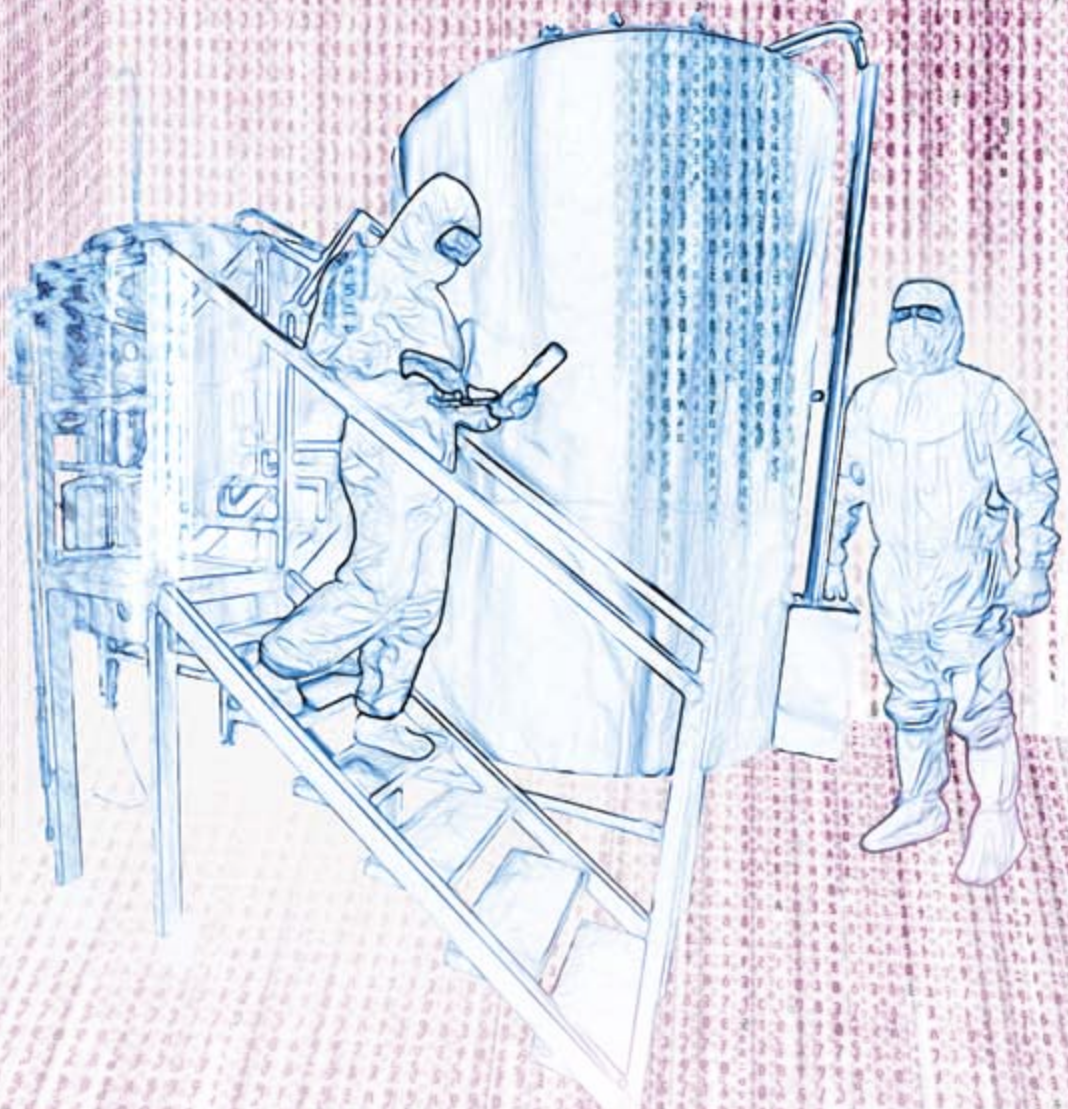
People • Science • Regulation

PDA Letter

Volume LI • Issue 3 www.pda.org/pdaletter March 2015



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22

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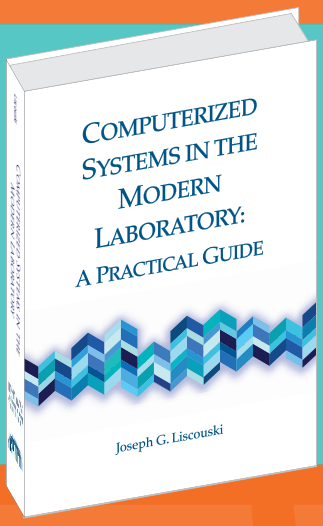

Computerized Systems in the Modern Laboratory: A Practical Guide

WRITTEN BY: JOSEPH G. LISCOUSKI

PDA MEMBER PRICE: ~~$265~~
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ITEM NO. 17329

The Bio/Pharmaceutical industry is at an interesting crossroads regarding the use of electronic technologies in laboratories. Laboratory management and staff must often evaluate tools that they don't completely understand, while facing pressure from vendors trying to make a sale. Furthermore, regulatory agencies are requiring senior management to justify the application of scientific electronic technology. *Computerized Systems in the Modern Laboratory* will provide laboratory staff and managers a solid understanding of the tools available, how to successfully purchase and implement the technology, and how to develop a plan for application and evaluation in order to meet regulatory requirements.

go.pda.org/CSML

ABOUT THE AUTHOR

Joe Liscouski, Executive Director, Institute for Laboratory Automation has more than 30 years of experience in the field of laboratory automation to include the design and development of automation systems, LIMS, robotics and data interchange standards. He has held symposia on validation, presented on technical material and taught courses on laboratory automation and computing in the U.S., Europe and Japan. His publication portfolio contains several authored books and specialized chapters, more than 30 technical papers on computing and automation, and an editorial defining the need for Laboratory Automation Engineering as a means of advancing the subject matter. His most recent work centered on the development of a new approach to technology planning and management for automation and computing in laboratories.

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pda.org/MAP

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pda.org/apmanagement

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pda.org/simulation

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PDA Letter

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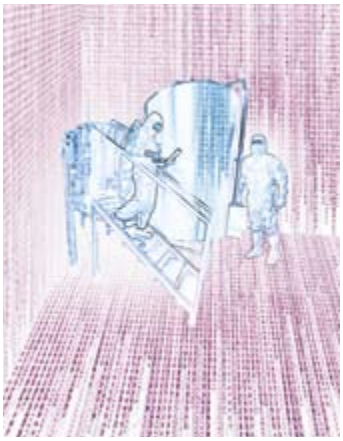
Cover



Cover Art Illustrated by Katja Yount

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Regulation

Voices of PDA

Contents

Features

PDA IN THE NEWS

Below is a listing of various news articles/websites that have mentioned PDA within the past five months.

BioProcess International

December 11, 2014

"The 2014 BPI Awards: Recognizing Excellence in Bioprocessing"
— Maribel Rios, Cheryl Scott and S. Anne Montgomery
tinyurl.com/mvoylh2

January 13, 2015

"The Single-Use Watering Hole: Where Innovation Needs Harmonization, Collaboration, and Standardization"
— James D. Vogel and Maureen Eustis
tinyurl.com/kvagbs2

GenomeWeb

December 15, 2014

"Study Shows Promise of NGS, qPCR to Detect Vaccine Contaminants"
— Andrew P. Han

IPQ Monthly Update

December 2014

"FDA's Center for Veterinary Medicine Using QbR and Other CDER-Tested Approaches to Decrease Review Times; CVM User Fees Drive Guidance Development"

"FDA Field Operation 2015 Priorities Include Alignment with Centers and Lab Optimization"

Pharmaceutical Technology

November 2, 2014

"Parenterals, Particulates, and Quality by Design"
— Cynthia Challener, PhD
tinyurl.com/kdot5n4

"Tackling Drug Shortages"
— Sean Milmo
tinyurl.com/knlrmw5

"Injecting Highly Viscous Drugs"
— Andy Fry
tinyurl.com/mupt4x8

January 20, 2015

"The Quest Continues for Quality Metrics"
— Jill Wechsler
tinyurl.com/o75gw6s

February 2, 2015

"Improving Visual Inspection Practices"
— Jennifer Markarian
tinyurl.com/lpmup9z

INTERPHEX Sessions to Build on *Aging Facilities Workshop*

PDA will be offering an exceptional education program at *INTERPHEX 2015,* an annual pharmaceutical and biopharmaceutical event dedicated to innovation, technology and knowledge, April 21–23 at the Jacob K. Javitz Convention Center in New York. Focusing on "Advancing Manufacturing Science," industry and regulatory experts will provide the latest updates on the changing manufacturing industry and address the critical issue of aging and modernization in three sessions over three days.

The first session on Tuesday, April 21 will address how continuous manufacturing and facility upgrades can increase efficiency along with present views from the U.S. FDA. The meaning of aging and modernization will be covered in the Wednesday, April 22 session, which will include a summary and readout report from the *2015 PDA Aging Facilities Workshop* held in March following the *PDA Annual Meeting.* The final session on Thursday, April 23 will take a first-hand look into aging and modernization from an analytics and facilities perspective and will also incorporate FDA's views on the subject.

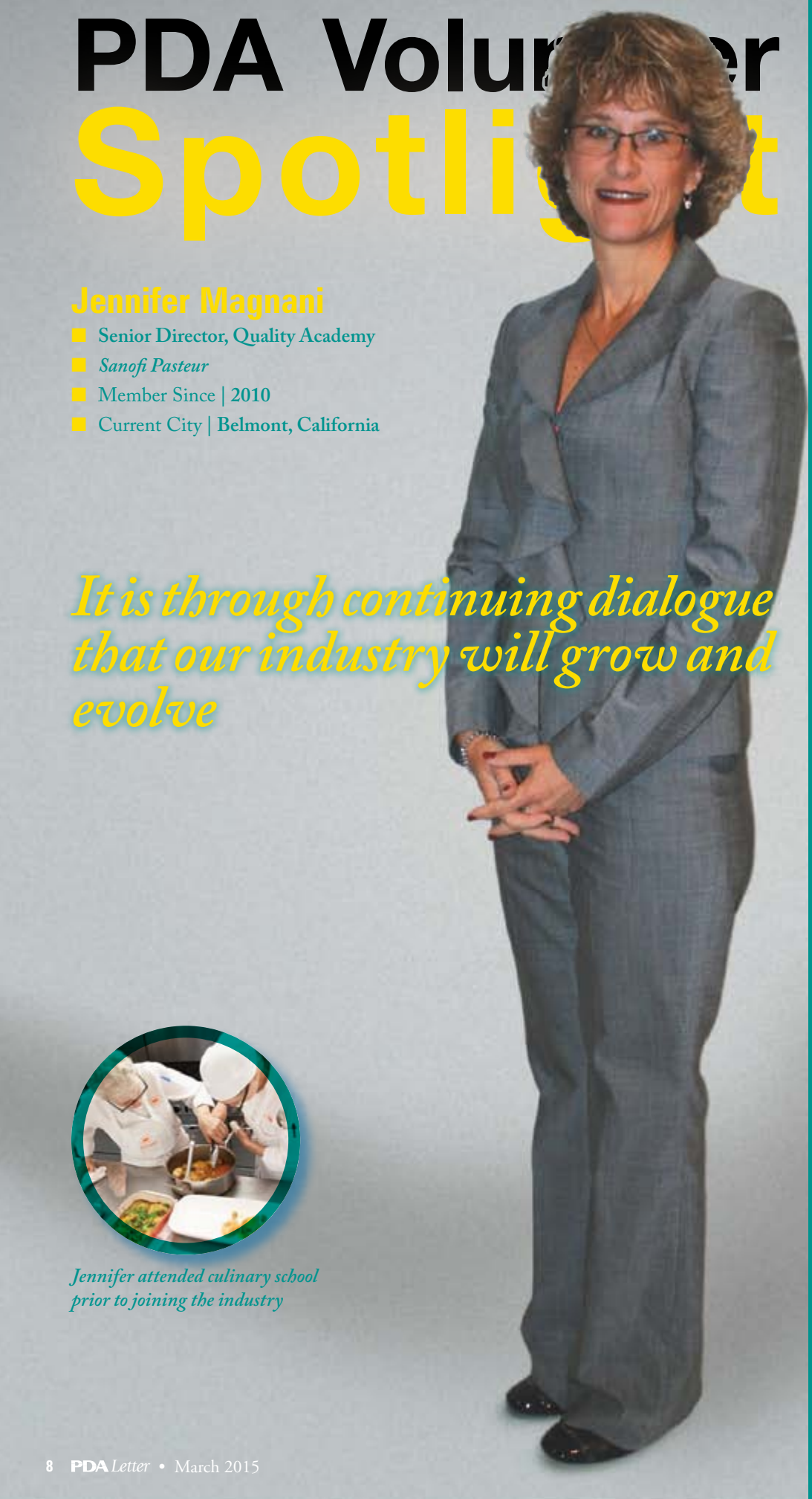
Throughout the conference, PDA will also be providing additional technical information through a series of presentations in the PDA Learning Center on the exhibit floor. These shorter talks will build on both the information shared at *INTERPHEX 2015* and content provided at the *2015 PDA Annual Meeting* in Las Vegas.

INTERPHEX 2015 registration is free, so register today to take advantage of the latest information on the topics most important to the pharmaceutical and biopharmaceutical manufacturing industry as well as access to the latest technology.

While you are there, be sure to visit the PDA booth (Booth #3679) in the Exhibit Hall to find out what's new for PDA members and spend some time networking with colleagues in the members-only lounge.

INTERPHEX

PDA Volunteer Spotlight



Jennifer Magnani

- Senior Director, Quality Academy
- *Sanofi Pasteur*
- Member Since | 2010
- Current City | Belmont, California

It is through continuing dialogue that our industry will grow and evolve

Jennifer attended culinary school prior to joining the industry

How can volunteers gain leadership roles at PDA?

Gaining a leadership role at PDA is achievable in so many different ways, but the most important is to **get involved.** There is no excuse not to. No matter your position or level of expertise/experience, there is a way to contribute to PDA and get noticed.

Here are some ways I got involved: authoring sections of technical reports, serving on conference and workshop planning committees, engaging in interest group discussions, attending local chapter meetings, presenting at local chapter meetings and working with the PDA Board of Directors on PDA's strategy.

How have you been able to manage volunteering for PDA and your job?

Balancing work, volunteering and life is not easy but its necessary. It just takes planning. You have to decide how important each one of these are, and how much time it will take to do each one well.

Start small when you volunteer for the first time and then when you are comfortable, move on to bigger, more time consuming roles.

How can PDA benefit someone new to the industry?

Very simply: knowledge! PDA is an organization filled with members that are leading industry experts from every technical space and support function within our field. Tap into it and build your network by connecting with PDA members. No matter what area of the pharmaceutical industry you are interested in, there are members you can talk to.

A new and easy way to gain knowledge and build your network is through PDA Connect[SM]. This online tool is a way to learn and share knowledge and experience. Just like we expect everyone in our company to speak up and ask questions, I would encourage all PDA members to participate in PDA Connect[SM].

What was your main takeaway from last year's *PDA/FDA Joint Regulatory Conference?*

It is hard not to say that the most memorable part of the conference was hearing **Janet Woodcock** speak about Quality Culture. As a matter of fact, I just watched it again on YouTube. I absolutely believe that the future of our industry depends on how pharma embraces the concept of living quality every day in everything we do.

Join the Conversation @ PDA CONNECT℠

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chapter update

Chapter Addresses Visual Inspection Challenges

Vishal Sharma, Vienni Training and Consulting

"Vision is the art of seeing what is invisible to others."
– **Jonathan Swift**

Visual inspection continues to remain a challenge for parenteral manufacturers both within India and across the globe. In line with PDA's spirit of connecting people, science and regulation®, PDA's India Chapter addressed visual inspection concerns with a workshop, Dec. 11–12, in Bangalore, India.

More than 115 industry professionals from all over India participated in the workshop, which covered the fundamentals of visual inspection methods and their application to injectables using a combination of lectures, breakout sessions and hands-on exercises to develop and practice inspection skills. These skills may be applied to both manual inspections, semiautomated and automated machine inspections.

Gaetano Baccinelli led a session focused specifically on manual and both fully and partially automated inspections. This session showcased differences that exist between the various types of visual inspection methods as well as the best strategies to adopt for visual inspection. He also discussed a case study on inspection of ampoules.

Visual inspection defect kits also served as a key topic. **Vikram Shukla** facilitated a discussion on preparing and qualifying visual inspection defect kits. The session took a deep dive into the process of qualifying defect kits, critical questions on type of defect kits, challenges in preparing defect kits, batch size of defect kits, selection of defects to be included—all important considerations for defect kit maintenance and expiry.

The co-chair of PDA's Visual Inspection Interest Group, **Markus Lankers,** PhD, also looked at qualification, this time of visual inspectors. Participants appreciated his detailed considerations on selection criteria of inspectors, their training

process, utilization of test kits, and performance monitoring of inspectors.

Following these presentations, the second half of the first day featured a breakout session on setting up limits for particulate rejects. The participants were divided into three groups of approximately 40 participants, each led by a team of PDA India Chapter volunteers.

Michael de la Montaigne opened the second day of the workshop with a discussion on inspection technology and new advances in terms of particle inspection, direct spin and full cap inspection at a single station, facilitating better automated inspection. This session closed with discussion on standard documentation and industry standard practices during visual inspection.

Next, Lankers facilitated a session on investigation of rejects. He started with reject classification and the lifecycle approach, followed by tools for classification and identification methods, investigation and root-cause analysis methods, and ending with modes for process improvement.

For an understanding of USP chapters concerning visual inspection, **Atul Awasthi**, PhD, analyzed the USP Subvisible General Chapters: <788> Injections Subvisible, <789> Ophthalmic Subvisible,

Workshop Speakers and Volunteers

Top row (l-r) R.R. Tuljapurkar, Cadila; Deepak Kabbur, Brio Pharma; Sandeep Kachhwaha, Dr. Reddy's Laboratories; Ranjit Menon, Zydus Hospira Oncology; Vikram Shukla, Zydus Hospira Oncology; Sumitra Pillai, Dr. Reddy's Laboratories

Front row (l-r) Ivy Louis, Vienni Training and Consulting; Tarun Chugh, Amneal Lifesciences; Sanjit Lamba, Eisai Pharmaceuticals India; Gaetano Baccinelli, Stevanato Group; Markus Lankers, PhD, Rad-ID; S.G. Belapure, Cadila Healthcare; Vishal Sharma, Vienni Training and Consulting

<771> Ophthalmic Products — Quality Tests, <1788> Methods for the Determination of Particulate Matter in Injections and Ophthalmic Solutions, <787> Subvisible Particulate Matter in Therapeutic Protein Injections, <1787> Measurement of Subvisible Particulate Matter in Therapeutic Protein Injections, and <1771>Ophthalmic Products — Performance Tests. Then, he covered the current Visible General Chapters: <1> Injections, <790> Visible Particulates in Injections, and <1790> Visual Inspection of Injectable Products

The second day's breakout session encompassed visual inspection challenges and their solutions. Again, the India Chapter's volunteers rose to the occasion to successfully lead this session.

Finally, Lankers closed the workshop by providing an overview on the activities of the PDA Visual Inspection Interest Group.

Feedback from the event was very encouraging and participants expressed a demand for more such events. Expect more to come from the India Chapter in 2015! Visit www.pda.org/chapters/asia-pacific/india to learn more about upcoming chapter events.

[Editor's Note: Interested in learning more about the latest in visual inspection? Consider attending the *2015 PDA Visual Inspection Forum*, Nov. 26–27, in Bethesda, Md. Find out more at www.pda.org/2015-pda-visual-inspection-forum.**]**

PDA Who's Who

Atul Awasthi, PhD, Director Analytical Research & Development, USP India

Gaetano Baccinelli, OPTREL

Michael de la Montaigne, Global Sales Director, Bosch

Markus Lankers, PhD, Managing Director, rap.ID Particle Systems

Vikram Shukla, Zydus-Hospira

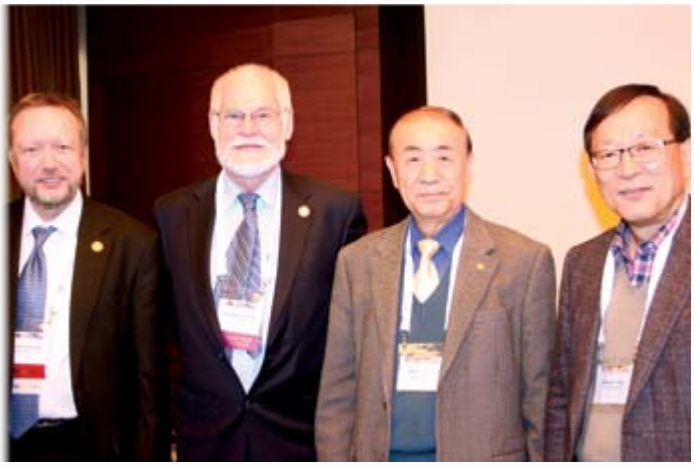
GMP for APIs (ICH Q7) PDA–PIC/S Training Course

January 22–23 | Seoul, South Korea

Opening Plenary

(l-r) Graeme McKilligan, MHRA; Stephan Rönninger, PhD, Amgen; Sang Bong Kim, South Korean Ministry of Food and Drug Safety (MFDS); Jeong Yeon Kim, PhD, MFDS; Woo-Hyun Paik, PhD, President, PDA Korea Chapter; Carmelo Rosa, U.S. FDA; Georg Rössling, PhD, PDA

Jeong Yeon Kim, PhD, MFDS, discusses how South Korean regulations apply to APIs.



PDA Board member Stephan Rönninger (far left) and PDA Europe President Georg Roessling (second from left) met with PDA Korea Chapter President Woo-Hyun Paik (second from right) and Byong Ho Youn, JW Life Science

Speaker Cormac Dalton, PhD, AbbVie (left), looks on while Graeme McKilligan (right) delivers a point while Carmelo Rosa looks into the audience.

PDA Visitors | PDA Headquarters

Process Validation for Oral Solid and Semi-solid Dosage Forms Technical Report Team for TR 60-2

(l-r) Josh Eaton, PDA; Bob Wissert, ConcordiaValSource; Michael Blackton, Eli Lilly; Igor Gorsky, ConcordiaValSource; Miguel Hernandez, Actavis; Darius Pillsbury, Ultragenyx; Scott Bozzone, PhD, Pfizer; Susan Griesemer, Mallinckrodt

See p. 16 to learn more about this group's activities.

TOOLS FOR SUCCESS

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How to Find Keywords for Your LinkedIn Profile

Joshua Waldman, Career Enlightenment

I'M OFTEN asked, "Well, I know I need keywords in my LinkedIn profile for LinkedIn search engine optimization, or SEO, but how do I know what keywords to use?" Here is a simple list of some great places to begin growing your keyword list for your LinkedIn and other social media profiles.

Use Your Brain

I'm not being cheeky by saying that. I think we often overlook our own common sense because the online tools are so convenient.

Sit down with a blank paper and come up with as many industry specific nouns as you can. Don't judge what happens, now is the time to get as big a list as possible. Later, we'll hone it down.

Use Related Job Descriptions

I always tell people that job boards are good for at least one thing—finding job descriptions to mine for keywords. Companies will often, but not always, include the keywords they look for when they screen resumes in these descriptions.

Visit three of your favorite job boards, like SimplyHired, Indeed or Monster. The location doesn't matter, just enter the job title you are aiming for. Copy three different job descriptions from three different job boards and copy them all into a word cloud generator (see next sections).

Get Official About it

The U.S. government publishes official job descriptions on a website called O*Net (onetonline.org). Here, you'll find many different ways organizations have described what you do. Enter your job description at the top. Then drill in to the different jobs and related industries. Start collecting the variations on how people describe what you do.

Again, grab this copy and paste it into the word cloud generator.

Cloudy with a Chance of Jobs

Word clouds show you visually which words in a body of text are used more frequently. This is handy when you want to quickly assess the most commonly used words in a body of text, for example, a job posting. So now, paste those job descriptions here: tagcrowd.com. Add some of these words to your list of keywords for LinkedIn SEO.

Make Your Top 10

Now that you have a long list of words for LinkedIn SEO, and probably a sense of how popular those words are, it's time to cross off the ones that won't work and keep the ones that will. I like to have a top ten list as ten is an easy number to manage and keep in mind while writing your profiles for LinkedIn SEO.

About the Author

Joshua Waldman, author of *Job Searching with Social Media for Dummies,* is the founder of Career Enlightenment (careerenlightenment.com) which offers professional LinkedIn profile writing services and career advice for the modern job seeker.

PDA TRI Internship Experience Launches Career in Industry

Kyle Nakashima

My name is **Kyle Nakashima.** I was an intern at PDA's Training and Research Institute (TRI) during the summer of 2012, just after my third year at the University of California, San Diego, where I studied chemical engineering. As an intern, I was fortunate enough to participate in a few classes offered at TRI, most notably the two-week long "Aseptic Processing Training Program," where I gained valuable knowledge and hands-on experience. This experience played an integral part in shaping my career path.

Now, a year removed from college, I currently work as a QC/QA Environmental Monitoring Technician at a contract manufacturing organization that manufactures parenteral drugs. For my job, I monitor the sterility of the air, surfaces, and critical components inside the Grade A and B cleanroom areas during fills using viable and nonviable air samplers, TSA settling plates, RODAC contact plates, swabs, and more. It turns out that I was already familiar with these concepts thanks to the training courses at PDA, where I learned about proper aseptic technique, gowning, equipment use, microbiology, etc., through lectures as well as from participating in a media fill.

From instructors covering a wide range of the industry, I also learned how to write SOPs, review U.S. FDA regulations, prepare for audits, adhere to cleanroom regulations, conduct risk analyses/CAPAs, and so much more. These are now part of my daily activities. The knowledge I gained not only helped position me as a highly qualified job candidate, but it also allows me to perform my job duties every day to the best of my ability.

I'll admit it was a little intimidating at first to be the only college student attending a class with professionals from some of the most successful companies in the world. Yet, I couldn't have imagined at the time how much the knowledge from the instructors at PDA would come in handy later on, and go on to influence the career path that I'm on now. My time at TRI offered me a rare glimpse into the industry that few college students get, and I would like to thank TRI staff **James Wamsley** and **Bob Dana,** PDA President **Richard Johnson,** and everyone else at PDA for this once-in-a-lifetime opportunity.

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snapshot

Task Force *Corner*

Technical Report Team Tackles Process Validation for Oral Solid and Semisolid Dosage Products in TR-60 Annex

Josh Eaton, PDA

A PDA technical report team is currently drafting a follow-up annex to *Technical Report No. 60: Process Validation: A Lifecycle Approach* that focuses on specific process validation considerations for oral solid and semisolid dosage products..

As in TR-60, this annex will present the material in terms of process design, process qualification and continued process verification (the three stages of process validation). These concepts will be applied in a practical way to oral solid and semisolid dosage drug products to assist the industry in gaining a clear understanding of the application of process validation specific to these technologies. The document will include explanations of unique terminology, discuss issues related to sampling and dosage uniformity, and feature several case studies.

The annex will comprehensively present material covering process controls and parameters, process performance qualification (PPQ), and methods for continuous process verification. Additionally, the technical report will also present the use of enabling tools such as process analytical technology (PAT), quality risk management (QRM), technology transfer, and knowledge management as they relate to process validation for the specific dosage forms. Case studies will include detailed process validation examples for new oral solid dosage and semisolid dosage products as well as validation of a legacy oral solid dosage product.

The team met for a two-day working session in December 2014 at PDA's headquarters in Bethesda, Md. and will meet again in person at the *2015 PDA Annual Meeting* in Las Vegas. Also at the Annual Meeting, **Michael Blackton,** Assistant Vice President, Site Operations, Eli Lilly, will present a summary of the technical report team's activities during the Process Validation Interest Group meeting March 16.

Members will be notified when the technical report becomes available and will be able to download the report for free.

Journal *Preview*

March–April Issue Chock Full of the Latest Research

What are the latest approaches to parallelism in bioassays? How can particles be visually detected using the Tyndall effect? What is the impact of mixing monoclonal antibodies using bottom-mounted mixers? Find out in the latest issue of the *PDA Journal of Pharmaceutical Science and Technology*.

Commentary

Lee Blaney, Kiranmayi Mangalgiri, Ke He, "Emerging contaminants: A potential human health concern for sensitive populations"

Research

Nacole D. Lee, et al., "Studies Of Protein Oxidation As A Product Quality Attribute In A Scale-Down Model For Cell Culture Process Development"

Francis Bursa, Kelly Fleetwood, Ann Yellowlees, "Parallelism in Practice: Approaches to Parallelism in Bioassays"

Emil M. Friedman, et al., "In-Process Microbial Testing: Statistical Properties of a Rapid Alternative to Compendial Enumeration Methods"

Ingunn Tho, et al., "Utilization of the Tyndall effect for enhanced visual detection of particles in compatibility testing of intravenous fluids: Validity and reliability"

Conference Report

Richard Levy, Robert Repetto, "PDA Single-Use Systems Cross-Organizational Workshop – Meeting Summary, May 14, 2014 – PDA Global Headquarters, Bethesda, MD"

Review

Dominick DeGrazio, "Adapting to Biology: Maintaining Container-Closure System Compatibility with the Therapeutic Biologic Revolution"

Yuh-Fun Maa, et al., "Mixing Monoclonal Antibody Formulations Using Bottom-Mounted Mixers – Impact of Mechanism and Design on Drug Product Quality"

Hana Morrissey, et al., "In Vitro Analysis of the Effect of In-Line 1.2 Micron Filters on Two Formulations of Propofol (2,6-diisopropyl phenol)"

Martha Folmsbee, "Evaluation Of The Effect Of The Volume Throughput And Maximum Flux Of Low-Surface Tension Fluids On Bacterial Penetration Of 0.2 Micron-Rated Filters During Process-Specific Filter Validation Testing"

Stephan Rönninger, Sandra Bush, "Knowledge Management and ICH"

Water Testing Lab Automates its Way to Efficiency

Simon in 't Veld, Vitens

How do you merge three regional water supply testing laboratories into one without losing efficiency and increasing errors? Build a state-of-the-art lab using the latest microbiology and chemical tests combined with automation and robotics, that's how.

An automated system moves samples through the laboratory for analysis

Vitens is the largest drinking water supply company in the Netherlands. It was founded in 2002 after a merger of three drinking water companies. At the time of the merger, the three companies each had their own regional water laboratory. Due to the merger, a new laboratory was built to replace the three regional laboratories. In the original laboratories, samples could be analyzed at the end of the afternoon due to the short distance between the sampling points and the laboratories. In the new laboratory, it was not possible to analyze the samples that early. Although sample collectors still take samples in the three regions, the samples have to be transported over a longer distance to the laboratory. At present, samples arrive at the laboratory around 8 p.m.

For this and other reasons, senior management set up the laboratory to rely on a high level of automation. In particular, the company wanted to avoid the expense of analysts working long evening shifts as well as to minimize the effect of the samples' late arrival in relation to the test results that became available. Solutions were provided by KIESTRA Lab Automation and Labman Automation. Analyses can be characterized as semiautomatic. Transport and handling of sample bottles and petri dishes in the laboratory is based on barcode reading. Microbiologists carry out a mix of classic and modern techniques in the microbiology laboratory. Standard culture methods for the detection of fecal contamination and other general water analyses are performed. Confirmation of suspicious colonies after culture is done with modern techniques like MALDITOF and real-time PCR. In the chemical laboratory, robots supplied by Labman Automation transfer water from bottle to tubes. Many inorganic analyses are also carried out completely automatically. Therefore, sample bottles are transported to a unit containing several analyzers (sample bottles are identical, the only difference is the conservation reagents, depending on the analyses that are carried out from the bottle, and the sterility of the bottles used for microbiological analyses). With the help of robot arms, subsamples are transferred to the analyzers. Total investment for the new laboratory was 12 million euros and the return on this investment was seven years.

The company also sought to minimize errors. The handling of about 2000 bottles in an evening containing approximately 330 mL of water (easily between 650 and 700 liters total) within a short time can easily lead to mistakes. Based on the information on the barcode, petri dishes with culture media are labelled automatically. Here, the unique barcode of the sample bottle is scanned. Then with the help of this barcode, the LIMS system sends a command to a label unit to print the right set of petri dishes.

Transportation of the petri dishes into the incubator is also done automatically. In this way, the right set of analyses is always evaluated. Also, the system avoids the problem of technicians putting petri dishes into the wrong incubator. Registration of the incubation period is done automatically. When the required incubation time is finished, the petri dishes are automatically transported out of the incubator to the analyst where the counting and screening is done.

To ensure that test results meet the required quality level, all analyses were validated before opening the automated laboratory. In this ISO 17025 accredited laboratory, validation was carried out in accordance to the guidelines of a national document issued by the Dutch Accreditation Council. The performance of the analyses was also checked by participation in ring trials for microbiological and chemical analyses.

Continued at bottom of page 20

Sterility Challenges, Complexities Require New Tools

Michael Sadowski, Baxter Healthcare

The sterile healthcare products industry has always faced challenges; however, today we have added complexities to consider. Companies are relying more on outsourcing and supplier sources for knowledge and support. Global regulatory authorities expect organizations to use complete process understanding and good scientific, product quality risk criteria to make and justify manufacturing decisions, best illustrated by recent efforts to revise the EU's Annex 1. New regulatory authorities such as Brazil's ANVISA are also launching or revamping sterile processing requirements. Pharmacopoeias face sterility-related revisions, as well such as USP <1116> Implications for the Microbiological Control and Monitoring of Aseptic Processing Environments. New product configurations and manufacturing technologies such as single-use systems and gas sterilants must be considered to design effective processes. In addition, new methods such as parametric release face questions concerning regulatory acceptance.

While these complexities are ever-growing, industry has responded with new tools and approaches. Quality Risk Management has become an essential instrument for ensuring development of high quality sterile product. There are even new approaches available for the continuing hazard of biofilm contamination. Nonetheless, it is more important today than ever to be aware of the trends in our industry, to keep up with new information, and to understand the implications and requirements these challenges present.

This year's *2015 PDA Aseptic Processing – Sterilization Conference* summarizes innovative and best practices recently developed and employed successfully to meet the growing complexities for the manufacture of sterile product with aseptic processing and terminal sterilization. In particular, the conference will address the latest methods for aseptic risk evaluation, post-aseptic fill lethal treatments, regulatory perspectives on risk, and new technologies for risk minimization. Another session will explore the impact of recent compounding regulations on small organizations as well as USP <797> Pharmaceutical Compounding Sterile Preparations.

To learn more, visit www.pda.org/2015-pda-aseptic-processing-sterilization-conference. Information about the PDA Education courses following conference can be found at www.pda.org/2015-pda-aseptic-processing--sterilization-course-series.

Packaging Playing a Greater Role in Future of Pharma

Ronald Iacocca, PhD, Eli Lilly, and Diane Paskiet, West

Where does industry stand with advancing science to ensure product quality and adherence to medicines? As quality standards for pharmaceuticals and delivery systems are being realized through risk-based practices, the industry is still confronted with critical present day issues while anticipating needs for the future of novel treatments.

The complexity of these issues spans a global landscape encompassing various phases of development, technology transfer, commercialization, and finally, the last mile to the patient. The pharmaceutical industry is challenged with developing and manufacturing quality products designed to meet the needs of patients, while packaging suppliers are faced with meeting ever increasing standards for container/closures and delivery systems. The analysis of human factors and systems engineering plays an ever greater role across the development cycle. With new technology bringing medical care from the clinic to the home, manufacturers and secondary packaging suppliers must now design features that improve patient adherence and compliance along with flexibility. And of course, the overall importance to strive for excellent quality in primary secondary packaging remains an important objective.

Can there be an evolution to the future state if common goals are recognized? These common goals include an understanding of the need to include packaging and delivery systems early in the development process, realization of the risks associated with packaging components and systems, and the importance of acquiring data to qualify packaging components and systems

In addition, a greater understanding of risk has led to a higher degree of scrutiny of present systems; mitigation of current risk is moving at a faster pace than innovation of new container closure materials and delivery systems. What lessons has the industry learned and how will that factor into future applications?

There are no easy answers to these questions but the *2015 PDA Pharmaceutical Packaging Conference* offers an opportunity to discuss these challenges and allow for interactive discussions to seek possible solutions. To learn more, visit www.pda.org/2015-pda-pharmaceutical-packaging-conference. For information about PDA Education courses following the event, please visit www.pda.org/2015-pda-pharmaceutical-packaging-course-series.

SUS Success Needs Knowledge Sharing, Transparent Partnership

Robert Repetto, PhD, Pfizer, and Morten Munk, NNE Pharmaplan

The global pharmaceutical industry is facing a new reality where the market is requesting new types of products and offering new reimbursement models, especially in the Western world where the industry's production facilities are becoming outdated and struggle to meet the increased requirements for more specialty products, typically biologicals. Additionally, an increased number of biosimilars and other generic products, combined with the globalization of the market and general unpredictability of the future, challenge the industry. The only way to win this battle and avoid undesirable drug shortage situations and keep new life saving products cost-effective to patients is for the industry to be even more agile. One of the important tools in this battle is single-use technology (SUT), also known as single-use systems (SUS). Along with other innovative production improvements, SUT has the potential to transform pharmaceutical manufacturing by offering tremendous opportunities to reduce costs, improve flexibility and cycle times, and most importantly, shorten the time needed to implement a manufacturing process for new, lifesaving drugs.

Successful implementation of SUT relies on the industry sharing best practices for the adoption of this emerging technology as well as a transparent partnership between SUS suppliers and pharma manufacturers. A key contribution in this effort is the PDA *Technical Report No. 66: Application of Single-Use Systems in Pharmaceutical Manufacturing*. But it requires an ongoing effort from suppliers, regulators and manufacturers to continue to build this transparent partnership that lies on a foundation of science and risk-based dialogue.

PDA's Single-Use Systems Task Force, responsible for producing TR-66, will host a June workshop that champions the philosophies outlined in the report and serve as a forum to further SUS development, supporting the transparent partnership approach advocated in the technical report. Additionally, the workshop will showcase how to implement a risk-based decisionmaking process for meeting regulatory expectations while using SUS, and present critical points to consider when implementing SUT.

Harmonization, best practices and transparency will be the defining enablers as SUT becomes more common. Suppliers, end users, manufacturers and regulators will need to use forums such as this work shop to keep pace with changing practices and paradigms due to the fast pace of SUS adoption. Consensus is still needed on quality systems, technical standards and compliance activities for SUS, allowing the audience to vast opportunities to expand this dialogue. The next few years will be an exciting and rewarding time for our industry and the patients we serve.

To learn more about, and sign up to this vital workshop, please visit www.pda.org/2015-pda-single-use-system-workshop. For information about PDA Education courses offered following the event, visit www.pda.org/assessing-packaging-and-processing-extractables-leachables.

Technology Column continued from page 17

In addition to the high level of automation, Vitens is also considering the possibilities of automating the remaining manual activities in the laboratory. In the near future, the company will work on developing a robot to automatically filter a sample and transfer the filter to a petri dish with culture media. In this way, the company automates the line between the transport of sample bottles and the counting and screening of the incubated petri dishes.

Besides the automation of classical microbiological methods, there is a change from the more classical microbiology to molecular-based analyses and online sensoring. When these new analyses are ready to be accepted, automation in the microbiological laboratory will strongly increase. Online sensoring on location will result in the availability of real-time data. This will make it possible to carry out analyses automatically in the field and no longer in the laboratory. At the moment, Vitens receives test results after the water has already been consumed. Online sensoring will allow rapid testing of water prior to consumption by the public. Examples of this kind of automated testing include Coliguard® (E.coli and coliform bacteria) and Bactiquant (quantification total bacteria) tests. Automation such as this will help to ensure public safety in addition to increasing operational efficiency.

To view a video of Vitens' automated process, visit tinyurl.com/o3zyonp.

[Editor's Note: Tricia Vail, a member of the *PDA Letter* Editorial Committee, toured Vitens' automated laboratory in 2014. Other industries offer "lessons learned" that pharma can explore. Expect more articles about practices in other industries in future editions of the *PDA Letter*.**]**

About the Author

Simon in 't Veld is the manager of the Department of Microbiology within the drinking water company Vitens. He has been working for more than 28 years in the field of drinking water microbiology.

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Recordings from the conference are available for purchase for **$275 Member/$315 Nonmember**. Price of recordings includes:

- Nine recorded sessions from the 9th Annual Global Conference on Pharmaceutical Microbiology
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- Access to 21 downloadable presentation handouts
- Unlimited playback of the recordings for 90 days from receipt of login information.

2014 PDA Pharmaceutical Quality Metrics Conference

Recordings from the conference are available for purchase for **$225 Member/$275 Nonmember**. Price of recordings includes:

- Seven recorded sessions from the 2014 PDA Pharmaceutical Quality Metrics Conference
- PowerPoint slides with synchronized audio
- Access to 18 downloadable presentation handouts
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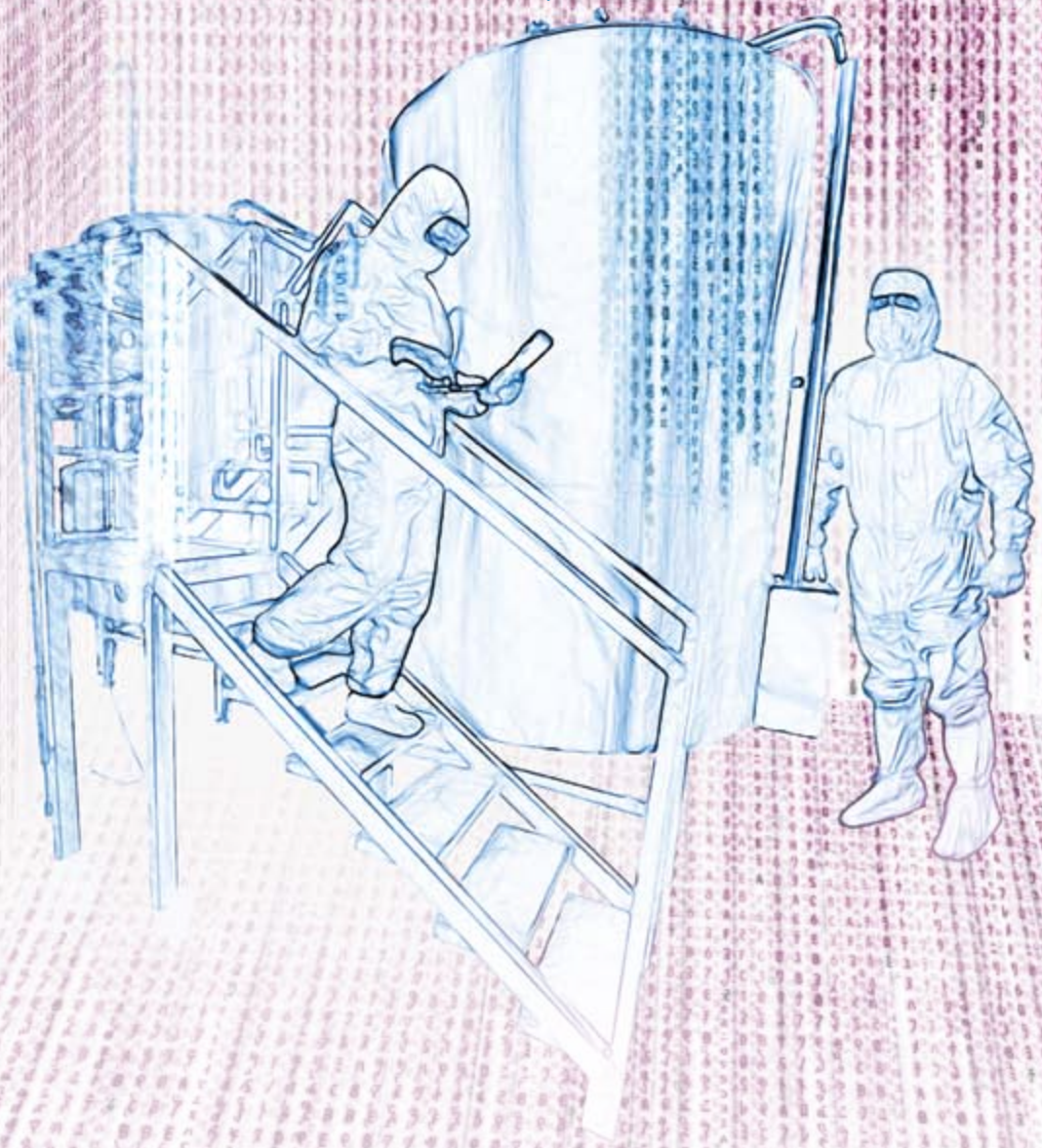
Want to Make the FDA Quality Dean's List? Take a Look at Your Metrics

Walter Morris, PDA



No one can say for sure what the ultimate impact of the U.S. FDA's pharmaceutical quality metrics initiative will be on both pharmaceutical manufacturers and the Agency's enforcement practices. A vision of what the future holds, however, materialized during the *2014 PDA Pharmaceutical Quality Metrics Conference* in Washington, D.C., Dec. 2–3.

The very first talk of the meeting offered a glimpse into a possible future state, and the final panel discussion with FDA and EU regulators helped further flesh out a possible vision. In between, conference attendees participated in breakout groups to offer feed-

Article at a Glance

- FDA can use a "Dean's List" to encourage and recognize companies with good quality
- EMA and MHRA observing FDA quality metrics activities
- How can manufacturing be brought into the discussion?

back on predefined quality metrics selected by FDA for consideration and also helped PDA further its effort to hone in on what constitutes a strong and reliable quality culture. Yet, the meeting concluded with many questions still needing answers and much more work to be done by the Agency, manufacturers and organizations like PDA if this vision is ever going to materialize.

Guy Villax, CEO, Hovione kicked off the meeting by introducing the idea of FDA Commissioner **Margaret Hamburg's** "Dean's List."

Villax noted a substantial discrepancy between the volume of product sold, dominated by generics, or "small pharma" companies, and the dominance of innovators, or "big" pharma companies, over total sales revenue. But at this and other conferences on quality metrics, employees of large companies compose most of the audiences. In addition, there is discrepancy in the role of manufacturing. Large pharma relies on innovation and patents to drive profits, whereas small pharma and generics companies rely on efficiency in manufacturing and other business elements.

Nevertheless, he asserted, patients and regulators demand the same quality product no matter what the source.

In discussing the current regulatory system which requires compliance with cGMPs, Villax asked, "What is more important to a patient, paperwork or a team that wants to do the right thing?" The quality culture, is important because it is what makes quality "sacred."

Villax used driving as an analogy to compare quality systems to quality culture. Quality systems are no greater than the roads upon which people drive, he said. There are well-defined rules about speeding, etc. Quality culture, on the other hand, is like the driver. It is the driver that anticipates when other cars are doing something wrong or if there is rain, etc.

Quality systems provide the evidence of compliance and are easy to regulate, legislate and enforce. They are useful to identify bad behavior, which is the "cornerstone of regulatory oversight." Quality systems can be established in the same way companies build a plant: easy to fake, but unable to drive good behavior.

Quality culture, Villax went on, addresses the unexpected. Quality culture is not definable but easy to spot. It is not explicitly assessed in inspections and virtually absent from regulations. It takes a long time to build, as it mirrors people's values and ethics. Finally, it is impossible to game or fake and is the central driver of good behavior or innovation.

When FDA issued the *Federal Register* notice in 2013 calling for industry input into its quality metrics proposal, Villax noted that only one company response—from Pfizer—mentioned quality culture. Villax quoted the company's submission: "Without the quality culture, product quality and business continuity are not assured."

While it might be difficult to define a strong quality culture, Villax noted that it is easy to see the lack of one. "Data integrity problems should raise flags," Villax said. "What's the point of a quality system if a culture of fraud dwarfs culture of quality?"

FDA's Dean's List is the Carrot

FDA must offer some incentives to effect change ***(1).*** But right now, "FDA does not drive good behavior, just good compliance," Villax explained. The Agency "excels in use of the stick, but the toolkit has no carrot."

A quality Dean's List is one way FDA can reward good behavior. Villax compared his idea of this Dean's List with the U.S. Occupational Safety and Health Administration's Voluntary Protection Program. Companies that do an outstanding job receive a VPP star. Villax stated that this star "clarifies what is a role model, rewards the role model, gets everyone proud, and is uncomplicated and inexpensive." The FDA quality Dean's List would be similar to the VPP.

Villax cautioned that whatever system is put in place, it cannot "reward just the firms who pay exorbitant amounts for flashy manufacturing technology, etc. Rather it must recognize those who make high quality product at an affordable price with reliable technology and strong systems."

Villax concluded that it is "time to give more weight to people and their values than to paperwork. FDA needs to reward good behavior; it needs the Dean's List."

He showed an image of a bell curve on which the left side represented firms that routinely run afoul of regulatory agencies (the one's the authorities regulate well), while the middle consists of the vast majority of firms that meet the expectations but do no more, and the exceptional firms that have strong quality cultures on the right side of the curve (see **Figure 1,** p. 27). The firms on the right would comprise the Dean's List.

As part of his talk, Villax suggested that inspections can play a huge role in the assessment of quality culture at pharmaceutical companies. FDA's Office of Surveillance in CDER's new Office of Pharmaceutical Quality is looking to do just that.

Following Villax's presentation, the Acting Director of the Office of Surveillance **Theresa Mullin** provided insight into how FDA intends to build a new surveillance program.

"FDA is not going to become some kind of super quality management board for industry," she first cautioned. Rather, the aim is to use "limited oversight resources to maximize public health protection."

The Office of Surveillance was created to strengthen FDA's knowledge of:

- Who manufactures drugs for patients
- Where are these drugs made
- How well are the drugs produced ➤

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SAVE THE DATE for PDA's 2015 Events

MARCH EVENTS

16–18
2015 PDA Annual Meeting
Las Vegas, NV
pdaannualmeeting.org

18–19
2015 PDA Aging Facilities Workshop
Las Vegas, NV
pda.org/Aging-Facilities2015

19–20
2015 PDA Annual Meeting Course Series
Las Vegas, NV
pdaannualmeeting.org/courses

23–27
GSA Schedule Contract GS-02F-113BA
2015 Aseptic Processing Training Program – Session 1, Week 1
(Week 2: April 13–17)
Bethesda, MD
pda.org/2015aseptic2

APRIL EVENTS

14-15
Aseptic Manufacturing
Berlin, Germany
europe.pda.org/AsepticManu2015

16-17
Introduction to Aseptic Processing Principles
Berlin, Germany
europe.pda.org/TCAseptic2015

20-23
Train the Trainer Week
Bethesda, MD
pda.org/trainer

27-29
GSA Schedule Contract GS-02F-113BA
Validation of Biotechnology-related Cleaning Processes
Bethesda, MD
pda.org/biotechclean

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

MAY EVENTS

4-5
Lyophilization Week
Bethesda, MD
pda.org/lyo

11-12
Recommended Practices for Manual Aseptic Processes
Bethesda, MD
pda.org/MAP

13
NEW COURSE
Risk Based Approach for Prevention and Management of Drug Shortages
Bethesda, MD
pda.org/prevention

14-15
Development, Manufacturing and Handling of Primary Packaging Containers, Drug Delivery Device Formats and Actual Market Trends
Bethesda, MD
pda.org/markettrends

18-19
2015 PDA Pharmaceutical Packaging Conference
Washington, DC
pda.org/packaging 2015

18-22
2015 Aseptic Processing Training Program – Session 3, Week 1
(Week 2: June 15–19)
Bethesda, MD
pda.org/2015aseptic3

20-21
2015 PDA Drug Delivery Combination Products Workshop
Baltimore, MD
pda.org/drugdelivery2015

20-21
2015 PDA Pharmaceutical Packaging Course Series
Baltimore, MD
pda.org/packagingcourses

22
Technical Development of Prefilled Syringes, Autoinjectors and Injection Pens
Baltimore, MD
pda.org/techdevelop

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Photo Source: Aseptic Vial Filling at Albany Molecular Research Inc.

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Without the quality culture, product quality and business continuity are not assured

The oversight strategy is global across all sites and local at given sites, so FDA needs reliable, high quality information to prioritize its inspections. "You need to have good documentation of those states of reality. You have to know what is going on enough to feel confident that you don't have to go someplace or that you can rely on the information you have that a facility is fine," said Mullin.

To do this, FDA needs high quality data. Current sources of information for the Agency are "fragmented, disparate and incompatible." In many cases it is "paper" and "entered into different systems." She listed several examples of compliance information, including field alerts, recall alerts, CMC supplements, annual reports and EIRs/483s. Putting this information together currently is a slow, clunky process for the Agency, and the current system actually hampers the Agency's ability to be strategic.

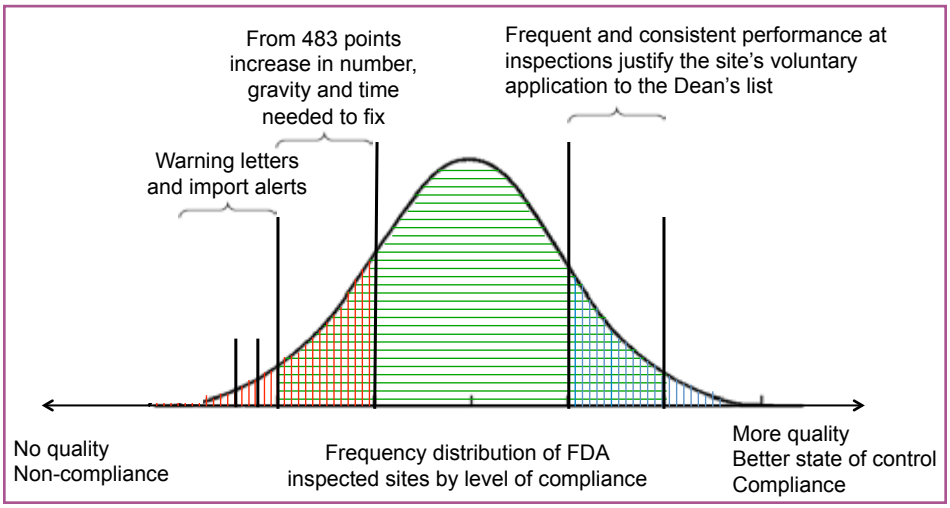
The Food and Drug Administration Safety and Innovation Act (FDASIA), under Titles VII 706 and 705, gives the Agency specific tools to establish a risk-based inspection schedule. Mullin explained that FDA needs to:

- Gather analyzable data for ongoing quality assessments
- Develop an effective and efficient process for quality surveillance inspection
- Create standards for consistently gauging and grading state of quality observed by investigators; specify positive range to build and expand on current structure of observations focused on failures and deviations.

The envisioned inspections will still be built around the system of rankings introduced over a decade ago, which uses a notional scale: extreme failure/critical GMP deviations; substantial failure/major; and unacceptable/minor. The thought is, Mullin said, to add new rankings to the notional scale to recognize firms along Villax's entire compliance curve: acceptable, enhanced, and well done.

FDA also will look at not just risk-based inspections, but tailoring them so that they are "rule-based, incorporating expert knowledge" and allow investigators to identify "signs and symptoms of quality culture." The inspections will be set up to "support consistent recording of observations by investigators." This will include electronic tools along with structured and streamlined inspection reports ensuring that investigators can readily produce accessible analyzable information of maximum downstream value for future decisions on a facility.

Figure 1 Villax's Quality Curve: Firms on the right would comprise FDA's quality "Dean's List"



EMA Joins the Discussion

Head of International Affairs, EMA, **Emer Cooke** provided the EMA's first public thoughts on FDA's metrics initiative.

She noted that European regulators have been discussing the program, but "haven't got to the stage where we thought we had a product we needed to engage with at the European level collectively."

Cooke expressed her "key signs" of constituted quality culture:

- clear and effective leadership from the top (ICH Q10)
- strategic planning for quality and supply chain security and resilience
- patient focus
- utilization of measurement analysis and knowledge management
- a clear workforce focus ("workforce is seen as an enabler of quality")
- manufacturing and quality seen to create a strategic advantage
- results are gathered, analyzed and fed back to facilitate continuous improvement

On a more tangible level, firms can be evaluated by staff levels, training, staff knowledge of tasks and quality system documentation, response to inspector queries, and ongoing interactions between manufacturer and authority.

Specifically regarding quality metrics and Europe, Cooke stated that there is "no formal European position." Nevertheless, "quality-metrics-like data is collected and reviewed during inspections," she said.

"We are very interested in learning more, starting a healthy international debate, and discussing the consequences in a more global context," she concluded.

The regulatory experience on quality culture was addressed by **Gerald Heddell,**

Director, Inspection Enforcement and Standards, MHRA, Heddell talked about his Agency's compliance management process. This process attempts to proactively address problems at firms before they escalate to serious compliance actions and plant shutdowns. He discussed three recent cases where the process helped firms correct serious problems without severe regulatory action.

The compliance management process is an example of how regulatory authorities can "influence behaviors in companies without going down the route of formal action, which is enormously time consuming for the company and the regulator and doesn't benefit the patient," said Heddell.

Regulators and firms must strive to forestall a "cycle of despair," in which those making the products:

- Don't know what to do
- Don't care
- Cannot cope
- Do only what is expected of them
- Give only what is measured
- Don't think the rules apply to them
- Feel the procedures are too complicated

Hallmarks of a good culture, Heddell went on, include a strong shadow of the leader. In other words, quality values are made clear from the CEO and the Board, that "walk the talk."

Tangible indicators of quality culture are:

- Robust quality systems
- A relevant organization
- Continuous improvement processes

Speaking for CBER, **Mary Malarkey,** Director, Office of Compliance and Biologics Quality, said the adoption of robust quality systems has had an "extremely positive impact" and quality metrics "has a place in terms of measuring those programs." CBER is engaged with CDER in the initiative. "We are working with them, and we [are] thinking it is extremely important."

New Office to Own QS Data

Russell Wesdyk, Scientific Coordinator, CDER, said that the Office of Pharmaceutical Quality symbolizes FDA's effort to transform itself into an organization that equally focuses on both compliance and quality. Enforcement will continue to be of highest enforcement, "but at the same time, we want to focus on quality and part of that is focusing on surveillance: looking at all products, all sites and how they are performing over the lifecycle," he explained.

The Office of Surveillance will serve as business owner of quality data systems and the pharmaceutical quality platform, developing and managing analytic and predictive programs and a new inspection paradigm and assessment program focusing on surveillance of quality.

Wesdyk touched on the metrics in which FDA currently is interested in receiving data:

- Lot acceptance rate
- Right first time rate
- Product quality complaint rate
- Invalidated OOS rate

He also reviewed many of the quality culture metrics that PDA's own Quality Metrics Task Force has helped identify. The remainder of the meeting was spent with participants breaking into smaller groups to interactively discuss the quality culture metrics.

The final sessions included summaries of the breakout group discussions and a panel discussion led by FDA and EU regulatory representatives. **[Editor's Note:** For a partial transcript of the regulatory panel, see "Metrics Conference Regulatory Panel" Sparks Lengthy Discussions," p. 31.**]**

The breakout discussion readouts were presented by the lead discussion facilitators: **Gabriele Gori,** Global Head of GMP Compliance and Auditing, Novartis Vaccines, **Anil Sawant,** PhD, Vice President, Enterprise Regulatory Compliance, Johnson & Johnson, and **Glenn Wright,** Senior Director, Project Management, Eli Lilly and Company. The PDA Quality Metrics Task Force is currently preparing a paper to discuss the conclusions derived by the conference discussions for publication in an upcoming issue of the *PDA Letter*. They are also working on the an analysis of the PDA Quality Metrics Survey conducted last fall (see p. 36 of the September 2014 *PDA Letter*), which also will be published later this year.

A lengthy Q&A session followed the readouts. The lead facilitators were joined with the following industry experts to broaden its scope of experience: **Deborah Autor,** Sr. Vice President, Strategic Global Quality and Regulatory Policy, Mylan, **Eric Drape,** Group Executive Vice President, Global Head of Quality, Teva, Guy Villax, **Jacqueline Elbonne,** PhD, Sr. Vice President, Global Quality, Merck, **Erwin Vanhaecke,** PhD, Head, Novartis Group Quality, Novartis, **Martin VanTrieste,** Sr. Vice President of Quality, Amgen, **Anders Vinther,** PhD, Chief Quality Officer, Sanofi Pasteur, and **Zena Kaufman,** Sr. Vice President, Global Quality, Hospira.

An interesting question was posed early in the panel discussion. One audience member noted that according to the readouts, more than 90% of conference participants viewed the traditional quality system is not suitable enough to create a quality culture at a site or within a company. While the result is not surprising, he said, it is a "staggering result when you think that we've had all these years of regulation designed to ensure that companies focus on quality product." He asked

the panel, "Where did we go wrong and what should we do about it?"

Mylan's Autor, who recently joined industry from FDA, stated, "If there's any flaw there, I think it's in thinking that the regulations form the ceiling of what we need to do, rather than the floor. I think, as an industry, we often lapse into doing what the regulator says because we're closely regulated, and not getting beyond that. GMPs, to me, lay out basic paperwork and processes that need to be followed, but certainly not enough to ensure high quality."

Sanofi's Vinther added, "I think that we could ask ourselves how good a job have we done to integrate quality into the general business of the company, and a good example is the quality system itself. Is the quality system written to the minimum standards or is it written in a way that actually makes good sense in the company?"

Teva's Drape stated, "Looking into the evolution of the pharma industry, the pharma industry has been, for many years, an industry of fat cats, and, therefore, the focus on the efficiency was not as important as in other industries that have lower margins. And our main focus has been on ability to pass inspections and not so much on efficiency in everything that we do. So we had QA organizations that [put] quality systems in place, and then as soon as the quality system was able to demonstrate that it was good enough to pass inspections, they were just pouring a huge layer of concrete on top of that to prevent any change of the system."

Merck's Elbonne expanded on Drape's remarks. "My experience has been, for companies that get into trouble, they start to figure out the cultural piece and how they need to really invent themselves to be successful and sustainable. I think companies that typically have been successful traditionally, passing inspections and getting products out of the door with a good quality, probably haven't had that incentive to really start to match the how piece—of how you engage people in those systems and processes, how they understand how the business processes relates to what they do on the shop floor."

Furthermore, Elbonne said, "We're starting to see, or hope to see, I think, a shift to more of a consistent view of how we engage people in the quality management system, which really is the way to build quality at this point."

Manufacturing/Ops. a Key Stakeholder

Another audience member noted to the panel the conspicuous absence of employees from operations and manufacturing at the conference. He asked the panel if they thought it was important to get those folks active in this process and, if so, how.

Villax recommended that PDA offer a discount at next year's meeting to "every quality person that brought in a manufacturing person."

VanTrieste said, "Clearly, a quality culture is not effective if it's only in the quality unit. It has to be across the company. And I think part of the reason that we don't get a lot of manufacturing people at this kind of event is because we say it's quality culture, and they naturally think quality means the organizational unit or quality means compliance, and not really product quality, efficiency and operational excellence. So I think quality culture is a good brand, but maybe the brand has to change a little bit. Maybe we need to think about what that branding is, not only to get people to come to conferences, but to be more effective in rolling it out in people, in organizations."

Drape added, "maybe also just a general question. How many manufacturing people, engineer people ever attend any PDA meeting? We must have those statistics, and is this meeting any different from those? My gut feeling is it probably isn't, which is different from when you go to an ISPE meeting. They have way more engineering and tech ops people. So I'm not sure it's only how we title it. I think it's also the audience that we target."

PDA's Chair, **Harold Baseman** stated from the floor: "That's a very good point. We do have statistics on that, and, actually, depending on what the subject matter is, we do have a different mix. I will say that at the ISPE meetings we're seeing more engineering people, design engineering, and so forth, but I'm still not exactly certain that we're grabbing that other group, that manufacturing group."

Vinther said it is "very important is make sure you bring somebody. So next time when you come, bring somebody from operations. I've done that several times."

Autor agreed that inviting someone from manufacturing or operations is a great idea, but, "I think it's like anything else, we have to make a business case." If you can make a business case to bring colleagues from manufacturing and operations, you will be successful, she added.

It would be impossible to cover all the fantastic dialogue that took place at the *2014 PDA Pharmaceutical Quality Metrics Conference,* but from beginning to end, the audience was engaged in helping to flesh out a vision for a new regulatory paradigm based on quality culture.

Reference

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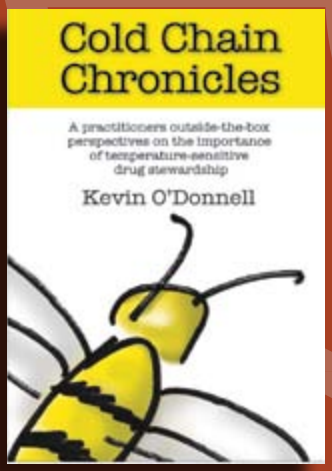

Cold Chain Chronicles

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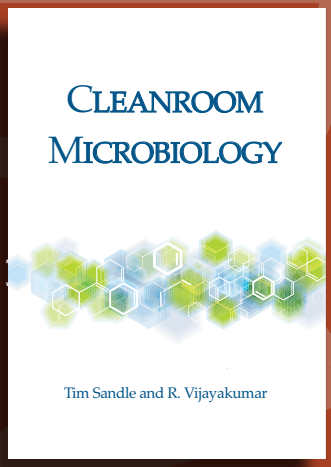

Cleanroom Microbiology

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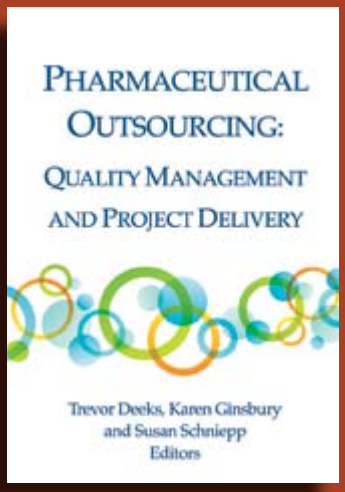

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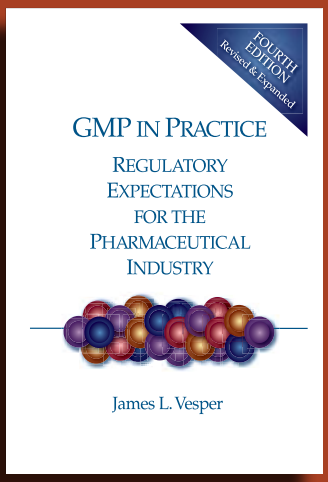

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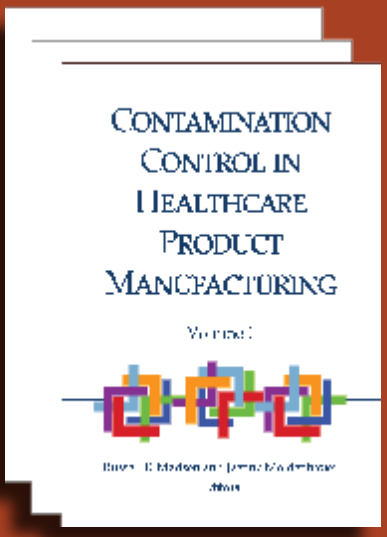

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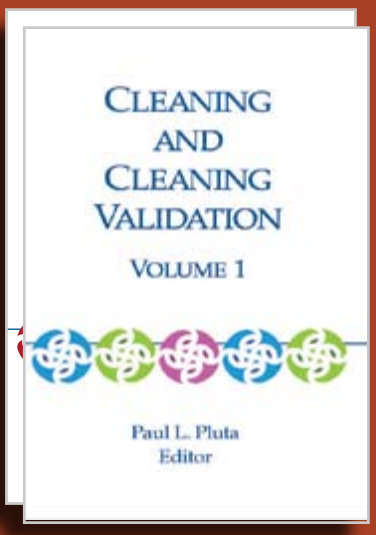

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Regulatory Take on Quality Metrics and Culture

Transcript of the final panel discussion at the *2014 PDA Pharmaceutical Quality Metrics Conference*

[Editor's Note: *The following is a transcript of the final remarks of regulatory representatives from the U.S. FDA, EMA and MHRA at the* 2014 PDA Pharmaceutical Quality Metrics Conference. *The statements have been reduced to a few key points by each speaker. The panelists were:* ***Janet Woodcock,*** *MD, Director, CDER;* ***Howard Sklamberg****, Deputy Commissioner for Global Regulatory Operations and Policy, FDA;* ***Ellen Morrison****, Assistant Commissioner for Operations, ORA;* ***Cynthia Schnedar****, Director, Office of Compliance, CDER;* ***Karen Midthun, MD****, Director, CBER;* ***Emer Cooke****, Head of International Affairs, EMA; and* ***Gerald Heddell****, Director, Inspection, Enforcement, and Standards Division, MHRA. Following these statements, the panelists fielded questions from the audience. The transcripts were prepared professionally by Malloy Transcription Services, and have been lightly edited for clarity by PDA Staff.***]**

WOODCOCK

To look at the quality of our activities, we are putting in place an evaluation unit, both for the premarket inspection and premarket review activities, and linking that to policy and guidance development. We will also have a process evaluation to make sure we're running the process correctly, and, of course, that's going to be challenging in the first few months of [setting up] our new organizations, so you may have to give us a little slack while we migrate from one modus operandi to another.

At [the Office of Pharmaceutical Quality], we are setting up the organization around these principles. OPQ's [start] will be in early January, and we hope, from the very beginning, to focus on the customer, the patients, and the providers. We want to have a holistic view of quality, and to that end I would tell you, with one of the proposed never-events I mentioned, quality has to include availability. We need breakthrough drugs to become available if they've proven that they're a breakthrough for a serious and life-threatening condition. It's no good to just show they work really well or they work better than anything else out there, but they're not available to the patients because of some manufacturing issue. We need to have continued availability of essential drugs. We really have to focus on that, and there maybe trade-offs there and we have to be willing to deal with those tradeoffs.

We need to check and evaluate our ability to execute when we do inspections. We need to make sure we're looking at your ability to execute. So we've done the premarket review—that's what is your design of the process and product and what is your ability to execute that—and then, for postmarket inspections, how well are you executing it? Are you actually executing what you proposed to do in making this, and reliably making a high-quality product? Quality metrics, which you've been discussing for a day and a half, I think, are a piece of this. They're one way, just one piece, one way to measure how well you're executing those manufacturing control strategies that you put into place, and how well you're also responding, hopefully, to problems in that proposed strategy, into the continuous improvement loop.

SKLAMBERG

I think, quite simply, without program alignment, the changes to which Janet spoke would not be possible, bluntly. Basically, as most of you know, program alignment is a shift, really—it's not really of [the Office of Regulatory Affairs], it's really the whole agency—to a much more specialized inspectorate, organized along vertically integrated program lines, as opposed to geography. What this means—and we have a largely specialized inspectorate now—but what this means is that a person who is doing pharmaceutical inspections or who is working on pharmaceutical policy in the quality area, or who is working in a laboratory doing work in pharmaceuticals will be a pharmaceutical person 100% of the time. Obviously, there are some functions, administrative and the like, that crosscut, but, by and large, a person who comes and does a drug inspection at one of your facilities will be a person who does drug inspections 100% of the time.

Why is that important? Well, it's important, obviously, because more specialization enables more expertise and more participation in the development and the understanding of why we're doing things. But as we are implementing a whole bunch of new laws and a whole bunch of new policies, and implementing this shift in the way we do business and the way we foster and encourage quality, and, at the same time, compliance and enforcement, you can't do all of those changes,

and understand everything that you're doing, and participate in them if you are, at the same time having to also understand the implementation of the Food Safety Modernization Act, while inspecting both. It's not possible for folks to do all that, as what we do gets more complicated, and as the products we regulate get more complicated.

MORRISON

We're very much involved, and I give credit to Dr. Woodcock for involving many of us at the senior level of the ORA inspection side, operations side, in the early discussions within CDER about the whole issue of pharmaceutical quality and how the inspectional approach will need to change…. We know that we'll be looking at metrics. We'll be looking at things that can be measured across firms. It's going to be done in a pilot project, because we do need to learn, initially, how things are going to go. But we will move from the traditional—and I grew up with the traditional, so I can say this—from writing 483s, potentially, and then very long EIRs, to a much more structured data approach that can be measured across firms, and measured across firms globally and measured across sectors. These new inspectional approaches will be data rich, we hope, in measurable data across firms, and I think that we're going to need to do a lot of training of investigators.

But I think we'll essentially be doing a better job with more data, and, again, we've shared all of the ORA data. As Janet's staff has observed, we have a graveyard of IT systems in FDA. So we have given over to the CDER platform on pharmaceuticals availability of all the data that we had in the ORA systems. We need to look at this together.

SCHNEDAR

Well, it's a very exciting time for me to be joining the FDA. I come from the Department of Justice, and I think one of the key lessons I've learned is not to view things in isolation. You have to look at the big picture. You need to have a team-based approach. So it's very exciting to be here at the FDA, with this tremendous transformation that's taking place, where that's really the message that's been going out.

Compliance: Still will have an enforcement function, but I think it's going to be much more strategic. It's going to be very closely linked with [the Office of Pharmaceutical Quality]. They'll be focusing on quality metrics; we'll be focusing more on when we do find there's a need for enforcement. But I think we're going to have a better view of when there is that need for enforcement, and we'll be more strategic. And we're looking forward very much to enhancing our relationship with ORA. I think the team-based approach is something that, certainly in my past agency, was very successful, and I think that it's something that compliance is very committed to—working with everyone in that fashion. So I'm excited.

MIDTHUN

We at CBER have a long history of engaging with our industry partners in preventive compliance efforts and we really understand the importance that quality plays in having a really important impact on products that, as Janet was saying, patients can use, and also avoiding, hopefully, absence of product for patients, which we all know is a really critical issue in many domains. And, as such, also, we have become very involved with CDER, ORA, and other centers in the Council for Pharmaceutical Quality, and working closely together I think we just recognize that, clearly, we have many common interests that, really, we want to learn best practices and share best practices across the FDA, and we really are embarking on this as a journey that I think we're doing together, with all of our partners in industry, as well.

I think we've recognized there are things that we have to learn. Those things we're going to have to feed back into the system to do things better, both on our side and also, as was addressed in the previous panel, industry, too. They're learning about best practices and quality indicators, and to the extent that they, too, can figure out how to share that in a broader way, I think that's going to really help all of us move ahead.

I think we can't underestimate the importance of quality and actually having good products available to our patients, and that's something that we are very focused on, and certainly within the Center for Biologics we recognize that many of our products are

made just by one or two manufacturers, and, as such, they're very, very important for the public health. So quality and really ensuring not only the product's made in quality but also ensuring that the culture is there that really is dedicated to that, is just really critical.

I don't think you just want it in the United States. We want it throughout the world

COOKE

I've been here for the last two-and-a-half days and I've been listening to all the discussion that's going on. I've been thinking a lot about its impact on what we might do in Europe, what we need to do globally to assure that the products that are manufactured really are of high quality to meet patient expectations, because, in fact, that's what international harmonization is all about.

I think we can only applaud what the FDA is doing. I think the focus on quality and measurable quality, and enabling a quality culture, it's what we all want. I don't think you just want it in the United States. We want it throughout the world. So I can't do anything but applaud what FDA is doing. I'm not sure we will adopt exactly the same approach in Europe. I think what we will try and do is work as closely as we can to ensure that companies don't have to collect different sets of data, because that just makes it more complicated. But we do have different systems—we have to take that into account—and we have to see what fits best in our own environment.

I think all the efforts that FDA is making on quality metrics, on the new inspection protocol, on trying to change the culture from compliance to quality; again, it's something that we have to applaud. Some of it is internal to FDA. I think quite a lot is internal to FDA. So it's when it gets to the interface of being external that we need to think about how we work together. But I think we're actually quite closely aligned, so I'm very pleased. Thank you.

HEDDELL

In terms of European processes, we have, over a period of years, moved more and more to introducing more of a risk-based approach to our processes. It's often used in conjunction with inspections, but I think, frankly, we need to talk about risk-based regulation, in general, not just inspections. And any risk assessment is only as good as the intelligence upon which it's based, and I agree with what Emer has said, in terms of applauding the FDA for moving forward in this area of metrics, particularly for beginning to consider the culture that underlies those metrics.

We want to be part of that with you. How we will adopt it, exactly how we will use the information, I don't know, but it represents a new source of intelligence that will allow a better assessment of risk, which will allow a better use of our resources and direction, as far as we're able, for industry and thereby, [leading to] better protection for patients. So we look forward to being part of this with the FDA. I guess one final comment, perhaps, is that companies tend to be multinational companies, many of them, and if they're being asked to put metrics together for one agency, why would it not be in our interest to try to make those metrics as common as we can.

The more I'm saying, the more I'm thinking, as well. In terms of the culture aspect, we've spoken about what to measure. To me, the culture is the motivation behind actually doing the right thing, so it's the how and the why associated with the what. We've talked about moving from quality control to quality assurance to quality systems to quality culture, and one is not replacing the other. The basic standards still stand. What is different is more of a recognition. People need the motivation to apply those standards, and that's where culture comes in. So it's delightful to be here. Thank you very much.

Making a Masterpiece of Manufacturing

A classic painting is the sum of its parts. Quality metrics are just one piece that comprises industry and PDA members' vision for manufacturing. A vision also reflected in CDER Director **Janet Woodcock's** concept of "a maximally efficient, agile, flexible pharmaceutical manufacturing sector. "

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> – **Girish Mulye,** *Genentech*

Validation of Lyophilization (May 6-7)
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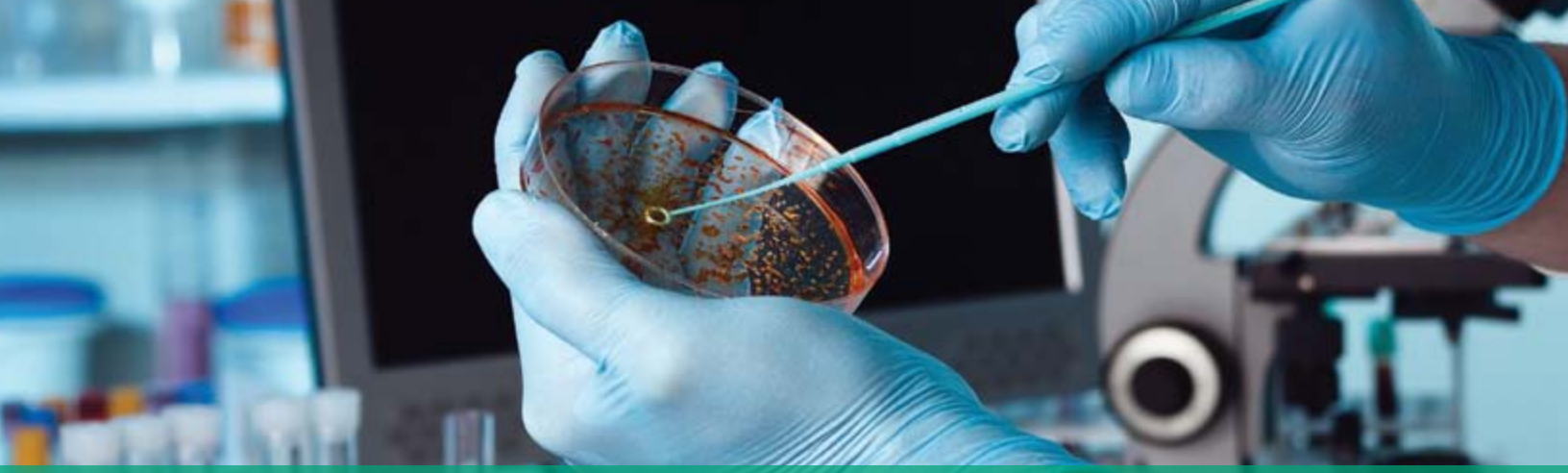

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Are Corporate Quality Policies Required?

The following blinded, unedited remarks are taken from PDA Connect℠, a new online forum that allows PDA members to discuss and share some of the most challenging issues confronting the pharmaceutical industry. The discussions on PDA Connect℠ do not represent the official views of PDA, PDA's Board of Directors or PDA members.

The PDA Letter will periodically publish selected dialogue from PDA Connect℠. Join at community.pda.org and continue the conversation!

Questioner

I was asked recently an interesting question:

"In which U.S. or EU GMP regulation is written that a global quality system is necessary for companies with more than one drug manufacturing site?"

I answered that this makes sense anyway and it is state of the art. Global quality procedures are also implemented in most larger companies.

But the question is: *"Do you have references to regulatory requirements?"* Is it written in guidelines, guides, etc.? Are there citations in Warning Letters?

I found references in ICH Q10 about general responsibility of the senior management in the ICH Q10 chapter "Management Responsibility".

In the EU GMP Guide I found references in § 1.3 and 1.5 "Pharmaceutical Quality System":

***"1.3** The size and complexity of the company´s activities should be taken into consideration when developing a new Pharmaceutical Quality System or modifying an existing one. The design of the system should incorporate appropriate risk management principles including the use of appropriate tools. While some aspects of the system can be company-wide and others site-specific, the effectiveness of the system is normally demonstrated at the site level."*

***"1.5** Senior management has the ultimate responsibility to ensure an effective Pharmaceutical Quality System is in place, adequately resourced and that roles, responsibilities, and authorities are defined, communicated and implemented throughout the organisation. Senior management´s leadership and active participation in the Pharmaceutical Quality System is essential. This leadership should ensure the support and commitment of staff at all levels and sites within the organisation to the Pharmaceutical Quality System."*

My interpretation is that the regulators are aware of company-wide risks in drug manufacturing. And they want to see company wide procedures.

- Do you agree?
- Do you have additional references to guidelines, warning letters, etc.?

Thanks for your answers!

Respondent 1

I remember some years ago, the U.S. FDA went on an inspection tour of half a dozen sites (United States, Europe and Asia) run by a specific company. They didn't expect one global quality system, but a consistent

Continued at bottom of page 41

No Surprises for FDA at Historic Advisory Committee Meeting

Denyse Baker, PDA

On Jan. 7, the U.S. FDA's Oncologic Drugs Advisory Committee voted 14 to 0 that the proposed granulocyte-colony stimulating factor drug EP2006 should receive licensure as the first U.S. biosimilar based on the totality of evidence presented by Sandoz, and FDA. This would be a biosimilar version of Amgen's Neopogen®—a product that treats lack of white blood cells caused by certain cancers.

CDER Director **Janet Woodcock,** MD, opened the meeting, remarking that this was a historic occasion and the culmination of many years of work. She thanked the FDA staff who shaped the standards and policies and explained how much has been done since Congress created the pathway for biosimilars as part of the Affordable Care Act in 2010. She compared current skepticism of the new program to that felt at the beginning of the generics program in 1984, and noted that today generics comprise 85% of dispensed prescriptions.

FDA also provided a primer on biosimilar development and the approval pathway. **Leah Christl,** PhD, who heads the biosimilars team in CDER, presented all the statutory requirements established by the Biologics Price Competition and Innovation Act of 2009 as well as FDA's current thinking about the biosimilar development pathway and shared some key aspects of anticipated additional guidance.

An audience member observed that the molecule in question is a single chain, nongylcolsylated, 175 amino acid protein making it a good first molecule for FDA to assess under the newly developed biosimilar approval pathway. Future molecules will be more complex, so the establishment of a baseline process and Agency expectations will be key for moving forward. FDA stressed several times that each case will be evaluated on its own merits. In this case, Sandoz/Novartis submitted an extensive analytical characterization data package, data from five nonclinical animal studies, clinical data including crossover studies with healthy volunteers and patients taking both the U.S.-licensed and EU-approved reference products. Their data package for the drug also had the benefit 7.5 million patient days of exposure from 60 countries where it has already been approved as a biosimilar. The weight of this information weighed heavily in favor of licensure approval with the committee members.

During the meeting, public speakers brought up a number of topics that were not resolved and will likely be explored over the next few years. These include distinguishing vs. common nonproprietary naming, accurate tracking and tracing of medications, extrapolation of biosimilar indications to those indications approved for the reference product without specific clinical trials, and whether to require postmarketing studies to address immunogenicity of a biosimilar.

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- Points to Consider for SUS Implementation and deployment
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- Challenges and Need for SUS Practices

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Moving Beyond "Read and Understand" SOP Training

Vivian Bringslimark, HPIS Consulting, Inc.

It used to be adequate enough to show training records as evidence of trained employees. And then regulatory inspectors began asking about the effectiveness of our training programs. So we added the ubiquitous "quiz" conducted at the conclusion of training, and for a while this was acceptable as a practice. These "quizzes" maybe measure knowledge retention, and possibly, comprehension, if they include challenge questions about real workplace situations. But having a quiz is no guarantee that the employee transformed the knowledge itself into a skill that can be performed correctly back on the job, especially when the original training was conducted via the "Read and Understand" technique.

As a means of accessing information, it is effective. But reading a procedure is not the same thing as training and qualifying a SOP. *Reading* the procedure is reading what the SOP contains. *Training* is closing a knowledge and skill gap and then applying that information back on the job. *Qualifying* is performing a procedure accurately without coaching. Given that GMP regulations are very clear, i.e., "thou shall follow the procedure," why would management take a less effective approach to ensure compliance?

The next part of the training effectiveness evolution came about when regulatory inspectors began asking how we qualify our trainers. And to the surprise of a lot of firms, the standard of "if they are trained, they can train others" is no longer sufficient. How do you know they are qualified? "Do you have a procedure/process" for that has become the new refrain.

Most Train-the-Trainer courses focus on presentation skills and managing a classroom environment. On-the-job qualified trainers deliver training on the floor, at the lab station or at the work space but *not* in a classroom. What they need is a workshop that focuses on the demands facing on-the-job trainers within the workplace environment **(Figure 1).**

Figure 1 On-the-Job Training: Train the Trainer Curriculum Key Topics

Structured OJT vs. Traditional OJT
Learning Styles and Trainer Preferences
SOJT Process/Methodology
Adult Learning Principles
Following a Training Plan
Employee Qualification
Equipment Trouble Shooting (Optional)

Industry Will Need to Evolve Again

At the *2013 PDA Pharmaceutical Quality Metrics Conference*, CDER Director **Janet Woodcock,** MD, announced that the U.S. FDA will shift their inspection focus to performance and away from compliance. What will this mean for industry? While industry task forces and committees have formed to address that question, I believe that the current 100% trained reports and SOP quizzes will not be enough to satisfy the performance challenge for training effectiveness. Industry will need to document how they qualify their employees. It's called *the Final Performance Demonstration* and it's documented as a *Qualification Event.*

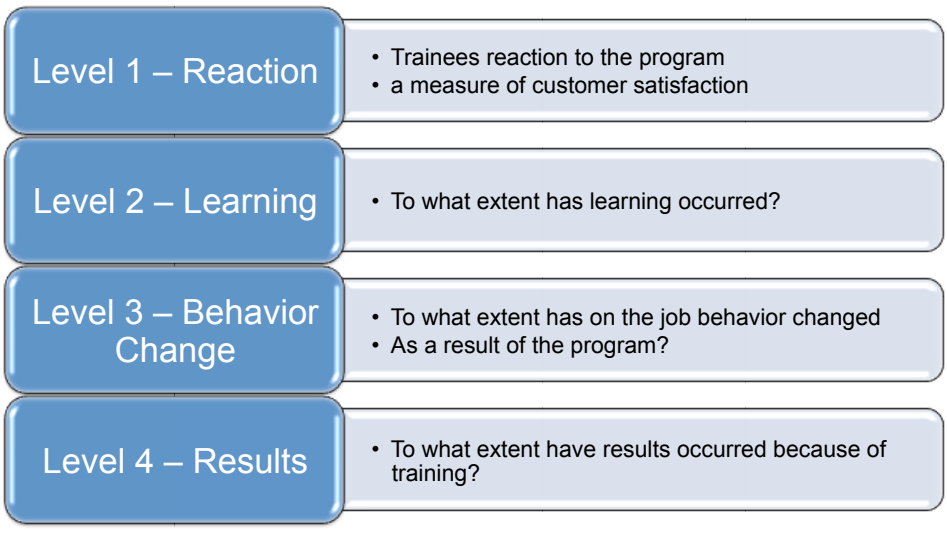
During the final performance demonstration, the Qualified Trainer observes performance and determines if the employee is qualified or requires more time to practice. These Qualification Events are "moments of truth" when the effectiveness of the training up to this point can actually be verified. This is the true measure of SOP training effectiveness, not a quiz or 100% trained report.

Qualification Events: Level 3 Evaluation

When you look at the well-known Kirkpatrick's Four Levels of Evaluation Model (**Figure 2**), you may recognize qualification events (final performance demonstration) as Level 3 – Behavior Change ***(1).***

When seen through the lens of human performance improvement, Level 3 can be seen not strictly as behavior change but as effective transfer. **Thomas Gilbert,** author of *Human Competence: Engineering Worthy Performance,* writes "behavior is a necessary and integral part of performance, but we must not confuse the two," ***(2).*** He explains that behavior is a means; not the end goal. Inherent in a behavior change is the presumption that it will lead to a change in the output(s); thus, an improved result. Without a concerted effort to go one step more and link

Figure 2 Kirkpatrick's Four Levels of Evaluation



Adapted from Kirkpatrick, DL & Kirkpatrick, JD. Transferring Learning to Behavior, 2005.

the behavior change to performance results, the connection is often lost. And so is the effectiveness of all that learning and on the job practice sessions.

So, when employees demonstrate procedures correctly, the Qualification Event is a successful knowledge *and* skill transfer back to the job. Thus, removing doubt about their ability to perform as expected and raising everyone's confidence that employees are complying with the required SOPs. This is the end goal achievement.

We've evolved with our training practices and will continue to enhance our training programs/processes to meet regulatory expectations regarding qualified to perform their job functions. Is your organization ready to step up and address the new regulatory performance challenge? Just how qualified are your employees? Can you back that up with "proper" evidence?

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2. Gilbert, T. *Human Competence: Engineering Worthy Performance*, San Francisco: Wiley, 2007.

About the Author

Vivian Bringslimark has 26 years of a unique mixture of education, life sciences industry experience and consulting engagements enabling her to provide human performance consulting services for improving people strategies.

Hear more about this topic from Vivian at the PDA Education course, "Qualifying Your SMEs as Trainers," April 20, during "Train the Trainer" week at PDA's Training and Research Institute in Bethesda, Md. To learn more, visit www.pda.org/train-the-trainer-week.

Are Corporate Quality Policies Required? continued from page 37

approach to quality. Maybe the word procedure is misleading in this context. I believe the regulators look for a corporate approach to quality and compliance.

One way I have seen this achieved is by having corporate guidance documents that govern local (site, country or business unit) quality systems.

References to a corporate system are given in Annex 16 6.3.2 and in Part III Site Master File 2.4

Questioner

Thanks for you view and your example. Probably we should talk about global quality policies. If industry wants to demonstrate a corporate quality approach, it has to write documents like policies that describes the big picture of a quality system in a corporation.

Thanks for the reference it is a great help.

Respondent 2

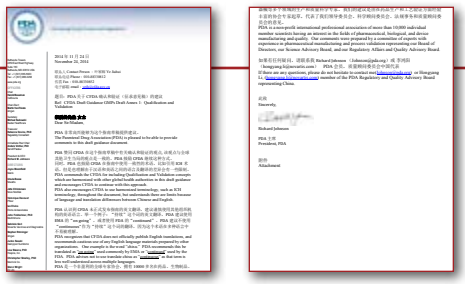
As per ICH Q10 and EU GMP, there is no requirement to have Global Policies and Procedures. However, it depends on the size of company. For larger companies with multiple sites across the globe, Global Procedures and Policies are useful to ensure Quality Systems consistency across all the sites of the company.

Respondent 3

I would like to share my experience when I worked at a large international pharma company (name of the company omitted in order to maintain confidentiality). This company implemented corporate quality policies that every site they owned around the world had to follow. However, there was a downside to this policy. When the regulatory agency found a critical finding during an inspection, they subsequently visited two other of the company's manufacturing sites to look for the same issue. The other sites got nailed too. True story.

PDA Urges Chinese FDA to be Cautious with Terminology

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



November 24, 2014

题目：PDA关于CFDA确认和验证（征求意见稿）的建议

Ref: CFDA Draft Guidance GMPs Draft Annex 1: Qualification and Validation

亲爱的先生/女士

Dear Sir/Madam,

PDA非常高兴能够为这个指南草稿提供建议。

The Parenteral Drug Association (PDA) is pleased to be able to provide comments to this draft guidance document.

PDA赞同CFDA在这个指南草稿中有关确认和验证的观点，该观点与全球其他卫生当局的观点是一致的。PDA 鼓励CFDA继续这种方式。

同时，PDA也鼓励CFDA在指南中使用一致性的术语，比如引用ICH术语，但是也理解由于汉语和英语之间的语言及翻译的差异会有一些限制。

PDA commends the CFDA for including Qualification and Validation concepts which are harmonized with other global health authorities in this draft guidance and encourages CFDA to continue with this approach.

PDA also encourages CFDA to use harmonized terminology, such as ICH terminology, throughout the document, but understands there are limits because of language and translation differences between Chinese and English.

PDA认识到CFDA未正式发布指南的英文翻译，建议谨慎使用其他组织机构的英语语言。举一个例子：“持续”这个词的英文翻译，PDA建议使用EMA的“on going”，或者使用FDA的“continued”。PDA建议不使用“continuous” 作为“持续”这个词的翻译，因为这个术语在多种语言中不易被理解。

PDA recognizes that CFDA does not officially publish English translations, and recommends cautious use of any English language materials prepared by other organizations. One example is the word “chixu.” PDA recommends this be translated as “on going” used commonly by EMA or “continued” used by the FDA. PDA advises not to use translate chixu as “continuous” as that term is less well understood across multiple languages.

PDA是一个非盈利的全球专家协会，拥有10000多名在药品、生物制品、器械等多个领域的生产和质量科学专家。我们的建议是由在药品生产和工艺验证方面经验丰富的协会专家起草，代表了我们领导委员会、科学顾问委员会、法规事务和质量顾问委员会的意见。

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

如果有任何疑问，请联系我Richard Johnson (Johnson@pda.org)或 李鸿阳(hongyang.li@novartis.com) PDA会员，质量顾问委员会中国代表

If there are any questions, please do not hesitate to contact me(Johnson@pda.org) or Hongyang Li, (hongyang.li@novartis.com) member of the PDA Regulatory and Quality Advisory Board representing China.

此致
Sincerely,
Richard Johnson
PDA 主席
President, PDA

PDA Commenting Task Force

Hongyang Li, Novartis (Leader) **Jeffrey Hartman,** Merck **Scott Bozzone,** PhD, Pfizer **Veronique Davoust,** PhD, Pfizer

[Editor's Note: For an analysis of these Comments, see *PDA Letter,* February 2015, p. 35.**]**

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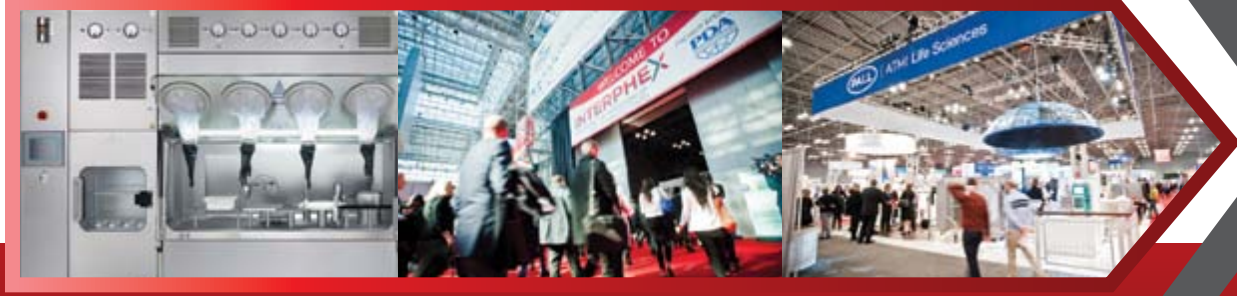

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Joyce Bloomfield, Merck

The Quality Metrics Advantage

The opportunity to explore, develop and progress our journey in defining quality metrics and quality culture is epic. Curiosity is quickly turning to certainty in a relatively short time, and PDA has been at the forefront of this journey. Our primary focus to collect and report industry feedback on the selection of quality metrics and proposed definitions began in 2013. In 2014, PDA formed a metrics definitions task force whose members reviewed proposed metrics and their definitions from industry. Their findings were published in a Points to Consider document in the *PDA Journal of Pharmaceutical Science and Technology* **(1).** In collaboration with the U.S. FDA, the task force then quickly turned to figuring out how to measure and evaluate a company's quality culture and to exploring the effect culture can have on product quality through an industry survey. This culminated in the second *PDA Pharmaceutical Quality Metrics Conference* last December where participants shared and further discussed the survey results. More feedback was collected from the conference participants through multiple working sessions, led by both industry and the FDA. PDA is now poised to share the results of this feedback and will publish a Points to Consider document on the merits of a strong quality culture program.

Industry has explored the options, debated the merits, and recognizes the importance of a strong quality culture to enable success. What we haven't fully explored during this journey is how to maximize the advantage that quality metrics data and a strong quality culture will eventually bring to our customer and business. Now, we need to turn our focus on how to best utilize the data we collect and take advantage of this valuable feedback to predict product performance in a complex supply chain.

In order to get the most from this journey, we must continue to diligently influence guidance that will benefit both industry and the FDA. We must also prepare to understand how to collect, store and analyze our data. The data we collect must be useful to reliably and consistently detect variability in product performance that will lead to continuous improvement opportunities. A strong quality culture program and a Quality Management System is the fundamental foundation with which to construct and successfully utilize metrics that matter. Ultimately, the greatest benefit will be to the patient through increased product quality, decreased product lead time, and lower product cost resulting in fewer drug shortages. We currently have a unique opportunity to turn our curiosity into a reality that will benefit the industry and future generations of patients.

Reference

1. Mendivil, S., et al. "PARENTERAL DRUG ASSOCIATION POINTS TO CONSIDER: Pharmaceutical Quality Metrics Updated September 2014." *PDA Journal of Pharmaceutical Science and Technology* 68 (2014): 535-545.

2015 PDA Visual Inspection Forum

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CALL FOR PAPERS AND POSTERS

The Planning Committee invites you to submit a scientific abstract for an oral presentation or a one-day poster presentation at the *2015 PDA Visual Inspection Forum*. Case studies are particularly desired. Commercial abstracts featuring promotion of products and services will not be considered. Abstracts are being sought on all aspects of visual inspection processes as applied to injectable drug products. Suggested topics for papers and posters include, but are not limited to:

- Fundamental investigations into inspection processes
- Development and control of manual inspection processes
- Selection and training of human inspectors
- Statistical considerations for sampling and assessing inspected product
- New developments in automated inspection technology
- Validation of automated inspection systems
- Particulate/Foreign Material identification
- Foreign material sources in the manufacturing environment and their control
- Preparation and use of standards in assessing visual inspection processes
- Definition and classification of defects and the preparation of defect libraries
- Case studies in the area of particulate or defect control and inspection
- Regulatory and compendial requirements affecting the visual inspection process
- Component quality and supplier qualification
- Special considerations for the inspection of biopharmaceuticals
- Detection and characterization of protein aggregation

Abstracts must be received by March 27, 2015 for consideration
Please visit pda.org/visual2015cfp to submit an abstract.

By submitting an abstract you confirm that you have received the required approval from your company to present if your abstract is selected. After **April 13, 2015**, you will be advised in writing of the status of your abstract. Papers accepted for oral presentation will receive one complimentary registration. To confirm your participation as a poster presenter and be listed in the brochure, you are required to register as a **paid full conference** attendee at the rate of **$1,795 member/$2,054 nonmember** no later than **May 1, 2015**. After May 1, 2015, poster presenters are required to pay the prevailing registration rate and will be listed in the online program agenda.

Attention Exhibitors: Registrations included with exhibitor packages are not eligible; exhibitors who wish to present a poster will be required to register as a **paid full conference** attendee.

QUESTIONS?

Contact PDA: **Jason E. Brown**
Senior Manager, Programs and Meetings
Tel: +1 (301) 656-5900 ext. 131
Email: brown@pda.org

ALL ABSTRACTS WILL BE REVIEWED

All submitted abstracts will be reviewed by the Program Planning Committee for inclusion as an oral or poster presentation.

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pda.org/visual2015

The Struggle for the Pharma Industry's Soul

Recently, I picked up *The Cave and the Light: Plato Versus Aristotle, and the Struggle for the Soul of Western Civilization,* by **Arthur Herman,** and despite the overly dramatic case the author makes about the intellectual divide in Western thought brought about by the two remarkable Greek philosophers, it is an engaging and thought-provoking read, particularly for anyone who enjoyed philosophy in college.

On the one hand is **Plato,** who viewed mathematics, particularly Pythagorean geometry, as holy, and believed that perfect "forms" existed beyond the physical world that people could realize only through the Socratic method, or philosophical dialectic. Plato argued that the physical world represented a cave in which humans were trapped, prevented from realizing the ideal forms of existence.

Aristotle broke with Plato, his mentor, after years of studying at Plato's Academy in Athens. Eventually, Aristotle decided that the physical world, or Plato's cave, was all there was to existence, and to get to any kind of true understanding, people must observe and study the world around them. Whereas Plato is the father of modern philosophy, Aristotle is the father of modern science and the scientific method, thus the "struggle for the soul of western civilization."

The book argues that Plato's school of thought lends itself to mysticism, religion and absolutist political beliefs, and might even be a direct precursor to Nazism and other horrible modern human-caused disasters. Aristotle's modern day adherents, on the other hand, are responsible for democracy, rational thought, the Declaration of Independence and putting a man on the moon. This is where the book goes too far, I believe.

Nevertheless, the book got me thinking about the journey **Janet Woodcock** mentioned at the *PDA Pharmaceutical Quality Metrics Conference* last December. Industry and the U.S. FDA—along with other regulators—are going to go on a "joint quality journey" over the next half decade, she said. Quality metrics, she further explained, might only be "one piece of this." Measurement, central to both Plato and Aristotle's beliefs, is becoming ever more important in the industry. After all, what are metrics? In our industry, we are referring to the second common definition: a standard of measurement. Aristotle would say that if firms measured their output, they could determine quality. Plato might say that too much focus on the details might lead a firm away from the perfect form of quality—the quality culture. Both are right, of course, and Janet captured this notion in her discussion of the journey.

Industry must both measure as much as it can in real time to determine what is going on in its processes and anticipate potential quality-related disruptions, while simultaneously striving to create a perfect quality culture with all the attendant characteristics discussed at the PDA meeting. Aristotle's observation and measurement is our metrics, and Plato's perfect forms, though not as mystical, represent our culture.

So as your firm embarks on this journey, don't feel you have to be on one side of the western civilization divide, because Janet's journey—the industry's journey, really—is going to require a lot of Aristotelian observing and measuring as well as an equal amount of Platonic searching for that perfect quality culture.

PDA Letter

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CALL FOR POSTERS

The Program Planning Committee invites you to submit a scientific abstract for a one-day poster presentation at the *PDA 10th Annual Global Conference on Pharmaceutical Microbiology*. Case studies are particularly desired. Commercial abstracts featuring promotion of products and services will not be considered. Suggested topics for posters include, but are not limited to:

- Advancements and New Technologies
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- Biologic Products/Biotechnology
- Contract Laboratories and Contract Manufacturers
- Endotoxin and Pyrogens
- Environmental Monitoring
- Filters and Filtration
- Globalization and Harmonization
- Investigation of Microbial Data Deviations
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- Microbial Control
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- Parametric Release
- Product and/or Labeling Attributes Potentially Impacting Sterility Assurance
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Abstracts must be received by March 20, 2015 for consideration
Please visit pda.org/micro2015cfp to submit an abstract.

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