People • Science • Regulation

PDA Letter

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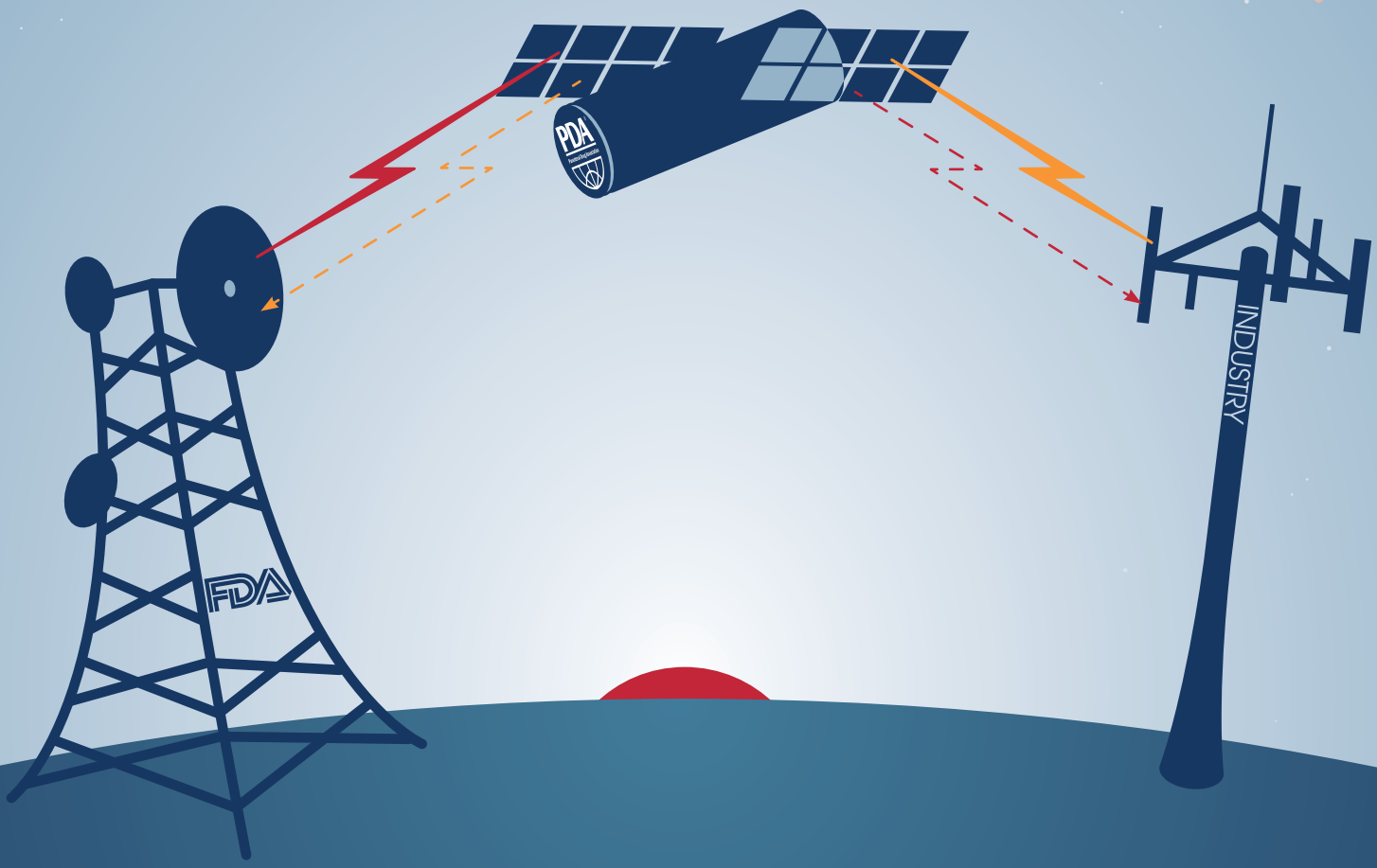

Keeping the Signals Clear:

Industry and FDA Collaborate on Innovation

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2015 PDA U.S. Continuing Education Courses

Save the Date for PDA's 2015 Courses

Check **www.pda.org/calendar** for an updated list of courses

Denotes Laboratory Courses

DATES	COURSE NAME	LOCATION
1/26 – 1/30 2/23 – 2/27	Aseptic Processing Training Program, Session 1	Bethesda, MD
2/9 – 2/13	Glass Quality, Visual Inspection and Foreign Material Identification Week	Bethesda, MD
3/9 – 3/13	Fundamentals of Aseptic Programming	Bethesda, MD
3/19 – 3/20	2015 PDA Annual Meeting Course Series	Las Vegas, NV
3/23 – 3/27 4/13 – 4/17	Aseptic Processing Training Program, Session 2	Bethesda, MD
4/7 – 4/8	Airflow Visualization Techniques and Practices	Bethesda, MD
4/20 – 4/23	Train the Trainer Week	Bethesda, MD
4/27 – 4/29	Validation of Biotechnology-related Cleaning Processes	Bethesda, MD
4/29 – 4/30	2015 PDA Aseptic Processing/Sterilization Course Series	TBD
5/11 – 5/12	Recommended Practices for Manual Aseptic Processing	Bethesda, MD
5/18 – 5/22 6/15 – 6/19	Aseptic Processing Training Program, Session 3	Bethesda, MD
5/20 – 5/21	2015 PDA Packaging Course Series	Washington, DC
5/22	Technical Development of Prefilled Syringes, Autoinjectors and Injection Pens	Washington, DC
5/27 – 5/28	Syringes and Elastomers: Understanding the Effects on Quality and Demonstrating the Production Process, Influences and Needs	Bethesda, MD
6/1 – 6/3	Management of Aseptic Processing	Bethesda, MD
6/9 – 6/10	Fundamentals of Cleaning and Disinfectant Programs for Aseptic Manufacturing Facilities	Bethesda, MD
6/11 – 6/12	PDA Pharmaceutical Supply Chain Course	Bethesda, MD
6/25 – 6/26	Assessing Packaging and Processing Extractables/Leachables	Washington, DC
7/21 – 7/23	Moist Heat Sterilization Week	Bethesda, MD
7/27 – 7/29	Risk-Based Qualification of Sterile Drug Produce Manufacturing Systems	Bethesda, MD
8/3 – 8/7 8/24 – 8/28	Aseptic Processing Training Program, Session 4	Bethesda, MD
8/12 – 8/14	Dry Heat Processes Used for Sterilization and Depyrogenation	Bethesda, MD
8/17 – 8/20	GMP Week	Bethesda, MD
9/2 – 9/3	Single Use Systems for the Manufacturing of Parenteral Products	Bethesda, MD
9/9 – 9/10	Fundamentals of an Environmental Monitoring Program	Bethesda, MD
9/22	Utilization of Statistical Methods for Production Monitoring	Bethesda, MD
10/12 – 10/16	Filtration Week	Bethesda, MD
10/19 – 10/21	PDA 10th Annual Global Conference on Pharmaceutical Microbiology Course Series	Bethesda, MD
10/21 – 10/23	Validation of Moist Heat Sterilization Processes	Bethesda, MD
10/26 – 10/27	2015 PDA Visual Inspection Forum	Bethesda, MD
10/28 – 10/29	An Introduction to Visual Inspection	Bethesda, MD
11/9 – 11/13	Quality Risk Management Week	Bethesda, MD
11/16 – 11/20	Quality Systems for Aseptic Processing	Bethesda, MD
12/1 – 12/4	Lyophilization Week	Bethesda, MD
12/7 – 12/11	Fundamentals of Aseptic Processing	Bethesda, MD

The Parenteral Drug Association presents the...

2015 PDA Annual Meeting

Manufacturing Innovation and Efficiency: Achieving Quality Performance in Sterile and Biopharmaceutical Operations

March 16-18, 2015
Red Rock Casino, Resort and Spa, Las Vegas, NV

The *2015 PDA Annual Meeting* is **the** most important conference to attend to gain the latest and most comprehensive information about traditional and biopharmaceutical science, manufacturing technology, quality and evolving regulations.

This year's theme, **Manufacturing Innovation and Efficiency: Achieving Quality Performance in Sterile and Biopharmaceutical Operations** is specifically focused on the challenges our industry faces as the manufacturing and regulatory environments continue to change.

At this meeting, you will hear from experts in manufacturing human error prevention, lean six sigma, process validation, manufacturing control strategies, quality metrics, track and trace, supply chain, drug shortage and global regulatory submission planning along with many other important topics. Leading industry experts will address today's manufacturing challenges through sessions focusing on Changing Manufacturing – Fulfilling Future Treatment Options and Financial Necessities, Fulfilling Future Treatment Options and Financial Necessities, The Importance of Science & Technology to Building A Quality Culture, Flexible Manufacturing – Current Solutions and Future Visions, and Biosimilars on the Doorstep – Challenges and Opportunities.

Highlights of this year's meeting include:

- 2.5 days, 15 concurrent sessions over 3 tracks
- 14 interest group meetings
- The ***2015 PDA Aging Facilities Workshop*** hosted immediately following the conference on March 18-19, 2015
- PDA TRI Courses hosted in conjunction with the conference on March 19-20, 2015
- And much more

For details and to register, visit

pdaannualmeeting.org

#PDAAnnual

Exhibition: March 16-17 Post-Conference Workshop: March 18-19 Courses: March 19-20

PDA Letter

Volume L • Issue 10 www.pda.org/pdaletter

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Cover Art Illustrated by Katja Yount

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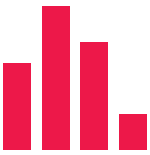

PDA TRI Thanks Summer Intern

The PDA Training and Research Institute wants to thank **Jocelyn Belmonte** for her hard work as the 2014 summer intern. Jocelyn is a student at Montgomery College in Maryland.

Jocelyn was most helpful assisting in the hands-on TRI laboratories and cleanroom, where she helped with the preparation of materials and equipment for TRI laboratory education courses.

Jocelyn was a huge help by performing a variety of administrative duties, including printing course notes and materials for students, preparing registrar reports and attendee badges, etc., and uploading course information to the website.

On her time here at PDA, Jocelyn said:

"Not having knowledge of the equipment used in the laboratories at the Training and Research facility made this internship a journey."

Attention PDA Bookworms!

Vote for your favorite 2014 PDA/DHI Technical Book at www.pda.org/2014authorsurvey. The author or editor that receives the most votes will win the PDA/DHI Technical Books Distinguished Editor/Author Award, which will be presented at the *2015 PDA Annual Meeting.*

PDA Defines 4 Pharma Quality Metrics

PDA's Pharmaceutical Quality Metrics Task Force has updated and published definitions for four key quality metrics in an updated version of its "Points to Consider: Pharmaceutical Quality Metrics," which was first posted on the PDA website in December 2013.

The definitions include the recommended methodology to calculate and report each specific metric. The metrics defined are:

- Product Quality Complaint Rate by Product
- Batch Reject Rate by Site
- Confirmed OOS Rate by Product/ Site
- Recalls by Product and Site

The paper, published in the September/October issue of the *PDA Journal of Pharmaceutical Science and Technology* (tinyurl.com/ljdrdq3), is free to the public.

The authors and contributors to the quality metrics points to consider paper are:

Steven Mendivil, Task Force Co-Chair, Amgen

Joyce Bloomfield, Task Force Co-Chair, Merck & Co.

Vince Anicetti, Coherus Biosciences

Denyse Baker, PDA

Ian Elvins, Elvins & Associates

John Farris, Amgen

Gabriele Gori, Novartis Vaccines

Robert Kieffer, RGK Consulting

Marty Nealey, Hospira

Pritesh Patel, Allergan

Anil Sawant, Johnson & Johnson

Susan Schniepp, Allergy Laboratories

Anders Vinther, Sanofi Pasteur

Glenn Wright, Eli Lilly and Company

Emer Cooke, the Head of International Affairs at the European Medicines Agency, and **Janet Woodcock,** the Director of the U.S. FDA Center for Drug Evaluation and Research, are featured speakers at the *2014 PDA Pharmaceutical Quality Metrics Conference.* More information on the workshop can be found at www.pda.org/metrics2014.

Education Advisory Board Launches; Other TRI Highlights

Bob Dana, PDA

As 2014 draws to a close, I want to give you an update on what's happening with PDA's education programs.

First of all, we are concluding another successful year for PDA education. We will have taught more than 1,250 students in over 70 courses offered in the United States this year. Our courses were offered in conjunction with every U.S. conference, at PDA's Training and Research Institute in Bethesda, Md. and in-house at several companies. We delivered three training courses exclusively for U.S. FDA personnel this year: one on aseptic processing and two separate sessions for Office of Regulatory Affairs field investigators covering aseptic processing, environmental monitoring, filtration and particulate matter/visual inspection. The student evaluations for all the training courses we conducted were overwhelmingly positive, which is a testimony to the excellence and professionalism of the more than 70 volunteers who taught courses for us in 2014.

Another highlight of the year was completing the process of having select training courses listed for availability to government employees under the provisions of the General Services Administration (GSA). Under this program, PDA offers prequalified courses and pricing to government employees to minimize the potential for contracting issues and maximize the opportunity for government employees to obtain required internal approvals to attend a qualified PDA course. The rigorous requirements we successfully met to obtain GSA listing speak to the quality and value offered by our education courses.

We continue to offer a number of courses based on PDA's technical reports. There were 29 such PDA-owned courses offered in 2014, all taught by instructors who were actively involved in the preparation of the technical reports. This arrangement gave students special insights into the logic and rationale behind the subject matter and provided a learning opportunity only available through PDA.

A significant development relative to PDA's education programs took place in September with the first ever meeting of the PDA Education Advisory Board

A significant development relative to PDA's education programs took place in September with the first ever meeting of the PDA Education Advisory Board (EAB). This Board is led by PDA instructors **Edward Trappler,** Lyophilization Technology, and **Brent Watkins**, Veltek Associates while I serve as the PDA staff liaison to this Advisory Board. The EAB will provide support for PDA's global education programs by advising on strategic plans and initiatives, and providing guidance on how to best position these programs to meet the new and challenging issues facing our industry. EAB is already in the process of reviewing the Education Strategic Plan which was presented to the PDA Board of Directors with a view toward making some specific recommendations.

And speaking of global education, the plan to achieve greater harmonization between the European and U.S. education programs is well underway. Several of the PDA-owned courses have been delivered in Europe and much of the "back-of-the-house" documentation used by both Europe and the U.S. has already been integrated.

Rebranding of our education programs is underway as well. As 2015 unfolds, look for many more references to *PDA Continuing Education* and fewer references to "European education" and "TRI courses." TRI is, of course, the acronym referencing the PDA Training and Research Institute in Bethesda, Md. TRI is a brick-and-mortar facility and it's one of the places where PDA's education programs are delivered. We are looking forward to a fully integrated education approach in 2015.

PDA's education department continues to be well served by our dedicated and loyal staff. Longtime employees **Stephanie Ko**, **James Wamsley** and myself were joined in 2014 by our new Coordinator of Laboratory Education, **Kim McIntire**. Kim is a recent graduate of the University of Maryland with a B.S. degree in Physiology and Neurobiology and, in only a few short weeks, has already made some significant contributions to our programs. And our special assistant, **Bethanne Bond,** continues to ensure that all our course presentations are well-polished and professional in appearance, as well as handling some other special assignments. Their efforts all contribute to making PDA's education programs so successful. And of course, as I always do at this time of the year, I want to thank all the 1,250 plus students who took PDA education courses in 2014. Without you, there would be no PDA education programs.

I'll close by wishing you, on behalf of all our staff, a safe, happy, healthy and prosperous 2015. We look forward to welcoming many of you to a PDA education course next year.

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* PDA Standard and Government members have the opportunity to download **new** Technical Reports free of charge within 30 days of publication. Print versions are available for purchase at the PDA Bookstore.

PDA Volunteer Spotlight

Igor Gorsky

- Senior Consultant
- *Concordia ValSource*
- Member Since | 2009
- Current City | Owings Mills, Maryland
- Originally From | Kiev, Ukraine

We work hard to benefit our patients

Igor loves the Abbott and Costello skit, "Who's on First?"

How has your work on Technical Report *No. 60 (2013): Process Validation: A Lifecycle Approach* contributed to your career?

Just after its completion, I was offered a great opportunity to work with a team whose focus is the promotion of the lifecycle principles outlined in TR-60. The principles of TR-60 have now become the core of what I do in the industry.

You have been a very active task force participant. How could someone else follow suit?

Hold tightly to your passion for a particular topic. Immerse yourself in its nuances and never stop learning as much as you can about it.

What was the first thing you did as a PDA member and how did it help you get to where you are now?

I had the fantastic opportunity to work on the revision of *Technical Report No. 29 (Revised 2012): Points to Consider for Cleaning Validation* under **Destin LeBlanc's** leadership and with a great team of professionals from around the globe. That experience allowed me to bolster my cleaning validation expertise, while simultaneously exposing me to the greater reaches of the field around the world.

Who do you admire most within your field?

I very much respect and admire **Hal Baseman,** the current chair of PDA. Hal's enthusiasm and passion for the modernization of our industry, coupled with his tireless work ethic, ignites a drive that is contagious.

What is the most challenging part of your job?

Unfortunately, I still find it challenging to entice others to the importance of strategic thinking and continuous learning, as well as the value of understanding the depths of knowledge management and the lifecycle approach.

When you were a child, what did you want to be when you grew up?

I really wanted to become an archeologist. I participated in several archeological digs in my native country of Ukraine until I was seventeen years old. The experience of being at those digs fed my passion for history as discovering ancient relics quite literally brought the past to life. I still find the field of archeology to be fascinating and enlightening.

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tales from the trail

Smooth Sailing South and a Hectic Trip North

Rebecca Stauffer, PDA

This summer and fall I attended two high-profile chapter events: the Southeast Chapter's Lab Conference on July 29 and the Delaware Valley Chapter's Vendor Night on Sept. 30.

My trip to the Southeast Chapter conference in Raleigh, N.C. went smoothly. I took the local Metro train to the airport without incident. Security was a breeze; I even had time to grab some tacos for lunch. The plane took off reasonably on time and landed reasonably on time. I figured I had gained the favor of the travel gods for my trip.

The all-day conference featured some very interesting and enlightening presentations. **Elayne Best** began with her talk on identifying key elements of a Laboratory Auditing Program. She also touched on recent data integrity concerns from U.S. FDA inspections of Indian facilities. Following a break, **Lindsey Colvin** discussed how her company implemented an automated environmental monitoring solution for manufacturing. She would also present this talk at the *PDA 9th Annual Global Conference on Pharmaceutical Microbiology* in October as one of the "Emerging Leaders" in the microbiology community. Next, **Michael Barron** talked about approaches to manage costs and mitigate risks in stability operations, providing a business case for stability studies. After lunch, **Patrick McCarthy, Sara Haddad,** and **Jeri Ann Boose**, PhD, presented a cast study on rapid validation and regulatory submission strategies while also utilizing a contract testing lab. Although theirs was a very specific case study not necessarily of interest to all attendees, their talk drew extensive questions and an ovation. **Karen Smith** then talked about strategies to investigate foreign particulates. And finally, **Michelle Cree's** presentation on new regulatory requirements for elemental impurity testing served as the concluding talk.

The conference was held on the campus of North Carolina State University in the building that houses the school's Biomanufacturing and Training Center (BTEC) program. On one of the breaks, I took the opportunity to walk around and see some of the training rooms where students can utilize all sorts of cGMP bioprocessing equipment.

During the conference, I also spent some time with **Michele Creech,** former president of the Southeast Chapter, who talked about the chapter's upcoming events and the chapter's overall direction. For more information about these upcoming events, please visit www.pda.org/chapters/north-america/southeast.

Unfortunately, the travel gods weren't as favorable when later I headed north to Malvern, Pa. for the Delaware Valley Chapter's Vendor Night. Thanks to a cracked rail on one of Washington, D.C.'s Metro lines, I found myself scrambling to find a cab in Northwest Washington. (Helpful hint for anyone planning to visit the Nation's Capital: while other major cities seemingly have more cabs than people, finding a cab in D.C. can feel like hunting for Sasquatch!) Fortunately, I flagged down a cab driving a mildly annoyed Senate staffer to the Capital building and he drove us both to our destinations, even leaving me ten minutes to spare.

By the time my train arrived in Paoli, Pa., I was flustered and frazzled. But the breathtaking foliage that welcomed me into southeastern Pennsylvania made it all worth it. Think rolling hills with trees crowned in crispy golds, reds, and oranges beneath a bright blue sky littered with clouds. ➤

tales from the trail

The rest of the trip to Malvern went smoothly, and I thoroughly enjoyed the Vendor Night. I spent time talking with current Chapter President **Jason Mattis** as well as Past-President **Art Vellutato, Jr.** In addition, I talked to several of the vendors and enjoyed a demonstration of an automated arm that could be used to pick up objects in a cleanroom environment. Representatives from Kimberly-Clark Professional also told me about their innovative RightCycle program, where they take clients' disposable cleanroom apparel and recycle them into raw materials used to make lawn furniture and other items.

I also sat in on the Process Validation Interest Group which met during this event as part of a new initiative to bring interest groups to chapter meetings. Here, I listened to **Scott Bozzone** and **Hal Baseman** lead a lively discussion on CpK values.

Later, **Mike Long** and **Jeff Hartman** gave an animated and interactive talk on process validation which drew considerable audience participation despite the late hour. And of course, Hal Baseman, PDA Chair and one of the leading process validation experts, put in his two cents as well.

As the new president of the Delaware Valley Chapter, Jason Mattis also discussed his plans for the chapter, including evenings devoted to topical presentations. For more information, please visit www.pdadelval.org.

And I also presented at both events, providing a short talk on publishing opportunities with PDA. Members of the publishing team will continue to attend chapter events to get the word out about writing and editorial opportunities at PDA. So if you haven't seen me at one of your chapter events, you will probably see me soon, but hopefully not atop a D.C. cab!

PDA Who's Who

Elayne Best, Sr. Auditor, Biogen Idec

Lindsey Colvin, Manufacturing Scientist, Pfizer

Michael Barron, Director, Business Development, Quality Chemical Laboratories

Patrick McCarthy, Technology Specialist, EMD Millipore

Sara Haddad, QC Analyst, Argos

Jeri Ann Boose, PhD, Sr. Director, Biopharmaceutical Services, Lancaster Laboratories

Karen Smith, Manager of Biotech and Pharmaceutical Services, RJ Lee Group

Michelle Cree, PhD, Strategy and Business Manager, Catalent Pharma Solutions

Michele Creech, QO Manager, Grifols

Jason Mattis, Investigator, GlaxoSmithKline

Art Vellutato, Jr., President/ CEO, Veltek Associates

Scott Bozzone, PhD, Sr. Mgr, Quality Systems & Techn. Svcs. Validation, Pfizer

Hal Baseman, COO, ValSource

Mike Long, Director Consulting Services, Concordia ValSource

Jeff Hartman, Director, Quality Systems Validation, Merck

Choose your Favorite 2014 Books Editor or Author

www.pda.org/2014authorsurvey

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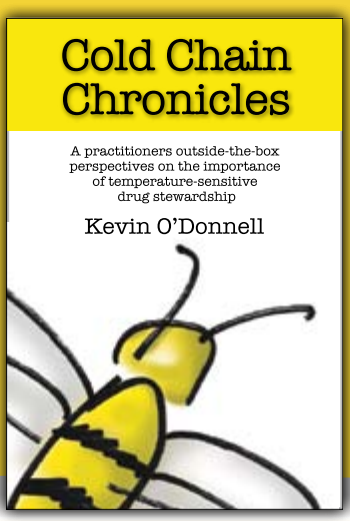
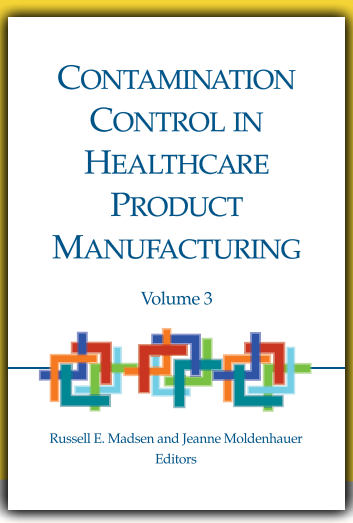
In recognition of the outstanding quality of their publications, PDA presents one distinguished Editor or Author with the PDA/DHI Award annually at the PDA Annual Meeting. This members' choice award is determined ***by you*** *so please take a moment to cast your vote online from October 15-December 31, 2014.*

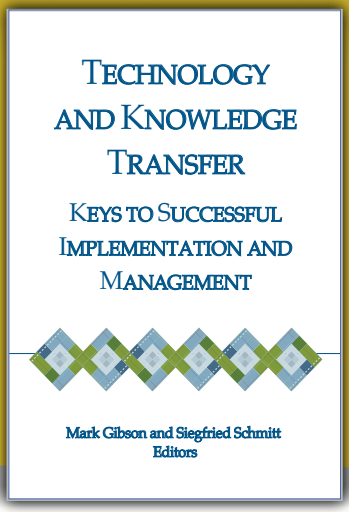
The Nominees:



Kevin O'Donnell
for Cold Chain Chronicles

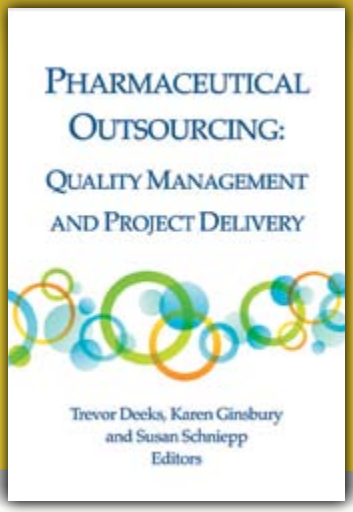
Russell Madsen and Jeanne Moldenhauer
for Contamination Control in Healthcare Product Manufacturing, Volume 2 & 3





Mark Gibson and Siegfried Schmitt
for Technology and Knowledge Transfer

Trevor Deeks, Karen Ginsbury and Susan Schniepp
for Pharmaceutical Outsourcing



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2014 PDA/FDA Joint Regulatory Conference

Plenary Sessions

Opening Remarks and P1: FDA's Views on Scientific Advances and their Impact on Manufacturing of the Future

(l-r) Hal Baseman, ValSource; Stephen Ostroff, MD, U.S. FDA; Monica Caphart, U.S. FDA; Richard Johnson, PDA

P2: Analytics & Manufacturing of the Future

(l-r) Madhu Balachandran, Amgen; Mansoor Khan, PhD, U.S. FDA

P3: The Cost of Poor Quality

(l-r) Maria Crowe, Eli Lilly; Janet Woodcock, MD, U.S. FDA

P5: Compliance Update

(l-r) Mary Malarkey, CBER, U.S. FDA; Alicia Mozzachio, CDER, U.S. FDA; Steven Silverman, CDRH, U.S. FDA; Ilisa Bernstein, PharmD, CDER, U.S. FDA; Douglas Stearn, ORA, U.S. FDA; Martine Hartogensis, CVM, U.S. FDA

P6: Center Initiatives

(l-r) Karen Midthun, MD, CBER, U.S. FDA; Bernadette Dunham, PhD, CVM, U.S. FDA; Lawrence Yu, PhD, CDER, U.S. FDA; Ellen Morrison, ORA, U.S. FDA

P6: Closing Remarks

Conference Co-chair Susan Schniepp, Allergy Laboratories, closed the *2014 PDA/FDA Joint Regulatory Conference.*

A1: Combination Products

(l-r) Carl Fischer, U.S. FDA; Steven Mendivil, Amgen; Mark Lee, PhD, U.S. FDA; Steven Hertz, U.S. FDA

C1: Design

(l-r) John Ayres, MD, Eli Lilly; Chris Stevenson, Baxter; Jeffrey Baker, PhD, U.S. FDA

B2: Manufacturing of the Future with Submissions

(l-r) Gordon Muirhead, PhD, GlaxoSmithKline; Rapti Madurawe, PhD, U.S. FDA; Mai Huynh, U.S. FDA

B1: FDASIA

(l-r) Ann Marie Montemurro, U.S. FDA; Betsy Fritschel, Johnson & Johnson; Alicia Mozzachio, U.S. FDA

C4: Supply Chain

(l-r) Steven Wolfgang, U.S. FDA; David Ulrich, AbbVie

B5: Drug Shortages

(l-r) Valerie Jensen, U.S. FDA; Catherine Gould, PharmD, U.S. FDA

2014 PDA/FDA Joint Regulatory Conference

Breakout Sessions

A5: Case Studies for Quality

(l-r) Alicia Mozzachio, U.S. FDA; Juergen Knoebel, Roche; Regina Brown, U.S. FDA; Patricia Gupta, Patti Gupta and Associates

A4: Quality Risk Management Systems

(l-r) Maria Guazzaroni Jacobs, PhD, Pfizer; Milind Ganjawala, U.S. FDA; Martin VanTrieste, Amgen

B4: Risk Based Control Strategies

(l-r) Mahesh Ramanadham, U.S. FDA; Robert Iser, U.S. FDA; Kenneth Hinds, PhD, Johnson & Johnson

C4: Supply Chain

(l-r) David Ulrich, AbbVie; Renee Kyro, AbbVie; Steven Wolfgang, PhD, CDA

C2: Customer Complaint Reviews & Trending

(l-r) Agnieszka Majcher-Dann, MD, Johnson & Johnson; Shane Killian, Johnson & Johnson; Solomon Iyasu, MD, U.S. FDA

C3: Aging Facilities

(l-r) Maik Jornitz, G-Con; Ghada Haddad, Merck; Glenn Wright, Eli Lilly; Susan Schniepp, Allergy Laboratories; Maridalia Torres, U.S. FDA; David Jaworski, U.S. FDA; Laurie Norwood, U.S. FDA


AUDITUTOPIA

2014 PDA/FDA Joint Regulatory Conference

Exhibit Hall/ Networking

Passport Drawing

Shan Jiang won a bottle of champaign from Aptar

Ananth Katta received a Jambox from Hyde Engineering & Co.

Maria Guazzaroni Jacobs won an Amazon gift card from Novatek

Tapashi Dasgupta took home a bluetooth speaker from Agilent

Robyn Parker won an iPad Mini from PDA

Veronica Atterbeary took home a bottle of premium whiskey from Complya

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9 Questions to Ask Your Manager During a Performance Review

Margaret Buj

1 What do you think went well this year?

Some managers are lousy at expressing appreciation. If your boss is one of those, you may need to ask for her positive views. Practically speaking, it's also helpful to know exactly what pleases your manager. (If the answer you get is "nothing," then you might want to start looking for a better boss!)

2 What do you think I should do differently next year?

This is a much better approach than asking what you did wrong in the past. If your boss is uncomfortable giving critical feedback, this question will often help you learn what he's really thinking.

3 What could I do to improve my rating in this area next year?

If you get a low rating on some particular objective or attribute, find out what you need to change. Try to agree on specific things that you can do differently. Understanding the change that's desired by your boss is usually more productive than arguing about the past. Unless your manager is more flexible than most, you're not likely to get that rating changed during your review.

4 How could I be more helpful to other people on the team?

In most work groups, the members are somewhat interdependent. Even if you have a great relationship with your colleagues, your manager may see opportunities for the team to be more collaborative. And just asking the question sends the message that you aren't only concerned with yourself.

5 What are your most important goals for the coming year?

Surveys have found that most employees really don't understand what their manager's goals are. If you know your boss's priorities, then you can provide useful information or assistance, which certainly won't hurt your next performance rating!

6 Is there anything I could do to make your job easier?

If you ask this question, your boss might faint dead away, since very few employees actually think about how to make life easier for their manager. Most of us typically view this the other way around: how can my boss make life easier for me?

7 How do you think our business is going to change in the future? What challenges do we face?

This question can help you see how your own work fits into the bigger picture and provide a heads up about future issues. It also sends the message that you are thinking about things beyond your own daily work.

8 What new knowledge or skills do you think I may need to develop?

You need the answer to this question to plan for your own professional development. Or, if your job is changing in undesirable ways, you may need to rethink your career plan.

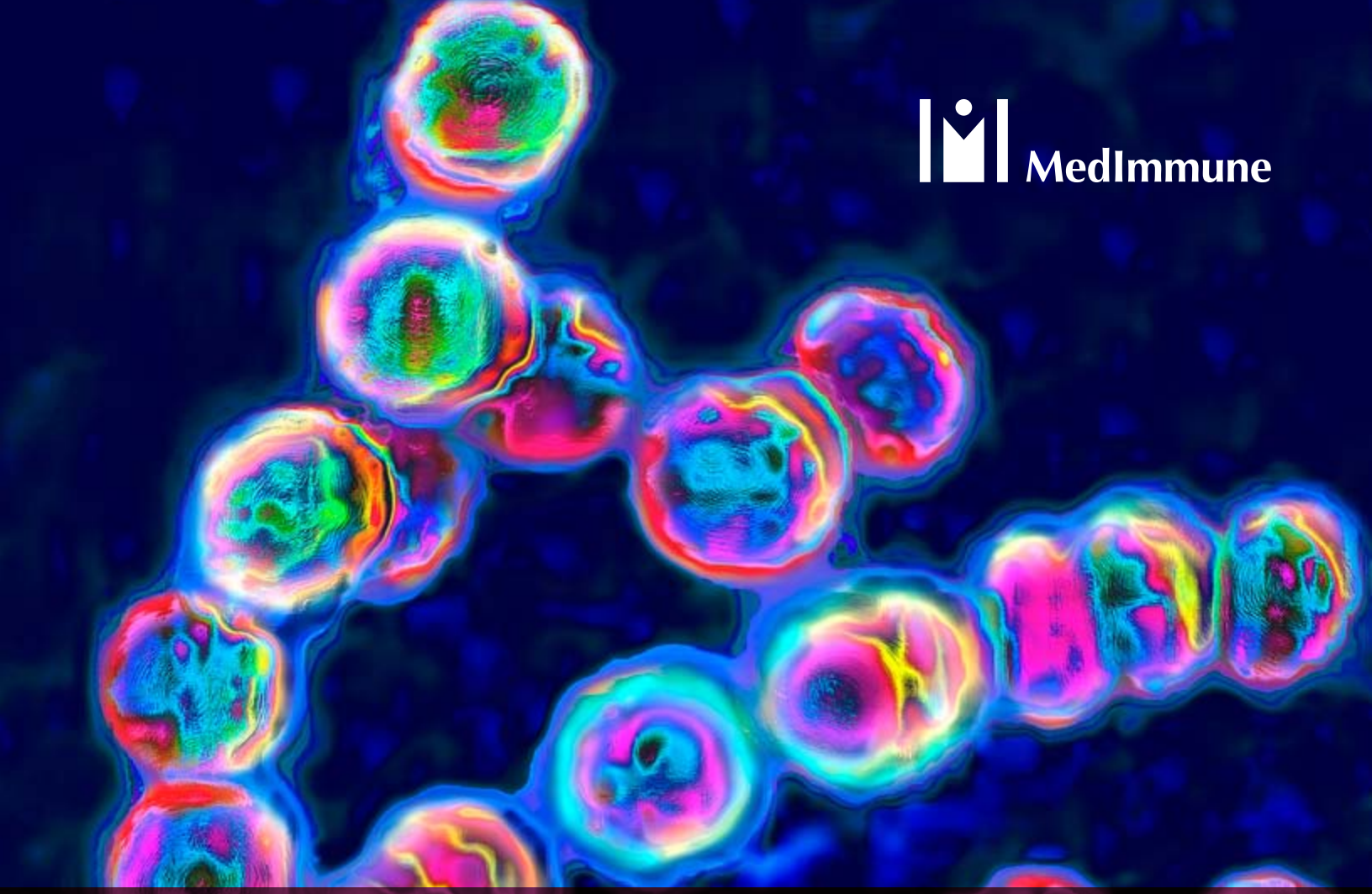
9 What career opportunities do you see for someone with my background?

If you hope to develop a career path in your current organization, you need to initiate that discussion. Don't wait for someone else to find an opportunity for you.

Hope these questions will help you make the most of your next performance review.

About the Author

Margaret Buj is an interview coach who's helped hundreds of professionals across Europe and the United States to get the jobs and promotions they really wanted. She also has eight years of experience recruiting for a variety of positions at all levels across Europe and in the United States, primarily in the technology and e-commerce sectors.



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AstraZeneca

snapshot

PDA to Address Concerns of Visible Particulates

Jahanvi (Janie) Miller, PDA

As visible particulates rise to one of the top concerns within the pharma/biotech industry, PDA plans to develop documents addressing this, such as the 2014 paper "Industry Perspective on the Medical Risk of Visible Particles in Injectable Drug Products." This paper provides a scientific and medically based risk-approach for evaluating the risk to a patient in terms of safety/efficacy in the event particulate matter contained within an injectable drug product is inadvertently administered to a patient.

Specific approaches to risk mitigation are not addressed in this paper; however, it does provide a review of current compendial inspection requirements for visible particles along with a review of the medical literature associated with any observed harm from such particles. Guidance is also provided on the assessment of risk in such circumstances, including consideration of the following key attributes: patient factors, route of administration and use of filtration at the point of administration, the volume administered, particle size and their fate within the body, particle type, source and amount, manufacturing process mitigation and the frequency of detection. As quality culture becomes a key movement within our industry, the importance of risk mitigation in relation to quality is becoming a prime focus.

Medical personnel were also involved in the development of this paper; the collaboration with these medical/safety personnel highlighted how integral they are in supporting and encouraging a corporate quality culture and awareness of patient safety. This paper will be published in the *PDA Journal of Pharmaceutical Science and Technology,* and PDA will continue to work on developing this topic in a series of documents in our journal as well as in the form of technical reports.

Journal *Preview*

Special November–December Issue Covers Virus Detection Conference

Guest editors **Arifa Khan** and **Dominick Vacante** provide a thorough overview of the *2013 PDA/FDA Advanced Technologies for Virus Detection in the Evaluation of Biologicals Conference* with articles covering the meeting.

Editorial

Arifa S. Khan, Dominick A. Vacante, "Introduction and Workshop Summary: Advanced Technologies for Virus Detection in the Evaluation of Biologicals—Applications and Challenges"

Conference Proceeding

Kavitha Bekkari, et al., "A Practical Approach to a Viral Detection Pipeline Using Existing Viral and Non-Viral Sequence Resources "

Paul Duncan, "Summary of the Advanced Virus Detection Technologies Users Group Efforts—2013"

Arifa S. Khan, et al., "New Technologies and Challenges of Novel Virus Detection"

Shasta D. McClenahan, Philip R. Krause, "The Potential Role of Advanced Technologies for Virus Detection in Development and Regulation of Vaccines"

Research

Christopher J. Wang, Szi Fei Feng, Paul Duncan, "Defining a Sample Preparation Workflow for Advanced Virus Detection and Understanding Sensitivity by Next-Generation Sequencing"

Technology/Application

Eric Cabannes, et al., "Whole Genome: Next-Generation Sequencing as a Virus Safety Test for Biotechnological Products"

Szi Fei Feng, "Modeling an Approach To Define Sensitivity of Viral Detection in Sample Matrices— Examples with Microarray Readout"

Review

Laurent Mallet, Lucy Gisonni-Lex, "Need for New Technologies for Detection of Adventitious Agents in Vaccines and Other Biological Products"

Paul Shabram, John L. Kolman, "Evaluation of A549 as a New Vaccine Cell Substrate: Digging Deeper with Massively Parallel Sequencing"

Tom Slezak, "Bacterial Genome Reference Databases: Progress and Challenges"

Carolyn A. Wilson, Vahan Simonyan, "FDA's Activities Supporting Regulatory Application of "Next Gen" Sequencing Technologies"

Jens Modrof, et al., "Parallel Evaluation of Broad Virus Detection Methods"

Siemon H.S. Ng, "Preliminary Evaluation of Next-Generation Sequencing Performance Relative to qPCR and In Vitro Cell Culture Tests for Human Cytomegalovirus"

Brenda Richards, et al., "Detection of Adventitious Agents Using Next-Generation Sequencing"

Interest Group *Corner*

Aging Facilities: A Regulatory Perspective from Puerto Rico

Rebecca Stauffer, PDA

The topic of "aging facilities" has gained considerable traction within industry. But as members of PDA's Facilities and Engineering Interest Group discussed at the *2014 PDA/FDA Joint Regulatory Conference*, determining what constitutes an aging facility can be tricky and depends on a number of factors. A facility can be considered "aging" not necessarily due to age; lack of maintenance and lack of technology upgrades plays a role as well. A well-maintained facility that is decades old but led by a management team embracing new technologies and processes could generally be considered modern.

Maridalia Torres, District Director, San Juan District Office, U.S. FDA, brought her perspective on the aging facilities topic. She has worked for the Agency in Puerto Rico since 1990. This location in particular faces its own unique aging facilities concerns.

"Having worked for the FDA in Puerto Rico for many years, I have seen my share of aging facilities," she said, explaining that in the 1970s pharma companies, drawn to the island by tax incentives, built numerous facilities in Puerto Rico. By 1990, there were well over 100 facilities on the 100x35 mile island. Now, the number of facilities on the island is less than that, due to a variety of factors, Torres explained. Those that remain and are also successful are the facilities where companies have kept up with new technologies, methods and processes.

Perhaps if they had stayed on top of the business...they could have survived

She then cited two examples from her experiences as an inspector where facilities—both run by well-known companies—closed due to failure to implement new processes and technology. One facility, which she referred to as a casualty "of changing times," received a hefty warning letter due to a number of deficiencies, including air ducts no longer up to standard. The second, a generics manufacturing that operated in Puerto Rico for 12–15 years, closed due to failure to maintain the infrastructure. Investigators found numerous areas with microbial contamination and even the presence of mold.

"The inspection led to multiple recalls of the firm's products and also led to a logistical nightmare…eventually the facility closed," Torres said. "They were not able from the get-go to overcome these problems," adding, "perhaps if they had stayed on top of the business in terms of maintenance and infrastructure, they could have survived."

As an investigator, she encouraged interest group members responsible for these types of sites to maintain communication at all levels—regional and national—with the Agency.

"Talk to us. We're not monsters. We're here to help," Torres emphasized. "I think it's very important we maintain a channel of communication"

In addition, any signs that a facility is having problems should not only be a signal to the Agency but "it should be a signal to your own site management" as well.

At the end of the session, interest group leader **Christopher Smalley,** PhD, Director, BioSterile Validation, Merck, encouraged attendees interested in aging facilities to consider joining a PDA task force that will draft a QRM series technical report on the topic. Smalley also announced the appointment of **Shelley Preslar,** General Manager, Southeast Operations, Azzur Group, as the new coleader of the interest group.

If you're interested in joining the task force or the Facilities and Engineering Interest Group or contributing to the technical report, please email the PDA Volunteer Coordinator at volunteer@pda.org.

About the Expert

Maridalia Torres is the Director of the FDA's San Juan District Office and part of ORA's Senior Management Staff. She began her career with FDA as Consumer Safety Officer in 1990, and was promoted to Drug Specialist in 1996 and Pre-Approval Program Manager for the San Juan District in 1999.

The Forecast for Global RIM is Cloudy

John Lawrie, Veeva Systems

The life sciences industry is faced with a conundrum. Now serving a global marketplace, it must meet all local regulations while also continuing to improve efficiencies and speed to market. As a result, the industry has engaged affiliates and remote, external distributors throughout the world to expand its footprint while maintaining needed flexibility to weather economic trends. The resulting network of small, regional affiliates/distributors/partner companies may not be networked with the central sponsor when handling submissions. As such, affiliates typically manage information in their own local systems and must duplicate their regulatory data along with a subset of their documents to be housed within the headquarters' system. This approach is not only inefficient but also increases the margin for error and noncompliance and limits sponsor visibility into critical documents and processes.

A recent study on Regulatory Information Management (RIM) practices conducted by Gens & Associates identified the need for "integrated and aggregated information regardless of function and geography" as a growing focus of the industry. Yet, many companies are still dealing with local systems, paper processes and tracking spreadsheets. Although there is often certain comfort in allowing affiliates to use their own systems that are tailored to local requirements, such practices lead to significant waste. A full 25% of local affiliate time is spent handling nonvalue activities such as duplicating data entry, finding information, and responding to requests from the central authority due to concerns on data quality. These activities represent a substantial expense, which could be greatly reduced with one global, authoritative system. With today's advanced cloud technologies, affiliates can easily and securely access the corporate system from anywhere, improving efficiency, accuracy, and compliance worldwide.

As an example, a global biotech company struggled to see what its regional affiliates and distributors had done with periodic safety update reports (PSURs) distributed via CDs. PSUR status updates were collected via email and phone calls, and then manually recorded in spreadsheets. Now, the company leverages a globally accessible cloud solution to distribute and track its safety update reports, increasing visibility and the reliability of meeting regulatory requirements.

A growing number of sponsors, in fact, are moving to cloud solutions to globally harmonize submissions processes. Small, local affiliates with little-to-no IT support and rudimentary tools can connect to the corporate cloud system anywhere there is an Internet connection, and retire old systems completely. Consolidating systems cuts administrative overhead and eliminates redundancy. For example, when affiliates update a specification, manufacturer, or label using a global cloud system, they no longer have to also update their local tools as well. Duplicate sets of information are eliminated and replaced by a single, trusted, authoritative source of information which fosters improved compliance.

Organizations with a central cloud system save resources by:

- Capturing the activities of both headquarters and their affiliates in real time
- Eliminating duplicate data entry
- Providing ongoing transparency into affiliate activities to improve compliance
- Aggregating information for better decision-making and audit readiness

One key caveat: to properly engage and collaborate with affiliates throughout the globe, a centralized cloud application must offer an easy user interface that's highly intuitive. "Often, when affiliates get full access to the native application…they become overwhelmed with the complexity of the system," explained **Steve Gens,** industry veteran and founder of consultancy Gens & Associates. "What works for the daily user doesn't work for casual users like those at the affiliates." To avoid overwhelming the occasional user with complicated functionality, the central system should incorporate a familiar, user-friendly interface while also provide the specific functionality needed to meet local requirements. The global system must track the documents, data, timelines and reports that are relevant in-region. This is the only surefire way to ensure affiliates will retire local systems so the organization can consolidate technology and improve overall efficiency.

About the Author

John Lawrie has nearly 20 years of experience in the pharmaceutical industry. He is currently director of product strategy for the Veeva Vault Submissions application. In this role, he is responsible for product direction in supporting regulatory submissions content management as well as Vault Submission's position within the overall Regulatory Information Management (RIM) landscape.

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Exciting Technological and Scientific Advances Drive Prefilled Syringe Market

Insights from the *2014 Universe of Prefiled Syringes*

Walter Morris, PDA

The first question that popped into my mind when I arrived in Huntington Beach, Calif. on October 5 was, *What is so big about the Universe of Prefilled Syringes?* I mean, we are talking about injectable technology, which has been around for hundreds of years. Really, what would possess almost 1000 people to congregate at this PDA event year after year for nearly a decade?

Well, it didn't take long for me to understand why this meeting has grown into one of PDA's largest. The amount and breadth of research that goes into the development of new prefilled/autoinjectable devices is remarkable. Plus, the technological advances and opportunities offered by smartphones and other new technologies is even more impressive. And all of the advances and potential future offerings are meant to improve the patient experience, create safer injectable products and safeguard such products from inadvertent and careless mistakes by users.

Markus Bauss, President and CEO, ConnectMeSmart GmbH, offered a glimpse into the endless possibilities for the pairing of injectable devices with smartphone and mobile medical applications.

Bauss started off his talk by discussing and demonstrating the "talking vial" circa 2007—a device coupled with a microchip attached to a vial that can read information out loud about the medicine, including dose and frequency. That same year, he noted, also saw the launch of the smartphone revolution with the introduction of the Apple iPhone. Now, he asserted, there exists endless opportunities to use these devices to enhance and improve drug delivery, patient compliance, safety, dosing accuracy, and supply chain integrity, to name a few.

Many reusable pen injectors already have included embedded electronics for many years for dose setting and tracking of injection dates. Now, with available technologies and networks, these devices can include additional functionality such as integrated reminders and transfer of injection data to personal Web-based health records.

Other companies in the diabetes market are developing smartphone-based blood glucose metering, while others are combing the glucose infusion and metering technology into one small device. Several developing products such as Bee and Timesulin allow for the wireless transfer of injection data.

Similarly, BETACONNECT™ allows multiple sclerosis patients to program injection speed, needle insertion depth and set injection reminders for Betaferon® administration. This device also allows patients to upload their injection records to a website via bluetooth or cable.

Who hasn't used YouTube to figure out how to change their oil, fix a hole in their wall, or do some other unfamiliar task? Well, now patients will be able to look increasingly at their smartphone to learn how to use their injectable product. No longer will they have to try to remember the often cursory training provided by their healthcare provider. Bauss demonstrated the NovoPen training app produced by Novo Nordisk.

And if you feel these technologies only can be applied to reusable products, you are wrong. Bauss also discussed how these solutions can be tailored to disposable products, too.

He closed his talk with a discussion of the regulatory landscape. Both the European Union and the United States regulate mobile medical applications. Of the 50,000 or more "mobile health" apps developed over the last few years, "only a couple of hundred have received certification by the FDA or CE approval in Europe as a medical device/medical product," Bauss reported.

According to a 2013 U.S. FDA guidance, a mobile medical app is classified as such if it meets the definition of a device in section 201(h) of the Federal FD&C Act and either is used as an accessory to a regulated medical product, or transforms a mobile platform into a regulated medical device.

In Europe, the Medical Device Directive applies if the mobile app or app/device combination is considered a medical device, and then all other applicable rules for risk management, quality, etc. apply.

Bauss explained that while the marketplace for mobile medical applications is only in its infancy, it is already exploding as more and more smartphone users worldwide (already >1 bil.) are becoming increasingly comfortable using the technology for personal health monitoring.

He concluded: "Connecting smartphones with the help of modern connectivity standards to areas where drug delivery devices are used opens up a world of completely new applications, to support patients in taking their medications."

Author Note: This is the first of a series of reports on the science and technology presented at the *2014 PDA Universe of Prefilled Syringes Conference* in Huntington Beach, Calif., Oct. 6-7. Next time, we'll look at how patient safety is driving the movement towards single-dose systems, though economics might present the biggest challenge to broader, worldwide implementation and acceptance.

2015 PDA Upcoming Events

SAVE THE DATE for PDA's 2015 Events

JANUARY EVENTS

22–23
GMP for APIs
Seoul, South Korea

FEBRUARY EVENTS

10 –11
PDA PIC/S Conference
Brasilia, Brazil

17–18
Pharmaceutical Microbiology
Berlin, Germany

MARCH EVENTS

3–4
Parenteral Packaging
Frankfurt, Germany

16–18
2015 PDA Annual Meeting
Las Vegas, NV

18–19
2015 PDA Aging Facilities Workshop
Las Vegas, NV

APRIL EVENTS

14–15
Aseptic Manufacturing/ Sterilization
Brussels, Belgium

MAY EVENTS

18–19
2015 PDA Pharmaceutical Packaging Conference
Washington, DC

19–20
PIC/S – PDA Workshop
Geneva, Switzerland

20–21
2015 PDA Drug Delivery/ Combination Products Workshop
Washington, DC

JUNE EVENTS

2–3
Advanced Therapy Medicinal Products
Amsterdam, Netherlands

9–10
Virus & TSE Safety Forum
Lisbon (Cascais), Portugal

9–11
2015 PDA Aseptic Processing-Sterilization Conference
West Coast Area

23–24
2015 PDA Single Use Systems Workshop
Washington, DC

23–24
Quality & Regulation
Brussels, Belgium

PDA
Parenteral Drug Association

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

SEPTEMBER EVENTS

15–16
Pharmaceutical Freeze Drying Technology
Copenhagen, Denmark

22–23
Monoclonal Antibodies
Berlin, Germany

28–30
2015 PDA/FDA Joint Regulatory Conference
Washington, DC

30–1 October
2015 PDA Manufacturing Initiative Workshop
Washington, DC

OCTOBER EVENTS

10–11
Pharmaceutical Cold & Supply Chain
Amsterdam, Netherlands

19–21
2015 Interphex PDA Educational Program
Puerto Rico

19–21
PDA 10th Annual Global Conference on Pharmaceutical Microbiology
Bethesda, MD

26–27
PDA Visual Inspection Forum
Bethesda, MD

NOVEMBER EVENTS

3–4
The Universe of Pre-filled Syringes
Vienna, Austria

TBD
PDA Vaccines Conference
Washington, DC

DECEMBER EVENTS

TBD
2015 PDA Metrics (or PAC) Conference
Washington, DC

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Report from PDA/FDA

Keeping the Signals Clear:
Industry and FDA Collaborate on Innovation

Advancing Collaboratively in Changing Times

Geetha Jayan, PhD, CDRH, U.S. FDA

"Collaboration," "Innovation," "Quality," "A new way of doing"...these were all buzz words that spanned most sessions of the three-day *PDA/FDA Joint Regulatory Conference,* held Sept. 8–10 in Washington, D.C.

Keynote speaker **Stephen Ostroff,** MD, Acting Chief Scientist, U.S. FDA, kicked off the conference, stating that this is a period of "rapidly expanding discoveries and opportunities" with scientific breakthroughs happening at an extremely rapid pace. This in turn, is driving—at unprecedented speed—innovation and the development of novel medical products. Furthermore, since FDA is charged with the regulatory oversight of medical products, this rapid period of change calls for continuing adaptation of the Agency's role in bringing innovative medical products to market. He then cited a few examples of such cutting edge technologies: the application of genomic sequences to diagnose and treat health conditions, development of 3-D printing to facilitate personalized medical care, application of stem cells in regenerative medicine, and biomonitoring with cell phones and other mobile devices.

The Agency, Ostroff further said, is going through a period of transformation in which innovation, collaboration and the global nature of business are key considerations. FDA's goal, he said, is to facilitate bringing to market innovative medical products that can benefit the public, as rapidly as possible. Breakthrough therapy (BT) designation, fast track designation, accelerated approval and priority review designation are examples of the Agency's expedited review programs for drugs and biologics ***(1).*** In addition, FDA and the Centers for Medicare & Medicaid Services (CMS) recently established a pilot program for concurrent review ***(2)*** to expedite patient access to safe and effective medical devices.

These new approaches at the FDA, he explained, require a collaborative mindset for bringing together expertise from the industry, academia, government and elsewhere. Although this is not a traditional model for the Agency, he indicated that the Office of the Chief Scientist is uniquely positioned to facilitate such collaboration and innovation through public/private partnerships.

Prior to Ostroff's talk, PDA Chair **Hal Baseman,** Chief Operating Officer, ValSource, PDA President **Richard Johnson** and meeting co-chair **Monica Caphart,** Deputy Director, Division of Human Resource Development, Office of Regulatory Affairs, FDA, opened the event. Their remarks reiterated the overarching theme of the conference and the pharmaceutical world's current state of affairs. That is, assuring total product lifecycle quality with customer-focused outcomes using innovative approaches and state-of-the-art science and technology as scientific discoveries and innovation happen at incredible speed.

This theme was expanded upon in the session following Ostroff's talk, "Analytics & Manufacturing of the Future." **Madhu Balachandran,** Executive Vice President, Amgen, presented certain perspectives on next generation manufacturing (NGM) and how NGM can play a role in avoiding drug shortages. He walked the audience through a NGM approach used at Amgen to mitigate a drug shortage. The approach included four main elements— Prevention (through a Quality System), Technology (to minimize damage to product), Inventory (to protect against surprise variations) and Diversification (to avoid single point of failure). **[Editor's Note:** For more on Balachandran's perspective, please see p. 36**].**

Article at a Glance

- FDA is going through a period of transformation
- Evolving paradigms driving a shift toward quality culture
- Rapid technological changes are driving new analytical models

Mansoor Khan, PhD, Director, Division of Product Quality Research Programs, CDER, followed Balachandran's talk with a presentation on some quality considerations for parenteral drug products, from a CMC perspective. He provided an overview of field alert reports and recalls on parenteral drug products during recent years and highlighted factors that were common to many recalls. Khan also pointed out the establishment of CDER's Emerging Technology Team (ETT) to assist innovative manufacturers better navigate the regulatory process. This team, he said, would facilitate the inspection and review of manufacturing facilities where novel pharmaceutical product development and production approaches are involved.

Continuing the focus on quality, on the second day of the conference **Maria Crowe,** President, Lilly Manufacturing, Eli Lilly, presented an example of Eli Lilly's "quality journey" as the company prepared to achieve its "safety first, quality always" motto. She discussed how Lilly applied a comprehensive framework for their manufacturing and quality management system—establishing integrated standards to document expectations, and define business processes for delineating how the work gets done are key components of this framework. The Lilly quality journey, said Crowe, has led to a focus on "continuous improvement, integration, and sustainability."

This was followed by a presentation from **Janet Woodcock,** MD, Director, CDER, who talked about how pharma's evolving landscape has warranted changes within the FDA. Some of the drivers of this change include increasing global manufacturing, expansion of contract manufacturing and just the sheer increase in volume of new drug products. She also talked about the progress of the "quality culture" at FDA. It aims to meet the needs of the evolving pharma landscape paradigm and enable the industry to stay the course on their quality journey of shifting from a "compliance-driven" to a "quality-driven" approach of doing business. Woodcock cited the recent implementation of expertise-based team reviews at CDER and the establishment of CDER surveillance programs as examples.

The last day of the conference gave a human element to the often high-level concepts discussed with a patient perspective from **Terri Sarisky,** Director, Quality Systems and Compliance, Merck. She walked the audience through her journey following her mother's diagnosis of glioblastoma multiforme (GBM). Sarisky said that it "took a village" to enable her mother's recovery stressing that the collaborative approach from doctors, nutritionists, medical radiologists and other caregivers was key for her mother's survival.

The conference attracted 852 participants. It gave ample opportunity to attendees for professional networking and also for hearing from a diverse group of stakeholders including regulators, the regulated industry and patients, all steps in the pathway to working together collaboratively to tackle a changing industry.

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2. U.S. Food and Drug Administration. "FDA-CMS Parallel Review." www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/ucm255678.htm (accessed Oct. 3, 2014)

About the Author

Geetha Jayan, PhD, is a Senior Science Health Advisor at FDA's Center for Devices and Radiological Health. Views/opinions presented in this article represent the author's and not the FDA's.

Industry, Regulators Share Insights and Look to the Future

Erin O'Brien, West

The *PDA/FDA Joint Regulatory Conference* proved to be a valuable opportunity for learning and information exchange regarding the key issues facing our industry, the initiatives championed by the U.S. FDA, and solutions emerging from the ranks of PDA membership. From the opening remarks on Monday, the stage was set for attendees to gain insight into many topics, starting with a look at how rapid scientific advances are driving the need for new manufacturing capabilities and analytical models.

Stephen Ostroff was the first plenary speaker, addressing the direction of the agency as we stand on the cusp of innovations in personalized medicines and genomics. He also addressed the range of new biological, chemical and radiologic threats requiring industry/government and academia to collaborate. The Medical Countermeasures Initiative is a front line defense to not just terrorist threats, but also natural disasters such as the current Ebola outbreak. "Extraordinary challenges bring great responsibility," he said, invoking **J. Robert Oppenheimer** and his memorable quote regarding "heroic days," giving attendees a call to action to use the scientific approach to address the great challenges of our time.

The second plenary session covered "Analytics & Manufacturing of the Future," with valuable perspectives from both Amgen and CDER. Next generation manufacturing and its role in preventing future drug shortages was discussed. Against a backdrop of increasing market and supply chain complexity, drug shortages have increased fourfold in the period of 2005–2011. Quality, capacity, and raw materials were cited as the key drivers. Regardless of cause, the resulting patient impact is unacceptable. Madhu Balachandran introduced the audience to concepts being used at Amgen to ensure supply interruptions are minimized, and described how, in concert with Next

ORA Director Addresses Operations, Foreign Inspections During Q&A

Rebecca Stauffer, PDA

On the last day of the *2014 PDA/FDA Joint Regulatory Conference,* senior compliance and Office of Regulatory Affairs leadership from the U.S. FDA provided a "Compliance Update." Following presentations from CBER, CVM, CDER, CDRH and ORA, panel participants took Q&A from attendees.

Douglas Stearn, Director, Office of Enforcement and Import Operations, ORA, took a number of questions from audience members. He addressed how his Office interacts internally with other FDA branches as well as with other parts of the U.S. government, such as U.S. Customs and the U.S. Department of Agriculture. Other questions directed at him concerned a perceived increase in inspections of foreign facilities by FDA.

"There's a lot going on," he said. "First, the dominant part of my Office, the Division of Import Operations, is one of our three divisions over at headquarters. We have multiple people across ports, stationed there, including districts across the United States. We work regularly with customs and our process has certain elements related to customs."

Stearn went on to point out that FDA is one of the federal agencies with entry authority under section 801 of the Food Drug and Cosmetic Act; his Office represents the Agency's interests to Customs.

In addition, "we work closely with all the product centers," relying on these Center's various experts for assessments about product risk. His Office also receives information about certain facilities' products, even sampling products if there are quality concerns.

Another audience member then asked Stearn about a perceived increase in foreign inspections. He agreed with the assessment that FDA inspections of foreign drug manufacturing sites will continue to grow.

He explained further that previously there had been "some concerns the Agency has had, and that industry has had, that there were areas out there that had not been inspected outside of the United States in the same way, or the same degree."

"It's not necessarily that they're foreign per se," he added. "It's important to note we're talking about huge categories. And I encourage caution—people make these very broad generalizations."

The Agency, Stearn emphasized, determines its level of surveillance based on a risk-based balanced approach.

About the Expert

Douglas Stearn currently serves as the Director of the Office of Enforcement and Import Operations. As the Director, he leads FDA's Office of Regulatory Affairs in matters related to compliance and enforcement activities, imports, and the systems used by FDA's field force, as well as serving as the principal advisor and spokesperson on these issues.

Extraordinary challenges bring great responsibility

Gen Manufacturing techniques, variation can be reduced and six sigma performance achieved. Balachandran enlightened the group regarding the Amgen approach to ensure supply: linking the four pillars of prevention, technology, inventory, and diversification. In an interesting analogy, he discussed how the U.S. Nuclear Navy's "Defense in Depth" program—which provides a systemic approach to deliver highly reliable operations in an incredibly risky field—might serve as a model to pharma.

Mansoor Khan shed light on the concerning number of Field Alert Reports (FARs) resulting from particulates, and their connectivity to drug shortages. Khan discussed the myriad reasons for these incidents, ranging from operator training to filter issues, impurity/degradation products, and API coming out of solution. He challenged the industry to consider the application of Process Analytical Technology (PAT) to improve product quality, and gave a lyophilization example relating to the use of in-process measures such as temperature to prevent later particulate formation.

In a session addressing the Cost of Poor Quality, attendees gained perspective from industry and regulators regarding the critical nexus between quality investments and business success. The cost of fixing quality issues continues to increase, and funds can be better invested in continuous improvement driven by risk assessment and scientific rigor. In the emerging paradigm of Quality Culture, compliance must follow from thorough product and process understanding…not vice versa. This becomes even more critical as breakthrough therapies will rely on advanced manufacturing initiatives. Strong leadership is critical to develop and maintain a true culture of quality. Manufacturing needs an equal seat at the table with the R&D and commercial organizations as pharmaceutical companies determine how to allocate spending—and there is opportunity as an industry to promote the "business case" behind proactive risk management and quality investment.

Besides the plenary sessions, there were a range of concurrent sessions to choose from. Quality by Design was a recurring theme in some of these sessions. **Chris Stevenson,** Sr. Manager, Quality innovation & Lifecycle Management, discussed the implementation of QbD on legacy products at Baxter, highlighting how the application of QbD to multisite products has allowed them to identify and benchmark optimization opportunities. **Jeffrey Baker,** PhD, Deputy Director, CDER, confirmed that while CDER is seeing increasing use of QbD in submissions, there are some differences. Good science abounds, but there are a range of approaches to translating that understanding to control strategies. He also debunked a few misconceptions, such as that there is no such thing as a "QbD" or "nonQbD" submission, and no such thing as too many or too few controls. QbD is not a program, brand, or deliverable; it is about understanding the significance of data—Baker likened it to comparing a pile of bricks (data) to a house (QbD).

Continued at bottom of page 52

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Developing a Robust Supplier Management Process | March 20

Explore current regulatory expectations regarding supplier management and learn to implement these concepts in your own company to reduce the risks associated with supplier management.

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Amgen's Next Gen Manufacturing: A Conversation with Madhu Balachandran

On September 2, the PDA Letter's ***Walter Morris*** *interviewed* ***Madhu Balachandran,*** *Executive Vice President, Amgen, Inc. on manufacturing of the future in advance of his presentation at the* PDA/FDA Joint Regulatory Conference *on September 8. Balachandran answered questions about Amgen's "Next Generation Manufacturing" facility opening soon in Singapore. Below are selected questions and answers; the full interview is available online as the October* PDA Letter *Podcast.*

PDA Letter: You will be talking at the *2014 PDA/FDA Joint Regulatory Conference* on the future of manufacturing. How is Amgen defining the future of manufacturing?

Balachandran: Good question, Walt. For us manufacturing of the future, or as we like to refer to it these days more appropriately as "next generation manufacturing," represents the advances in manufacturing from today's technology. The way we define this next generation approach has to do with increasing the productivity of each cell. Scientists at Amgen, and I imagine at other companies, have refined the techniques of producing and adapting cell lines so that each cell is much more productive than the cells used to be as recently as five years ago. Each cell in our case is typically a Chinese hamster ovary cell. The increased productivity that we've seen from these cells, coupled with the ability of the equipment and our engineering systems to accommodate much greater cell densities—meaning there are many more of these cells in a given volume than before—results in much more protein of product that can be made in a given engineered system than before. That is really the heart of the advance in next generation manufacturing or Manufacturing of the Future.

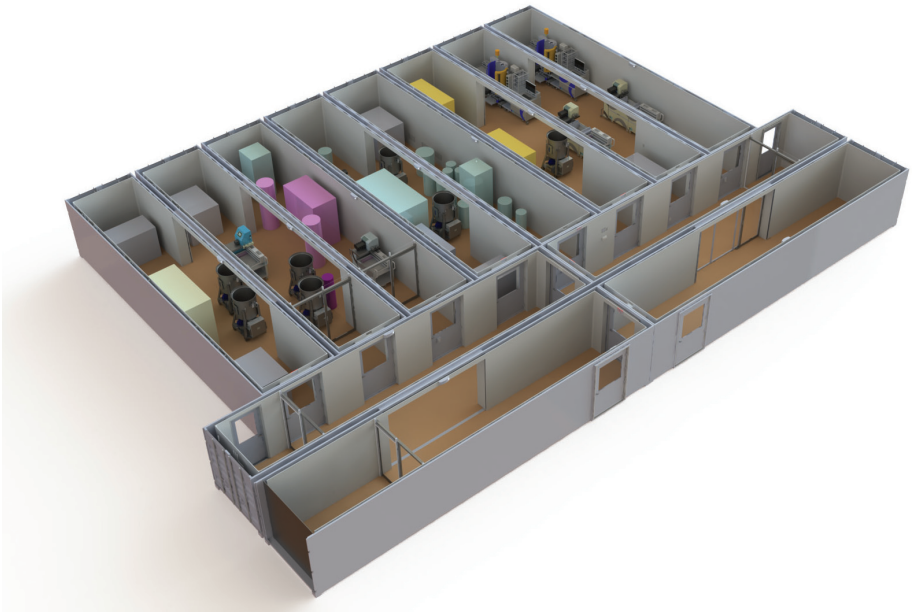
Then you combine that with the ability to use portable equipment, which is much smaller now because for a given volume you are producing a lot more drug. You combine that further with single-use systems—disposable technology based on plastics—you then have the ability to use modular, portable, flexible engineered plants. These pieces can be put together and reconfigured any way you want. You can build them a lot faster. You can produce them for much lower capital cost and you can operate them with fewer people. Together, that is what we like to think of as representing next generation manufacturing.

PDA Letter: What is the genesis of the new platform and the new efficiency in the cell banking?

Balachandran: At Amgen, as with other companies in the industry, we are growing all over the world. We are now attempting to reach millions of patients with our existing medicines as well as our pipeline medicines, requiring the production of much greater quantities of proteins when compared to the past. The current manufacturing systems for making such proteins and biologics are very complex. If you saw one of our cell culture manufacturing plants, they are very big in size, very impressive to look at because they are filled with gleaming stainless steel equipment, but they are capital intensive. They take up a lot of land area and require large staff to operate and produce the product. They take a long time to build and qualify, commission, and get licensed.

As we grow the world over with an expanding pipeline of products, the demands for capacity are increasing. And if we didn't make a change, we would have to invest high proportions of the company's resources to build these factories. There was a real necessity for us to innovate and make advances in engineering in the manufacture of biologics which is why we initiated this a few years ago. We hope we will be successful with our first enterprise in Singapore.

PDA Letter: This isn't just about smaller plants with smaller footprints and using disposable equipment. You indicated that the company has innovated and improved the output of the cell banks themselves. Is this home-grown knowledge that led to these advances or is Amgen incorporating knowledge from elsewhere? Is this something other companies are experiencing?



Modular facilities offer a flexible approach to manufacturing (image courtesy of Biologics Modular)

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As we grow the world over with a growing pipeline of products, the demands for capacity are increasing

Balachandran: The answer to that question is a complicated one. It is a blend of everything that you hinted at. We have a lot of proprietary knowledge undoubtedly behind the advances in next generation manufacturing coupled with advances that are happening elsewhere, both in academia as well as at other companies. The advances are mainly in increasing use of disposables and superior engineering approaches.

As I mentioned at the outset, if I could point to one significant advance, it is the ability of the cells to produce more. This requires nurturing the growth and development of the cells in the appropriate environment so that they can flourish and grow and continue to be productive and produce the desired protein. That requires experience and knowledge of biological systems as well as development and formulation of proper nutrients and media that contain these nutrients so that the cells can be nurtured and kept in a healthy state so that they can produce the desired protein at the appropriate levels of throughput.

PDA Letter: Companies like yours must have such immense experience with this platform that you naturally are deriving efficiencies year after year. Now, you mentioned this next generation facility with the smaller footprint, and you mentioned that it is in Singapore. Why did Amgen choose to build a facility there as opposed to other biotech hotspots in the United States or Europe?

Balachandran: There were a number of candidate locations that first came to mind. As you might know, our flagship operation, by far our largest manufacturing operation, is in Puerto Rico, so that would have been a natural obvious location to invest further in. We have a presence in Ireland and Rhode Island which were also candidates that we examined and considered as viable alternatives. The reason we finally decided on Singapore is because of our growth in Asia. It is strategically important for Amgen to have a presence in Japan, China and the Far East. We chose to increase our presence there because there are people there who need our medicines as much as patients in Europe and the western world. There is good business symmetry to locate our next significant manufacturing location in Singapore concurrent with our plans to grow there as well. This enables our supply chain to operate significantly and effectively. Singapore also has its advantages, including an outstanding university system, a number of talented life science and engineering graduates emerging out of the great universities in Singapore. There is a flourishing pharmaceutical industry there that accepts and absorbs these graduates in order to develop their careers. There is also a growing and thriving research environment that is taking root in Singapore. We felt that the combination of business and environmental reasons made the most sense for a new Amgen location in Singapore.

About the Expert

Madhavan (Madhu) Balachandran is Amgen's executive vice president, Operations. Balachandran oversees the company's global manufacturing operations, quality, product and process engineering, and capital projects.

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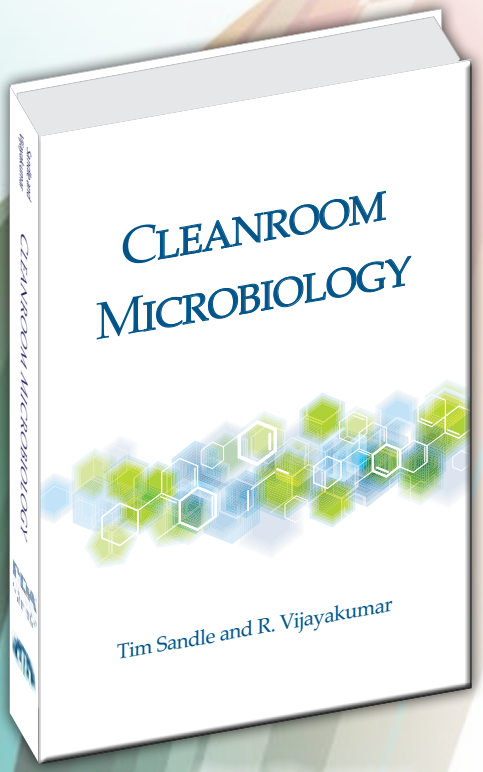

Item No. 17323

Cleanroom Microbiology

By Tim Sandle and R. Vijayakumar

Pre-order your copy by December 31, 2014 and save 15%. Enter Campaign code CM during check out.

While there are books on cleanrooms available, these focus almost entirely on the physical and rarely address microbiological risks. Similarly, there are various books on microbiology (even a few about pharmaceutical microbiology), yet these books rarely mention cleanrooms, or, where they do, give controlled environments limited coverage. To the authors of Cleanroom Microbiology, these two domains, normally separated by different functions, are inseparable. This book is about cleanrooms and controlled environments in relation to the pharmaceutical and healthcare sectors and is applicable to both the sterile and non-sterile pharmaceutical sectors with its focus on cleanroom microbiology.

go.pda.org/cleanroom

TIM SANDLE has over twenty-five years of experience in pharmaceutical microbiology. Tim is the site microbiologist at the Bio Products Laboratory and he is a visiting tutor at the University of Manchester, where he teaches pharmaceutical microbiology. In addition, Tim is a longstanding committee member of the Pharmaceutical Microbiology Interest Group (Pharmig).

DR. VIJAYAKUMAR is an Assistant Professor of Microbiology in the College of Science, Zulfi, Majmaah University in the Kingdom of Saudi Arabia. He has over twelve years' experience in the field of Pharmaceutical and Clinical Microbiology. He has a doctorate in Microbiology from Bharathidasan University, India. His past experience in the sterile pharmaceutical industry includes (Aurolab, India) as Microbiology Manager where he was involved in QC and QA activities.

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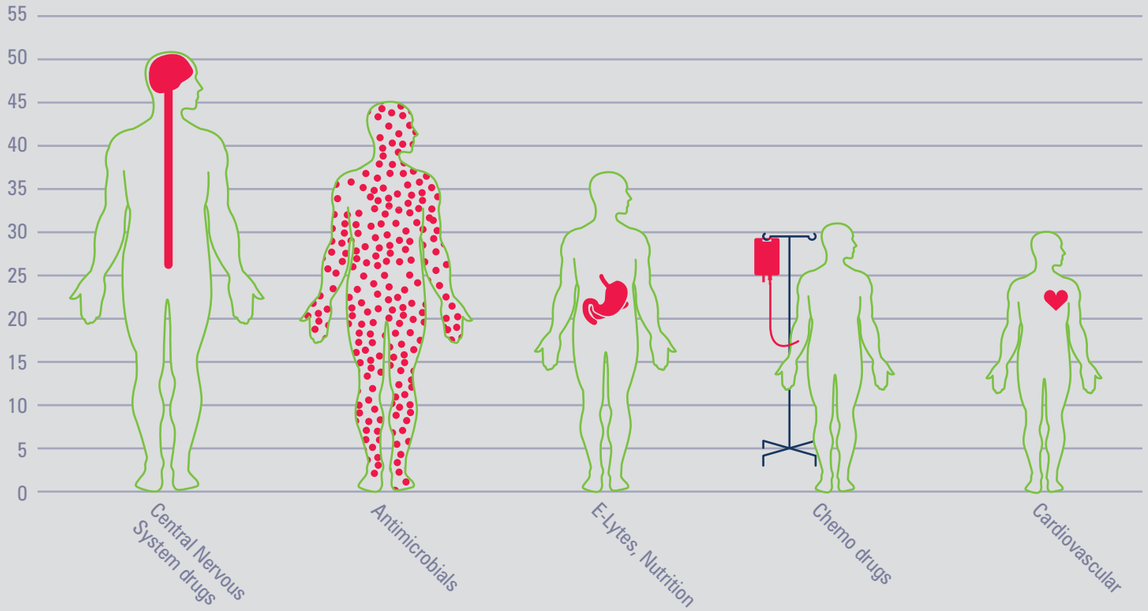
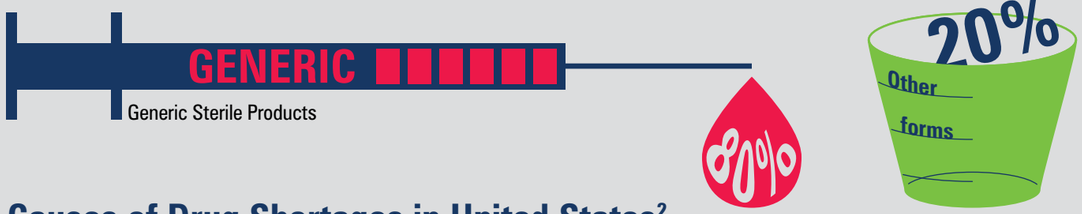
Key Takeaways From the *2014 PDA Drug Shortage Workshop*

The Top 5 Classes of Drugs in Shortage Are Used for Serious Ailments[1]



Shortages by Dosage Form[1]



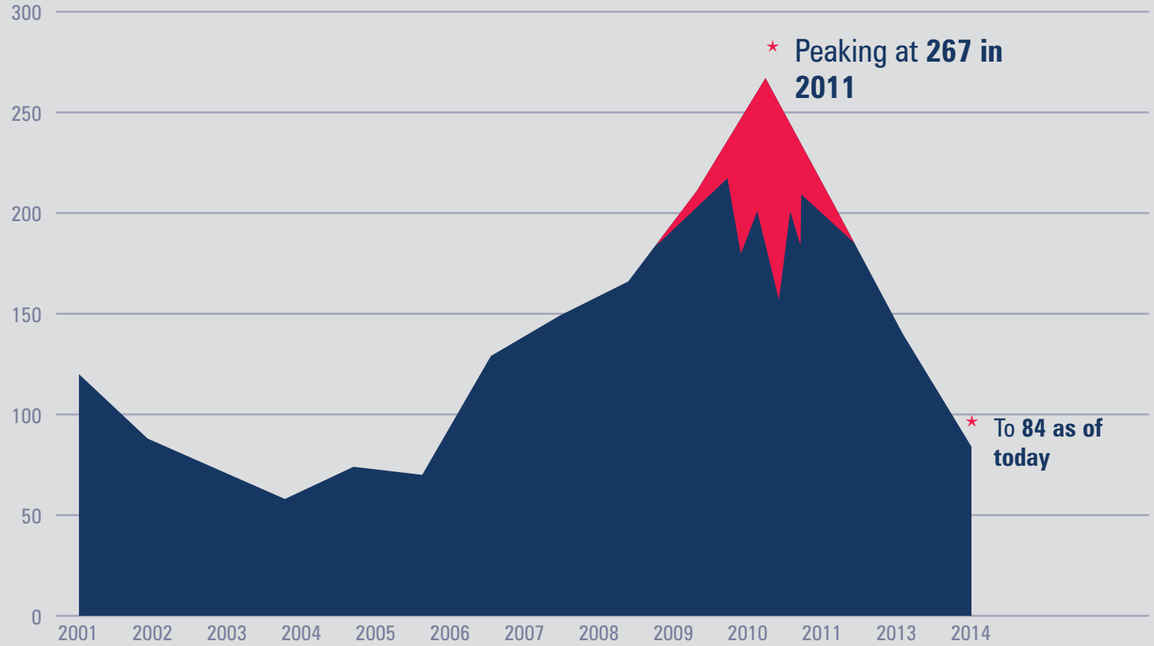
Causes of Drug Shortages in United States[2]

64% Quality issues

27% Raw Materials shortage

9% Other

The numbers of drugs in shortage has fallen[1]…



BUT

Of 1137 new shortages reported since 2008,

25% **remain unresolved[1]**

What can you do?

Start with PDA's upcoming technical report on drug shortages. This report will offer a practical risk triage model for companies to prevent and manage shortages.

Sources

1. Benjamin, B. "Drug Shortages: Current Trends And Impact On Care." Presented at the 2014 PDA Drug Shortage Workshop, Washington, DC, September 2014
2. Jensen, V. "FDA Response to Drug Shortages." Presented at the 2014 PDA Drug Shortage Workshop, Washington, DC, September 2014

snapshot

Report from PDA/FDA

Interest Group *Corner*

Regulatory Affairs Interest Group Learns about QbR Submissions from FDA Expert

Rebecca Stauffer, PDA

During his presentation on Question-based Review (QbR) for ANDA submissions at the Regulatory Affairs Interest Group meeting at the *2014 PDA/FDA Joint Regulatory Conference,* **Robert Iser,** Director, Division of Chemistry IV, Office of Generic Drugs, CDER, FDA, stressed that the Agency does not require QbR submissions for generics but the format does offer advantages over other types of submissions.

"It's not a requirement but it does facilitate the review and submission process," he said. "Makes it more efficient, matter of fact, than using other formats for the submissions."

But what is QbR? According to Iser, "QbR is a general framework for the science and risk-based assessment of product quality… QbR contains important scientific and regulatory review questions."

These questions relate to product design, product performance, risk to product performance, and the control strategy.

"It takes a lot of the questions that we have as we're reviewing and puts them down in a format that's easily used by the industry," he said. "This really helps to streamline the reviews."

QbR arose out of the growth of the Quality by Design (QbD) paradigm and other enterprises that followed the FDA's Pharmaceutical cGMPs for the 21st Century initiative. ICH Q8–Q10, plus the quality systems guidances, also laid the foundation for QbR. The Office of Generic Drugs started the transition to QbR in 2004, finalizing the questions for the generics industry by early 2005. In 2007, QbR was fully implemented within OGD. Now, close to 100% of ANDA submissions utilize the QbR approach.

Iser also explained that the questions used as part of QbR are not static and his office routinely receives feedback on the questions. The goal of QbR is to streamline the submission process.

"The whole point of QbR is to lead to a higher quality submission," Iser emphasized.

An audience member asked Iser about CBER's views on QbR. He explained that while CBER has not taken on a project to implement QbR into their submission process, his group has been having discussions with the Office of Biotechnology Products within CDER on how QbR can help those teams with their reviews and submissions for biologics products.

QbR Tied to CDER Reorganization

As far as NDAs, Iser said that NDA sponsors tend to use QbR questions as a guideline. His group has been involved in internal discussions that resulted in a QbR template that could be used for a small molecule NDA or ANDA, or a large molecule NDA. Utilization of QbR beyond ANDAs would also reflect the vision of the Office of Pharmaceutical Quality (OPQ), the new super office at the Agency, which will house all the quality assessment activities for NDAs, ANDAs and the BLAs that fall under CDER purview. The idea is that OPQ would be responsible for a total quality assessment of products, utilizing integrated teams that follow risk-based thinking as well as lifecyle and knowledge management.

The new office would also coordinate compliance activities as different silos within the agency collaborate in this area, ideally avoiding disconnect between application reviewers and compliance officers overseeing preapproval inspections through sharing of information prior to inspection.

Once the super-office is set up, "If OPQ is doing what they're supposed to be doing, you shouldn't hear things from someone in an inspection that says 'the reviewer doesn't know' and you shouldn't hear someone from the review side saying 'the investigator doesn't know,'" said Iser.

In addition, OPQ will feature a better platform for facilitating sharing of knowledge. Iser acknowledged that companies submit a lot of information about their products in their submissions and in the past the Agency has not accessed or used it well.

"One of the tenets of OPQ is to share this knowledge better," he said.

Before Iser's presentation, interest group coleader **Ruhi Ahmed,** PhD, Sr. Director, Regulatory Affairs, Ultragenyx, announced that she and **John Finkbohner,** PhD, Senior Regional Policy Director, MedImmune, have been elected as coleaders for the Regulatory Affairs Interest Group.

Anyone interested in joining this interest group is encouraged to contact PDA's Volunteer Coordinator at volunteer@pda.org.

About the Expert

Robert Iser has been with the Office of Generic Drugs since 2003. He is currently the Director of the Division of Chemistry IV. Since joining OGD, Iser has been involved in numerous OGD and CDER committees and working groups.

Group Yields New MHRA Inspection Data Report Format

David Churchward, MHRA and Stephan Rönninger, Amgen

In October 2012, the UK regulatory agency MHRA reached out to a number of national and international industry associations including PDA, the Association of the British Pharmaceutical Industry (ABPI), British Generic Manufacturers Association (BGMA), International Society for Pharmaceutical Engineering (ISPE), and the Research Quality Assurance-Group (RQA), as well as the UK's National Health Service, to form an "inspection trending focus group." PDA's Regulatory Affairs and Quality Advisory Board (RAQAB) and PDA's Inspection Trends Interest Group jointly supported this effort on behalf of PDA.

As a result of the efforts of this focus group, the content and format of the annual MHRA inspection report was revised and is now available for the benefit of the industry (www.mhra.gov.uk/home/groups/pl-a/documents/websiteresources/con464241.pdf). The group provided an understanding of how industry uses trend data and suggested ways to improve future MHRA reports to promote greater learning opportunities. This facilitated a more effective use of existing data collection tools available to MHRA at present.

Types of Deficiencies Remain Mostly Unchanged

The report's executive summary lists the most common GMP deficiencies by defect category for 2013, along with graphs outlining five-year trends for these defects This is further elaborated in the report with concrete examples of the most frequent deficiencies found. The report ends with four key areas for attention by manufacturers.

What can be concluded from these inspection activities? Well, for one, the most frequently encountered deficiencies found in inspections by MHRA over the previous five years have remained relatively consistent, with the exception of "contamination, chemical/physical (or potential for)." This has increased significantly. Deficiencies relating to "Quality Systems" are by far the most relevant observations made by inspectors. The ratio of "critical" observations raised per inspection increased during 2013 due to a cluster of data integrity issues that carry potential impact to public health.

The top five deficiencies listed in the report, include:

1. Investigation of anomalies: Deviations
2. Quality Management
3. Investigation of anomalies: CAPA
4. Contamination, chemical/physical (or potential for)
5. Supplier and contractor audit

Based on changes in the regulatory environment, in addition to intelligence from other agencies, the inspectorate has identified a number of focus areas. These areas of focus are: data integrity, implementation of new supply chain requirements according to the Falsified Medicines Directive (FMD), and cross-contamination risks—this, particularly in light of impending changes to chapters on "Premise and Equipment" (chapter 3) and "Production" (chapter 5) of the EU GMP guide.

Looking to the future

Further improvements to address other points raised by the focus group will be considered; MHRA's goal is to implement as many remaining requests from the group as possible. To achieve this, the Agency plans to develop an IT solution which will permit greater detail on inspection data collated in the future. Further enhancements being explored include trending of deficiencies by individual paragraphs of the EU GMP guide and also publishing an anonymized raw data set for stakeholders to perform tailored analyses specific to their needs.

The data shows areas of commonality between the critical and major inspection findings by inspections conducted by MHRA and those from other agencies (e.g., the U.S. FDA). There are clear benefits in learning from the experiences of others when identifying common areas of quality and regulatory focus. Ultimately, the focus group encourage regulators and industry to

Continued at top of page 55

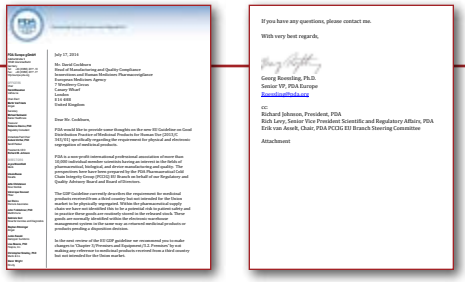
Your Local PDA Connection

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.

PDA PCCIG Comments on EU GDP Guideline

For the comments grid, visit www.pda.org/regulatorycomments



July 17, 2014

Mr. David Cockburn
Head of Manufacturing and Quality Compliance
Inspections and Human Medicines Pharmacovigilance

European Medicines Agency 7 Westferry Circus Canary Wharf London E14 4HB
United Kingdom

Dear Mr. Cockburn,

PDA would like to provide some thoughts on the new EU Guideline on Good Distribution Practice of Medicinal Products for Human Use (2013/C 343/01) specifically regarding the requirement for physical and electronic segregation of medicinal products.

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. The perspectives here have been prepared by the PDA Pharmaceutical Cold Chain Integrity Group (PCCIG) EU Branch on behalf of our Regulatory and Quality Advisory Board and Board of Directors.

The GDP Guideline currently describes the requirement for medicinal products received from a third country but not intended for the Union market to be physically segregated. Within the pharmaceutical supply chain we have not identified this to be a potential risk to patient safety and in practice these goods are routinely stored in the released stock. These goods are normally identified within the electronic warehouse management system in the same way as returned medicinal products or products pending a disposition decision.

In the next review of the EU GDP guideline we recommend you to make changes to 'Chapter 3/Premises and Equipment/3.2. Premises' by not making any reference to medicinal products received from a third country but not intended for the Union market.

If you have any questions, please contact me.

With very best regards,
Georg Roessling, Ph.D.
Senior VP, PDA Europe
Roessling@pda.org

Richard Johnson, President, PDA
Rich Levy, Senior Vice President Scientific and Regulatory Affairs, PDA
Erik van Asselt, Chair, PDA PCCIG EU Branch Steering Committee

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GSA Schedule
Contract GS-02F-113BA

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SESSION 1:
Week 1: January 26-30
Week 2: February 23-27

SESSION 2:
Week 1: March 23-27
Week 2: April 13-17

SESSION 3:
Week 1: May 18-22
Week 2: June 15-19

SESSION 4:
Week 1: August 3-7
Week 2: August 24-28

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- Learn to incorporate proper documentation practices into your aseptic processing program to facilitate regulatory compliance

Learning Objectives

Upon completion of this course, you will be able to:

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- Limit risk for manual product contamination with airflow visualization studies
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Regulatory Briefs

Regulatory briefs are compiled by PDA member volunteers and staff directly from official government/compendial releases. Links to additional information and documentation are available at www.pda.org/regulatorynews.

North America

Launch Date Announced for Office of Pharmaceutical Quality

The U.S. FDA announced on Oct. 16 the launch date of the Office of Pharmaceutical Quality. OPQ is scheduled to launch January 1, 2015 with **Janet Woodcock,** MD, as the first acting director, supported by **Lawrence Yu** as Deputy Director.

Organizational Changes Planned at FDA Office of Regulatory Affairs

The U.S. FDA recently announced changes in the organizational structure of the Office of Regulatory Affairs. To ensure better collaboration with Centers as well as efficiency, each Center will have a single senior executive within ORA responsible for each commodity program. ORA will also work with other Centers on new initiatives for inspections and training.

New Guidance Clarifies Adulteration Circumstances

On Oct. 22, the U.S. FDA released a guidance, *Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection,* per Section 707 of the Food and Drug Administration Safety and Innovation Act (FDASIA). This guidance defines the types of actions or inactions that the Agency considers as constituting delaying, denying, or limiting an inspection, or refusing to permit an inspection.

U.S. FDA Compliance Data Available Through Public Dashboard

As part of the Presidential Memorandum on Regulatory Compliance, issued January 2011, the U.S. FDA has released a new online dashboard that allows public access to information on the Agency's compliance, inspection and recall activities. Providing data from FY 2008 to FY 2013, the dashboard includes information on inspections, warning letters, seizures and injunctions, and statistics specific to recalls. This data will be updated semiannually.

Hosted in a cloud environment, the data can be downloaded, manipulated through the selection of filters, rearranged to format datasets and columns, drilled down, and exported. The dashboard can be accessed here: govdashboard.fda.gov.

U.S. FDA Releases 2015 Fiscal Year Regulatory Science Priorities for Generics

On Oct. 3, the U.S. FDA published its 2015 regulatory science priorities pertaining to generic drugs in accordance with GDUFA. These priorities were prepared based on comments received at the May 16 public meeting and through public dockets. Priorities include: postmarket evaluation of generic drugs, equivalence of complex products, equivalence of locally acting products, therapeutic equivalence evaluation and standards, and computational and analytical tools.

U.S. FDA Plans Further Decisionmaking on Biomarkers

Under the Prescription Drug User Fee Act Reauthorization of 2012, the U.S. FDA is mandated to advance the use of biomarkers, which are key in the development of personalized medicines. As part of this plan, the Agency partnered with the Brookings Institution to host a public workshop Sept. 5.

During the workshop, the following were topics of discussion: the need for clear standards for the evidence supporting biomarker use, infrastructure and policies promoting development of tests to identify patients for clinical trials, new models for clinical trials that accelerate biomarker development, and methods for assessing treatment effects in small populations.

The information gathered in this workshop will be used to guide the Agency's decisionmaking with regard to biomarkers.

U.S. FDA Outlines When it May Refuse an ANDA Due to Lack of Justification of Impurity Limits

On Sept. 17, the U.S. FDA released the draft guidance, *ANDA Submissions—Refuse to Receive for Lack of Proper Justification of Impurity Limits.* This draft guidance is aimed at applicants submitting abbreviated new drug applications (ANDAs) for approval of drug products with new strengths, and highlights specific deficiencies of information that may lead the Agency to refused to receive an ANDA.

These deficiencies are: failing to justify proposed limits for specified identified impurities in drug substances and drug products that are above qualification thresholds, failing to justify proposed limits for specified unidentified impurities that are above identification thresholds, and proposing limits for unspecified impurities (e.g., any unknown impurity) above identification thresholds.

Europe

Chapters Now Finalized in EU GMP Guide

The European Commission has published the final version of Chapters 3, 5, and 8 of the EU GMP Guide. Chapter 3 covers premises and equipment, Chapter 5 covers production, and Chapter 8 covers complaints, quality defects and product recalls. These chapters will be effective March 1.

EDQM: Undeclared APIs Now a Major Problem in Europe

Sept. 10–11, the European Directorate for the Quality of Medicines & Healthcare (EDQM) held its second symposium on strategies to combat counterfeit and other illegal medicinal products. The symposium consisted of representatives from forensic and customs laboratories, national food and drug regulatory agencies, enforcement groups and the European Commission. According to

Continued at bottom of page 55

EMA Official Outlines Drug Shortage Problem; Discusses Initiative

Rebecca Stauffer, PDA

During her presentation on EMA initiatives addressing drug shortages in Europe at the *2014 PDA Drug Shortage Workshop,* **Sabine Haubenreisser,** PhD, EMA Liaison Official at the U.S. FDA, described the issue in terms one might use to characterize a severe illness.

"Shortages related to manufacturing issues, they are very problematic," she said. "They can have a rapid onset, they can very quickly go from huge to chronic, they can take a very long time to resolve, and you'll need a multidisciplinary team to address the issue."

While the issue of drug shortages has been a major focus for both the FDA and companies in the United States, EMA has also been involved in responding to shortages due to manufacturing issues within the European Union. In general, most drug shortages within the European Union are handled at the local level by National Competent Authorities. EMA becomes involved if the shortage concerns a centrally authorized product, a nationally authorized product referred to the EMA or if there is a shortage of a noncentrally authorized product affecting more than one Member State.

Just like in the United States, EU manufacturers are required to notify regulatory authorities under certain conditions if there is an expected shortage.

"In case there will be a cessation of product on the market, the marketing authorization holder must notify the supervisory authority within two months and give the reason for the shortage," said Haubenreisser. "And if there is a suspension or recall of the medicine, then the marketing authorization holder must notify the competent authority immediately."

The issue of globalization and the complexity of the global supply chain is a key factor in European drug shortages. She further explained that the European Economic Area is an important destination and source of medicines and ingredients.

"There is a globalization of manufacturing which brings about a complexity of the supply chain. And such a complex supply chain is obviously vulnerable because at any time, at any stage of each step something can go wrong," she said.

EMA Efforts to Address Drug Shortages

The last half of Haubenreisser's talk highlighted EMA's efforts to tackle the issue of drug shortages. Initially, the Agency initiated discussions among its scientific committees, including the Committee for Medicinal Products for Human Use (CHMP), Coordination Group for Mutual Recognition and Decentralised Procedures (CMDh), Paediatric Committee (PDCO) and Committee for Orphan Medicinal Products (COMP), along with other regulatory agencies. This culminated in a workshop held in September 2012 that led to the development of an implementation plan.

"The implementation plan aims at developing a common understanding of what is a critical medicine. This is pretty close to, as well, with what the FDA has defined as an 'essential medicine,'" said Haubenreisser. "The implementation plan also foresees a framework for the risk benefit assessment of a given shortage for a given medicine."

The plan also recommends development of a decision tree that outlines how a National Competent Authority can escalate a shortage to the EU level.

In addition, "the implementation plan is aimed to raise awareness of the impact of shortages but also to stimulate your reaction and it should stimulate as well improvement in business continuity planning. It aims at better promoting proactive risk management by the Marketing Authorization holders."

Haubenreisser concluded by suggesting ways for industry to address the issue.

"For one, it's important to shift from reactive to proactive risk management. It's important to explicitly assess supply chains and transport risk as part of procurement and contract management and proper governance process," she said.

Communication with EMA as soon as a company is aware of a shortage is also important, she stressed. This communication should also be ongoing at every stage of a shortage.

Collaboration and communication with both regulators as well as across industry through associations can serve as a "treatment plan" for resolving shortages as well as for developing proactive, preventive "cures" for the issue. While a shortage obviously has severe implications for patient safety and access to lifesaving medicines, companies involved face further risks.

"They [shortages] can come about with costs due to recalls but also reduce public confidence in the organization," Haubenreisser emphasized.

About the Expert

Sabine Haubenreisser joined the EMA in 1997 where she held positions as support to the Head of Human Unit, as Project Manager in the Sector of New Chemical Substances, as Secretary to the Mutual Recognition Facilitation Group and from 2001 to 2009 as Specialised Group Leader of the Team Anti-Infectives, Immunology, Gastroenterology and Musculoskeletal in the Post-Authorisation Human Unit. In May 2012 she was appointed as EMA Liaison Official at the U.S. FDA and is based at the FDA headquarters in Silver Spring, Md.

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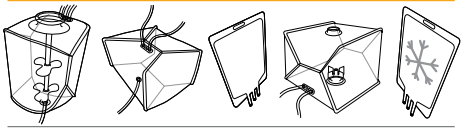

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The closing plenary of the 2013 PDA Pharmaceutical Quality Metrics Conference

Amgen's Martin VanTrieste discusses the U.S. FDA's proposal for offering quality metrics

Mark Sebree of BD Rx talks about his company's new line of generic sterile injectables

Lawyer Cathy Burgess speaks about greater U.S. FDA regulatory oversight of cGMPs

Katja Kotter of Vetter addresses the new combination products rule

Yuexia Li, Jeffrey Baker and Cesar Matto offer perspectives on transitioning to U.S. FDA careers after many years in industry

Dr. Jack Levin, codiscoverer of the LAL test, discusses his research into this groundbreaking assay

Lonza's Allen Burgenson discusses potential threats to the supply of LAL and alternative assays

Amgen's Madhu Balachandran discusses the future of manufacturing

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A European Perspective on Quality Metrics

Anil Sawant, PhD, Johnson & Johnson

As the U.S. FDA's momentum to collect quality metrics keeps building, one major question keeps arising: is this a U.S.-only effort or is Europe moving in the same direction?

This leads to further questions. What is the EMA perspective on quality metrics? Are quality culture and quality systems maturity viewed the same way in Europe as in the United States? Will there be universally accepted definitions for metrics?

PDA has been one of the leaders in facilitating dialogue between industry and regulators on the topic of metrics. During the *2013 PDA Pharmaceutical Quality Metrics Conference,* technology enabled the attendees to provide instant feedback on various proposed metrics which helped shape PDA's position on the subject. At the 2013 conference, every attendee's voice was heard and among those voices was the request to explore the role of quality culture and quality system maturity.

This year's quality metrics conference is a result of that feedback as well as feedback received during conference sessions on quality metrics at the *2014 PDA Annual Meeting* and the *2014 PDA/FDA Joint Regulatory Conference.* The PDA Metrics Task Force has been working on building the foundation for the 2014 conference. This fall, PDA conducted a first-of-its-kind Quality Culture Survey—sent out to both executives within industry and to PDA membership at large. The results of this groundbreaking survey will be presented during the 2014 meeting and there will be lots of opportunity for attendees to discuss the findings of the survey.

In addition, attendees will not only hear the latest thinking from FDA regulators, but will also get a European perspective from distinguished speakers such as **Emer Cooke,** Head of International Affairs, EMA, and **Gerald Heddell,** Director of Inspection, Enforcement and Standards, MHRA. FDA speakers will also provide an opportunity to learn more about the upcoming guidance on quality metrics.

To learn more, please visit www.pda.org/metrics2014. For information about the PDA TRI course following the conference, visit www.pda.org/metricscourse.

Tug-of-War Exercise Illustrates Importance of Quality Culture

Jahanvi (Janie) Miller, PDA

Quality Culture has become the driving force within many organizations. Yet challenges remain with regard to implementing or emphasizing it. In August, at a workshop at the *GMP by the Sea* conference, **Robert Darius,** VP, Quality Unit, GSK, led an activity to illustrate the importance of quality.

He asked attendees to divide themselves into teams based on which of the following categories they fell under; business, manufacturing or quality. Needless to say, there was an unequal divide; however, what everyone was not aware of, was the tug-of-war exercise being set up on the lawn. The three ends of the tug-of-war ropes represented the teams (quality, manufacturing and business). A circle on the ground represented the design space that the junction of the ropes had to stay within to prevent occurrence of a quality incident.

Since there wasn't an even distribution of experts, the teams failed to maintain equilibrium.

The team that struggled the most? The quality team with the least number of representatives.

After multiple tries, along with compromise, collaboration, and active communication; the group stabilized the focal point to the center of the design space; this was the intent of the exercise all along. The impact of this exercise was very notable. Many people seemed unaware of the challenges faced by the other departments they work with. All who attended this workshop took away the clear message that to successfully achieve a common quality goal, all involved must actively communicate, taking into account the capabilities and the need to meet the standards of their sister departments.

PDA continues to ensure members are aware of the latest thinking on quality. In September, PDA released its Quality Culture survey; preliminary results will be launched at the metrics conference in December.

Keeping the Signals Clear: Industry and FDA Collaborate on Innovation continued from page 34

The advent of continuous production was discussed by **Gordon Muirhead,** PhD, Vice President Oral Solid Dosage Forms, GlaxoSmithKline. Such processes are very amenable to QbD in comparison to batch processes. PAT provides the right metrics to reduce variability—enabling companies to measure more meaningful parameters than blending time, for example, and focusing instead on properties indicative of blend thoroughness. On the flip side of "manufacturing of the future," the dilemma of aging facilities was covered. The reasons to update facilities are myriad: high process variability, improper or outdated analytics, equipment age and resulting issues obtaining spare parts, to name a few. **Maik Jornitz,** President, G-Con, discussed the important efforts of PDA's Aging Facilities Task Force, which has subgroups dedicated to facilities, processes, and analytics and seeks volunteers. **Ghada Haddad,** Associate Director, Engineering, Merck, shared her experience and challenges in "renovating and innovating" an existing facility, to upgrade equipment and processes (isolators and VHP) while increasing capacity.

Marla Phillips, PhD, Director, Xavier Health, Xavier University, brought unique insight to pharma/supplier relationships. A Xavier study revealed that contrary to popular belief, lack of reliability of incoming materials was not due to "poor supplier performance," but was more attributable to issues caused by manufacturers themselves; Xavier continues their work with industry to develop and codify Good Supply Practices (GSPs).

Plenary sessions on the final day were kicked off with a compelling "Patient Perspective" session, in which **Terry Sarisky** shared the personal story of her mother's fight against brain cancer, and the critical role that innovation and clinical research can play in saving and improving patient lives. Various FDA leaders then participated in panel discussions regarding Compliance and Center Initiatives. Following the reorganization of FDA, there are multiple agency priorities, ranging from Food and Drug Safety and Innovation Act (FDASIA) and Drug Quality and Security Act (DQSA) implementation, to quality initiatives and preparedness activities.

Overall, the event celebrated the advances of our industry, the important alliance between industry/regulatory/academia, and highlighted the fact that, despite the noble efforts we undertake, the increasing complexity of our challenges creates new risks, which require new approaches and a redoubled focus on quality.

About the Author

Erin O'Brien joined West in 2009. In her current position as Senior Director, Marketing, she leads West's marketing efforts for the Pharmaceutical Packaging Systems Division in North America.

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Recordings from the entire workshop are available for purchase for **$280 Member/$320 Nonmember**. Price of recordings includes:

- Eight (8) recorded sessions from the 2014 PDA Packaging Conference
- PowerPoint slides with synchronized audio
- Access to sixteen (16) downloadable presentation handouts
- Unlimited playback of the recordings for 90 days from receipt of login information.

2014 PDA/FDA Joint Regulatory Conference and Drug Shortage Workshop

Recordings from the conference and workshop are available for purchase for **$425 Member/$475 Nonmember**.
Price of recordings includes:

- Fifteen (15) recorded sessions from the 2014 PDA/FDA JRC and four (4) recorded sessions for the Drug Shortage Workshop
- PowerPoint slides with synchronized audio
- Access to thirty-eight (38) downloadable presentation handouts
- Unlimited playback of the recordings for 90 days from receipt of login information.

For more information on all PDA conference recordings please visit:

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Group Yields New MHRA Inspection Data Report Format continued from page 43

extend further opportunities for collaboration and data sharing to achieve a common goal—the reliable supply of quality medicines to patients globally.

About the Authors

David Churchward is Expert GMDP inspector at MHRA. In his current role, Churchward is responsible for the GMP Inspectorate's compliance management activity, including membership of the MHRA's Inspection Action Group, and leads the agency team responsible for delivering data integrity inspection strategy and training.

Stephan Rönninger is the Head of External Affairs Europe, International Quality at Amgen. In his current role, he is responsible for providing leadership, feedback, support and represent in external activities impacting Amgen's operations functions with and for associations such as PDA and EFPIA.

Regulatory Briefs continued from page 47

participants, undeclared APIs and other active substances in products offered for sale remain a pressing issue within Europe. These products are often purchased from the legal market as well as acquired from uncontrolled sources.

EMA to Release Clinical Reports to General Public

On Oct 2, EMA's Management Board adopted a new policy to publish clinical reports contained in all applications for centralized marketing authorizations. The Agency hopes this new policy will better allow the general public to understand its decisionmaking as well as avoid duplication of clinical trials, foster innovation and encourage development of new products. Information that may be considered commercially confidential will be redacted.

The policy will be effective January 1, 2015 and will apply to all authorizations submitted after that date.

Africa

African Medicines Regulatory Harmonization Program Designates Regional Centres of Regulatory Excellence

The African Medicines Regulatory Harmonization Project has announced that ten institutions and institution partnerships were designated as Regional Centres of Regulatory Excellence (RCOREs). These centers will participate in the development of a regulatory workforce across Africa through hands-on training within companies or regulatory authorities.

Richard Johnson, PDA President and CEO

2014 Proves a Busy, Productive Year for PDA

I am pleased to report that 2014 has been another very successful year for your Association. With the help of countless volunteers and our hardworking staff, PDA continued Connecting People, Science & Regulation®. All of this activity was guided by your input and the PDA 2010–2015 Strategic Plan. We will be updating this strategic plan to guide our activities for the next five to ten years.

I would like to highlight a few elements of our activities this year.

People

We continue to bring people together to learn from each other and develop new insights at meetings, such as the:

- 69th *PDA Annual Meeting* in San Antonio, Texas
- 23rd annual *PDA/FDA Joint Regulatory Conference* in Washington, D.C.
- 11th *Universe of Prefilled Syringes and Injection Devices* conference in Huntington Beach, Calif.
- Microbiology conferences in both the United States and Europe
- Parenterals meeting in Munich, Germany
- PDA/PIC/S workshop on implementation of ICH Q7 in the United States, Europe and South Africa
- And many others

We've expanded our training activities in the United States and around the world, with more than 50 courses, including:

- Enhancements to our premier aseptic processing courses
- Gaining GSA Schedule approval to enhance our ability to serve our government members
- Augmenting in-house training to stakeholders around the world
- And many others

We also continue to enhance the value of PDA membership to you by expanding our reach into new areas (e.g., a new chapter in Singapore) and by boosting volunteer recognition and recruitment initiatives

Science

We've focused our resources to continue delivering outstanding publications, including:

- A PDA Points to Consider document on pharmaceutical quality metrics
- *PDA Technical Report No 65: Technology Transfer*
- *PDA Survey: 2013 PDA Objectionable Microorganisms for Nonsterile Pharmaceutical, Consumer Health, Medical Devices, Dietary Supplement and Cosmetic Products*
- *PDA Technical Report No. 13 (Revised 2014): Fundamentals of an Environmental Monitoring Program*
- *PDA Technical Series: Sterilization — Compilation of Technical Reports and Journal Articles on Pharmaceutical Sterilization*
- PDA Points to Consider document on the medical risk of visible particles in injectables
- *PDA Technical Report No. 66: Application of Single-Use Systems in Pharmaceutical Manufacturing*
- And several others

Regulation

We keep expanding our global reach and working effectively with global regulatory authorities to enhance pharmaceutical science and advance health of patients, by providing science and technology-based input on regulations and guidelines related to PDA strategic areas, utilizing PDA's volunteer and membership base; bringing sound scientific and technical information to the regulatory process; maintaining valuable and effective relationships with global regulators, and educating members on current regulatory expectations; and engaging with regulatory agencies for the development and adoption of PDA technical reports.

Of course, we have continued to manage your Association's resources by following a five-year rolling financial and marketing plan to sustain and balance major activities.

2015 promises to be another busy year of Connecting People, Science and Regulation®, but none of it will happen without the support and volunteer efforts that make these activities so valuable. If you would like to volunteer in a task force, interest group or a committee, visit www.pda.org/volunteer.

Please email us or stop by and let us know how we are doing. Remember, this is your Association. Our doors are always open, and we would love to hear from you.

PDA Seeks a World With Just One Post-Approval Change Process

Anders Vinther, PhD, Sanofi Pasteur

At the cutting-edge *PDA Drug Shortage Workshop* in September in Washington D.C., we talked about ways regulators and industry can work together to reduce drug shortages. We covered many topics including the need to reduce incidents of quality-related manufacturing issues which are often the cause of drug shortages. This will be covered in a new PDA technical report that will include templates that can be used directly by companies and also to meet requirements in the United States and European Union for reporting drug shortages.

Also during the workshop, the topic of drug shortages caused by the complexity of Post-Approval Change (PAC) processes around the world came up. While each country might have a very standardized process for reporting and handling PAC, collectively there is a wealth of processes used globally. The complexity comes from different reporting levels, different documentation requirements and different approval timelines for the same type of change, and then some of the changes require a preapproval inspection prior to being effective. Hence, although a company would prefer to have just one manufacturing process and associated test methods applicable worldwide, over time the one originally submitted process may end up in several—even dozens—of processes run in parallel or sequence depending on the approval status. This makes the role of logistically managing all these versions at the same time difficult, and also creates a potential for a shortage if one regulatory PAC approval takes longer than anticipated or the demand suddenly increases for one version of the process outside current stock level.

The complexity of regulatory PAC processes globally can make companies think twice before they implement a new method capable of detecting a broader range of adventitious agents, or a process change that improves the overall process capability and reduces the OOS rate, simply because of the risk of a drug shortage in the future or because it is not financially viable with several parallel processes and test methods. One can argue that the current global PAC process complexity incentivizes companies to keep things the way they are rather than facilitating continual improvement, state of control and product realization—which are exactly the objectives of ICH Q10.

At PDA we have decided to attack the problem by creating what we call "global Change Protocols" or "gCPs". So what do we mean by that? Well, imagine if we had just one standard protocol for certain types of postapproval changes and our companies would use this protocol globally for all health authorities. The protocol would suggest reporting category, requirements for validation of the change, comparability studies needed and how the change could be implemented. An example of a gCP is moving from traditional microbial control systems to rapid micro methods, or introducing single-use systems at specific process steps. With the gCP we have the potential to standardize certain types of PAC globally and thus expedite the change through the regulatory system based on solid scientific data and agreed upon requirements—and ultimately reduce drug shortages and promote ICH Q10 objectives.

The gCP approach that we have now initiated is right at the core of the PDA mission and strategy of promoting science and regulations®—and it has the potential to drastically reduce drug shortages when fully implemented by regulators and industry.

If you are as excited about this PAC initiative as I am, let us know and get involved in creating one or more gCPs.

Third PDA/FDA JRC Continues Spirit of Collaboration

When I first started working at PDA in September 2012, barely a week later I was at the *PDA/FDA Joint Regulatory Conference* in Baltimore. This was my first taste of this signature meeting where regulators and members of industry (and even some from academia) come together to discuss the pressing issues affecting the pharma and device world. Now I've experienced my third Joint Regulatory Conference and the dynamic atmosphere and lively discussions were no less this year than in 2012.

We hope the articles in this issue offer you a taste of this year's conference. **Geetha Jayan** and **Erin O'Brien,** our cover story authors, volunteered to cover the meeting for the *PDA Letter.* Both noted the spirit of collaboration and innovation imparted by plenary speakers such as the U.S. FDA's **Janet Woodcock** and Amgen's **Madhu Balachandran.** We also interviewed Balachandran in advance of his talk; this was recorded and uploaded as the October *PDA Letter* podcast. We've included a transcript of portions of this interview in our Features section.

Our Science and Regulation Snapshots also feature reports from two of the PDA interest groups that convened during the meeting.

Following the conference was the *2014 PDA Drug Shortage Workshop.* This issue's two-page infographic showcases some sobering statistics delivered in the opening plenary of this workshop. Stay tuned for an upcoming PDA technical report that offers risk models for preventing shortages.

And don't forget to check out the PDA Photostream for some photos of the *2014 PDA/FDA Joint Regulatory Conference*. If you were hoping for photos of me attempting the Electric Slide at the gala, expect to be disappointed!

I hope to see everyone again in September at next year's *PDA/FDA Joint Regulatory Conference* in Washington, D.C.!

—**Rebecca Stauffer,** filling in for **Walter Morris** this issue.

PDA Letter Editorial Committee Seeks Volunteers! Email stauffer@pda.org for more information.

Correction

In the October issue, **Robert Kieffer's** name was misspelled in the article, "Quality Culture Not Just Technological; Skills Key, Too," on page 21.

The *PDA Letter* podcast is available at www.pda.org/pdaletter.

This month: Madhu Balachandran

PDA Letter

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