-PDA-Regulatory-Comments/Final-Submission-of-PDA-Comments-on-FDAs-Draft-Drug-Shortages-Strategic-Plan-March-13-2013.aspx (accessed January 6, 2014)
3. PDA Points to Consider: Pharmaceutical Quality Metrics; Parenteral Drug Association, Inc.: Dec 19, 2013. www.pda.org/pdf-1/PDA-Pharmaceutical-Quality-Metrics.aspx (accessed January 6, 2014)

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PARTICLE MEASURING SYSTEMS

Metric Session Readout Reports Highlight Industry Views

Report from the 2013 PDA Pharmaceutical Quality Metrics Conference

[Editor's Note: *The following is a modified transcript from the breakout session readouts during the closing plenary session of the* 2013 PDA Pharmaceutical Quality Metrics Conference *held Dec. 9–10 in Bethesda, Md. Here,* ***Anil Sawant,*** *PhD,* ***Joyce Bloomfield, Glenn Wright*** *and* ***Sue Schniepp,*** *who all served as facilitators for the conference's breakout sessions, discuss participants' selections of particular metrics and the reasons behind them.***]**

ANIL SAWANT: So, the No. 1 metric that we picked was "confirmed product quality complaint rates"—again, the term "confirmed," of course, led to lots of lively discussion, and I will talk a little bit more about "confirmed product quality complaint rates," "confirmed OOS rate for drug substance and drug product," "process capability by product," "critical investigation rate," and "batch rejection rate." These were the top five that we voted on.

When we had the option of adding four more, interestingly enough, every group came up with some very good recommendations, but none of them made it to the top five. So, I have just listed them, and the lesson perhaps from this is, if given time, we can come up with additional metrics. We can come up with a lot of metrics, and we could have lots of discussion, but, you know, they didn't make it to the top five.

The other feedback that we got is definition, definition, definition

What were the critical themes that we found? Most underlying comments were related to where we are today—and I guess the feedback was—today, industry more ready to report lagging indicators such as batch failure rate, complaints, but not industry moving in the direction of leading indicators, such as process capability, not ready yet for every product. And that is some of the feedback that we got through sessions, that every product, perhaps the older products, are not there yet. Companies might not have that kind of information. So we believe we should consider a phased—or FDA should consider a phased approach to implementing this—start collecting metrics, see how the system works, including the mechanism for collection and then build on it. I think most companies will have worked on metrics, starting small and then building and adjusting the metrics as they go along.

The other feedback that we got is definition, definition, definition. It is very important to define these metrics, especially terms such as "critical," "confirmed," "effectiveness," and the feedback that we have is the definitions need to be common and specific, so a lot of discussion around how do we go about defining. Either we define these terms or consider not having these terms associated with any of these metrics, because they are too subjective.

JOYCE BLOOMFIELD: So, we were in the same place, pick top five for site metrics and quality system metrics, and we didn't distinguish between the two, so this is combined. And what we found is that, No. 1, "confirmed OOS rate" was one of the top five. "CAPA effectiveness" is one of the top five. "Batch failure rate," "critical investigations and deviations rate by site," "environmental monitoring and grade A&B areas, the excursions," and then we had one that popped up that everyone felt strongly should be included. So, we couldn't come up with five; we came up with six. And "right first time" was one that we added that we thought was important.

We also polled and asked for which way to best report the metric "confirmed OOS rate by site," and our results are to do a direct comparison: 25% of the group thought it should be direct, and 75% thought that it should a trend comparison.

Another question we asked was what is an objective measure for "CAPA effectiveness by site" as far as "direct" or "trend." By site was 45%, and CAPA effectiveness—I'm sorry...."direct" was by 45%, and "trend" was 55%, so it was almost a 50-50 split on this one, and we said, "hey, maybe we could even report this both ways."

And a couple of themes that came out while we did this was that those top five that were selected was based on a concept that there would be a need for a specific definition for each metric in order to ensure that we're doing an apples-to-apples comparison, and I think that's the theme that you saw also from Session A. And we also thought that some metrics could possibly consolidated to report. For example, "confirmed OOS rate" and "batch failure rate" might be something that's really a combined type of metric. ➤

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GLENN WRIGHT: The poll question we asked was to pick the top two that you feel to be most challenging. You initially look at this, and you say, "Well, you know, I don't know how many of them will be really that challenging," but then as you get into the definitions, it becomes fairly clear. When you look at this output graph, when we started to get into the definition of "process capability," CpK, PpK, you really started to understand that there were some real challenges with that and how you would implement that and how that would work, and there is a lot of good comments about that. One of the really interesting comments was an idea we hadn't even thought of, which was maybe the metric initially isn't a metric on actual numbers. Maybe it is percent of specifications that have CpK's or PpK's developed for them, that's all, because we know that as we talked on Day 1, the number of companies doing this is fairly low. So if you were to do something like this, it would really have to be a transition. It would be a multiyear kind of effort. So, that was really interesting. There were some things that popped up out of the discussion like that.

The other one that was really interesting was "critical investigations." Again, as you got into the specifics on definition, that term "critical," which sounds pretty easy—hey, "critical investigation"—all of a sudden, it goes about five different ways, and you really start to stumble with how you are going to define that. So the results out of that poll really said that those two were probably going to be the most difficult, and it was very interesting, because they were so—the percentages were so different for those two.

It would be a multiyear kind of effort

Then we moved on to site metrics, and we asked the same question after a long discussion. There again, there was a couple that really came out as, "Boy, these two are really, really difficult." They don't sound that difficult, but as we got into the discussion about CAPA effectiveness, how do you actually get that measure? That is a pretty tough thing to actually measure across companies. So how do you get that CAPA effectiveness? That was one where you look at it and you say, "Boy, that's going to be hard to define," and our work really proved that out today. The other one was, again, "critical investigation rate." That term "critical," where does it cut? Where does it cut for critical? We talked about, "Boy, would you have to have a list of everything that is critical," so you could say, "Okay, for all these, you would count these." It really became a good discussion. So those two were the ones that by far were looked at as the most challenging. This is not the final list of metrics or anything. This is just a good idea of—I think today's work was really great, because what it showed you was that until you actually do get to the granularity of the definition, you are not really sure which metrics are actually going to be usable. You are going to have to get to the granularity of the definition.

And then we asked some additional polling questions, and these were equally interesting. For your company, do you have one set of standard metric definitions across all of your manufacturing sites for all of your products produced? And 36% said "yes," 25% said "no", and 39% to some level. This was really a good question, because it really shows you where we are as an industry, which is we are kind of disconnected a little bit, even internally, with metrics and how we report those up through the companies. So that was a very interesting result.

…So how many metrics do you think the FDA should initially request? You look at that number three, and you realize that about 50% of the people really felt strongly that three to four metrics was probably the right area. Amazingly, there was a few people who said zero metrics. And then some wanted more than eight, which is really ambitious….

Then we asked this question about reporting frequency: "Which one do you think would be right for the products and site metrics," and again, you look at that and really the largest percentage was yearly broken down by quarter, just yearly straights, and then it fell down from there…

…Metric data submitted could be compared directly or could be trended with the trends being compared, if you had to choose one method, which do you feel would be most appropriate? And that was really interesting, because 81% really said they would like to see the trends compared and not the direct comparison of numbers, so that was an overwhelming number.

SUSAN SCHNIEPP: Our session was focused on culture, and we had about eight questions that we polled the audience on….

We asked the group to discuss what are the elements of quality culture, what are the elements of an antiquality culture, then to discuss the responsibilities of the employee in a quality culture and management in a quality culture.

And then we took off with our first polling question: "Does your organization use metrics to measure quality?" We had 93% say "yes," 5% said "no," and 2% were unsure. If they answered "yes," they were then instructed to respond to questions 2 and 3. So we were probing a little bit deeper into the quality metrics question. So, the second question was, "Did your organization experience unintended consequences when the metrics were introduced?" 58% said "yes," 26% said "no," and 16 % were unsure.

This person who got rewarded for putting out the fire was actually the one who set it

Then those people who answered "yes" to question 1 continued to answer question 3, and the question was, "How long did it take to implement the use of metrics such that you had a handle on unintended consequences and had meaningful data to compare?" And 43% said it took only one year, 42% said it took two to three years, and 17% said it was greater than three years to implement that.

Now, the people who answered "no" to question 1 were instructed to answer then on question 4: "Is your organization planning on implementing metrics in the future?" And 100% of those people said "yes."

And then we asked "how long or what is your time frame for implementing the quality metrics?" 55% said they would do it within a year, 27% said within two to three years, 9% said greater than three years, and 9% said "don't know." Now, I should clarify this is the statistics across all four discussion groups, okay?

Then we went on to discuss—we asked each group to discuss some of the elements that you find present in a quality culture. We just pulled some of the common themes from all of the groups that reported in, and No. 1, I would say is communication and transparency. There needed to be good communication and transparency between employees and management. Management commitment and engagement was No. 2, really a very clear theme across all of the groups. Technical expertise and having the confidence and the knowledge about the job that you are doing, to be able to share that expertise with management, whether they are operational or quality. Standardized criteria and requirements was thought to be so that everybody knew what was expected of them in the organization. This was kind of an interesting one, cross-functional vision, that it wasn't a departmental vision, but a vision that had to be across all of the departments, all of the sites. And that a good reward and recognition process, system program to reward the good behavior and recognize good behavior, to reinforce it across the organizations.

We then asked the group to list elements present in an antiquality culture. I called it "dysfunctional" and "anti," but a culture that didn't promote a good quality behavior. Again, overwhelmingly, pretty much across the groups, the police mentality; finger pointing; arsonist firefighting—you know, the guy who creates the problem three months before, rushes in after it turns into a blazing fire and says "I know how to solve this problem," then gets rewarded for solving the problem. But if you do the root cause analysis, you will find this person who got rewarded for putting out the fire was actually the one who set it, so that's what we described the arsonist firefighter mentality—silo mentality, fear of failure, inability to make a decision or to express your thoughts because of for fear of failure or having people perceive you as failing; and then quality reporting to operations. I guess there are still models out there where quality would report into operations, and that was considered definitely not encouraging a quality culture.

So then we moved on to our next polling question. Based on the discussion that we had about what elements were in a quality culture or in an antiquality culture, we asked the audience to tell us what kind of culture they thought they were working in. 42% indicated that they felt they were in a good quality culture; 4%, which kind of surprised me that it was so high—I really was surprised by that—said they were in a bad culture, because I consider antiquality bad culture; 53%—and I don't think this was a surprise—said that the culture was a mixture of both, there were good elements and there were poor elements within their culture; and 1% weren't sure if they were working—in what culture they were working in.

We went ahead and discussed metrics and how they helped to foster a quality culture, and some of the ideas that the group brainstormed were that it eliminates subjectivity. The metrics are visible to everyone, that it allows and helps and encourages benchmarking for improvement across sites within sites across departments. Training side by side with operational colleagues was also a

metric that people thought was very encouraging to a quality culture. It helped identify synergies between sites and across systems, and operations, it was thought was good when operations actually presented their own metrics instead of having the quality people present operational metrics.

Then we had a polling question. Based on that discussion, we asked the audience did they think the use of metrics helped to foster a quality culture. 41% said "absolutely," 54% said "usually," 1% said "no direct relation," and 1% said it "typically undermines a quality culture." And then we had 5% that weren't sure. So the majority of people were kind of on the "usually, it helps foster the quality culture."

Our last polling question—and this led to a very lively conversation. I think it was the most lively of the day: "Who is responsible for establishing the quality culture, the employee, the management, or both?" 1% said it was the employee, 38%—this surprised me—38% of the people across the group said it was management's responsibility to establish the culture, and 61% said both. And I think there was some debate on is it management's responsibility to establish the culture and then the employee's to maintain it, and that seemed to be where people split off and said—the 38% said, "But you used the word 'established,' and that to me means the management sets up the parameters which we're going to operate under..."

This transcript continues online with the February PDA Letter *podcast. This, and our other podcasts are available at www.pda.org/pdaletter.*

PDA PtC ID's Range of Useful Metrics

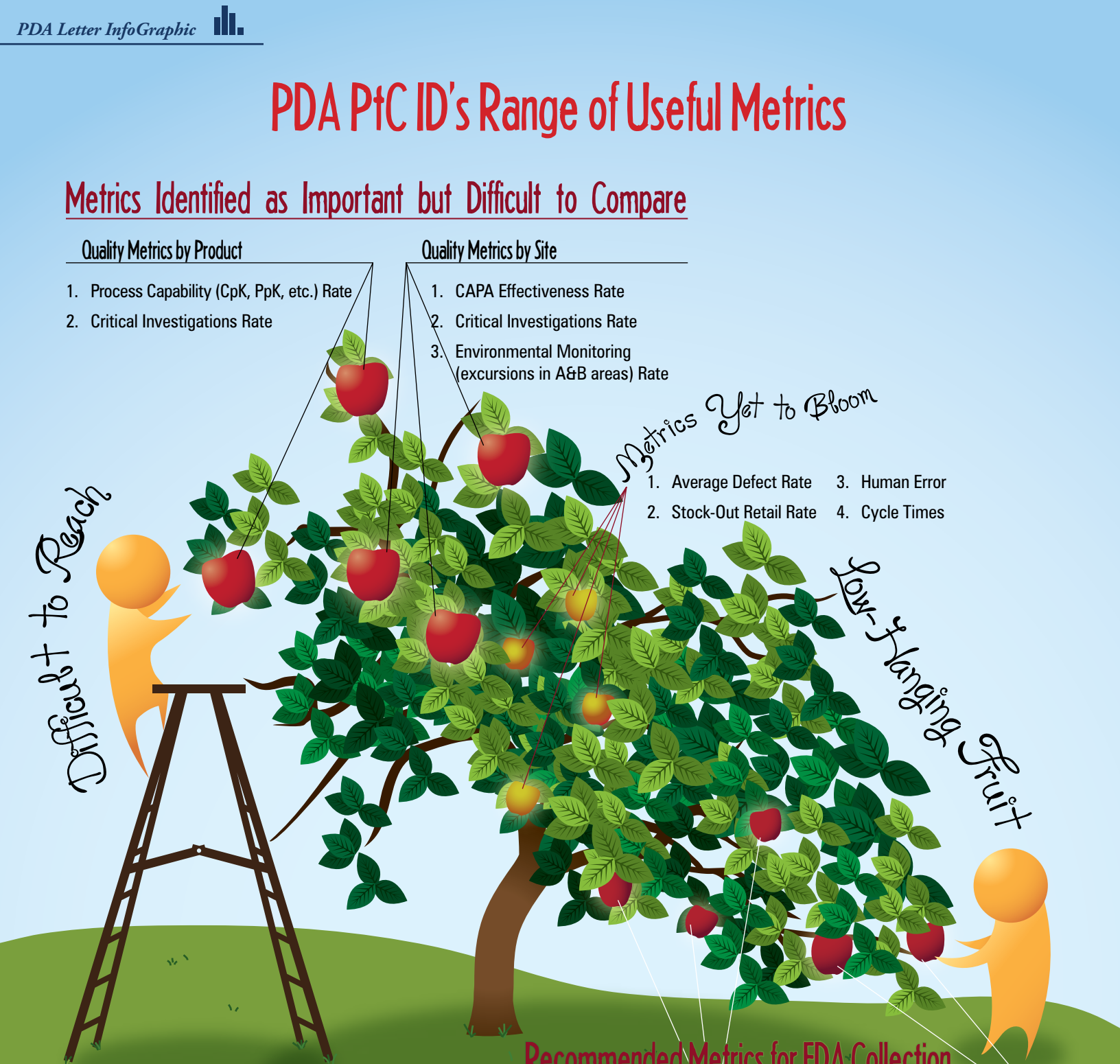
Metrics Identified as Important but Difficult to Compare

Quality Metrics by Product

1. Process Capability (CpK, PpK, etc.) Rate
2. Critical Investigations Rate

Quality Metrics by Site

1. CAPA Effectiveness Rate
2. Critical Investigations Rate
3. Environmental Monitoring (excursions in A&B areas) Rate



Metrics Yet to Bloom

1. Average Defect Rate
2. Stock-Out Retail Rate
3. Human Error
4. Cycle Times

Recommended Metrics for FDA Collection

Trend Metrics Collected per Product

1. Batch Reject Rate by Product
2. Confirmed Product Quality Complaint Rate by Product
3. Confirmed OOS Rate (Drug Substance & Drug Product) by Product

Trend Metrics Collected per Site

1. Confirmed OOS Rate (Drug Substance & Drug Product) by Site
2. Batch Reject by Site

Methodology

These metrics were developed based on breakout discussions conducted during the *2013 PDA Pharmaceutical Quality Metrics Conference,* held Dec. 9–10 in Bethesda, Md., and summarized in a Points to Consider document sent to the U.S. FDA on Dec. 13.

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- ☑ **Technical Report No. 30 (Revised 2012):** Parametric Release of Pharmaceutical and Medical Device Products Terminally Sterilized by Moist Heat
- ☑ **Technical Report No. 48:** Moist Heat Sterilizer Systems: Design, Commissioning, Operation, Qualification and Maintenance
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snapshot

Interest Group *Corner*

GMP Links to Pharmacovigilance Interest Group Pushes for Greater Physician Role in the GMP Quality System

Rebecca Stauffer, PDA

Product development requires the incorporation of clinical expertise in the assessment of safety issues, stressed **John Ayres,** MD, Sr. Medical Director, Eli Lilly, at the GMP Links to Pharmacovigilance Interest Group meeting held during the *2013 PDA Visual Inspection Forum* in early October. He emphasized the benefits that can be gained from the mutual involvement of on-staff medical experts and development teams.

"I think as a clinician in this business that there is a real opportunity to take all of the good science and the work that's been done and to bring in physicians in your businesses and to get them trained in what you do," he said. "This has to be something that physicians in our industry get engaged [with]," and added that physicians also need to "understand the portfolio in your development process."

A former practicing physician himself, Ayres was also involved in founding the interest group, which was established in 2012 for the specific purpose of facilitating clinical expertise and patient experiences into the GMP quality system, forcing companies to consider the impact of certain attributes, such as quality attributes and product attributes, on safety and efficacy.

"This forum was established, as you can see, to consider how we assess CQAs [clinical quality attributes] for their impact on safety and efficacy, evaluating these attributes through the lifecycle," he explained, pointing out the group's other goal involves communicating "to the broader pharmaceutical community and industry, the value and limitations of safety surveillance."

As an example of a safety surveillance limitation, Ayres pointed to the U.S. FDA's Adverse Event Reporting System database.

"You have to understand the limitations of that dataset relative to some of the questions that are being answered, and you can't rely wholly on that information coming through," he explained as the dataset relies heavily on waiting for an event to be reported but many events are most likely not recorded in the database. In addition, the information gained from the database is only as useful in how it is utilized.

"As you think about these attributes, you're really asking the question 'are the changes that we see over two years—how are those translated into issues that they are relative to the performance of a patient and pharmacovigilance tools for monitoring these attributes?'" Ayres said.

Returning to the pressing issue of greater physician engagement, he then explained that Eli Lilly involves clinical staff at each milestone of the development process as part of a continuous review process. At each milestone, any signs that have been picked up from assessment data are discussed and examined as far as relevance.

"I like this milestone approach, because I think that we all pause at these decision points and have a discussion around the attributes that we're seeing…we're collecting data along the way, and what I'm suggesting is that you look at your clinical data," he said.

Furthermore, each group that meets for one of the milestones uses a special tool he called an *impact score.*

"Each of those milestones has a group that gets together," Ayres said. "We're looking at these elements as well as a few others, but asking ourselves 'are we getting information here relative to this specific product?'"

For example, a high impact score might mean that the team needs to gather additional information or develop a more rigid control strategy. The impact score serves to drive discussions and result in a specific response addressing the issue.

Safety signals and pharmacovigilance was another area where Ayres felt called for greater physician involvement. According to him, adverse safety signals present the threat of being misinterpreted, resulting in loss of product, unless there was clinical input.

"What we don't want to have happen is that we put a lot of work into developing and manufacturing a drug product that has beneficial properties to patients," he said. "And you don't want to have it trashed because you start getting a safety signal that's not related to the drug product, and regulators start reacting to that, [then] *you* start reacting to that. "

Moving on to product safety assessments, he identified two types of assessments: prospective and retrospective. Retrospective safety assessments occur following a deviation, such as a product complaint or an adverse event. Prospective safety assessments involve conducting analysis and review in anticipation of an event, and for Ayres are "where I want to live, primarily because I think this gets me earlier into the product lifecyle, and it could be more anticipatory of the types of events you might want to see, and to recognize that much of what's relevant to safety is predicated on a quality culture and control strategies and capability."

But he urged audience members to continue focusing on the GMP environment, no matter the type of assessment.

"If it's GMP, keep it GMP. But try to get safety in as a proxy to make those decisions," he said, and to ask if "the changes that ➤

Volunteer Opportunities at PDA

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- Author/Contributor to the *PDA Journal*
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- Speaker
- Chapter Leader
- Task Force Member
- TRI Instructor
- Interest Group Leader

PDA Committees:

- Program Planning Committee
- Membership Committee
- PDA Letter Committee
- Education Committee
- Audit Committee

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- Interest Group Member
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we make in our manufacturing environment, whether it's a site change or a change control, is it really having any impact downstream on the patient?"

During the Q&A following his presentation, Ayres addressed how a company could engage physicians during the development process.

"I think that you have to be patient with your physicians," he admitted. "This is an emerging process. I think it's a two or three year process. And you just have to get them at the table."

Additionally, he emphasized the fact that physicians who can write well are a prime asset as they will need to draft various assessment reports.

Ultimately, the interest group plans to explore additional ways companies can elevate the role of physicians in pharmacovigilance. Other topics to be addressed by the interest group include extraneous particulate matter assessments, data mining methods and utility, manufacturing investigations for adverse events, portfolio risk assessments to prevent counterfeiting, clinical assessments and the design space, and the impact of pharmacovigilance legislation on quality.

Ayres stressed that the interest group will continue to push to facilitate expansion of medical expertise in the pharmacovigilance lifecycle.

"This has to be something that physicians in our industry get engaged and understand the portfolio in your development process," he stressed. "The FDA and the EMA, they can't police this...this is a self-regulated industry…and it's up to us to put these systems in place and demonstrate we're on the same page as they are."

If you are interested in joining the GMP Links to Pharmacovigilance Interest Group, please contact PDA's Volunteer Coordinator at volunteer@pda.org.

[Editor's Note: See Ayres' remarks about CDER Director **Janet Woodcock's** presentation at the *2013 PDA/FDA Joint Regulatory Conference* on p. 42.**]**

About the Expert

John Ayres, MD, serves as the Health Hazard Evaluation physician and Sr. Director, Product Safety Assessments for Eli Lilly. In this role, he works closely with the company's development functions, manufacturing, quality, and pharmacoviligance to evaluate the human safety risk potentially associated with product quality attributes, manufacturing deviations, linked to product complaints, or related to anticounterfeit medication issues.

Report from the 2013 PDA/FDA Joint Regulatory Conference

Drug Shortage Issue, Solutions Highlighted

Allen Jacques, Pfizer, with Rebecca Stauffer, PDA

In 2013, the drug shortage issue served as a major topic for both industry and regulatory following publication of an article in *Clinical Pharmacology & Therapeutics* outlining the link between manufacturing quality and drug shortages ***(1).*** At the start of a new year, the issue shows no chance of dying down and many within industry and regulatory continue to look for possible solutions.

At the *2013 PDA/FDA Joint Regulatory Conference* in Washington, D.C., **Allen Jacques,** VP, Network Planning, Pfizer, offered an industry perspective on the issue. **Marta Wosinska,** PhD, Director for Economics Staff, CDER, U.S. FDA, one of the authors behind the article, provided her perspective on the topic.

Jacques started his talk by explaining the complex nature of global pharmaceutical supply chains due to the number of products, product configurations, and different stages of manufacturing. This, combined with customer demand volatility, manufacturing supply variability, capacity constraints and a complex regulatory environment, results in a challenging environment for ensuring product supply. For this reason, Pfizer has established robust Sales and Operations Planning (S&OP) processes to ensure a comprehensive understanding and modeling of these variables in optimizing supply chain output and meeting customer demand. This also enables the ability to predict supply capabilities and proactively identify and mitigate future supply gaps. This is a key first step in preventing drug shortages and triggering agency notifications when mitigation isn't possible.

He then described the transition from S&OP to their Drug Shortage Review Team which assesses probable future supply outages and makes determinations on agency notifications. Once a determination to notify has been made, a Rapid Response Team is formed that consists of a regulatory specialist, supply chain expert, and regulatory representatives from all impacted markets. This team is responsible for global messaging and regular follow up until a shortage is closed.

Next, Jacques gave an example from two years ago when Pfizer's demand for aseptic oncology products increased by 30% above capacity due to competitor supply issues. This example demonstrated their ability to increase capacity and fill this gap but also showed the long lead time involved due to tech transfer, validation, filling and approval lead times. ➤

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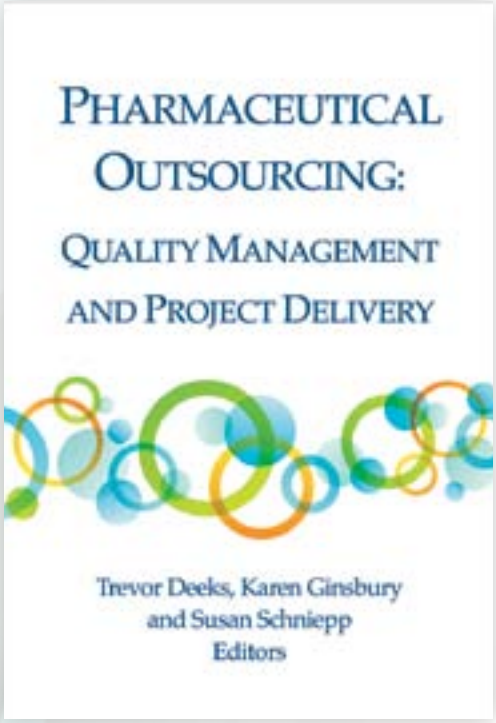

Item No. 17316

Pharmaceutical Outsourcing: Quality Management and Project Delivery

Edited by Trevor Deeks, Karen Ginsbury and Susan Schniepp

Many companies are looking to contract providers for managing various aspects of the drug development process. Contract organizations have services that range from research activities to clinical trial management and oversight to manufacturing of the clinical supplies and commercial product to packaging and labeling as well as product testing. Virtual companies may have multiple contracts with multiple service providers for multiple phases of the drug development process and the drug manufacturing process. To complicate the matter, there is little guidance from regulatory authorities regarding the use of contract providers. This book is intended to set forth and explore the best practices for contract organizations from various perspectives: the contract organization, the contracting organization and the regulators.

www.pda.org/outsourcing

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Item No. 17951

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3 Microbial Identification: The Keys to a Successful Program (single user digital version)
Edited by Dona Reber and Mary Griffin
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He then concluded with the following key areas on how drug shortages can be prevented:

- High service level targets with inventory to buffer demand and supply variability
- Forward-looking, robust S&OP processes
- Cross-licensing of API, drug substance and drug product sites to provide sourcing flexibility
- Internal and external redundant capacity
- Robust internal manufacturing and quality processes
- Robust contractor selection and quality control processes
- Capacity investments in known areas of risk, e.g., sterile injectables

Following Jacques' presentation, Wosinska offered a regulatory overview. She pointed out that of all the drugs involved in shortages, sterile injectables have comprised the majority of shortages since 2010. Wosinska defined the FDA's definition of a shortage as a situation where "total supply of all clinically interchangeable versions of an FDA-related drug is inadequate to meet the current or projected demand," and emphasized that the Agency primarily focuses on shortages of medically necessary products with a significant impact on public health.

Ultimately, two things happen before a shortage: one or more manufacturers cease or slow down production, and other manufacturers lack the capability to make up for lost production.

She further described the layered causes of drug shortages. Lack of incentives results in quality problems that lead to supply disruptions which lead to shortages. Magnifying the issue, the sterile injectable market is highly concentrated with just seven firms controlling the U.S. generics market. Contract manufacturing adds to this concentration as some branded products are made by facilities with a large portfolio of generics.

A related issue, Wosinska cited, is that the facilities manufacturing these products are highly specialized. This concentration of dedicated production lines can result in storage clusters. Even more challenging, manufacturers have little backup capacity—less than 2% of sterile injectable ANDAs list more than one facility in the application.

She then pointed out that FDA's authority on the matter is limited, although the Agency requires early notification if companies plan to temporarily or permanently discontinue products, preferably six months in advance. Early notification has greatly helped limit shortages by allowing time to coordinate a response. And, as of the passing of the Food and Drug Administration Safety and Innovation Act (FDASIA) in 2012, early notification is law.

But early notification does not address the manufacturing problems that cause disruptions in drug supply. This is important as the end users of the product cannot make the connection between issues with the product and sterility problems. In fact, many assume that the manufacturing processes in place produce reliable quality products.

Wosinska theorizes that FDA's focus on both safety and access of medication makes it harder to enforce quality. If there was no such regulatory flexibility, then economic theory indicates that manufacturers would attempt to improve drug quality. Yet safety and access are important as well. The Agency is currently evaluating strategies for incentivizing quality, including reorganizing CDER to include an office dedicated to manufacturing quality, development of standardized quality metrics and publicly recognizing quality improvements by manufacturers.

In fact, several weeks after her presentation, the Agency released its Strategic Plan for tackling the drug shortage issue ***(2).*** This strategic plan includes the following tasks outlined for the Agency: streamlining internal processes, improving data and response tracking, clarifying the roles and responsibilities of manufacturers, enhancing public communication about drug shortages, developing methods for incentivizing and prioritizing manufacturing quality, using regulatory science to identify early signs of an impending shortage and developing new strategies to address the issue.

In the end reducing the number of drugs in shortage will require a partnership between industry and regulatory working together to address the quality issues that result in shortages of drugs.

[Editor's Note: PDA will host a breakfast roundtable session on drug shortages at the *2014 PDA Annual Meeting* on April 9. To learn more, visit www.pdaannualmeeting.org.**]**

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2. Strategic Plan for Preventing and Mitigating Drug Shortages, U.S. Food and Drug Administration: October 2013 www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf

About the Author

In 2010, **Allen Jacques** assumed the role of Vice President of Network Planning for Pfizer and leads a team that is responsible for the production and capacity planning for Pfizer's manufacturing network, meeting Pfizer's global customer requirements, and issuing identification and mitigation via S&OP processes.

Quality Culture: An Opportunity for Patient-Focused Paradigms

John D. Ayres, MD, Eli Lilly

During the past decade, considerable work involving regulators and pharmaceutical scientists resulted in the adoption of guidance documents for pharmaceutical development, quality risk management and pharmaceutical quality (ICH Q8–10). These provide for a structured way to define product critical quality attributes, the design space, manufacturing process and relevant control strategy. With these foundational underpinnings, scientists and regulators are afforded a common environment where the infrastructure necessary to assure quality predictive drug substance and product can be developed and assessed. Building on these concepts at the *2013 PDA/FDA Joint Regulatory Conference* in Washington, D.C. in September, U.S. FDA CDER Director **Janet Woodcock,** MD, challenged industry and regulators to take the next "big step forward" and identify "clinically relevant" attributes, and fashion the design space, control strategies and quality systems needed to deliver the next generation of pharmaceutical and biologic therapeutic products to patients in need.

Woodcock noted that many of the current registered product specifications have no direct link to the patient and wondered if those attributes should be identified as "specifications," or even "quality attributes," or if they simply take a different place within the control strategy. This might include, for example, a parameter where a greater range of variability could be permitted—reducing the resources that would be necessary to otherwise control that parameter—as long as that variability did not impact the product's attributes in a clinically relevant manner.

You can access a video of Janet Woodcock's talk at the *2013 PDA/FDA Joint Regulatory Conference* on PDA's YouTube page here: y2u.be/KzUs14UiGdM.

Among the additional points that Woodcock made in her talk, a few stand out. First, she reiterated that one of CDER's goals is that "high quality medicines be produced without excessive regulatory oversight." But in order to achieve that goal, she pointed out, both industry and regulators will need

to create new archetypes. For the pharmaceutical industry, that means moving from fragmented quality systems in their organizations to a "culture of quality" where each component is fully focused on providing the highest possible quality product to the customer: the health care provider and patient. She indicated that one important aspect of the process must involve eliminating "never events" such as repackaging errors that find toxic substances relabeled as innocuous consumer products or shortages of essential lifesaving drug products. In a "culture of quality," failure modes, or manners in which product or supply might be adversely impacted, will have been proactively identified, and control strategies and systems adopted to prevent their occurrence. In addition, "in-use" assessments should be conducted to ascertain the impact of end user interaction with the product and design or other changes initiated as appropriate, if product impact is identified.

For regulators, Woodcock reiterated that it is essentially a change in focus from individual events such as deviations, recalls or complaints to metrics-based surveillance. The approach will permit a more comprehensive assessment of performance and serve as a better determinant that an organization operates within a "quality culture." The importance of this shift to metrics-based assessments, she explained, is that "a culture of quality is the most important determinant that quality product gets to the patient." **[Editor's Note:** For an overview of PDA's *Pharmaceutical Quality Metrics Conference,* please see p. 22.**]**

Ultimately, it is the pharmaceutical company that is responsible for quality. As a result, FDA shall evaluate a company's performance in conjunction with the quality culture it has established. If quality is part of the company's DNA then its actions will all be customer-focused through the product lifecycle from discovery and development through commercialization and continuous monitoring of both product quality and patient experiences.

The evolutionary process of moving from compliance—the low bar—to a culture of quality will certainly have its bumps and probably more questions than answers as that first "big step forward" is taken. But the prospect afforded to make the highest quality product available to health care providers and patients will, in Woodcock's words, be "well worth the effort."

The opportunities for both industry and regulators embedded in this challenge in addition to other timely issues will be explored at the *2014 PDA/FDA Joint Regulatory Conference.* This event will provide an excellent chance to offer one's input and hear industry and regulatory leaders discuss their perspectives on these important matters of interest.

[Editor's Note: Please see p. 38 for the "About the Author."**]**

PDA Chair Harold Baseman, ValSource

Chair's Message

As we enter 2014 and consider the challenges another year brings, it is difficult not to reflect on the accomplishments of the past year. 2013 was truly a remarkable year for the Parenteral Drug Association. While other industry associations struggled with declining membership, smaller conference attendance, reduced output and lowered expectations—PDA continued its upward trend.

PDA conducted more than 20 conferences in the United States and Europe. Highlights included another successful Annual Meeting in Orlando, Fla. in April and the *PDA/FDA Joint Regulatory Conference* in September, which broke attendance and revenue records. This record was quickly overtaken by PDA's largest event to date—the *Universe of Pre-filled Syringes and Injection Devices* meeting held in Basil, Switzerland in November. Attendance and revenue, however, are not the primary goals. PDA's mission is about *connecting People, Science, and Regulation*©. To that end, PDA hosted several very important interactive meetings and workshops between regulators and industry, in an effort to spotlight areas where we could work together for the good of the public health.

2013 was also a banner year for the PDA Training and Research Institute. TRI conducted over 60 lecture and hands-on laboratory courses at the TRI facility in Bethesda, Md. and in conjunction with major PDA conferences as well as training programs at company sites. After capital improvements to the Bethesda facility, TRI rolled out a series of new aseptic processing courses which build on its renowned two-week, hands-on aseptic training course.

Continuing on ways to disperse information, and connect industry, PDA published a record number of technical reports, including milestone efforts on process validation, quality risk management and glass defects. PDA technical reports are written by volunteer industry and regulatory experts. They are carefully vetted and meticulously prepared. The *PDA Journal of Pharmaceutical Science and Technology,* the *PDA Letter,* and PDA-sanctioned books continued to be hallmarks of the industry.

PDA moved forward on its Strategic Plan, including the establishment of new U.S. and global chapters, meetings in China and Japan, outreach to both emerging and European markets, and education strategies. PDA's European operations had its best year ever, emphasizing the importance of maintaining PDA as a global association. At the headquarters, the PDA continued investing in member services by implementing new internal management systems, designed to better address member needs.

The reason for the success of PDA can be summed up in three words: staff, volunteers and members. From the executive and senior staff, to the managers, to the rest of the staff for their extensive support, the PDA staff works tirelessly to serve members.

The PDA is a volunteer-driven organization, boasting over 1,000 volunteers working as interest group leaders, task force contributors, advisory board members, chapter officers, planning committees, etc. I would like to highlight the work of two volunteer groups in particular. The first are the advisory boards, the SAB (Science Advisory Board), the BioAB (Biotech Advisory Board), and the RAQAB (Regulatory Affairs and Quality Advisory Board). These volunteers have a truly unique position in our industry. They advise the PDA Board of Directors on matters related to two of our core values—Science and Regulation. All technical reports, bulletins, surveys, PDA position papers and regulatory comments are coordinated and vetted by one or more of these groups. As a member of the Board, when I see advisory board approval, I am confident in our position and you should be too.

The second volunteer group I want to single out is the Board of Directors. I have never sat on a Board with more of a strategic sense and purpose. The past Board Chairs that I have had the privilege to serve under have done a phenomenal job of doing what was needed to stabilize the organization. I want to thank those Chairs, as well as Board members leaving the Board, new Board members, and remaining members for all they have done, will do, and are continuing to do. I want to also take this opportunity to thank our good friends **Sue Schniepp** and **Steve Mendivil** for their service to the Board, welcome **Joyce Bloomfield** and welcome back **Veronique Davoust** and **Martin VanTrieste,** and especially thank **Anders Vinther** for his leadership these past two years.

This brings us to the final group, you, our members. There is no PDA without you. You set PDA's course and its path for the future.

And now a word about 2014. What will we see in the coming year? My opinion is that we are likely to see more globalization, more technological advances, a continuation of the return to science and risk-based decision making, a sound working partnership with global regulators, a need for education, a focus on manufacturing excellence, and the emergence of the next generation of leaders.

Where does this leave the PDA? It leaves us right where we belong. Serving you, our members. Thank you. I wish you a happy, healthy, prosperous 2014 and I hope to see you soon.

PDA President Richard Johnson

President's Message: Reflections and Forecasts

It has been my honor to serve as President for PDA for these past several years, and many of the efforts begun since I started have come to fruition. 2013 was a year of several major accomplishments, and I will only scratch the surface by listing some of them. Like everything we do, they can be organized in terms of *People, Science, and Regulation*©:

People

In 2013, PDA increased membership for the fourth straight year, and saw record levels of participation and attendance. We expanded the PDA community with new chapters in India and Singapore, and have begun working with our partners in Russia on a training facility. Several of our events set new records in terms of attendance, but most gratifying to us is the level of satisfaction with the quality of the events. Everyone at PDA is focused on performing at the highest level of quality for you, our members. For all of you, who sent messages of appreciation and thanks for the quality of our activities, let me thank you on behalf of the PDA staff. We are highly aware that the quality of our events begins with the volunteers who contribute their innovation, expertise and enthusiasm.

Science

PDA published more technical reports in 2013 than in any year of PDA's history. While this is significant, what is more significant is the continued high quality of the documents that our volunteers have produced. We have also established a pipeline of projects that promises to keep our output at this level. Our members, and the industry as a whole, benefit from this sharing of best practices, and everywhere I go in the world I hear how valuable these technical reports are to industry and regulators.

Regulation

PDA has a long history of working to help regulators develop the best guidance and bring their message to the industry. PDA also serves as an independent voice in helping clarify difficult issues. In 2013, we continued this tradition with a record number of regulatory comments for regulators around the world. Working with various regulators, we hosted several meetings that helped to advance understanding, including the *PDA/FDA Joint Regulatory Conference,* the *PDA/FDA Improving Investigations Workshop,* and the *Pharmaceutical Quality Metrics Conference.* We also had meetings with the CFDA in China, PIC/S and the Irish Medicines Board.

The *Pharmaceutical Quality Metrics Conference* in December was extremely successful, with more than 300 attendees actively participating in the discussion. From their feedback, PDA completed our Points to Consider document on quality metrics in December. Let me offer special thanks to the Committee and participants for their efforts (see story on p. 22).

In 2014, we will continue this momentum across all of our activities, with a focus on our strategic plan initiatives. We will continue to improve our member benefits with new tools for communication and collaboration among members, and enhancing the volunteer experience.

PDA will continue to "connect People, Science and Regulation" through our conferences and workshops worldwide, including

- The 68th *PDA Annual Meeting* in San Antonio, Texas April 7–10
- New collaboration with INTERPHEX in New York, N.Y. March 18–20 and Puerto Rico October 16–17
- The *Universe of Prefilled Syringes and Injection Devices* conference in Huntington, Calif. November 6–8
- Key regulatory conferences, including the *PDA/FDA Joint Regulatory Conference* as well as meetings on PIC/S Q7 training, QbD and drug shortages
- More than 20 large and small events

We will be expanding our training to industry and regulators worldwide, building on our prominence in aseptic processing and our growing portfolio in quality systems.

We will continue expanding our portfolio of technical reports that are leading the way to practical science-based implementation of technologies and quality systems, including new topics like *Bioburden and Biofilms* and *Comparison of Global Sterile GMPs*.

2013 can be summed up as the most successful year in PDA's history, with higher attendance, more members, and record number of publications. With your participation, 2014 promises to continue this effort. Please join us in connecting People, Science and Regulation©.

PDA Makes the Connections!

Okay, I won't say what the connections are, because you see it on all PDA materials, but we did it again and, as often is the case, with tremendous results. Of course I'm talking about PDA's response to the U.S. FDA's call for suggestions on pharmaceutical quality metrics. Just as in previous instances when PDA stepped up to help with regulatory initiatives, such as the roll out of ICH Q7 or revising aseptic processing guidance, PDA was able to deftly recognize, organize and connect those members of our community with the right expertise in quality metrics/systems, etc., with the FDA officials developing the latest compliance initiative. Those experts not only responded to the initial *Federal Register* announcement, but they identified a need to develop a more extensive report and pull in the opinions of other experts in the field.

The results are ongoing, but so far, it produced a jam-packed quality metrics workshop, an informative Points to Consider (PtC) report for FDA and plans for ongoing work in 2014. Oh, yeah, and all the feature content in the February *PDA Letter.* Besides the cover story on the conference and the PtC, we've included a transcript of the breakout session "readouts," delivered by members of the PDA metrics committee, who also doubled as session facilitators, and we dissect the PtC in the issue's Infographic.

Mentioning the Infographic reminds me to commend the incisive and intelligent feedback we received in creating the issue's cover and Infographic by the members of the *PDA Letter* Editorial Committee Art Subcommittee. The group really helped and challenged us in our effort to visualize abstract concepts. I'm not sure we met all of their expectations, but in the end, we are confident that our designs (well, **Katja Yount's** designs) are more to the mark because of their help. We also extended our outreach to a few members of the metrics committee.

Finally, the metrics conference provides us the perfect *PDA Letter* Podcast for February. If you don't feel like reading the transcripts, you can hear the unadulterated remarks from each speaker online.

If you miss the programming section and the TRI section, don't fret. Those articles are getting beefed up with more science and regulatory information to truly drive home the value of PDA's offerings. You now can find information on PDA meetings and courses in the Science, Regulatory and Features sections of each issue.

I really enjoyed working on this month's issue. I hope you enjoy reading it!

PDA Letter

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Manufacturing of the Future

This year´s conference will particularly address burning topics relevant to a fast changing and highly regulated environment such as Dedicated Facilities, Continuous Processing, Multi-Product-Lines as well as Flexible and Single-Use Factories. Practical approaches to the challenges in development and manufacturing of biopharmaceutically and biotechnologically derived products in the current GMP environment, and Quality by Design perspectives will also be discussed.

The rapidly evolving international environment in which biopharmaceutical industry is working confronts us with new challenges daily. Innovations and new developments offer solutions to some of these challenges.

A host of international experts will share their experiences by presenting the latest practices, methods and Case Studies associated with the industrial development and production of vaccines & biopharmaceuticals. Risk Management concepts applied to these new technologies and innovative operations will be discussed as well.

If you are operating in the biopharmaceutical business, whether in a large or small firm, this annual international survey of current best practices makes for the ideal lead into 2014, and an opportunity to network with opinion leaders and experts in these fields.

There will be plenty of time for questions and discussion, making for a very interactive and fruitful meeting.

We will be pleased to meet you in March 2014, and would also like to take this opportunity to celebrate the 10th anniversary of the French PDA Chapter.

Jean-Luc Clavelin, *Co-Chair, Consultant*
Christophe Grimm, *Co-Chair, Sartorius Stedim Biotech*

25-26 March 2014
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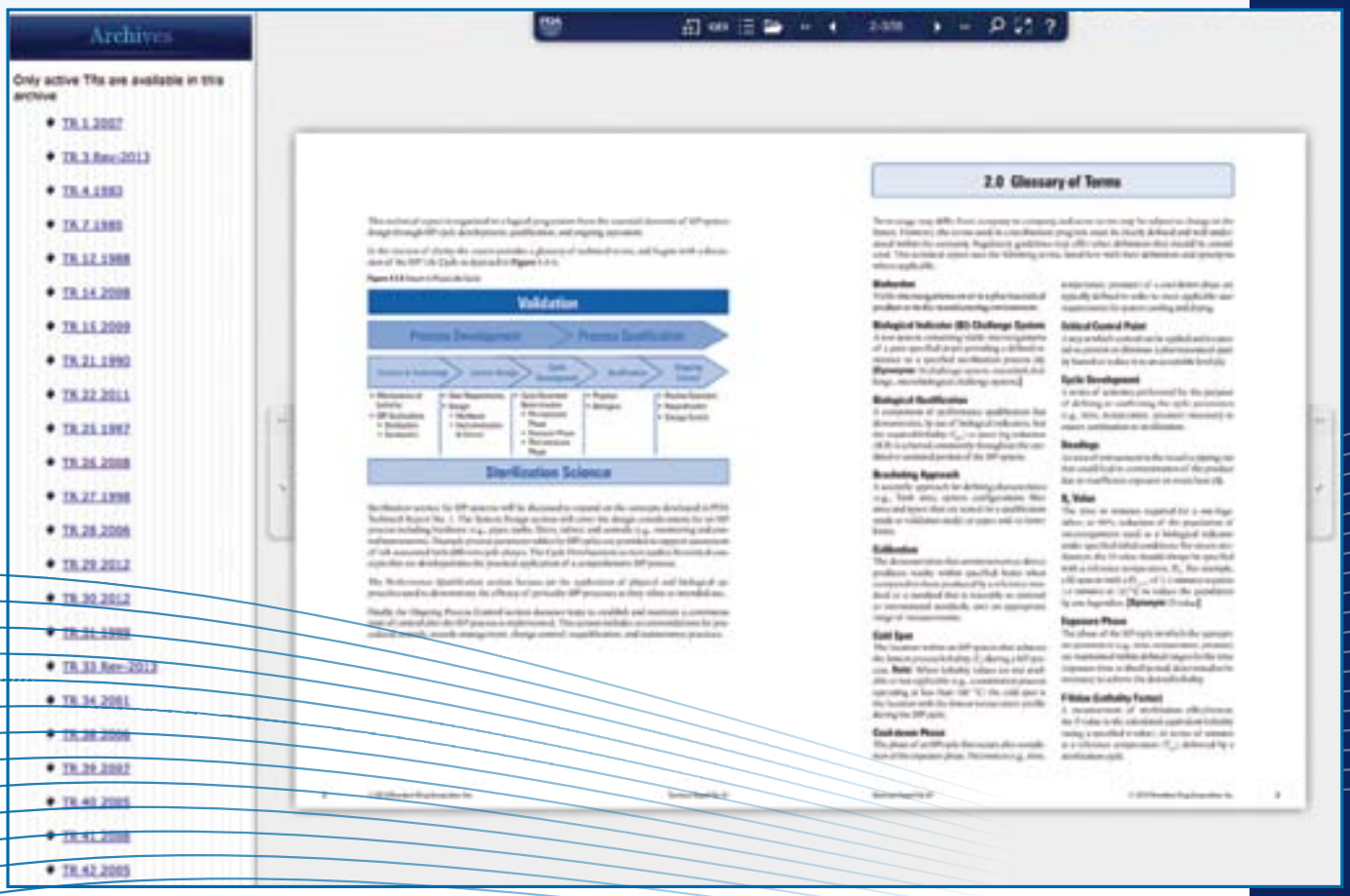

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