People • Science • Regulation

PDA Letter

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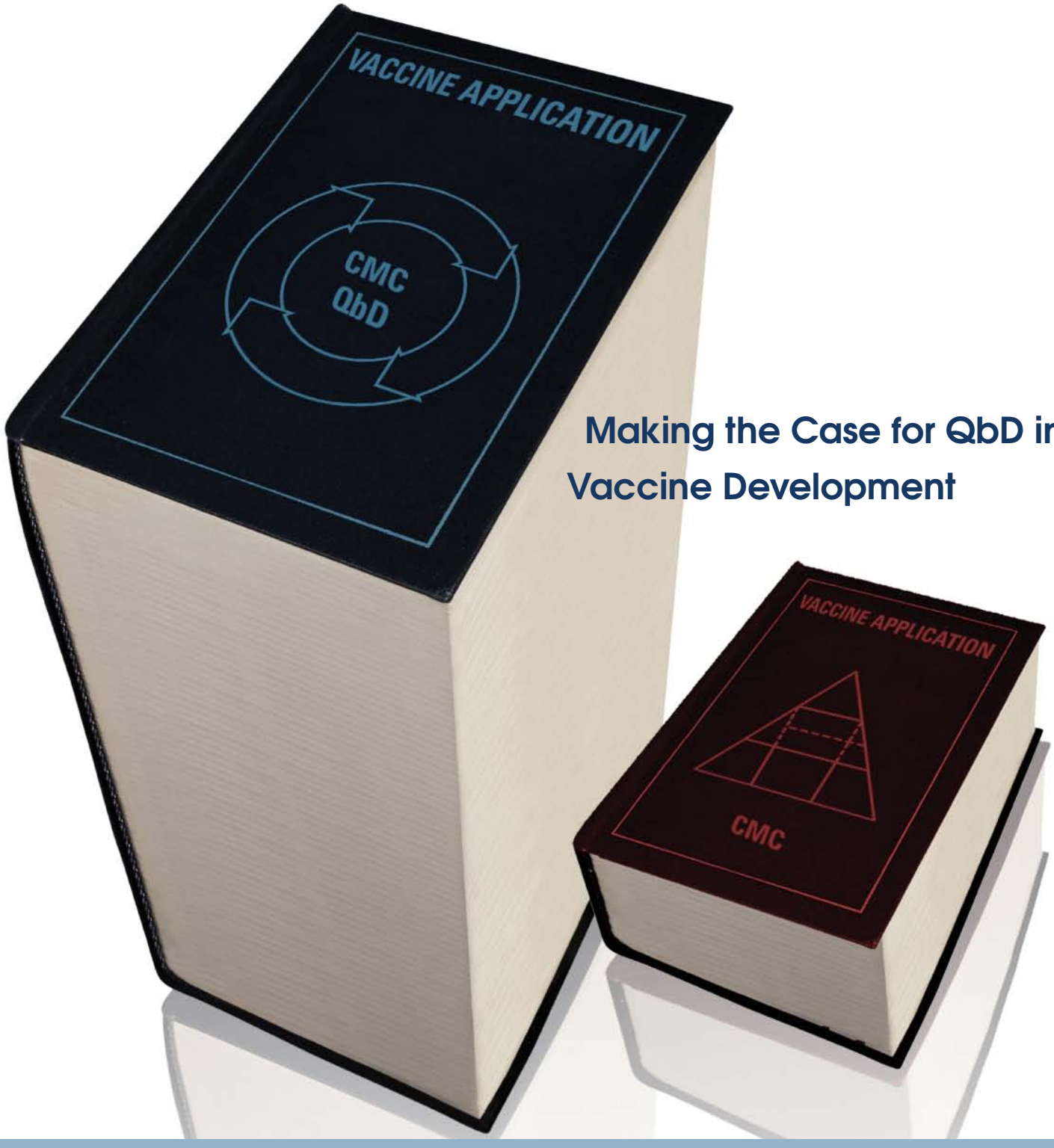


Making the Case for QbD in Vaccine Development

20

Final Chance to Save! Register by March 1st and Save Up to $200!

PDA Parenteral Drug Association

> **"The subject matter experts assembled from the global pharmaceutical industry were full of valuable insights and recommendations. I walked away with an immense amount of practical solutions to many issues."**
>
> **EJ Brandreth**, *Althea Technologies*

The Parenteral Drug Association presents...

2013 PDA ANNUAL MEETING

Modern Sterile Product Manufacture – Exploring Best Practices and Seeking New Approaches

April 15-17, 2013

The Peabody Orlando | Orlando, Florida

A critical goal for us to remain competitive is that we need to become more efficient and effective by applying best practices and approaches. PDA's premier event, the *2013 Annual Meeting* will provide sessions led by industry leaders and will give you the opportunity to share opinions and concerns about the scientific and regulatory topics being presented.

The PDA Annual Meeting provides outstanding educational opportunities in the areas of quality, sterile product manufacturing and biological science as well as valuable peer-to-peer networking events among many other benefits.

Leading the discussions:

Firelli Alonso-Caplen, PhD, *Pfizer, Inc*

Joyce Bloomfield, *Merck Sharp & Dohme*

Patrick McCormick, PhD, *Bausch & Lomb, Inc.*

Martin VanTrieste, *Amgen, Inc.*

Damon Asher, PhD, *EMD Millipore Corporation*

Carl June, MD, *University of Pennsylvania Abramson Cancer Center*

Peter Steiner, PhD, *ESBATech, a Novartis Company*

Thierry Ziegler, PhD, *Sanofi-Aventis*

Following the conference, there will be a post-conference workshop, *2013 PDA Human Factors and Human Error Reduction Workshop* on April 17-18.

Want to learn more? From April 18-19, six in-depth training courses will be held. These courses for professionals involved in developing and manufacturing quality pharmaceutical products will cover a range of topics from recommended practices for manual aseptic processes to the validation of moist heat sterilization processes.

www.pda.org/annual2013

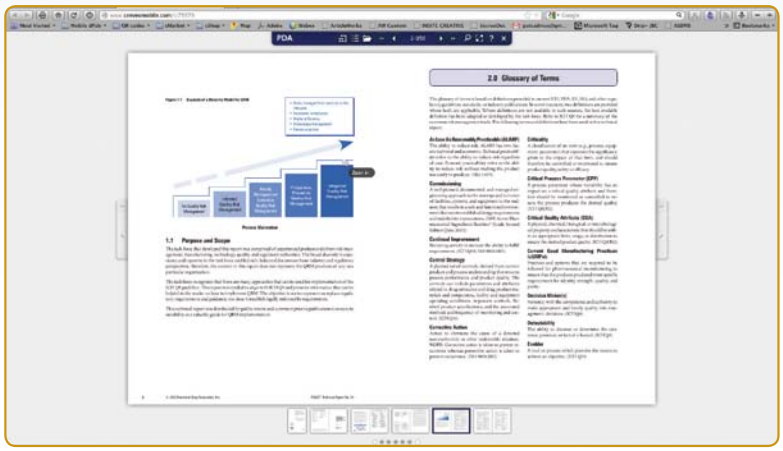
Exhibition: April 15-16 | Post-Conference Workshop: April 17-18 | Courses: April 18-19

Now Available

New PDA Member Benefit Just Added

PDA MEMBERS ONLY:

Welcome to Your Technical Report (TR) Portal



In this new portal, PDA members are able to view the complete library (or collection) of PDA Technical Reports (TR).

The Technical Report Portal is accessible to current Standard and Government members only and is for online viewing only. After logging in with your PDA ID number and password, you are able to view the documents but cannot print, share or copy them. As a reminder, sharing your PDA ID number and password is not allowable under PDA's membership rules and may result in loss of privileges.

All print versions of the PDA Technical Reports are available for purchase at the PDA Bookstore.

PDA members are able to download electronic versions of newly released Technical Reports free of charge within 30 days of publication as a standard member benefit. Make sure PDA has your current email address to receive notifications when a new Technical Report is available for download.

PDA Technical Reports are highly valued membership benefits. They are global technical documents, prepared by member-driven Task Forces comprised of content experts, including scientists and engineers working in the pharmaceutical and biopharmaceutical industry, regulatory authorities and academia.

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www.pda.org/trarchive

PDA Letter

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

Cover

Cover Art Illustrated by Katja Yount

Departments

Contents

Features

PDA TRI CPE Credits Go Electronic, Will No Longer Be Mailed

Effective Jan. 1, 2013, PDA will no longer mail paper Statements of Credit for course attendees receiving continuing pharmacy education (CPE) credits. The Accreditation Council for Pharmacy Education (ACPE) has collaborated with the National Association of Boards of Pharmacy (NABP) to create CPE Monitor, an electronic service for tracking CPE credits.

To view and track CPE credits, you will need to set up a NABP e-Profile, obtain an e-Profile ID, and then register for CPE Monitor. This can be done by visiting the NABP website: www.nabp.net.

To receive CPE credits for PDA conferences or courses, you will now be asked for your e-Profile ID number and date of birth on a form that will be distributed at the end of every conference and course. This form can then be turned in to the registration desk or mailed to PDA within two weeks of participation in the conference or course.

For more information on CPE Monitor, please visit to the ACPE website at www.acpe-accredit.org/cpemonitor or the NABP website at www.nabp.net/programs/cpe-monitor/cpe-monitor-service.

A COLLABORATIVE SERVICE cpe monitor FROM ACPE AND NABP ™

PDA Volunteer Spotlight

Marsha Hardiman

- Senior Manager, Biological Services
- *Medtronic*
- Member Since | 2000
- Current City | Santa Ana, CA
- Originally From | Connecticut, USA

If you weren't doing this job, what would you have done?

Pastry Chef, I love to bake!

Name your favorite magazines

PDA Journal of Science and Technology, O, The Oprah Magazine*, Newsweek*

If you could go back in time and talk to yourself in high school, what advice would you give yourself?

Study hard and play hard

What is the most challenging part of your job?

Making sure my staff gets 50% of my time that is focused on growing them when the day-to-day workload gets crazy.

What skills do you think someone needs to be successful in your position?

Strong technical background in microbiology and good influencing skills

What is the best professional leadership book you read and recommend?

The 7 Habits of Highly Effective People

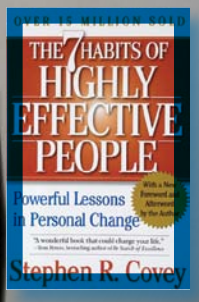
What do you think is the biggest challenge in the industry right now?

I am micro-centric so I think microbial contaminations, such as the meningitis deaths, have been a big issue. Loss of contamination control in a facility will not only cause compliance risks but can kill people as we are now sadly reminded with this outbreak.

How did you first hear about PDA and why did you join?

Good question – I joined when I was a microbiology supervisor in Boston and wanted some of the technical reports for my lab. Then I started going to meetings. Over the years I have become more actively involved and look forward to many more years of involvement. PDA is very personally rewarding to me and makes me a stronger microbiology leader in the industry.

I have built lasting friendships and I am very appreciative of the opportunities that PDA has given me.



Marsha recommends The 7 Habits of Highly Effective People

20-21 March 2013
RAMADA Hotel
Berlin-Alexanderplatz
Berlin | Germany

The Parenteral Drug Association presents...

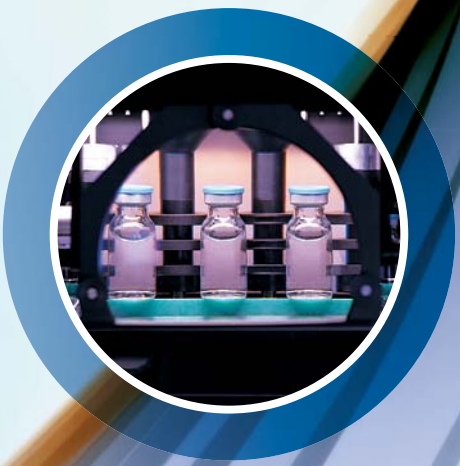
2013 PDA Training Course

An Introduction to Visual Inspection

A hands-on training course

The training course covers the fundamentals of visual inspection methods and their application to injectable products. It will be a combination of lecture/discussion and hands-on laboratory exercises used to develop and practice practical inspection skills. The skills developed through this course may be applied to both manual human inspection and automated machine inspection.
Upon completion of this course you will be able to:

- Identify applicable international regulatory and compendial requirements for visual inspection
- Apply the critical parameters which must be controlled for reproducible inspection results
- Use appropriate statistical tools to assess and compare inspection methods
- Develop consistent validation strategies for visual inspection processes and equipment



TRAINING COURSE | EXHIBITION | IG MEETING

https://europe.pda.org/TCVisInsp2013

7 March 2013
Prague | Czech Republic

The Parenteral Drug Association presents...

2013 PDA Europe Interest Group Meeting

Pre-filled Syringes

Update on IG activities

Focus topic: Container Closure Integrity of Pre-filled Syringes
- Methods, IPCs in manufacturing
- Transportation impact

Dose accuracy
- Technical solutions, labeling
- Impact of size and volume

Other topics, Q & A and Discussion

https://europe.pda.org/IGPrefilled2013

New Keck Student Chapter Hosts First Event

Michael Choy, Director of Communications, PDA KGI Student Chapter

Amgen, Gilead and Medtronic…these three giants of the biotechnology and medical devices industries were represented at the *Quality, Regulatory, and Operations Event* (QRO Event) that took place Nov. 9 at Keck Graduate Institute (KGI) in Claremont, Calif. PDA's KGI Student Chapter sponsored the event. KGI students and alumni filled the lecture hall to hear the distinguished guest speakers talk about current issues in the biotechnology industry.

As the first student chapter in Southern California (as well as part of PDA's Southern California Chapter), the KGI Student Chapter was founded this past May and quickly established itself as one of the leading student-led organizations at KGI. The student officers, **Jennifer Lee** (President and Founder), **Joanna Naymark** (Vice President), **Michael Choy** (Director of Communications), and **Naren Vinayak** (Treasurer), are supported by 40 student members to continue the founding success of this professional organization. The student members form teams to work on projects that contribute to the growth of the chapter, and the QRO event was organized and executed by members **Jason Ross** and **Alison Blaschke**.

Vince Anicetti, PDA Fellow and Adjunct Professor at KGI, serves as the Faculty Advisor to the KGI Student Chapter. Vince's professional connection was exemplary of the professional networking experience the students found useful and served as the key to securing the speakers, all of whom are executives at their respective companies. **Rick Lit,** PhD, VP, Regulatory Affairs and CMC at Amgen, spoke about the emerging field of biosimilars, while **Mickey Yraceburn,** Associate Director, Manufacturing at Gilead discussed the future of bioprocessing and outsourcing trends. Lastly, **Marsha Hardiman,** Senior Manager, Biological Services at Medtronic , echoed the issues discussed by the other two speakers and included a discussion regarding current quality control policies in medical devices.

(Top l-r) Vince Anicetti, Joanna Naymark, Michael Choy, Naren Vinayak
(Bottom l-r) Marsha Hardiman, Mickey Yraceburn, Rick Lit

After the lecture portion, the PDA student chapter members joined the guest speakers and Vince in the KGI library for an intimate reception and were able to put their professional networking skills to the test by standing shoulder to shoulder with these executives. **Paige Stein,** Manager of Media Relations at KGI, captured these moments in her article featured on the KGI website (www.kgi.edu), with the comment that the efforts from the students and faculty advisor brought a wonderful level of professionalism to KGI campus.

Working under the mission of bringing the real-world education to campus, the KGI student chapter continues to plan future events with top-notch professionals in the life sciences industry.

Contact

Jennifer Lee, jlee13@students.kgi.edu

Joanna Naymark, jnayma13@students.kgi.edu

Michael Choy, mchoy14@students.kgi.edu

Naren Vinayak, nvinay14@students.kgi.edu

2012 Cold Chain Management & Good Distribution Practice Conference

Sessions

Supply Chain Integrity and Security

Charles Forsaith, Purdue Pharma; Maryann Gribbin, Johnson & Johnson; Mark Seitz, Eli Lilly & Co.

Pharmaceutical Supply Chain Temperature Controlled Solutions — Case Studies

Karl Kussow, FedEx Custom Critical; Neritan Mustafa, Genzyme Corporation; Michael English, Merck Sharp and Dohme

Regulatory & Industry Consensus on Data-Driven Approaches to Ensure the Quality of Pharmaceuticals in Distribution

Jay Crowley, U.S. FDA; Arminda Montero, Abbott Laboratories; Paul Harber, Modality Solutions; Sally Wong, Merck & Co.; Robert Seevers, Eli Lilly & Co.

Migration from Cold Chain to Temperature Controlled Good Distribution Practice

Barry Conlon, Freight Watch; Tim Valko, Amgen; Robert Satek, Abbott Laboratories; Henry Ames, Sensitech

Passport Drawing

PDA

Karen Hurbour received a $100 gift card

Lufthansa Cargo AG

Mike Montana received a scale model of a Lufthansa airplane

Panther Logistics

Stephen Kim won a sizeable gift basket

Berlinger USA

Christina Galey received a watch

Envirotainer

Ed Church won a leased container

Tss

Lorant Kovacs received an excellent SWAG bag

Exhibitors Hall

During the conference, attendees had a chance to view the products and services offered by PDA sponsors.

2012 PDA/FDA Pharmaceutical Supply Chain Conference

November 13–14 | Bethesda, Md.

Global Pharmaceutical Supply Chain Integrity — Overview

Steven Wolfgang, U.S. FDA; Lucy Cabral, Genentech, Inc.; Allan Coukell, Pew Health Group; Rick Roberts, University of San Fransisco California

Assuring Supply Chain Integrity Through Monitoring & Metrics: Information, Sharing & Information Technology

Sue Schniepp, Allergy Laboratories, Inc.; Mac McGary, GT Nexus; Mary Devlin, Drinker Biddle & Reath

Enhancing Manufacturing & Distribution Systems to Assure Supply Chain Integrity: Quality Management Systems Approaches

David Ulrich, Abbott Laboratories; Gwyn Murdoch, Eli Lilly & Co.; Sharon Yanushi, Kuehne + Nagel, Inc.

Global Initiatives in Europe and the US

Matthew Anderson, Merz, Inc.; Gerald Heddell, MHRA; Paula Katz, JD, U.S. FDA; Michael Rose, Johnson & Johnson

Pharmaceutical Supply Chain Security — Connecting Industry, Regulatory, and National Law Enforcements

Barry Brandman, Danbee Investigations; Matthew Anderson, Merz, Inc.; Brian Johnson, Pfizer, Inc.; Gregg Goneconto, U.S. FDA

Friedrich Haefele, PhD, Conference Co-Chair, Boehringer Ingelheim Pharma; Stefan Merkle, PhD, Conference Co-Chair, Cilag AG, and Georg Roessling, PDA Euroope

Michele Arduini, IMA Life, chats with other attendees at the conference

Plenary Session 4: Manufacturing Technologies

Mauro Giusti, Eli Lilly; Torsten Müller, Cilag; Jim Nadlonek, Bausch + Ströbel; and John Shabushnig, Pfizer

Participants of the PDA & PIC/S course, "Rapid Microbiological Methods Training Seminar," held at Hotel Hesperia Tower, Barcelona, November 7-8, 2012

snapshot

Experts Explore QRM in Upcoming Technical Reports

Jahanvi (Janie) Miller, Senior Project Manager, Scientific & Regulatory Affairs, PDA

The Chair of the Paradigm Change in Manufacturing (PCMO℠) initiative, **Stephan Rönninger,** PhD, has dedicated a great deal of effort to advance the scientific application of the ICH Q8, Q9 and Q10 series into industry best practices. Since December 2008, the PCMO program has facilitated communication among the experts from industry, academia and regulatory bodies as well as experts from the respective ICH Expert Working Groups and Implementation Working Group.

Risks and risk management are constant and existing concerns. PDA has worked in collaboration with the PCMO leaders to ensure that best practices are developed to enhance the application of Quality Risk Management (QRM). Reflective of this initiative, PDA is currently developing three additional technical reports which compliment *Technical Report 54, Implementation of Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations*. The groups of authors of the technical reports come from diverse industries and share the common goal of exemplifying real life examples and applications of QRM.

These three reports are primarily intended to align with ICH Q9 and provide real world examples of how to apply risk management tools across the product supply chain; from the starting materials, active pharmaceutical ingredients (APIs) and excipients, through to manufacturing, labeling, packaging, and shipping. These complimentary technical reports highlight best practices of implementing QRM.

The first of three technical reports, led by **Ruhi Ahmed,** PhD, of Ultragenyx, provides an in-depth overview of general approaches to implementing QRM in manufacturing of biotechnological bulk drug substances. This report covers seven case studies on application of QRM throughout the product lifecycle of biotechnological bulk drug substances in a clinical and biopharmaceutical setting.

The second technical report, led by **William Harclerode** of Forest Laboratories, provides risk assessment, analysis, and management best practices delivered in four individual case studies covering the manufacturing of drug products. This report addresses application of QRM to control of visible particulates, combination products, technical transfers/scale ups and supply chain.

The final piece of this complementary set of technical reports, led by **Ghada Haddad** of Merck, provides a high level overview of the packaging and labeling portion of the product lifecycle. The details of this technical report are developed through five case studies that address various forms of drug products and best practices on how to effectively apply QRM during the packaging and labeling process of these products.

Managing risk in the product supply chain can help minimize negative impact on patient safety and health globally. The high-level QRM principles discussed in these technical reports provide a comprehensive best practices package for pharmaceutical and biopharmaceutical professionals to actively implement QRM into their current practices. Companies will be able to adopt and implement new concepts as well as promote advanced risk management strategies base on their needs. Robust QRM strategies will also ensure a higher level of quality for their products.

For more information about PCMO, and to get involved, go to www.pda.org/pcmo.

Tech *Trends*

Plant-Based Production Grows Up; Insect Cell Production Offers Less Bugs

Rebecca Stauffer, PDA

The earliest vaccines were quite simple. Initial vaccinations for smallpox ranged from inhaling rumpled scabs from victims of the disease to **Edward Jenner's** inoculations of cowpox which successfully prevented transmission of the deadly disease ***(1).*** Now, vaccine manufacturers are utilizing a number of more complex tools to develop products, including plant-based protein production with *Nicotiana benthamiana* and insect cells in the manufacturing of influenza vaccines. Some are even using a patient's own cells to develop therapeutic cancer vaccines.

At the *2012 PDA/FDA Vaccines Conference* in December, industry experts **Vidadi Yusibov,** PhD, Executive Director, Fraunhofer USA Center for Molecular Biotechnology, and **Penny Post,** PhD, Vice President of Regulatory, Protein Sciences Corporation, presented case studies of new developments in vaccine manufacturing while **Michael Havert,** PhD, Biologist, Office of Cell, Tissue, and Gene Therapies, CBER, U.S. FDA, provided regulatory insights on new vaccine technology.

Continued on page 17

Interest Group *Corner*

Vaccines IG Seeks to Expand Regulatory Discussion

Rebecca Stauffer, PDA

The Food and Drug Administration Safety and Innovation Act (FDASIA) served as a focal point of discussion at the Vaccines Interest Group meeting during the *2012 PDA/FDA Vaccines Conference* in December, along with other regulatory issues.

Panelists included interest group members **John Finkbohner,** PhD, Senior Director, MedImmune, **Rebecca Devine,** PhD, Consultant, and **Norman Baylor,** PhD, President and CEO, Biologics Consulting Group. Finkbohner gave a brief presentation on FDASIA, stating the law has certain provisions impacting biologics and vaccine manufacturers. In particular, he cited a key legislative revision concerning pediatric medicines.

He noted that timelines are defined for pediatric study plans mandated under PREA [Pediatric Research Equity Act], but moreover it [FDASIA] expands the applicability of the Best Pharmaceuticals for Children Act to include biologics. The initial pediatric study plan must now be submitted to the FDA within 60 days of an End-of-Phase 2 meeting, which used to be recommended under the guidance but now is a mandated deadline.

Other important provisions of the law impact antibiotic development, expedited approval times, allowance for patent exclusivity extensions, expanded inspection authority for the U.S. FDA, and specific legislative language concerning new oversight authorities covering drug shortages. The latter provisions, he thinks, will impact those involved in quality and compliance areas.

"Also, there's a new registration system for facilities that is mandated that includes importers," he said.

FDASIA provisions concerning drug supply chain oversight expands FDA inspectional authority, Finkbohner said, and suggests "the potential for virtual inspections. A number of enhanced authorities are given to the Agency relative to sharing compliance information across borders as well as allowing the Agency to compel the submission of documentation for headquarters review that previously would have been reviewed during inspection."

Going further, "mutual recognition of foreign inspections is now authorized under this new legislation as well as information sharing with foreign governments," he said.

Cross-border information sharing brings up the concern of protection of confidential information and trade secrets, "but there are provisions in the legislation that address Freedom of Information exemptions and the kinds of controls that need to be in place before the FDA will exchange information on compliance or inspections. For example, with say MHRA,

Continued on page 16

Journal *Preview*

Jan/Feb Issue Covers Hot Topics

Two hot topics appear in the first issue of the *Journal in 2013: Validation and Glass Delamination.* Christopher Sloey, et al., present their research on determining the propensity of glass to delaminate. To make the determination, the authors used the direct stress method. Harry Yang's article analyzes whether FDA's new process validation guidance changes the number of batches are needed for validation.

Editorial

Govind Rao, "The PDA Journal—At the Confluence of Academia, Government, and Industry"

Research

Harry Yang, et al., "Environmental Monitoring: Setting Alert and Action Limits Based on a Zero-Inflated Model"

Dheeraj T. Baviskar, et al., "Development of Matrix-Type Transdermal Delivery of Lornoxicam: In Vitro Evaluation and Pharmacodynamic and Pharmacokinetic Studies in Albino Rats"

Varsha B. Pokharkar, et al., "Pioglitazone Solid Dispersion System Prepared by Spray Drying Method: In Vitro and In Vivo Evaluation"

Christopher Sloey, et al., "Determining the Delamination Propensity of Pharmaceutical Glass Vials Using a Direct Stress Method"

Rajeshri Dhurke, et a., "Improvement in Photostability of Pantoprazole Sodium by Microencapsulation"

Harry Yang, "How Many Batches Are Needed for Process Validation under the New FDA Guidance?"

Case Studies

Xiaolin Cao, et al., "Identification and Root Cause Analysis of Cell Culture Media Precipitates in the Viral Deactivation Treatment with High-Temperature/Short-Time Method"

Technology/Application

Gideon Halperin, "Frequency Analyses Can Be Improved by a Modified t-test in Sample-based Preclinical Efficacy Studies"

http://journal.pda.org/

Interest Group Corner continued from page 15

they would need to certify that the U.K. government and the statutes they have in place…will protect the trade secret information that might be shared," Finkbohner said.

Ultimately, "the FDASIA legislation has a number of provisions that impact a broad range of pharmaceutical interest areas," said Finkbohner, affecting segments of the vaccine development community.

Devine then expanded discussion on FDA inspections, highlighting issues that came up when PDA met with Agency representatives about inspections.

"One of the major issues that FDA is seeing as a recurring issue for inspections is failure to perform adequate investigations," she said. "These types of observations are repeatedly being found, and I think many of the compliance staff at the Agency are getting concerned about what's going on in the industry in terms of how investigations are conducted and the thoroughness of them."

Quality systems are another concern, Devine said. She believes the number of quality defects leading to recalls in recent years will focus the Agency's inspectors on quality systems.

Devine warned that some within FDA think the industry takes a "myopic view" when it comes to deviations and other quality problems. "There is perhaps a shortage of resources, and, of course, there is always the ever-present pressure to get product out the door, so the quality unit is often under a little bit of duress to follow up on all of the investigations and close them out," she said.

Devine thinks companies need to take a forward-thinking, long-term view of investigations. This requires a proactive approach involving all levels of management. She suggested PDA can help with courses, workshops and conference presentations to help vaccines manufacturers learn how to properly conduct and document investigations and root-cause analysis.

During the Q&A session, Baylor addressed international regulatory issues, saying that when he worked at FDA, "one of the things that I really wanted to start, and started some discussions on, was looking at clinical trials from a global perspective and perhaps when you get to the area of a Phase II study, being able to have collaboration between the FDA, EMA, Health Canada, [and] others, where you could design studies that would benefit all of the regulatory authorities. Having some kind of collaboration where one trial would be sufficient to satisfy all of the authorities. That reduces cost because we know…that's one of the largest costs of vaccines—the clinical trials."

The Vaccines Interest Group worked with the *PDA Letter* on a survey regarding QbD, and several participants at this meeting agreed to answer the questions. The results are presented on p. 28.

The Vaccines Interest Group plans to meet at PDA's Annual Meeting in March. The group hopes to continue dialogue within PDA to ensure that the interests of vaccine manufacturers remain at the forefront. The interest group has extended an invitation to vaccine manufacturers to join the group so that regulatory issues can be identified and discussed with the goal of seeking solutions to the issues discussed.

About the Experts

Norman Baylor, PhD, is currently the President and CEO of Biologics Consulting Group, Inc., headquartered in Alexandria, Virginia. Prior to joining BCG, Inc., Dr. Baylor was the Director of the Office of Vaccines Research and Review (OVRR) in the Food and Drug Administration's Center for Biologics Evaluation and Research.

Rebecca Devine, PhD, is an independent regulatory consultant with over 30 years of experience in the regulation of biological products. She began consulting in 1999 after leaving the Food and Drug Administration. She joined the FDA in 1979 as a Microbiologist, and held various positions in the Center for Biologics Evaluation and Research (CBER) throughout her 20 year FDA career. When she left FDA she was the Associate Director for Policy at the Center for Biologics Evaluation and Research.

John Finkbohner, PhD, joined the regulatory affairs department at MedImmune in 2006. In early 2012, he transitioned to leading the Regulatory Policy function at MedImmune, where he is responsible for driving regulatory policy development and advocacy.

Tech Trends continued from page 14

Yusibov's presentation focused primarily on plant-based production using expression systems. While plant-based has been around for a few years, the industry is utilizing plant-based production in new and innovative ways.

"Most of the people, when you talk about plants, think about edible vaccines growing on the fields," said Yusibov. However, "this field has grown and evolved tremendously."

In Yusibov's experience, plant-based production was not ready for human products because it was not grounded in GMPs, unlike production methods utilizing animal cells and microbial systems. When he started working with plants in 2001 at Fraunhofer, he explained, "one of the major elements missing...was GMP production, so there has not been any case when anybody tried to make products for human use under GMP conditions in plants."

The company ultimately chose to develop plant-based methods in a GMP environment. Yusibov's group now uses *Nicotiana benthamiana* as its raw material plant. Although related to tobacco, it has little to no nicotine in it, depending on the plant line. The plant's seeds are small—approximately one gram—but four weeks after planting will yield an average biomass of one kilogram.

As an example of a plant-based vaccine, Yusibov highlighted an influenza vaccine that was used for Phase I clinical trials.

"One good thing about plants, is that unlike some other platforms, particularly when it comes to fermentation, there's a fairly predictable linearity of your process scale up," said Yusibov, which means that what happens with a small group of plants can be extrapolated for larger groups.

Fraunhofer's revolutionary process for avian influenza vaccine received the attention of the Bill & Melinda Gates Foundation, which gave the company an $8.7 mil. (USD) grant to support further development work. The company also has received several grants from the U.S. Defense Advanced Research Projects Agency (DARPA). Some of the DARPA funds went towards the company's fully-automated manufacturing facility in Newark, Del., wherein robots execute all the operations in the plant.

Insect Cells in Cancer Vaccine Production

Following Yusibov's presentation, Post presented a case study also highlighting a flu vaccine, this one developed using insect cells. Her company uses a core technology platform called the Baculovirus Expression Vector System (BEVS).

"The first step that we do is engineer the baculovirus with a gene of interest," she said. "For the influenza vaccines in this case, it's the gene for hemagglutinin. Baculoviruses

are very specific to insect cells, and we use a strong promoter that generates a high yield of the protein of interest."

The cells are then cultured in a bioreactor and infected with an engineered virus. Then the cells are incubated for around 72 hours, followed by purification of the substance before formulation.

Post has found a number of safety advantages to using insect cells.

"For the insect cells as with plants, there are very few known adventitious agents that can replicate in both insect cells and mammalian cells," she said. "The exception [is] the arboviruses which are transferred by biting insects, for instance, West Nile encephalitis or Eastern equine encephalitis. Our cells are derived from caterpillars and other nonbiting insects."

So far, two products developed using insect cells have been approved by the FDA: Cervarix, a human papillomavirus vaccine produced by GlaxoSmithKline, and Provenge, a cancer immunotherapy produced by Dendreon.

FDA Issues New Tech Guidances

Havert, a gene therapy reviewer, gave an overview of his Agency's framework of regulations affecting therapeutic cancer vaccines. His talk offered an overview of the development of regulatory guidelines of these new technologies, which are intended to help patients overcome immune suppression responses to tumor antigens.

"In a nutshell, these are largely unproven technologies. There are significant challenges in terms of break in tolerance in cancer patients and overcoming immune suppression…I think, with the significant research in this area—the developments in technology and science—we're starting to see better and better products, and these products are starting to bear fruit as clinical responses are observed," Havert said.

Break in tolerance is a large issue as unlike other infectious diseases that express antigens, cancer vaccines must handle a patient's self-reactive immune response.

"Cancer vaccine antigens are largely present during development of an immune system response," he said. The goal of a cancer vaccine is to activate remaining T-cells in the patient to respond to the tumor.

Regulatory considerations for cancer vaccines using genetically engineered T-cell therapies include manufacturing processes, ancillary materials/reagents, manufacturing challenges, timing of testing, and final product release. The manufacturing process involves collecting samples from the patient, in general from peripheral blood. Ancillary materials and reagents involve cell selection devices, cytokines and antibodies, and cell lines for expansion. Manufacturing challenges include patient-specific lots—meaning that there is limited product for testing and mix-ups need to be prevented—reproducibility of the product lots, and aseptic processing is required during manufac-

turing. Each lot must also be tested prior to release, although final results may not be available before release, which means there needs to be flexibility when testing is done. Final release testing involves analyzing sterility, mycoplasma, purity, identity, potency, and, if applicable, replication of the competent virus if working with retroviruses and lentiviruses.

As a regulator, he emphasized that measures of potency for therapeutic cancer vaccines are more complex, and as a result his office looks closely at potency testing.

"We do ask more as these products are becoming more complicated...we do ask more of the tests that are done," he said.

References

1. Freedman, Joshua E. "The Earliest Vaccines," *New York Times*, June 10, 1984. www.nytimes.com/1984/06/10/magazine/l-the-earliest-vaccines-245604.html (accessed December 7, 2012).

About the Experts

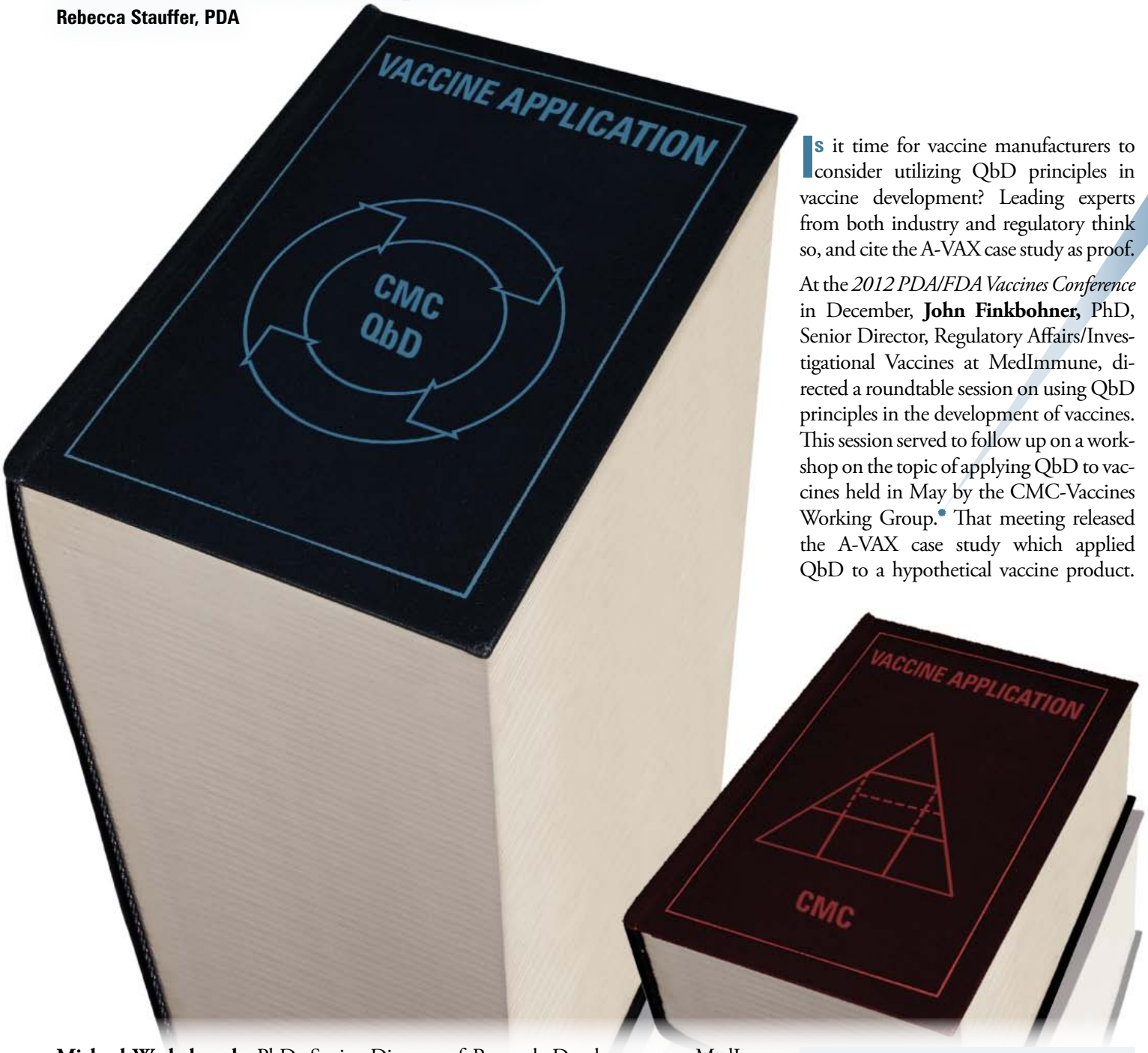
Michael B. Havert, PhD, is a biologist for the Office of Cell, Tissue, and Gene Therapies, CBER, at the U.S. FDA. Since 2004, he specializes in CMC reviews of gene therapy and therapeutic INDs using viral based vectors.

Penny Post, PhD, is currently Vice President of Regulatory at Protein Sciences Corporation (PSC) in Meriden, Connecticut. She joined PSC in 2000 and has served various management roles within the company in the process development, quality, and manufacturing departments.

Vidadi Yusibov, PhD, the Executive Director of Fraunhofer USA Center for Molecular Biotechnology, is responsible for the oversight of all plant-based vaccine and therapeutic development programs. He has been involved in different aspects of plant molecular biology, including molecular farming, with a major focus on transgenic plants and plant viruses since 1985.

Making the Case for QbD in Vaccine Development

Rebecca Stauffer, PDA



Is it time for vaccine manufacturers to consider utilizing QbD principles in vaccine development? Leading experts from both industry and regulatory think so, and cite the A-VAX case study as proof.

At the *2012 PDA/FDA Vaccines Conference* in December, **John Finkbohner,** PhD, Senior Director, Regulatory Affairs/Investigational Vaccines at MedImmune, directed a roundtable session on using QbD principles in the development of vaccines. This session served to follow up on a workshop on the topic of applying QbD to vaccines held in May by the CMC-Vaccines Working Group.* That meeting released the A-VAX case study which applied QbD to a hypothetical vaccine product.

Michael Washabaugh, PhD, Senior Director of Research Development at MedImmune, provided an update on the A-VAX case study.

"Quality by Design is sometimes referred to as an enhancement approach to development," he said, stating that the enhancement is just a way to systematically evaluate characteristics of quality.

"So, why do a case study for vaccines?" he asked. "Compare and contrast monoclonal antibodies with vaccines…the bottom line is monoclonals are relatively well-understood relative to the platform. The mechanisms of action are understood much better than vaccines. So we considered looking at vaccines because of the difficulty in

Article at a Glance

- A-VAX case study serves as a potential model for QbD and vaccines
- Regulatory relief and targeted quality profile are two takeaways from the case study
- Vaccine manufacturing is a multi-step process amenable to QbD

In April 2012, PDA announced plans to coordinate the CMC-Vaccines Working Group (CMC-VWG) on the utilization of QbD principles in vaccine development with representatives from five vaccine manufacturers (GlaxoSmithKline, MedImmune, Merck, Pfizer and Sanofi Pasteur). The development of this team followed a similar approach which led to the creation of a case study in 2009 applying QbD to development of a monoclonal antibody (the A-Mab case study). Working with PricewaterhouseCoopers, the CMC-VWG developed the A-VAX case study, outlining a strategy for using QbD in the development of a fictional vaccine. The A-VAX case study was released in May 2012. PDA served as a partner to the CMC-VWG, disseminating the case study and facilitating public discussion of its implications.

The A-VAX case study can be accessed on the PDA website here: www.pda.org/Home-Page-Content/CMC-VWG-A-VAX.aspx.

characterizing quality of understanding mechanisms and how the mechanism of action could be exploited and used."

Washabaugh listed a number of compelling reasons to use the enhanced approach in vaccines development. For one, he said, it will modernize development. Here, vaccines manufacturers can take valuable lessons from biologics manufacturers who have pursued the QbD approach.

Second, there is a need for a more reliable supply of vaccines to meet public health demands "The assumption is that with a better understanding of your product and your process you should be able to maintain the supply," he explained.

Next, Washabaugh provided some background on the working group which consists of 70 individuals from the following five companies: GlaxoSmithKline, MedImmune, Merck, Pfizer and Sanofi Pasteur. The group also worked with both U.S. and European regulatory agencies. Its goals were to establish a platform for discussion between regulatory and industry, as well as develop and highlight a framework for illustrating the feasibility of QbD for vaccines (the case study). The hope is that the A-VAX case study will provide a greater understanding of QbD and its application to vaccines and showcase QbD's value to senior management.

After giving a summary of the A-VAX case study, beginning with the Quality Target Product Profile through the risk assessment workstream and formulation and process development to upstream and downstream procedures, he addressed the regulatory implications of QbD implementation.

On the regulatory aspects of QbD, Washabaugh said, "You have the traditional approach for development versus this enhanced Quality by Design systematic approach." The latter is a more target-specific application that looks at specific unit operations that are critical to processes.

During the development of the case study, Washabaugh said the discussion on hybrid filings was key. The team demonstrates how to discuss QbD, how the control strategy evolved and how to document information at certain points.

Ultimately, he said that industry is likely to use QbD for certain process steps in vaccine development. QbD could be used to focus on areas where an enhanced approach may offer added process knowledge that could be beneficial for anticipated post-licensure changes.

Washabaugh took two takeaways from the A-VAX case study: the importance of having a targeted quality profile and the term "regulatory relief."

"What I saw was that 'regulatory relief' was interpreted as one of two things… there was a discussion around whether it was a timeline-driven decision or a data-driven decision," he said. He believes there will be balance between timeline-based and data-driven decisions.

"If you expected 'regulatory relief' to mean a more rapid filing or registration, you'll be disappointed," he added. "There's about 30% to 40% more work involved in terms of generating the characterization needed to understand the product. So the companies that seem to be more satisfied are the ones who used it as a lifecycle approach."

QbD Regulatory Aspects Considered

Following Washabaugh's presentation, **Robin Levis,** PhD, Deputy Director, Division of Viral Products, Office of Vaccines Research and Review, offered

Combining Analytical Methods with QbD Equals Success

Earl Zablackis, PhD, Sanofi-Pasteur

Quality by Design is being applied to process development throughout the pharmaceutical industry for better process understanding and control. It is logical, therefore, to apply the same concepts to analytical method development (AMD), since analytical methods are measurement systems for production processes and are, accordingly, an integral part of a QbD process. QbD for analytical methods parallels QbD for a manufacturing process. The intent of QbD is to build quality into a process; in consequence, application of QbD to AMD should lead to reduced method variability and increased method robustness as well as offering a sound basis for demonstrating and documenting the suitability of the method for its intended use.

Applying QbD principles in method development can provide the desired development path that will match scientific understanding and risk-based compliance, ensuring that required method performance is integrated with processing. The business case (translated to cost savings) for QbD has been analyzed extensively ***(1);*** and integration of QbD for analytical methods would contribute positively to the business case for QbD in general.

QbD tools can be applied to the AMD process from method selection to method qualification and validation. The use of risk assessment tools throughout the AMD process is used to identify method factors that can potentially affect method performance. Using risk assessment tools provides a systematic approach and assessment process for developing and documenting method development, i.e., a guide for what method parameters are important and how they should be addressed.

One of the simplest and clearest benefits of using QbD tools during AMD can be

obtained by using design of experiments (DoE) studies for robustness and intermediate precision during method development. DoE evaluations are more cost-effective than one factor at time (OFAT) analyses, and depending on the design used, are more useful for understanding factor interactions that cannot be delineated with OFAT analyses. Additionally, if robustness studies are designed to include multiple responses (more than just the reportable value), limits for system suitability criteria can be obtained as well through these systematic DoE studies.

Coming in Fall 2013, the PDA *Analytical Method Development and Validation Workshop,* (See p. 38 for more details about this workshop.) has included a session to explore recent applications of QbD to AMD and the links to QbD in biotech manufacturing process development. The session will offer discussions on application of QbD principles to the AMD process and integration of analytical methods into biotech QbD manufacturing.

Reference

1. Junker, B. 2012. Building a Business Case for Biopharmaceutical QbD Implementation. *BioPharm International,* 25: 40-47.]

About the Author

Earl Zablackis, PhD, is a biologist and carbohydrate biochemist who has spent the last 15 years in industry. He is currently at Sanofi Pasteur in the Manufacturing Technology group as Principal Scientist and Director of Analytical Method Validation.

At some level, vaccines should be amenable to the introduction of QbD and the enhanced development and review

a more in-depth look at the regulatory aspects of QbD.

"It hasn't been that long ago that we actually tried to put on paper what the definition of quality was with respect to both the development and the manufacturing of vaccines, and how we as regulators review them. In 1987 was the first real process validation guideline which tried to define quality of product," she said. "The quality, safety and effectiveness—the big three for us—really must be designed and built in to the product."

To achieve the latter, Levis said that each step of the manufacturing process must be controlled to maximize the probability that the finished product meets all three points.

"If we jump forward some 25-30 years from there, we're still talking about quality initiatives," she said, citing the Agency's *Pharmaceutical CGMPs for the 21st Century* initiative and the ICH Q8-Q11 guidelines.

Levis touched on FDA's history with QbD, which began in CDER with the goal of enhancing and modernizing regulation then moved to CBER in 2008.

"So, ultimately then, how can we implement the principles of QbD to biologics, [and] take what was very nicely outlined in the A-VAX case study and put it to real use?" she asked. "So what would be the perfect product for the QbD approach? The product is designed to be safe and effective in the clinic—that's an absolute must. The process is designed to consistently meet product critical quality attributes. The impact of starting raw material materials and process parameters on product quality is well-understood. The process is evaluated and updated to allow for consistent quality over time. The critical sources of process variability are identified and controlled. And appropriate control strategies are developed.

"At some level, vaccines should be amenable to the introduction of QbD and the enhanced development and review," she added.

Levis highlighted key unit operations that could be amenable to QbD. She emphasized that if any of the steps applied to a manufacturing operation, QbD should be considered. These process steps include: ones that are well-understood and can be reproduced, results from product-specific testing that verify the adequacy of the process, variables and controls that are well-understood, the capability of precise process monitoring, equipment that can be controlled in restrictive limitations, and scale-up and process transfers that could potentially predict outcomes.

Pick Your Spots with QbD

"So, if you look at QbD and vaccines, better product and process characterization leads to better vaccine product quality," she emphasized.

While it has been argued that vaccines are too complex for QbD, Levis said that the success of implementing QbD for vaccines means understanding that vaccine development is a multi-step process and to select those process steps that are amenable to characterization for QbD.

In terms of critical QbD elements, Levis said that risk assessments should be different for vaccines due to the fact that the product is generally administered to healthy individuals so the tolerance for safety issues is quite low and changes in efficacy may not initially be apparent.

"It's really important the risk assessment tools capture the full range of risks and even unlikely problems, and so I think that's going to be an area where both industry and we [regulators] are going to have to expand our discussions," she said.

Another critical element, is a robust system that identifies unexpected changes in the process and investigates the ➤

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2013 PDA UPCOMING EVENTS

FEBRUARY EVENTS

5-6
Modern Biopharmaceutical Manufacturing
Lyon, France
https://europe.pda.org/Biopharm2013

7
Freeze Drying of Vaccines Training Course
Lyon, France
https://europe.pda.org/TCBiopharma2013

11
Pre-Conference Workshop on VHP Decontamination
Ulm, Germany
https://europe.pda.org/WSParDrug2013

11-15
Aseptic Processing Training Program – Session 1, Week 1
(Week 2: March 4-8)
Bethesda, Maryland
www.pda.org/2013aseptic1

12-13
Parenteral Drug Development – Clinical Trial Materials
Ulm, Germany
https://europe.pda.org/ParDrug2013

26-27
Pharmaceutical Microbiology
Berlin, Germany
https://europe.pda.org/Microbio2013

28
Microbial Contamination Control in the Pharmaceutical Industry Training Course
Berlin, Germany
https://europe.pda.org/Contamin2013

28-1 March
The A to Z's of Biofilm Control, Monitoring, Validation, and Excursion Investigations of Pharmaceutical Water Systems Training Course
Berlin, Germany
https://europe.pda.org/Biofilm2013

28-1 March
Rapid Microbiological Methods Training Course
Berlin, Germany
https://Europe.pda.org/TCRMM2013

MARCH

5-6
Development of a Freeze Drying Process – From Formulation to a Robust Process Training Course
Prague, Czech Republic
https://europe.pda.org/TCFreezeDrying2013

5-6
Parenteral Packaging
Prague, Czech Republic
https://europe.pda.org/ParPack2013

7
Interest Group Meeting Freeze Drying
Prague, Czech Republic
https://europe.pda.org/IGFreezeDrying2013

7
Interest Group Meeting Pre-filled Syringes
Prague, Czech Republic
https://europe.pda.org/IGPrefilled2013

8
Container Closure Development Training Course
Prague, Czech Republic
https://europe.pda.org/TCCCD2013

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

Save these dates!

EVENTS

18-19
2013 PDA Analytical Methods Development & Validation Workshop
Baltimore, Maryland
www.pda.org/amd2013

18-22
Pharmaceutical Products Supply Chain Integrity: A Five Day Training Series
Bethesda, Maryland
www.pda.org/pharmaintegrity

19
Interest Group Meeting Visual Inspection
Berlin, Germany
https://europe.pda.org/IGVisInsp2013

20-21
An Introduction to Visual Inspection Training Course
Berlin, Germany
https://europe.pda.org/TCVisInsp2013

APRIL EVENTS

2-4
Preparation of Virus Spikes used for Virus Clearance Studies and Virus Filtration Training Course
Bethesda, Maryland
www.pda.org/viruspikes

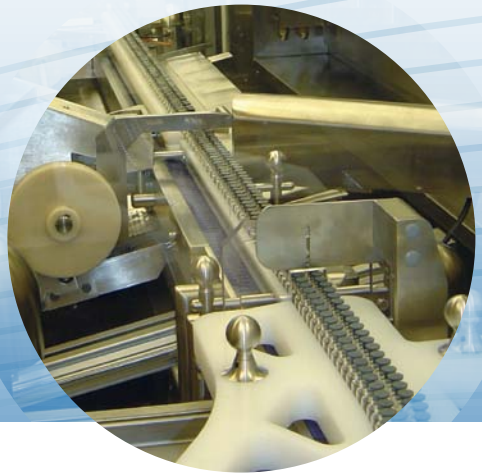
8-12
Aseptic Processing Training Program – Session 2, Week 1
(Week 2: May 6-10)
Bethesda, Maryland
www.pda.org/2013aseptic2

15-17
2013 PDA Annual Meeting
Orlando, Florida
www.pdaannualmeeting.org

17-18
2013 PDA Human Factors and Human Error Reduction Workshop
Orlando, Florida
www.pda.org/humanfactors2013

18-19
2013 PDA Annual Meeting Course Series
Orlando, Florida
www.pdaannualmeeting.org/courses

30-1 May
An Introduction to Visual Inspection – Session 1
Bethesda, Maryland
www.pda.org/visualinspectionlab1



unexpected changes, assigning causes.

Agency Gaining QbD Experience

Levis said that the Agency is looking at QbD being used for some blood products and certain operations at facilities. Inherent benefits of QbD include improvements in process control and monitoring, better change control, enhanced process capability, and a proactive approach for handling process control.

So what does the future hold for QbD, particularly at the regulatory level? "The concepts of QbD are starting to be applied to biological products. Some sponsors come to us to start that discussion," Levis said. "While there is a lot of experience reviewing changes to manufacturing, there isn't a lot of experience with the application of QbD across the Agency, especially in biological products such as vaccines. More experience and examples are needed to establish some of the review/inspection paradigms for the future."

"From this point then, we're encouraging the QbD approach for greater process understanding and better control over the process," she said. "We need to gain additional experience with submissions—we've had very few discussions at this point. QbD should also provide for better submissions and more consistency for regulatory decisions. And future discussions on regulatory submissions [are] ongoing."

She concluded by urging further dialogue between industry and regulators.

"We have to continue the collaboration established to define how QbD and other approaches to quality systems will be applied to the development and manufacturing of vaccines," she stressed.

About the Experts

John Finkelbohner, PhD, joined the regulatory affairs department at MedImmune in 2006 and led the regulatory support efforts for investigational vaccine development for nearly six years.

Robin Levis, Phd, is the Deputy Director for the Division of Viral Products in the Office of Vaccines Research and Review at CBER. Previously, she was a regulatory coordinator at the U.S. FDA. She has a doctorate from Washington University in St. Louis.

Michael Washabaugh, PhD, is a Senior Director at MedImmune, Inc. He has demonstrated expertise and experience in launching biopharmaceutical products, recruiting, building talent, collaboration, change implementation, and shaping strategy.

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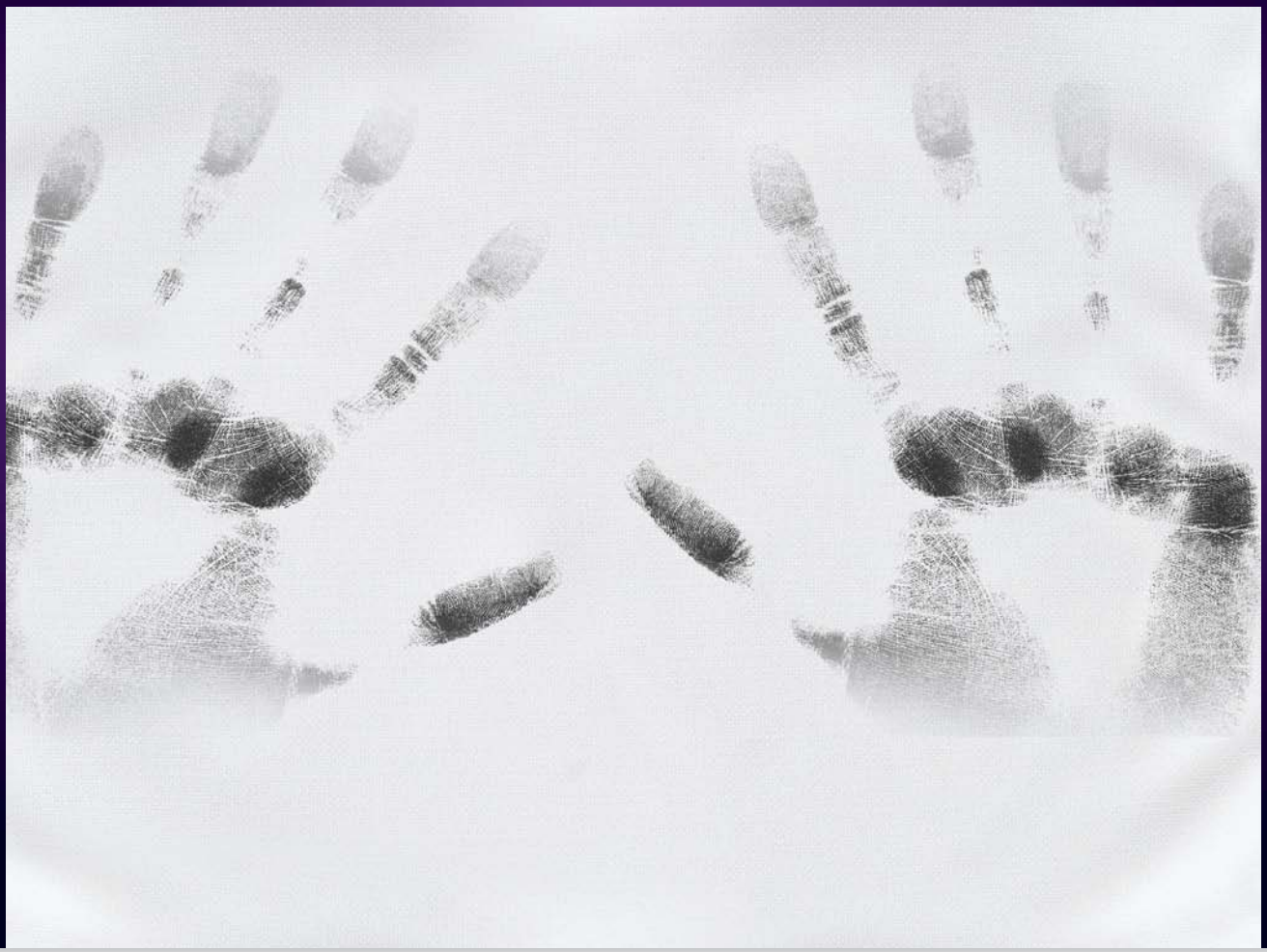

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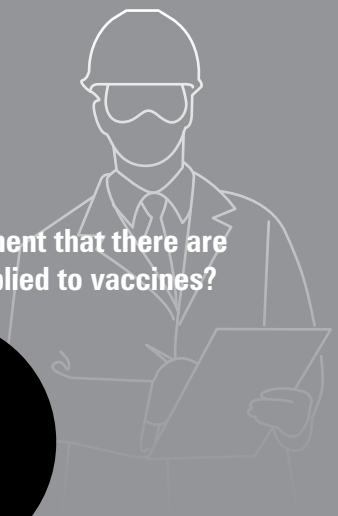
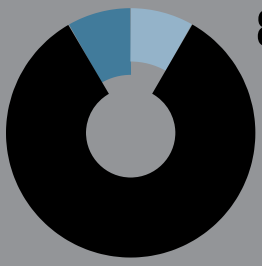
QbD and Vaccines: PDA IG Members' View



What does QbD mean to your organization?



83.3% A scientific, risk-based, holistic and proactive approach to pharmaceutical development

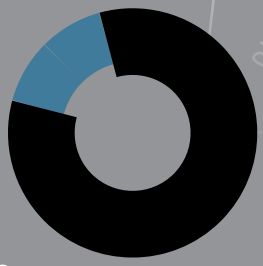
8.3% Assessment & Management

8.3% Other

Would you agree with the assessment that there are principles of QbB that could be applied to vaccines?

83.3% Yes

16.7% Unsure

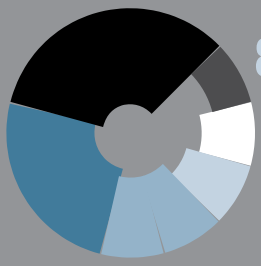


What do you see as the biggest challenge to implementing QbD for vaccines?

33.3% Linking clinical and process parameters

25% Assay variability

16.7% Lack of a broad regulatory and industry definition of QbD pertaining to risk assessments



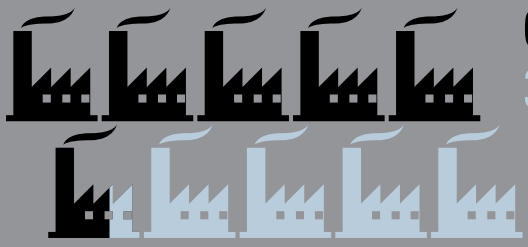
8.3% Designing appropriate quality systems

8.3% Designing appropriate quality systems *and* linking clinical and process parameters

8.3% Other

QbD Utilization Among Vaccine Manufacturers

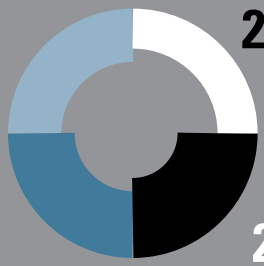
Does your company employ QbD?



66.7% Yes

33.3% No

What is the reason for not implementing QbD?



25% Too costly

25% Lack of familiarity with QbD

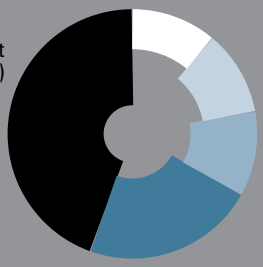
25% The regulatory benefit is not clear and QbD has not been harmonized internationally (i.e. no widely accepted definition)

25% Not easily applied to established vaccine manufacturing

What is the business case for following QbD principles?

44.4% Robustness of product and product availability (i.e. avoiding shortages)

22.2% Better process understanding resulting in simpler and more efficient tech transfer/scale-up



11.1% Better process understanding resulting in simpler and more efficient tech transfer/scale-up *and* QbD needs to fully understand all the CQA before addressing process elements

11.1% Opportunity for process improvement adaptation, transfer and comparability.

11.1% Opportunity for process improvement adaptation, transfer and comparability, *and* improved patient experience, process understanding, lower risks, lower costs, better speed to market, less defects (waste), more productive employees…

Methodology

The PDA Letter worked with the Vaccines Interest Group to conduct this survey on QbD in vaccines manufacturing to get a sense for the uptake of QbD principles within their operations, and if not, why. We also wanted to ascertain what QbD means to their companies. 100 members of the IG received the survey, and there was a ten percent response rate. The Vaccines IG met at the December *2012 PDA/FDA Vaccines Conference* (see article on p. 15); three additional responses were obtained, bringing the overall response *rate to 13%.*

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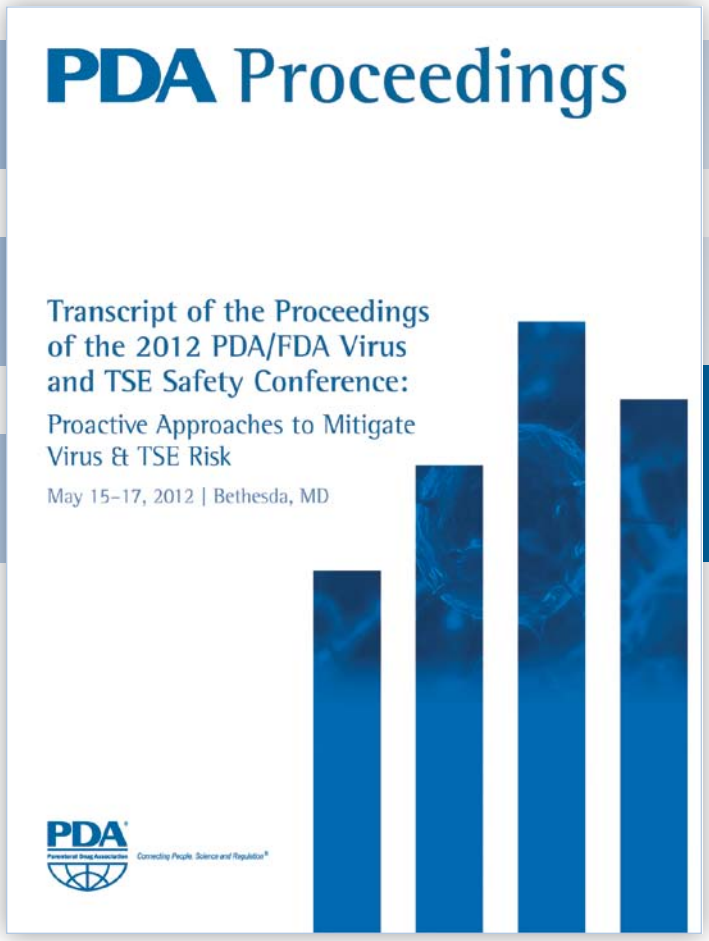

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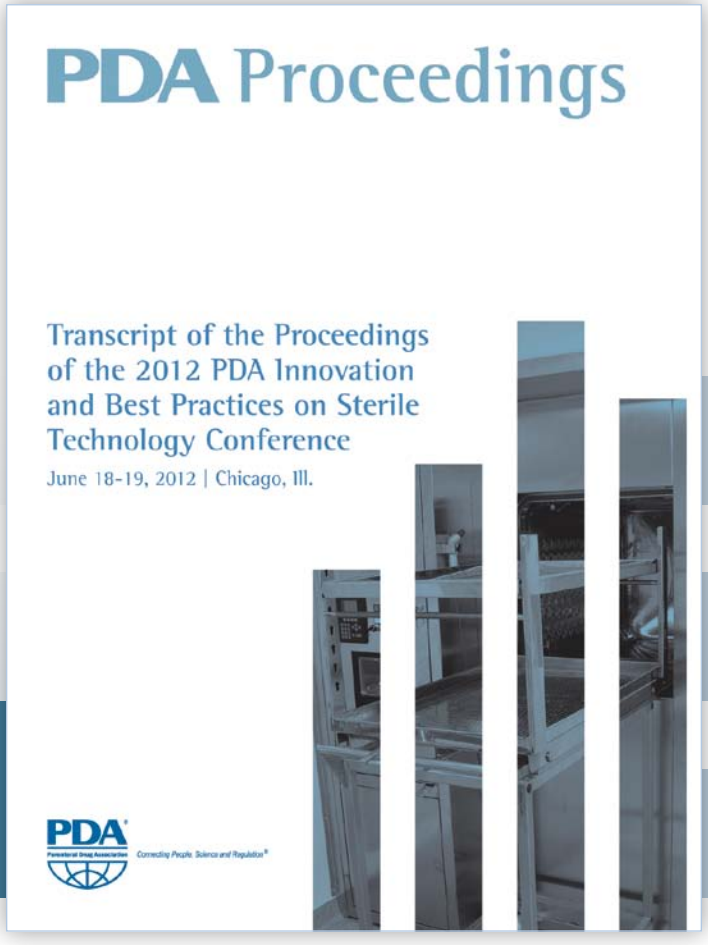

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Networking, PDA Involvement Keys to Success for Lisa Skeens

Rebecca Stauffer, PDA

Are you looking to make a career change in the coming year? Do you want to move up to a management position? Are you curious what skills hiring managers are looking for in potential hires? The beginning of a new year marks a time when many people evaluate their careers and make plans look for a new role or explore options outside of their current employer. With this in mind, the *PDA Letter* reached out to PDA Board Member **Lisa Skeens,** PhD, who recently made a major career move by joining Hospira as Vice President of Global Regulatory Affairs following a 20-year career at Baxter.

Lisa Skeens (right) stands with Zena Kaufman (left) and Hassana Howe, PDA Director of Membership

Skeens' story provides a good example of how important interpersonal relationships built through organizations like PDA are in advancing a career. From her involvement with PDA, she built a strong relationship with a fellow volunteer, **Zena Kaufman**, Senior Vice President of Global Quality at Hospira. Kaufman informed Skeens about the position at Hospira, which led to her taking the position in 2012.

Skeens began her career at Baxter as a Global Regulatory Affairs Associate with plans to eventually move in to management.

"I was hired into a role that was a rotational program where they were starting employees to fast track them in to senior management," she said. "It was always my goal to look at senior management and to move into senior management. So from the very beginning, I was kind of managing my career with that goal in mind."

To prepare herself to move in to management, she made a point of finding mentors. She emphasized that while many people think they need a formal mentoring relationship, she always sought more informal mentors.

"I looked at different people for different types of mentoring," she said. Working with business leaders provided opportunities at learning how to communicate effectively and lead meetings. She sought out mentors among senior regulatory staff to learn how they achieved their career goals and what they sought to accomplish.

"Then I looked for people outside of my own company," she said. "That's where PDA was excellent, and I had some really good mentors and role models in some of the people that were involved in PDA."

PDA also exposed her to "Some really strong women leaders…who were really strong mentors and PDA leaders." Women like former PDA Chair **Nikki Mehringer,** Senior Director of Quality, Global Medical Affairs, Eli Lilly, and Director **Jennie Allewell,** Head of Regulatory Affairs, Lonza AG, were role models for Lisa.

Her involvement in PDA also helped her gain expertise and experience.

"One of the ways you differentiate yourself within your company is being involved in an association like PDA. You not only get to discuss all the scientific, technical things that are going on, but you get to influence those," she said, highlighting how her involvement led her to work on U.S. FDA draft guidances. She then took this expertise and brought it back to her company, drawing positive attention to herself. This involvement also led her to expand her network, benchmark other companies, and develop relationships with others in the industry who could serve as sources of information.

"That was important to me, especially because I stayed in one company for so long. It enabled me to understand how things were done in industry through some of that networking and being on committees," she said.

For her, the key to networking success is "Getting involved. I didn't just go to meetings and introduce people and network that way. It really is getting involved. Get involved on a committee…networking is okay but building relationships with people is even stronger."

She admits that volunteering requires time and effort.

"You make time for it because A) you enjoy it, and B) you know you're going to get so much more back," she said.

Additionally, through networking, "I've built really strong relationships with people and it helped me, both from an understanding FDA perspective—which in regulatory is really strong—in addition, to building that network within industry."

Skeens then offered advice for others considering making career moves in 2013.

"People need to decide what they want to do and be comfortable with some changes. And be open to a lateral change.

Networking is okay but building relationships with people is even stronger

Be open to doing a different role that will get you different experience," she said, citing examples of individuals moving from quality to regulatory or even to project management.

She also suggests that anyone looking to make a career change seek some type of global experience.

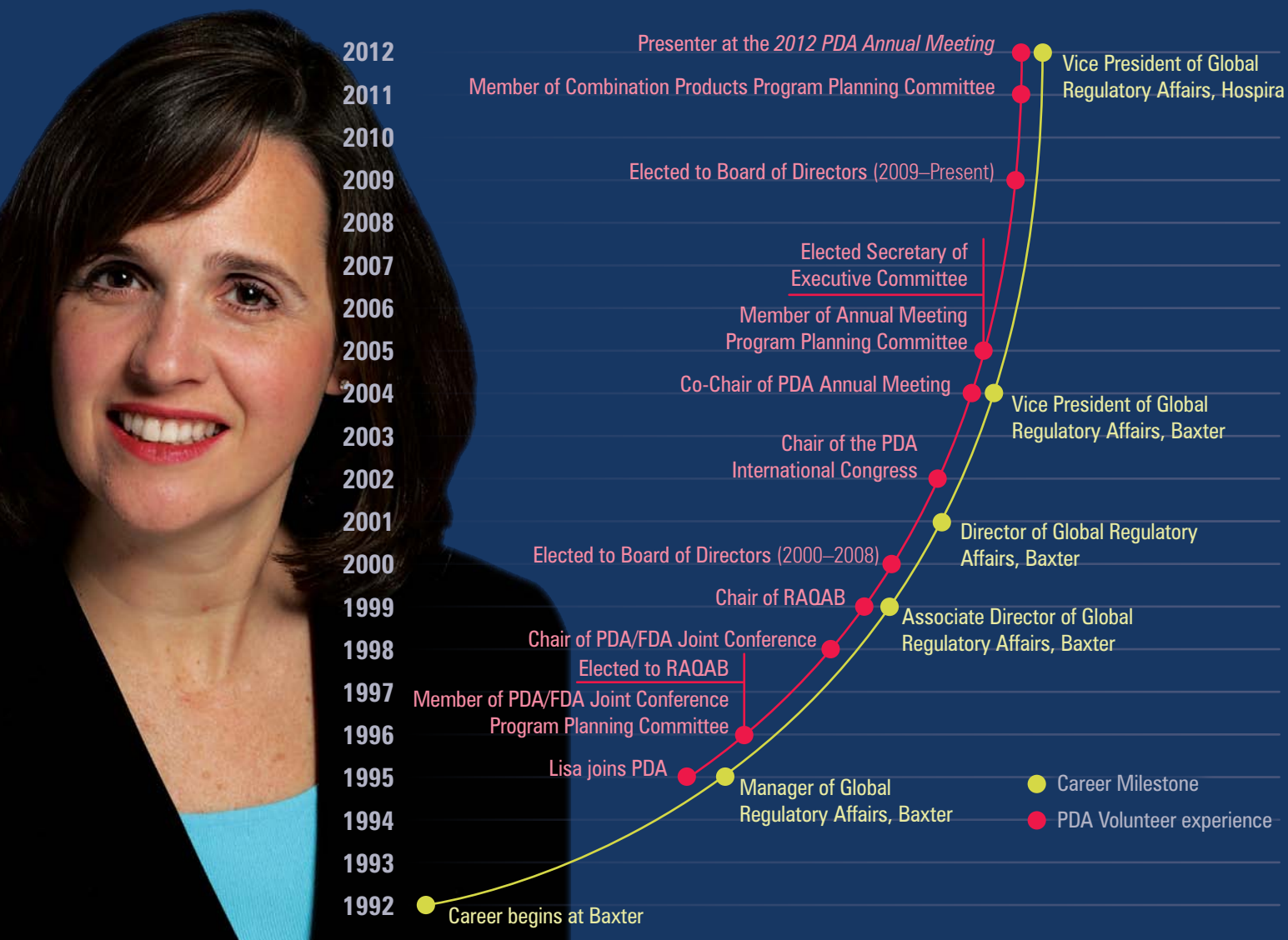
"If you're in a role that's just in the U.S.," she said, "you might want to consider something that's going to advance your experience and expertise, like taking a job that is a more global job in nature than maybe just working with FDA."

As a hiring manager, what qualities does she look for in a candidate?"

"I'm always looking for expertise and experience," she said. In the area of expertise, she looks for candidates with a strong scientific background, preferably with an advanced degree. Such a candidate also needs to demonstrate an eager willingness to learn.

"I expect people to have, not just a surface level of expertise, but a deep sense of expertise in the areas they've worked in,"

Lisa Skeens' Career and PDA Volunteer Highlights



she said. "From an experience perspective, I'm looking for people who have a diversity of experience and also a depth of experience."

So what advice does Skeens have for aspiring managers?

"You need to be preparing yourself for the different levels. So you need to make sure that you're very planful in your career moves and that, again, you can build on your experience and your expertise," she said.

New roles need to be selected carefully, Skeens says. Find out if the new position is going to give you the expertise and the experience that you need to go do something else and will it allow you to differentiate yourself against other people with similar backgrounds?"

Additionally, she recommends to explore opportunities to gain transferrable skills, such as a stint in project management. Taking on extra projects also helps, such as joining a business strategy team.

Outside of PDA, she has worked with other associations and professional groups, including the Biotech Industry Association (BIO), Advanced Medical Technology Association (AdvaMed), Drug Information Association (DIA), and the Regulatory Affairs Professionals Society (RAPS).

"But I've loved PDA because it's such a member-driven organization and a scientific organization," she said. "So those two things have differentiated it versus other trade associations."

She reminds anyone considering moving up the career ladder or switching roles to remember that the process takes time.

"I realized it doesn't happen overnight," she said. "You have to have the expertise and the experience to allow you to keep moving. So it was all about 'what experience do I need?' and 'what expertise do I need?' in order to get to the next level and get to the next position."

Skeens' career arc demonstrates how committing oneself to your career, including a willingness to get involved with your peers across the industry, can lead to advancement. Skeens' new position at Hospira represents a major step forward in her career, as she is now head of the company's entire worldwide regulatory affairs function. Who knows, the next stop for Skeens could be CEO.

Parenterals Conference Draws 200 to Spain

Conference Co-chairs Friedrich Haefele, PhD, Boehringer Ingelheim Pharma, and Stefan Merkle, PhD, Cilag AG

Almost 200 professionals from the pharmaceutical industry, from technology and equipment suppliers to government agencies convened in Barcelona, Spain Nov. 6-7 for the *2012 Parenterals: Contribution of Biologics to Public Health*. This symposium focused on the manufacture of biopharmaceutical products. Presentations covered numerous areas impacting the manufacturing of biopharmaceuticals, including: new guidelines on manufacturing and validation, manufacturing environment, manufacturing technologies, components (such as elastomers, containers, devices and efficiency), and cost and compliance.

Frank Mathias, PhD, CEO of Medigene and Chairman of the Board of vfa bio, a group representing biotech interests of German pharmaceutical companies, gave the introduction. He noted that despite the challenge of meeting expectations for public health, the industry is still the most promising source to solve unmet medical needs.

The second keynote presentation given by **Jeffrey Baker,** Phd, Deputy Director, Office of Biotechnology Products, CDER, U.S. FDA, provided insights into his perception of the currently ongoing change process in regulatory expectations towards CMC dossier content.

After **Cristina Gómez-Chacón,** from AEMPS, the Spanish regulatory authority, gave an update on new guidance impacting the industry, the stage was set for **Friedrich Haefele,** PhD, Boehringer Ingelheim Biopharma, who focused on recent trends and challenges for the industry, concluding there is not a single successful way through the demands ahead of us but a variety of solutions that may be followed on a case-by-case basis.

The afternoon sessions were more technical with presentations by **Günther Gapp,** PhD, Head, QA/QC Microbiology, **Eleonora Spanò,** PhD, Validation Specialist, Institut Biochimique SA, and **Norbert Hentschel,** Director, Global Technical QA Biopharma, Boehringer Ingelheim.

The coffee break offered another opportunity to interact with the exhibitors before the third and last session of the day which included presentations by **James Drinkwater**, Chairman, Pharmaceutical and Healthcare Sciences Society, **Jackie Horridge,** PhD, Senior Field Applications Scientist, Azbil BioVigilant, **Miguel Nogueras,** Phd, Global Manager of QA Microbiology, Abbott Laboratories, **Edwin Hoppenbrouwers,** Director, New Product Introduction, Catalent Pharma Solutions, and **Gloria Berrios,** Senior Research Scientist, Eli Lilly.

The first session of the second day titled, "Manufacturing Technologies," comprised a comprehensive approach to characterize and evaluate extractables from polymeric consumables used in the fill and finish process, including a user perspective on computer integrated manufacturing architecture practiced at Eli Lilly.

After the coffee break, the second session focused on components, i.e., elastomers, containers and devices, with presentations by **Roland Guinet,** PhD, Consultant, rGmp Compliance, **Zai-Qing Wen**, PhD, Principal Scientist, Amgen, and **Paolo Golfetto,** R&D Manager, Nuova Ompi.

The last session's topic was compliant efficiency and cost optimization. Here, **Andrew Pocock,** Team Consulting, provided examples in the area of device development and selection while **Wolfgang Epple,** Associate Director, Parenteral Production, Cilag, and **Sandra Schinzel,** PhD, Manager, Operational Excellence, Roche, discussed aseptic fill and finish.

Immediately following the conference, PDA Europe and PIC/S hosted an invitation-only, two-day course, "Rapid Microbiological Methods Training Seminar."

In hindsight, the overall goal of the symposium—to provide a forum to discuss actual challenges and trends in the manufacture of biopharmaceutical drugs—was accomplished. At times, lively discussions were entertained, plus, the exhibitors found adequate opportunity to network with attendees. Barcelona is always worth a trip, but this PDA symposium provided valuable insights beyond the fact that there's a correlation between the number of Nobel laureates and chocolate consumption!

The Barcelona skyline at dusk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North America

Axelrad Moves in to Advisor Role

Effective Jan. 6, **Jane Axelrad**, Director of the Office of Regulatory Policy (ORP), CDER, U.S. FDA, assumed a new position as senior advisor to **Janet Woodcock**, MD, Director, CDER. She will serve as a lead for the Center on managing policy and oversight issues concerning pharmacy compounding. This follows an outbreak of fungal meningitis due to contaminated steroid injections provided by a compounding pharmacy.

As of Feb. 1, **Nancy Hayes** will serve as acting director of ORP until a permanent replacement is brought on. Immediately following Axelrod's departure, **Denise Esposito** served as acting director before assuming a management position elsewhere at FDA.

U.S. FDA Extends RFID Feasibility Studies Expiration Date

In late December, the U.S. FDA announced that the expiration date for complying with the policy guide, *Radiofrequency Identification (RFID) Feasibility Studies and Pilot Programs for Drug* to Dec. 31, 2014. This guide shows how the Agency plans to use enforcement discretion regarding certain regulatory requirements that would be applicable to studies of RFID technology involving medicines. Ultimately, the Agency hopes to facilitate RFID studies and to give industry the opportunity to gain experience with the technology as well as analyze its effectiveness on the drug supply chain.

Draft Guidance Available on Submissions Using eCTD Specifications

The U.S. FDA has posted a draft guidance concerning regulatory guidelines for the electronic submissions of applications for drug products, including NDAs, ANDAs, BLAs, and INDs. The guidance outlines requirements for electronic submissions in an FDA-approved format. At this time, the Agency can process and review submissions using eCTD specifications.

Comments on the draft guidance are due March 4.

Draft Guidances on Safe Reporting Requirements for INDs and BA/BE Studies Available

The U.S. FDA posted in late December, a draft guidance on the safety reporting requirements for bioavailability and bioequivalence studies. The guidance only represents the Agency's current thinking on the topic and is not binding. Alternative approaches can be used if the approach in question satisfies applicable statues and regulations.

In the past, sponsors investigating INDs often reported numerous events that did not contribute to the safety profile of a drug, including serious adverse occurrences likely to have been caused by an underlying disease, adverse experiences common in the study population regardless of exposure to the drug, and adverse experiences that were end points of the study. The Agency believes these should not have been reported as IND safety reports. The guidance also offered additional safety reporting requirements for bioavailability and bioequivalence studies exempt from IND requirements.

In addition to the above draft guidance, the FDA also posted a similar draft guidance on the same topics for small businesses.

U.S. FDA Guidance on 510(k) Submission Criteria Now Available

On Jan. 2, the U.S. FDA posted the guidance, *Refuse to Accept Policy for 510(k)s.* This guidance specifies the criteria and procedures the Agency will use to determine when a 510(k) submission is administratively complete. After the draft of the guidance was posted in Aug. 2012, the Agency received comments concerning checklist questions related to performance data as well as comments on checklists identified as "analysis" or "discussion" as criteria for acceptance and relevant prior submissions. The Agency has addressed these comments in the guidance.

Key Regulatory Dates

Comments Due

March 4 — Draft Guidance on Submissions Using eCTD Specifications

Premarket Approval Applications Acceptance and Filing Reviews Guidance Posted

Superseding the U.S. FDA's May 2003 guidance on premarket approval filing, there is a new guidance available on the acceptance and filing review criteria for premarket approval applications (PMAs). Due to recent changes in the law, including the reauthorized Medical 88 Device User Fee Amendments of 2012 (MDUFA III), acceptance review has taken on a larger role in encouraging quality PMA applications and allowing FDA to allocate resources more adequately on completed applications. The new guidance includes a modified PMA filing checklist.

New Guidance on eCopy Medical Device Submissions in Effect

Effective Jan. 1, the U.S. FDA announced that the final guidance concerning the eCopy Program for medical device submissions is available. The eCopy Program is a new electronic review program for medical device submissions intended to expedite the efficiency of the review process. The new guidance contains standards

Continued on page 43

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Workshop to Showcase Analytical Method Lifecycle Steps

2013 Analytical Methods Development & Validation Workshop • Baltimore, Md. • Fall 2013

Stephan O. Krause, PhD, MedImmune, Committee Chair

PDA is pleased to host the *2013 Analytical Methods Development & Validation Workshop* later this Fall. The purpose of this workshop is to offer attendees an in-depth view of all analytical method lifecycle steps. This workshop continues the discussion topics of the previous PDA workshop sessions from June 2011. The program will begin with a plenary session that will provide a roadmap to the audience for the various stages of the analytical methods lifecycle. The guidance developed by PDA's task forces will be used as a basis. In addition, a regulatory overview will be provided by the U.S. FDA in this introduction session.

The workshop will feature a variety of regulatory and industry speakers knowledgeable about the details of method development and validation. Featured speakers include FDA representatives from CBER and CDER, as well as **Stephan Krause,** PhD, Principal Scientist at MedImmune, task force chair of PDA *Technical Report No. 57: Analytical Method Validation and Transfer for Biotechnology Products* and author of *Validation of Analytical Methods for Biopharmaceuticals: A Guide to Risk-Based Validation and Implementation Strategies*. The workshop will also feature some of the foremost scientists from regulatory agencies, task force contributors, the U.S. Pharmacopeia, and leading pharmaceutical companies, including Merck, MedImmune, Sanofi Pasteur, GlaxoSmithKline, Amgen, and Genentech, whose representatives will speak on the various aspects involved in method development and validation.

Representatives will speak on the various aspects involved in method development and validation

The primary workshop objectives are:

- To focus on the entire lifecycle of analytical methods from development to post-validation maintenance, based on PDA technical reports and representing a joint industry/regulatory perspective on this topic

Continued on page 41

Human Factors Affect the Manufacturing Environment

2013 PDA Human Factors and Human Error Reduction Workshop • Orlando, Fla. • April 17-18 • www.pda.org/humanfactors2013

Miguel Nogueras, Abbott Medical Optics

In several meetings over the last year, regulators have highlighted the continuing occurrence of old problems. Unfortunately, these problems often contribute to inefficient production, compliance failures, or drug shortages. Knowing there is a problem is one step — understanding the root cause, and taking action to prevent recurrence, is our collective challenge. As the old saying goes, "to err is human," and this certainly applies to our industry. Human involvement continues to be an important part of pharmaceutical manufacturing despite advances in automation.

Human factors is an area of science that focuses on a range of different topics, including ergonomics, workplace safety, human error, product and process design, human capability and human-computer or man-machine interaction. To learn more about the human factor and its impact on manufacturing, PDA invites you to attend the *2013 Human Factors and Human Error Reduction Workshop* which follows the PDA Annual Meeting this spring.

How often have you seen an investigation report that attributed the cause of the failure to "human error"?

What is a use error (also formerly known as human error)? It is an inappropriate or undesirable human decision or behavior that reduces, or has the potential for reducing, effectiveness, safety, or system performance, while executing an action that led the task or system outside its acceptable limits. A use error has an adverse impact on a process, product, person or a group of people. More importantly, an error is not known until after the fact. It is critical that we understand use errors due to the impact on quality, efficiency, cost, morale, and other components of manufacturing.

Notably, we often spend most of our efforts in training and disciplinary action, rather than **error-proofing.** Hence the high numbers of non-conforming reoccurrences with the same failure mode.

Along with studying use error and error-proofing, the workshop will also focus on cognitive workload, process design, ergonomics, and warnings and labels. In this workshop, we will discuss the impact to a process by cognitive workloads, whether they are overloaded or under-loaded. During Use Error Training attendees can learn how to further evaluate a process taking under consideration important elements such as the ergonomics associated to the process and the individuals interacting with the process. And finally, we will study warnings and labels as issues can arise from human interpretations of such content. Data published since the 1980s has shown that although there is a high percent of the human population who acknowledges/notices labels and warnings, significantly lower numbers comply with the required instructions from a label.

> ***"To err is human" remains a valid observation of human behavior***

Break out of the vicious cycle of failure/retraining!

During the *2013 PDA Annual Meeting* you will have the opportunity to participate in a world-class workshop where we will discuss not only the theory behind human factors, but also the perspectives from regulators regarding the use of human factors during process design and evaluation of non-conforming events. The training will provide real life experiences as well as tools used in the manufacturing environment to design and redesign a manufacturing process with the goal of preventing or eliminating reoccurring non-conformance. In today's work environment, re-thinking how to design a process to reduce the propensity for use error is a highly important skill. Besides, "to err is human" remains a valid observation of human behavior and illustrates the necessity for studying human factors, particularly in an industry where use error could impact patient safety and a company's bottom line.

Next PDA/FDA Glass Quality Conference is on the Horizon

2013 PDA/FDA Glass Packaging Conference • Bethesda, Md. • May 15-16 • www.pda.org/glass2013

Committee members Thomas Schoenknecht, PhD, Schott AG, and Roger Asselta, Genesis Packaging Technologies

On behalf of the program planning committee, we would like to invite you to the third conference co-sponsored by PDA and the U.S. FDA on the important topic of glass quality. The great success of the first two conferences together with the substantial increase of recalls related to material defects convinced us to revisit the topics discussed last year and ask industry leaders for their updates on the topics driving the industry.

In our industry, glass has been the traditional container material for pharmaceuticals for more than 200 years. With plastic materials constantly improving, we saw plastics replacing glass for oral solids and most oral liquids decades ago, however, glass is still the dominant packaging material for parenterals. The expansion of proteins and other biotech products together with new drug delivery systems such as autoinjectors has changed the design landscape for primary container solutions such as cartridges and syringes substantially. In parallel, the technical requirements and specifications for standard containers, such as vials or ampoules, improved as well.

When analyzing glass issue-related recalls of the last 18 months, glass delamination, or the formation of glass lamellae in drug product proved a substantial challenge for the parenteral drug industry. The conference will provide updated information on the root cause of this phenomenon from the glass converting industry perspective and the steps that have been taken to mitigate the risks associated with the glass delamination challenges.

Aside from the issue of container standards, glass supplier reliability and pharmaceutical manufacturer handling and distribution best practices will be discussed by industry experts, sharing knowledge about all necessary technologies to maintain and ensure container closure integrity and product sterility assurance throughout the product lifecycle of sterile injectable pharmaceutical and biopharmaceutical products.

Further, alternate materials and material combinations including coating solutions for containers will be discussed providing insights into the latest industrial developments. Also, the increasing interest in industry and regulatory about state of the art inspection technologies will be addressed in a special session where standards for subvisble ➤

In our industry, glass has been the traditional container material for pharmaceuticals

inspection and technology to visualize stress and tension in glass by birefringence measurement will be shown.

PDA is also hosting an exhibition where glass and alternative material utilizing drug delivery packaging solution providers, glass inspection companies and other pharmaceutical manufacturing service providers will show their latest offerings and hot issues from the market place can be discussed during the various networking possibilities offered by the conference program.

In addition you can deepen your knowledge about pharmaceutical packaging and related topics in parenteral drug manufacturing by participating in one of the PDA TRI educational courses that will be offered immediately following the conference.

We, the Committee, are convinced that this event will offer a great opportunity to learn and talk with industry peers, regulatory authorities and suppliers about the changing environment in packaging science and technology.

We look forward to seeing you at the *2013 PDA/FDA Glass Quality Conference* in Washington, D.C.

Workshop to Showcase Analytical Method Lifecycle Steps continued from page 38

- To learn from other industry experts how to prepare and submit this documented evidence to the agencies
- To give participants opportunities for questions and feedback in 30 minute Q&A sessions following each plenary session, as well as in a unique hour-long "Ask the Experts" panel discussion

Anyone working with method development, validation, or interested in understanding the analytical method lifecycle and how it relates to the product lifecycle is invited to attend this workshop.

TRI Combines Viral Filtration and Viral Spikes Courses

Bethesda, Md. • April 2-4 • www.pda.org/viruspikes

Scott Lute, U.S. FDA

Last year, TRI offered the popular courses, "Virus Filtration" and "Preparation of Virus Spikes Used for Virus Clearance Studies" for TRI for the first time. In an effort to make the course more efficient, TRIS has combined into one, "Preparation of Virus Spikes used for Virus Clearance Studies and Virus Filtration."

Not only will this make the course more efficient but instead of lasting four days, the new course will be three days, so attendees can spend less time away from the office. Otherwise, attendees will receive the same amount of information. Scott Lute, who taught the previous courses, will return for a second time covering the issues of virus filtration and virus preparation. Previously, he was an active participant in the PDA Virus Filter Task Force, which standardized nomenclature of both large and small pore virus filters.

Both topics have seen considerable interest in recent years, even resulting in PDA *Technical Report No. 27, Preparation of Virus Spikes used for Virus Clearance Studies and Virus Filtration* and PDA *Technical Report No. 41, Revised 2008, Virus Filtration.* The risk of contamination in biotechnological and biological therapeutic products exists because these products are manufactured using materials derived from animal or human origin. As a result, global regulatory agencies require manufacturers demonstrate the viral safety of these products, often with spike/removal validation studies. When validating industrial bioprocesses, viral filtration unit operations must be scaled down to represent a larger scale.

Participants will learn how to critically select virus filters and design a virus filtration process ensures safe use of therapeutic biological products as well as understand the complexity and variability of virus spikes, including methods to enhance quality control.

Participants will leave the course with increased knowledge on the viral safety of biotech products

This course will consist of both classroom lecture and lab work. The lab-based work will include testing model virus preparations and performing viral clearance studies at the laboratory-level using model bacteriophage. Participants will also gain a greater understanding of TR-41 and TR-47.

Participants will leave the course with increased knowledge on the viral safety of biotech products from an instructor with strong technical knowledge as well as manufacturing experience held at TRI's well-equipped, state-of-the-art laboratory.

We urge anyone involved in the viral safety area to attend this retooled TRI course.

About the Author

Scott Lute has been with the U.S. Food and Drug Administration since 2002 in the Bioprocessing laboratory in the Division of Monoclonal Antibodies. He has studied viral clearance by biotech downstream processing associated with monoclonal antibody manufacturing.

Regulatory Briefs continued from page 36

for electronic submissions and identifies submission types that require an eCopy in order for the submission to be processed.

Europe

EMA Restructuring to Affect Event Attendance

In December, EMA announced plans to review the Agency's operations, with a focus on expanding efficiency of scientific activities as well as enhancing information and communications-related technology. This review is expected to result in reorganization of staff in 2013.

This process will impact the Agency's involvement in external meetings through much of the first few months of the year. Attendance by EMA staff at outside events may be cancelled. Participation via video conferencing or teleconferencing, however, may be used as an alternative.

EMA will contact event organizers directly if EMA staff is scheduled to speak.

[Editor's Note: In this edition of the "Voices of the Board," the *PDA Letter* wants to recognize the two newest board members, chosen by PDA members in 2012, and thank outgoing board members for their years of service. Next issue, we will continue with articles from the board.**]**

Board of Directors Includes Two New Members

PDA welcomes two new directors to the 2013 Board of Directors, **Stephan Rönninger,** PhD, and **Ian Elvins.** We are excited to usher in these two new board members. Both have considerable industry experience and their expertise will be valued by the Board as well as throughout the organization. We are confidant both these individuals will represent the interests of PDA's members and be of service to the organization.

Ian Elvins has over 30 years' experience in the pharmaceutical industry, with responsibilities in quality, manufacturing, and technical areas. He is a microbiologist by background and has worked in Italy, Switzerland, Ireland and currently, the United States. He has held many diverse roles within our industry, from supervisor of an API facility to plant manager of a parenterals production site, which manufactured both lyophilized and liquid fill (syringes) products. For the last three years he has held the position of Head of Global Quality and Regulatory Affairs for the Swiss CMO, Lonza AG. In this role he is responsible for all aspects of quality and regulatory affairs in all of Lonza's sites worldwide.

Stephan Rönninger holds a PhD-engineering degree in organic chemistry from the Technical University of Darmstadt, Germany and performed post-doctoral studies at the University of Zurich, Switzerland. He has been with Roche since 1992 with responsibilities in quality assurance, quality management, and quality risk management. Currently he is the Head of External Relations Europe/Japan of F. Hoffmann-La Roche Ltd based in Basel, Switzerland. His main focus is in global quality and compliance; he collaborates with many stakeholders (e.g., authorities, associations, and competitors) on these topics and others. In addition, he comments on quality management and good manufacturing and distribution practice (GMDP) topics. He also represents Roche in the European Industry association EFPIA and EFPIA in ICH Q9, Q-IWG and ICH Q7.

PDA Bids Farewell to Two Board Members

In addition to gaining two new members, **Martin VanTrieste**, and **Zena Kaufman's** terms on the Board have ended. Both have provided a number of contributions as board members over the past few years. While we will miss their input as board members, Martin and Zena will remain fully dedicated volunteers serving PDA in a variety of roles.

Martin VanTrieste joined the Board in 2007. He is currently Senior Vice President of Quality at Amgen. He partnered with PDA, PQRI, and the U.S. FDA on the development and roll out of the FDA Aseptic Guidance Document and its related compliance tool. Additionally, he has been involved with the Science Advisory Board and has served on several program planning committees. In January 2013, PDA announced that a new award in his name, the Martin VanTrieste Pharmaceutical Science Award, will be awarded annually for contributions that have advanced pharmaceutical science.

He will also be one of the speakers at the 2013 Annual Meeting in Orlando, Fla.

Zena Kaufman joined in 2010. She is currently Senior Vice President of Global Quality at Hospira. In 2006 and 2007 she served as chair of the RAQAB Advisory Board. She has also served on program planning committees and has been involved with the PDA Midwest Chapter in addition to her work with the Quality Systems, Inspection Trends, and Visual Inspection of Parenterals Interest Groups.

She is currently on the program planning committee for the 2013 *PDA/FDA Improving Investigations Workshop* which will follow the joint regulatory conference with FDA.

editor's message

Vaccines IG Helps with QbD Infographic

The PDA Letter Editorial Committee (PLEC) very much thought it would be valuable to hear how QbD was being applied in vaccines manufacturing. As it turned out, that was a a hot topic for the PDA Vaccines Interest Group as well. So Editor **Rebecca Stauffer** worked with members of both groups to devise a brief survey on the topic which resulted in this issue's Infographic on page 28. PLEC members **Rainer Newman** and **John Paul Bevel** helped Rebecca formulate the questions. With the help of IG leader **Frank Kohn,** Rebecca promoted the survey to the Vaccines IG members via email and at their gathering during the *2012 PDA/FDA Vaccines Conference* last December. Over 100 PDA members were solicited, and we received a response rate over 10%.

Rebecca took advantage of her visit with the Vaccines IG and wrote an IG Corner for this issue's Science Snapshot. She learned that the group is very interested in FDASIA, as are many of us.

The whole issue of QbD and vaccines product development was a topic of several talks at the *2012 PDA/FDA Vaccines Conference.* Rebecca attended the QbD session and also turned around a nice report for this issue.

PDA members told me at the *2012 PDA Annual Meeting* that they want to see more career-related information in the *PDA Letter,* and we are striving to provide it. In this issue, we linked up with PDA Director **Lisa Skeens** to discuss her recent career move from Baxter to Hospira. Lisa was more than generous in talking about her career and offering advice to those wondering how to get ahead in our industry.

Last month, we rolled out the new-look "Volunteer Spotlight," and in this issue, we offer a completely redesigned and renamed "Faces & Places." The new "PDA Photostream" mimics the way most of us look at and take photos nowadays, with our handheld smart devices! **Katja Yount** did a great job with the new design.

PDA Letter Corrections

In the January issue, we found a few mistakes. For one, in the "Faces & Places" (p. 11), the U.S. FDA's **Kalavati Suvarna's** name was mispelled. Our apologies to her for the error.

In addition, the cover story "Proposed CDER Office Seeks to Change Quality Paradigm in Industry" mentioned the now famous ICH quality guidelines that are helping to change the quality paradigm, but left out one of the most important, ICH Q10 Quality Systems. I appreciate reader feedback which helped us set the record straight.

Finally, in our zeal to have pithy headlines, we mistakenly shortchanged the scope of the upcoming TRI *Pharmaceutical Supply Change Integrity* course series in "TRI to Offer Five-Day Course Training Series" (p. 42). Author and course instructor **Rafik Bishara** noted our error, and we hope it was clear from the content of the article that cold chain shipping was not the only topic covered during the week-long series.

Authors Wanted

We are currently seeking articles on Process Validation (due March 4); Careers (due March 25); Sterile Processing (Apr. 4); Outsourcing (July 3); Disposable Systems (Aug. 2); Filtration Validation (Aug. 2).

Contact me or Rebecca with your proposals: morris@pda.org or stauffer@pda.org.

PDA Letter

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PDA Global Headquarters — Bethesda Towers
4350 East West Hwy., Suite 200
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900 Fax: +1 (301) 986-0296
info@pda.org
www.pda.org

PDA Europe — Adalbertstr. 9
16548 Glienicke/Berlin Germany
Tel: +49 33056 23 770 Fax: +49 33056 23 7777
petzholdt@pda.org

PDA Training & Research Institute
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Preparation of Virus Spikes Used for Virus Clearance Studies and Virus Filtration
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www.pda.org/viruspikes

2013 Aseptic Processing Training Program
Bethesda, Maryland
www.pda.org/2013aseptic

- Session 2: April 8-12 and May 6-10, 2013
- Session 3: June 3-7 and June 24-28, 2013
- Session 4: August 26-30 and September 23-27, 2013
- Session 5: October 14-18 and November 4-8, 2013

Annual Meeting Course Series
April 18-19 | Orlando, Florida
http://pdaannualmeeting.org/courses

- Recommended Practices for Manual Aseptic Processes (April 18)
- Steam in Place (April 18)
- Biofilms (April 18)
- Single Use Systems (April 18)
- Process Simulation Testing for Aseptically Filled Products (April 19)
- Validation of Moist Heat Sterilization Processes: Cycle Design, Development, Validation and Ongoing Control (April 19)

An Introduction to Visual Inspection – Session 1
April 30-May 1 | Bethesda, Maryland
www.pda.org/visualinspectionlab1

MAY 2013

PDA Container Closure Components and Systems Workshop Course
May 13 | Bethesda, Maryland
www.pda.org/containerclosurecourse

- Assessing Packaging and Processing Extractables/Leachables

PDA/FDA Glass Packaging Conference Course
May 17 | Bethesda, Maryland
www.pda.org/glasscourse2013

- Identification and Classification of Nonconformities in Ampoules, Syringes and Injection Devices for Pharmaceutical Manufacturers

PDA/FDA Process Validation Workshop Course Series
May 22-23 | Washington, D.C.
www.pda.org/provalcourses2013

- Utilization of Statistical Methods for Production Processes – New Course (May 22)
- Process Validation and Verification: A Lifecycle Approach (May 22-23)

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

Laboratory Courses

The PDA Training and Research Institute is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education.

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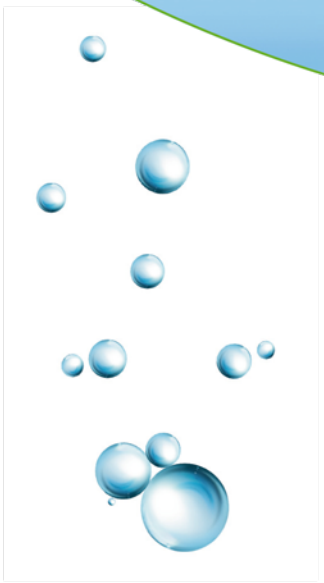

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