People • Science • Regulation

PDA Letter

Volume LIII • Issue 3 www.pda.org/pdaletter March 2017

Reaching for Next Gen Biopharma Manufacturing

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The Parenteral Drug Association presents the...

2017 PDA Annual Meeting

Innovation in Manufacturing Science and Technology

April 3-5, 2017 | Anaheim, California

Anaheim Marriott

Exhibition: April 3-4 | 2017 Cell and Gene Therapy Workshop: April 5-6 | Courses: April 6-7

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Learn more and register at pda.org/2017Annual

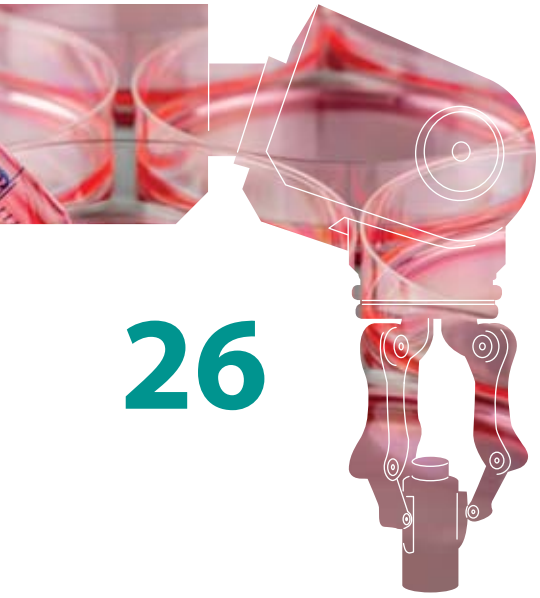
Following the Meeting, on **April 5-6**, PDA will offer the *2017 PDA Cell and Gene Therapy Workshop* to provide a more in-depth look at how these new therapies will impact the industry. ***Learn more and register at pda.org/2017CGT***

On **April 6-7**, PDA Education will be hosting five courses as part of the *2017 PDA Annual Meeting Course Series* to help you further advance your knowledge. ***Learn more and register at pda.org/2017AnnualCourses***

March 2017 PDA Letter

Show Issue

This year's Annual Meeting takes place in Anaheim, Calif. and will offer in-depth presentations on the next wave of manufacturing innovation. Throughout this issue are a number of articles highlighting talks, courses, and other events at this signature PDA meeting.



Reaching for Next Gen Biopharma Manufacturing

Rebecca Stauffer, PDA

Robotic arms. Gloveless isolators. Manufacturing pods. Process modeling. Big data. Automation. Welcome to the future—or "next generation"—of pharmaceutical manufacturing, "Industry 4.0." Pharmaceutical manufacturing is on the precipice of a paradigm change, particularly when it comes to biologic products.

Cover Art Illustrated by Katja Yount

Leveraging Video to Improve Operations

If a Picture is Worth a Thousand Words, What is a Video Worth?

Colleen Walson-Billin, Amgen

According to YouTube, they have over a billion users, almost one-third of all people on the Internet, and, every day, people watch hundreds of millions of hours of YouTube videos, generating billions of views. It's also been reported that videos increase people's understanding by 74%. If a video is worth a thousand words, a video is worth 1.8 million words per minute.

An Inside Look at Industry 4.0

The terms "Industry 4.0" and "Industrial Internet of Things" keep getting bandied around. But what do they mean?

PDA Letter

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Departments

Digital Exclusives

> **On the Issue** | Keeping it Clean
PDA Education instructor **Mary Carver** discusses cleaning and disinfection for aseptic processing

> New Approach to Validation for New Manufacturing Technologies
Learn about a next generation approach for validation of automation, facilities, utilities and equipment

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pda.org/eu-AnnualMeeting2017

13-14 June 2017

Hilton Berlin

Berlin | Germany

Letter to the Editor

Concerns About Example Used in September Cover Story

The September issue of the *PDA Letter* includes a well-written article by **Dr. Donald Eddington** ("Heads or Tails: Statistical Methods for Interpreting Multiple Biological Indicator Results," p. 22) that describes a statistical means for working with biological indicator results. We have no concerns at all with his discussion of statistics, which is the primary focus of the article. Our concerns relate to the vapor decontamination process example used to elucidate the methodology and are listed here:

- The biological indicator population required to demonstrate sterilization is not fixed at a population of 1×10^6 spores per unit ***(1).*** In biodecontamination processes where the objective is nonabsolute, complete destruction of biological indicator populations in the range of 10^3-10^4 is globally accepted ***(2–5).***

- The subject of "rogues" is misdirected. It should be noted that the unfortunate term "rogue biological indicator" arose out of failed efforts to decontaminate isolators and their contents using vapor phase hydrogen peroxide (VPHP). It is considered convenient by some to term a positive biological indicator as a "rogue" and endeavor to dismiss the positive as anomalous. Growth positive biological indicators, however, can arise from either a cycle unable to achieve complete kill or produced in such a way that spores are unable to react with vaporized, or more likely, condensed H_2O_2. In our experience, the layering or clumping of spores which has been confirmed microscopically is more likely to arise at biological indicator populations targeted to be $\geq10^6$ spores/carrier.

- The use of the Halvorson-Ziegler equation is associated with biological indicator evaluation in a Biological Indicator Evaluation Resistometer (BIER) in which the sterilizing conditions are both precisely controlled and highly reproducible. Applying this method to evaluation of vapor processes where neither of these conditions is present is suspect. The conditions within an isolator or other vessel may not be sufficiently uniform and, as a result, it is inappropriate to think of biological indicators placed throughout the vessel as "replicates" as the Halvorson-Ziegler equation requires ***(6).***

- The inclusion of a D-value is erroneous in that there are no proven means to determine a D-value for vapor processes. Vapor sterilization biological indicators are labeled with "D-values" for marketing reasons alone. BIER conditions for the assessment of vapor biological indicators have not been established and, as such, it is impossible to know the D value, or even propose a survivor window that might be germane to the user's purposes. These so-called "D-values" are based upon injection rates, and not the required agent concentration, relative humidity, temperature, and dew point necessary for a sterilizing gas biological indicator. The dual phase nature of vapor processes precludes the determination of a D-value for the biological indicator. The calculations in this article that rely on a D-value, while correct in format, should not be used with a labeled "D-value" for a vapor process.

- The suggestion that biological indicator populations for biodecontamination should be increased is heading in the wrong direction. The limited penetration of vapor processes is a problem, as is the manufacture of biological indicators at a targeted population of $\geq10^6$ spores/carrier. We have seen biological indicators manufactured from a single spore crop manifest large differences in survival time with increasing spore population, and we have seen biological indicators from the same spore crop take three to five times longer to kill at 10^6 populations than at 10^4. Under identical sterilization conditions, the spore kill rate should effectively follow first order kinetics, and thus, the kill rate (D-value) should be not be impacted by spore population. We have personally observed biological indicators inoculated at populations of ~10^2 to 10^4 demonstrate the expected independence from concentration effects. At higher concentrations of 10^5 to 10^6, however, we see evidence of concentration dependent kill rates.

Continued at bottom of page 7

Next Gen: Not Just for Pharma Tech

Way back in the good old days of the mid-2000s, I was knee-deep in my journalism classes learning how to compose a compelling opening, interview sources, track down pertinent information, and navigate the *Associated Press Stylebook*. Naturally, we touched on new forms of journalism and storytelling (I even took a class on it!), but the main focus was always writing for print.

Little more than a decade later, times *really* have changed.

In fewer than five years on the *PDA Letter,* I've been part of a major upgrade to the Letter website, posted audio podcasts, and even coordinated our relatively new series of "On the Issue" videos. I'm not just a writer and editor, I'm a Web content producer, sound engineer, scriptwriter, director...and I'm sure I'll wear more hats in the future. Naturally, all these new forms of storytelling have required me to learn new skills.

In some ways, this mirrors what is happening in parenteral manufacturing. The cover story (p. 26) looks at how biologics manufacturers are responding to next generation technologies such as flexible isolators, robotics, modular manufacturing, etc. Our second feature looks at Amgen's innovative mySOP training videos (p. 30). And this issue's infographic offers an example of an Industry 4.0 pharmaceutical facility (p. 34). All these new technologies will require those working in plants to learn new skills. As batches become smaller, even personalized for individual patients, flexibility is not just important for equipment but for the job skills of those operating the equipment as well.

And this year's Annual Meeting will feature numerous sessions on how companies are responding to these changes in technology. I'm excited about these talks and look forward to covering them in the Letter. If you see me at the conference, let me know what you think about these changes and how the Letter can cover them in future issues. To paraphrase a tired cliche, "the *PDA Letter* should be the only constant" in our industry.

Rebecca Stauffer

Letter to the Editor continued from page 6

- We have also personally noted that the vendor claimed "D values" for *G. stearothermophilus* BI's used in the testing of VPHP cycles listed as 0.3-0.4 minutes at concentrations of 10^3 to 10^4 and at 1.5 minutes or more at 10^6. Although we do not consider these true D-values, this observation is clear evidence of concentration dependent resistance, and we hypothesize that this, rather than any inherent problem with biological indicators, is the cause of the misnamed rogue biological indicator phenomenon. Increasing the biological indicator population exacerbates the problems commonly seen with biological indicators intended for use with VPHP and is completely unnecessary in biodecontamination as well as sterilization. We believe this problem can be alleviated only when the stubbornly held and completely unnecessary belief that challenges the notion that biological indicators must have a 10^6 spore population is finally dispelled.

— James Agalloco, Agalloco & Associates

James Akers, Akers Kennedy & Associates

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2017 PDA Annual Meeting

FDAers to Cover New Science and Tech at Annual

What do adventitious agent control strategies, virus detection technologies, and continuous biomanufacturing have in common? Well, for one, they represent areas of advancement within the pharma industry, and they are also topics that three US FDA regulators will discuss at the *2017 PDA Annual Meeting*.

- **Patricia Hughes,** PhD, Team Leader, Biotech Manufacturing, FDA, will present "Microbiological Control and Adventitious Agents" in session "A1 — Advances in Analytical Sciences & Quality Control Strategies," Monday, April 3, 2:00 p.m.
- **Arifa Khan,** PhD, Senior Investigator, CBER, FDA, will present "Virus Control, Safety, and New Technologies for Virus Detection," in session "A1 — Advances in Analytical Sciences & Quality Control Strategies," Monday, April 3, 2:30 p.m., following Hughes' talk
- **Rapti Madurawe,** PhD, Division Director (Acting), Process Assessment I, CDER, FDA, will present "Small Molecule/Continuous Biomanufacturing" in session "C1 — Future Facility Design," Monday, April 3, 2:30 p.m.

Additionally, breakfast sessions will feature regulatory-focused talks on implementation of new technologies, post-approval changes, knowledge management, quality risk management, data integrity and GMPs for personalized medicines.

For a more personalized view of the importance of parenteral drug manufacturing, in the opening plenary, keynote speaker **Suleika Jaouad** will chronicle her journey as a twentysomething diagnosed with cancer.

More information about these sessions can be found at the *2017 PDA Annual Meeting* website: www.pda.org/2017annual.

First PDA TR of 2017 Offers Best Practices for BFS

PDA's first technical report of 2017 offers the latest best practices on blow-fill-seal (BFS) technology. *Technical Report No. 77: The Manufacture of Sterile Pharmaceutical Products Using Blow-Fill-Seal Technology* features practical considerations for companies using this technology as a replacement for standard fill-finish practices.

PDA worked closely with the BFS International Operators Association (BFS IOA) to develop this document.

BFS refers to technology that integrates plastic blow molding and aseptic filling on a single machine with the final container being created within the machine just prior to aseptic filling. The final container is then hermetically sealed immediately after filling in one continuous operation.

Technical Report No. 77: The Manufacture of Sterile Pharmaceutical Products Using Blow-Fill-Seal Technology is now available for purchase from the PDA Bookstore (www.pda.org/bookstore). Full members can download a free copy of TR-77 until March 16; all members can view it at the PDA Technical Report Portal.

Nominate a Candidate for PDA Board of Directors

PDA's Nominating Committee seeks member recommendations for nominees as candidates to fill Board of Director positions for the 2018–2020 term. Nominees must be current PDA members in good standing. This year's committee is chaired by **Hal Baseman,** Immediate Past Chair of the Board of Directors.

If you are interested in being considered or want to recommend someone, send the recommendation by email to nominate@pda.org or via mail to PDA Global Headquarters, Bethesda Towers, Suite 600, 4350 East-West Highway, Bethesda, MD 20814, USA, attention: Nominating Committee. Please include any supporting information which may make it easier for the Nominating Committee to evaluate your recommendation. Nominations are due May 15.

If you have any questions, feel free to contact PDA president, **Richard Johnson** at johnson@pda.org or Hal Baseman at hbaseman@valsource.com.

PDA Volunteer Spotlight

Derek Duncan, PhD

- Director, Product Line
- *Lighthouse Instruments*
- Member Since | **2003**
- Current City | **Amsterdam, The Netherlands**
- Originally From | **Detroit, Michigan**

PDA has given me great opportunities to connect with others in my field

What has been your most memorable experience volunteering for PDA?

The 2016 *PDA Europe Annual Meeting*. It was my first time serving on a conference planning committee and it was also the first annual meeting in Europe.

What do you like about speaking at PDA conferences?

I enjoy speaking and have appreciated the discussion that followed my talks within the PDA community.

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

Statistical product and process studies. I think more of these studies are needed to have statistical confidence in process/product quality.

Why did you start volunteering with PDA?

I connect very much with PDA's emphasis on science-based approaches, and the PDA Europe team, under **Georg Roessling's** leadership, has been a lot of fun to work with!

Looking back, what is one thing you wish you'd known when you started out in your career?

That good communication is the solution to half of all problems.

What was a professional milestone you achieved in 2016?

I published an article in the *PDA Journal of Pharmaceutical Science and Technology*. **[Editor's Note:** See p. 23 of the January *PDA Letter* to read an abbreviated version of this article**.]**

Anything else you want to tell us?

I applied to be a space shuttle astronaut but did not get chosen, so going into the pharma industry was a good second choice!

The Parenteral Drug Association presents the...

2017 PDA Pre-filled Syringes Interest Group Meeting

May 10, 2017 | Bethesda, MD

PDA Training and Research Institute

#PDAPFS

2017 PDA Combination Products Interest Group Meeting

May 11, 2017 | Bethesda, MD

PDA Training and Research Institute

#2017Combo

Register before Mar. 17 and save up to $200

Double your information and networking opportunities with ***two back-to-back*** PDA interest group meetings!

The *2017 PDA Pre-Filled Syringe Interest Group Meeting* will take place **May 10** and the *2017 PDA Combination Products Interest Group Meeting* will take place **May 11** at PDA's newly expanded training facility. Each one-day, attendee-driven meeting will offer extended discussion with industry experts and peers on hot topics.

To ensure an effective environment for interactive discussions, attendance to each meeting is limited, so make sure to reserve your spot early by visiting **pda.org/2017PFS** (Pre-filled Syringe) or **pda.org/2017Combo** (Combination Products).

Extend your learning when you take part in PDA Education's *Technical and Regulatory Challenges of Drug Delivery Combination Products – Prefilled Syringes, Autoinjectors and Injection Pens* course on May 12. Register today at pda.org/2017TRC

Chapter Learns about EU and US Regs from Experts

Kathleen Souza and Corinne Miller, PhD, MilliporeSigma

On Nov. 9, more than 120 attendees packed the Hilton Boston in Woburn, Mass., to learn the latest in global inspection trends from two experts at the PDA New England Chapter's fall dinner meeting.

Prior to the talk about trends, past and present chapter leaders made several important announcements. First, former Chapter President **Jonathan Morse** announced that **Janelle Velez** won the student chapter's scholarship, which is awarded annually to a student of recognition attending Middlesex Community College. Velez has completed her program at Middlesex Community College and now attends Boston University where she is studying biomedical laboratory and clinical sciences. Sponsors Masy BioServices, Avista Pharma, Integrated Commissioning & Qualification (ICQ) and Lyophilization Technology, Inc., contributed to the scholarship.

Next, **Myron Dittmer,** Chair of the Nominating Committee for the chapter's board election and another past Chapter President, announced the new board members:

- **Amnon Eylath** (President)
- **Laurie Masiello** (President-Elect)
- **Daniel Eylath** (Secretary)
- **Shawn Sherry** (Treasurer)
- **Steven Jones** (Member-at-Large)
- **John Masiello** (Member-at-Large)
- **Elisabeth Piquet** (Member-at-Large)
- **Roger Deschenes** (Member-at-Large)

Following the announcements, the highlight of the evening began. PDA's **Rich Levy** moderated the panel, "Global Inspections and Trends," featuring consultant **Ann McGee** and veteran US FDA inspector **Thomas Arista.**

McGee's talk, "EU and US GxP: Similarities and Differences," compared the two regulatory frameworks, including how each region approaches GMP inspections. She also discussed the role of a Qualified Person (QP) in the European regulatory system. Her talk drew upon her unique background as an experienced professional in the pharmaceutical industry, both as a regulator and pharmaceutical consultant. Current hot topics for Europe include cross-contamination control, supply chain GDP, excipient risk profiles and outsourced activities other than manufacturing and analysis. She closed by briefly describing the EU approach to inspection, pointing out that, in the European Union, inspectors usually have some type of industry experience and announce plans to inspect a facility in advance. Inspections typically last just one week.

Arista, a member of the ORA National Expert Cadre of Field Investigators, discussed global inspection trends, based on

his expertise as an inspector of domestic and international pharmaceutical manufacturers. He emphasized that the EU and US aseptic regulations share similar principles and considerations, but the two regions approach inspections differently. He encouraged the use of alternative methods that rely on good science, risk assessment and readily available data to defend conclusions to an investigator. Arista also talked about what global harmonization means for inspections. For example, the US Code of Federal Regulations permits FDA officials to share nonpublic information with foreign counterparts for law enforcement/regulatory efforts. He discussed this in terms of the Generic Drug User Fee Program with emphasis on leveling the playing field around the world through equal scrutiny of firms. He explained that the goal is to ensure drug quality through international agreement, with an eye toward a more standardized method of inspections.

The panel discussion that followed featured numerous questions on the QP system in European Union, its biggest challenges, any needed changes and the possibility of implementing this system in the United States. Additionally, a number of questions were posed on harmonization, with topics ranging from future reduction of importation testing requirements between mutually equivalent countries, and regulatory filings with nonharmonized compendial methods, to whether global harmonization of site inspections would change their frequency.

The New England Chapter hosts Elisabeth Piquet and **Eric Chapdelaine** thanked all the event sponsors and expressed that they looked forward to seeing attendees at the next dinner meeting.

PDA Who's Who

Thomas Arista, Investigator/National Expert, Pharmaceutical & Biotechnology, US FDA

Eric Chapdelaine, Quality Control Manager – Specifications, Alnylam

Roger Deschenes, Senior Specialist, External Quality, Merck Sharp & Dohme Corp .

Myron Dittmer, Principal Consultant, MFD & Associates

Amnon Eylath, Senior Director, QA, Broad Spectrum GxP Consulting

Daniel Eylath, Quality Associate III, Alkermes

Steven Jones, President, Validation Support, LLC

Rich Levy, PhD, Senior Vice President, Scientific and Regulatory Affairs, PDA

John Masiello, Executive Vice President, Masy BioServices

Laurie Masiello, President & CEO, Masy BioServices

Ann McGee, Managing Director, McGee Pharma International

Elisabeth Piquet

Jonathan Morse, President, Complya Consulting Group

Shawn Sherry, Strategic Account Manager, CMIC

Janelle Velez, Intern, Novartis

2017 PDA Annual Meeting

Make Sunny Memories at the *2017 PDA Annual Meeting*

For those of you planning to attend the *2017 PDA Annual Meeting* in Anaheim, Calif., this year's gathering should offer lots of opportunities for sharing fun in the sun and making memories with old and new colleagues alike. This year's exciting events include:

Sunday, April 2

PDA 11th Annual Walk/Run Event

Registration starts at 6:30 a.m.; race begins at 7:15 a.m. The registration fee includes a t-shirt, race bib, light refreshments and unlimited fun with colleagues, family and friends. Participants can sign up for either the 5K run or 3K walk. Cost: $45 per person (attendees and guests welcome). Proceeds support Global Genes, a patient advocacy organization composed of various groups representing patients with rare diseases (https://globalgenes.org).

Meet and Greet Reception

Enjoy light refreshments with your colleagues after picking up your badge and conference packet. 4:00–5:30 p.m. near the registration area.

pda.org/2017Annual

Monday, April 3

Orientation Breakfast

New to PDA? Learn what benefits PDA can offer you as a member and what *you* can offer PDA. PDA staff and volunteers will show how you can get involved. 7–8 a.m. (*Sponsored by Amgen*)

Networking Reception

End the day by joining your fellow attendees in the Exhibit Hall for refreshments and camaraderie. Begins at 5:30 p.m.

Tuesday, April 4

Red Carpet Reception

After a full day attending sessions, be a star for an evening at our Red Carpet Reception. Strut your best outfit or go casual. No paparazzi, we promise!

This reception is included in the cost of full conference registration. Additional tickets for guests can be purchased for $70 at the registration counter. The reception will be held from 5:30 to 7:30 p.m.

Take advantage of other networking opportunities during morning and afternoon refreshment breaks, and don't miss the networking luncheon on Tuesday in the Exhibit Hall.

2017 PDA Annual Meeting

Container Closure Integrity Critical for New Biologics

Lei Li, PhD, Eli Lilly and Company

Drug product package systems, such as vials and prefilled syringes, must provide a barrier that protects drug product stability and sterility throughout the entire shelf life. Manufacturers are required to demonstrate that systems are capable of maintaining microbial barrier integrity. When it comes to biologics, these products may even require that package systems maintain integrity in stringent environmental conditions (such as frozen or cryogenic environments).

The recent industry trend toward combination product development and patient-centered drug delivery has driven increasingly innovative package design using a wide selection of new packaging materials—all this has implications for testing the integrity of microbial barriers. In addition, more package systems are fully integrated with delivery devices. The package systems not only have to meet the traditional requirements of protecting drug product but also need to enable other system requirements such as proper device functionality. These new requirements lead to customized package design with increased system complexity and, in many cases, present a high level of technical risk for maintaining container closure integrity (CCI). Therefore, CCI testing plays an increasingly important role in informing material selection, derisking of system design and verifying CCI performance.

Upon product filling and sealing, package systems experience downstream processes, ranging from device assembling, packaging, storage, and distribution, all the way to patient use. These processes may introduce additional mechanical stresses and expose the containers to unfavorable environmental conditions that may affect CCI. For example, additional mechanical stress that occurs on a sealing component during device assembly may affect its seal quality. Frozen or cryogenic temperatures during transportation and storage may critically affect sealing capability of elastomer components. These process-related risks to CCI must be assessed and the potential impact on product sterility and stability considered. Appropriate CCI testing should be integrated into process development studies to detect and control the risk of temporary or permanent loss of integrity.

In response to increasing regulatory expectations and industry needs, the pharmaceutical industry has witnessed significant technical advancements in CCI testing technologies. Advanced technologies, such as high voltage leak detection (HVLD) and vacuum decay, have demonstrated improved detection capabilities compared to conventional dye and microbial ingress methods. Many of the technologies have been used for on-line inspection and/or drug product stability testing. Even these advanced technologies, however, have limitations; there is no "one-size-fits-all" solution that can be applied to all product–package configurations and meet all process development CCI testing needs. The recently revised USP <1207> Package Integrity Evaluation—Sterile Products promotes a risk- and science- based approach and uses the package integrity profile database as a tool to ensure CCI throughout the package design and development, validation and routine manufacturing phases. Under this framework, pharmaceutical and packaging industries are experimenting with best practices to de-risk packaging design and verify continued package integrity throughout the product lifecycle.

The upcoming new PDA course, "Container Closure Systems and Integrity Testing," scheduled to follow the *2017 PDA Annual Meeting*, aims to better equip the industry with information about advanced CCI testing technologies as well as practical business approaches to effectively detect, mitigate and control package integrity. First, the course features lectures by industry experts, on-site instrument demonstrations, and hands-on exercises for advanced CCI testing techniques. The combination provides participants with a unique opportunity to not only learn the working principles but also personally experiment with these relatively new technologies and instruments, including tracer gas detection (e.g., helium leak detection), electrical conductivity and capacitance, vacuum decay leak detection, laser-based gas headspace analysis, mass extraction leak testing.

Furthermore, the course introduces a practical and meaningful risk-based methodology to construct a package integrity profile database using appropriate CCI testing methods. Such an approach starts with a thorough understanding of the construction of package materials, system design and manufacturing processes. The CCI failure modes and effects associated with each aspect are identified based on which type of CCI study is needed. In most cases, a series of CCI tests must be applied in concert with product development, including initial design confirmation, machinability studies and product stability testing, to ensure CCI is achieved and well maintained. The comprehensive results from these studies establish the package integrity profile database and inform CCI control strategy development.

Finally, the course uses case studies and group discussions to promote active participation among students, instructors and industry experts. These open-ended discussions should provide insight into the fast-evolving regulatory landscape and novel applications of CCI testing technologies.

Container Closure Systems and Integrity Testing

Anaheim, Calif.
April 6–7
www.pda.org/2017annualcourses

Continued at bottom of page 16

4 Reasons Leaders Are Readers

Jeremy Kingsley, OneLife Leadership

"The man who does not read has no advantage over the man who cannot read."

— **Mark Twain,** American author and humorist

You've probably heard the phrase "Readers are leaders." If you've taken the time to research the habits of well-known leaders, you'll see that most list one habit in common: reading. Leaders make time for it in their busy schedules. Why do leaders feel this is so important?

1 Reading Serves as a Reminder of Important Concepts

Many leaders reread the same article or book multiple times. It's not because they didn't understand the concepts the first time. It's because the concepts are so important to the leader that they want to be reminded of why they are important. Leaders are readers because they want to keep the best business concepts in the forefront of their thoughts.

2 Reading Presents New and Thoughtful Ideas

Like anyone else, leaders must be exposed to new and thoughtful ideas. The key is to choose books that are insightful. Don't be afraid to read something outside the norm. For example, a physician who runs a small medical clinic may generally only read medical journals. But picking up a a book on business management could provide the physician great insight into how the practice could be managed more efficiently.

You may not feel as if you're in tune with a particular book—that happens sometimes. But in the future, that book may inspire your own new ideas.

3 Reading Gives Leaders an Advantage

Steve Siebold, author of *How Rich People Think*, spent years interviewing 1,200 of the wealthiest people about their habits. One commonality? They were regular readers. And they didn't just read for fun. Rather, they read for knowledge. **Mark Cuban** reads for almost three hours a day. Why? Because he understands that reading provides knowledge accessible to anyone.

Yet, not everyone will take the time to read. Cuban understands that this creates a distinct advantage for him. He's not alone. In fact, **Warren Buffett** is known for his reading habit as well. He's one of the richest men in the world. Buffett is known for reading between 600 to 1,000 pages each day. Buffett estimates that he spends around 80% of his time reading.

4 Reading Encourages Better Decision Making

Reading gives us access to experiences that are not our own. It exposes us to how other people approach problems in business and in life. This gives leaders more options to make better decisions. Through reading, leaders are exposed to different perspectives that may encourage them to take a new or different approach to conflicts. It also promotes tolerance of other viewpoints.

Reading is one of the best possible ways to become a better leader. Take some time to find some great books—biographies, bestsellers, and stories from people you respect. You won't regret it.

About the Author

Jeremy Kingsley is a professional speaker, leadership expert and bestselling author. Learn more at www.jeremykingsley.com.

Eye on Education continued from page 15

Upon completing the course, participants will be able to compare and contrast various CCI testing technologies and understand their applicability, advantages and limitations. Through case studies, participants will become familiar with establishing a package integrity profile database using appropriate test methods in support of new product marketing approval and commercial CCI control strategy development. Furthermore, the best practices for CCI method development and validation will be discussed.

About the Author

Lei Li currently serves as an engineer advisor at Delivery and Device R&D, Eli Lilly and Company. He has nine years of experience in the pharmaceutical and medical device industry, with a focus on developing API and drug product packaging in support of clinical development and product commercialization, and establishing cold chain distribution for biologic products.

Make PDA Your Bio/Pharmaceutical Manufacturing Resource

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For more than 70 years, PDA has been providing high-quality, expert manufacturing resources to the industry.

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SNAPShot

New Year, New Name, New Activities for BioAB

John Geigert, PhD, BioPharmaceutical Quality Solutions, BioAB Chair

PDA's Biotechnology Advisory Board is now officially the Biopharmaceutical Advisory Board (BioAB). This new name better represents the scientific and technical information this advisory board provides to PDA's board of directors and its membership regarding biopharmaceutical manufacturing, quality and regulations.

But BioAB is more than an advising group. Its members actively participate and take leadership roles in numerous PDA events. And 2017 is proving to be an active year with BioAB members involved in three major upcoming events:

2017 PDA Annual Meeting

Michael De Felippis, PhD, Senior Research Fellow, Bioproduct R&D, Eli Lilly & Company and Vice-Chair of BioAB, and **Morten Munk,** Senior Technology Partner, Global Business Development, NNE Pharmaplan, are co-chairing this signature PDA event in April, assisted by **Laurie Graham,** Acting Director, OPQ, US FDA, and a number of other PDA volunteer members from across the bio/pharmaceutical industry on the conference planning committee.

2017 PDA Cell and Gene Therapy Workshop

Due to the increasing importance of cell and gene therapy products, BioAB has designated this area of biopharma as a major initiative for the advisory board, led by volunteers **Vijay Chiruvolu,** PhD, Senior Director, Product Sciences, Kite Pharma, **Michael Blackton,** Vice President, QA CMC, Adaptimmune, and **Karen Walker,** Global Head, Quality, Cell and Gene Therapy Units, Novartis. All three have been heavily involved in developing this workshop on these "next wave" biopharmaceutical products. It is scheduled to follow the Annual Meeting in April.

2017 PDA Biosimilars Conference

Vince Anicetti, Executive Director, Quality, Coherus Bioscience, and **Stephan Krause,** PhD, Director, QA Technology, AstraZeneca Biologics, are co-chairing this year's biosimilars conference in June, assisted by **Michael VanDerWerf,** Director, Regulatory Affairs, Teva, Laurie Graham, and **Jens Schletter,** PhD, Head, Regulatory CMC Group Biopharmaceuticals, Sandoz. BioAB has been heavily involved in this area as biosimilars are already market-approved in both Europe and the United States, with many more in various stages of clinical development or under active regulatory authority market approval review.

PDA's BioAB members continue to work hard to cover emerging developments and technology in biopharma. The advisory board hopes these three PDA events offer members a chance to learn more about the latest biopharmaceutical trends and challenges as well as debate these topics with other members.

Meeting *Preview*

Interest Group Schedule

As always, relevant interest groups will meet in the afternoon for the first two days of the *2017 PDA Annual Meeting.* Below is a schedule of interest group meetings that fall under the Science and Biopharmaceutical Advisory Board umbrellas. Note: All interest group meetings are open to meeting registrants. (For Regulatory and Quality Advisory Board interest group meetings, see p. 37.)

Monday, April 3	Tuesday, April 4
4:15 – 5:30 p.m.	4 p.m. – 5:15 p.m.
Advanced Virus Detection Technologies Interest Group Facilities and Engineering Interest Group Filtration Interest Group Microbiology/Environmental Monitoring Interest Group Packaging Science Interest Group	Process Validation Interest Group Sterile Processing Interest Group Visual Inspection of Parenterals and Lyophilization Interest Groups (joint meeting) Pre-filled Syringes Interest Group

SNAPShot

Journal *TOC*

PDA Points to Consider on Post-Approval Changes Available in March/April Issue of PDA Journal

The March/April issue of the *PDA Journal of Pharmaceutical Science and Technology* features a PDA Points to Consider paper from members of the Post-Approval Change: Innovation for Availability of Medicines (PAC iAM) technical report team (journal.pda.org).

Research

Alberto Biavati, Michele Poncini, Arianna Ferrarini, "Complexing Agents and pH Influence on Chemical Durability of Type I Molded Glass Containers"

Dennis Jenke, et al., "Simulated Leaching (Migration) Study for a Model Container-Closure System Applicable to Parenteral and Ophthalmic Drug Products"

Paul Faya, James D. Stamey, John W. Seaman Jr., "A Bayesian Approach to Determination of F, D, and Z Values Used in Steam Sterilization Validation"

Kurt Brorson, et al., "Mycoplasma Clearance and Risk Analysis in a Model Bioprocess"

Technology/Application

Harry Yang, et al., "Characterizing the Overall Derivatization of Conjugated Oligomeric Proteins"

Eric Hilario, et al., "An Improved Method of Predicting Extinction Coefficients for the Determination of Protein Concentration"

Commentary

Raja Mazumder, Vahan Simonyan, Jeremy Goecks, "Biocompute Objects—A Step towards Evaluation and Validation of Biomedical Scientific Computations"

Klaus Wuchner, et al., "Container Closure Integrity Testing—Practical Aspects and Approaches in the Pharmaceutical Industry"

PDA Paper

Emma Ramnarine, et al., "PDA Points To Consider: Technical Product Lifecycle Management: Communication and Knowledge Exchange between Marketing Authorization Holders and Health Authorities"

Group Seeks "ADDoPTion" of Digital Design

*On April 4, **David Royle** will discuss the recently launched UK project, Advanced Digital Design of Pharmaceutical Therapeutics (ADDoPT), in session "C3 — Selecting and Introducing New Technologies," at the* 2017 PDA Annual Meeting. *This project, involving collaboration between industry and academia, seeks to make digital design techniques widely available in the industry. Royle answered a few questions for the* PDA Letter.

Can you tell us more about the specific digital design techniques being developed?

In the context of ADDoPT, digital design combines research insight with qualitative and quantitative mechanistic modeling to provide links between raw materials, manufacturing processes, and the needs of the patient. It spans all unit operations, processes and procedures used during the manufacture of medicines and their impact, both upstream on the efficiency of product and process design, and downstream on product performance. It encompasses:

- Detailed mechanistic models (constructed around the underlying mechanisms indicated by science and engineering principles) for key manufacturing unit operations and underpinning fundamental physical and chemical properties of quality-critical solid, solution and particle forms
- Predictive tools that exploit our understanding of crystalline structures to support the design of more robust manufacturing processes and the identification of the most appropriate controls
- Advanced systems for process control and optimization of pharmaceutical processes that incorporate hybrid modeling to combine the benefits of mechanistic models with the classical data-driven techniques used in automation

How does process system modeling tie in to digital design techniques?

Conventional, largely empirically based, modeling capability in the pharmaceutical industry is approaching the limiting point of incremental development. Advanced process modeling involves applying detailed, high-fidelity mathematical models of process equipment and phenomena, usually within an optimization framework, to provide accurate predictive information for decision support in process innovation, design and operation. The resultant models are used to explore the process decision space to enable better, faster and safer decisions by reducing uncertainty. This approach differs significantly from that of traditional process simulation.

ADDoPT partners are working across the pharma value chain to define a system for top-down, knowledge-driven digital design and control for drug products and their manufacturing processes. This is bringing together a wide range of predictive models and insight from industrial case studies at the pharmaceutical companies, allowing for more targeted future experimentation and a better understanding of risk, resulting in better design and scale-up for robust products and processes.

Are there plans to reach out to global regulators as well?

Regulators such as EMA and the US FDA are supportive of Quality by Design (QbD), an approach that aims to ensure the quality of medicines by employing statistical, analytical and risk management methodology in their design, development and manufacturing. One of the goals of QbD is to ensure that all sources of variability affecting a process are identified, explained, and managed by appropriate measures. This enables the finished medicine to consistently meet its predefined characteristics from the start—so that it is "right first time." We believe that the pharmaceutical manufacturing industry's ability to deliver QbD will be significantly enhanced by the better knowledge of drug products and their manufacturing processes/value chains, and more efficient methods for the design and control of a wider range of manufacturing process which the project will deliver. Our dissemination strategy and implementation plans include engagement with the UK's MHRA Innovation Office to discuss how the ADDoPT systems framework can be integrated within the CMC sections of new product registration.

There are pharma companies moving toward more flexible forms of manufacturing (modular units, compartmentalized equipment). How could these companies benefit from digital design techniques?

Although the emphasis in ADDoPT is on new tools and methodologies for batch manufacture (where there is a huge installed asset base that will persist for several decades), the project's industrial case studies variously cover both batch and continuously operated manufacturing processes, existing and yet-to-be designed processes, and in-house and outsourced manufacture. The project consortium is well-positioned to make use of insights from previous collaborations and to transfer knowledge into new flexible manufacturing approaches through the extensive involvement of partners in related projects and activities. Examples include the EU Seventh Framework project "F3 Factory" that studied fast, flexible, and sustainable modular production technology (which included ADDoPT partners AstraZeneca and Britest) and the current UK AMSCI-funded REMEDIES (RE-configuring MEDIcines End-to-end Supply) project, which is identifying innovative ways for clinical and commercial supply chains to capitalize on new technologies with the potential to improve medicine manufacturing and supply and offering more personalized, faster and cheaper drug delivery.

About the Expert

David Royle is a chartered chemical engineer with over ten years' experience in the pharmaceutical industry at AstraZeneca.

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A Trending Policy for Automated Visual Inspection

The following conversation has been taken from PDA Connect℠, an online PDA forum that allows members to discuss 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 *periodically publishes selected, unedited dialogue from PDA Connect℠. Join the conversation at community.pda.org!*

The unedited, blinded discussion is from the Visual Inspection of Parenterals Interest Group Forum.

Questioner

We are working to establish a trending policy for automated inspection but are curious as to how others have started their own. We do have an existing manual inspection trending policy, but the rates established for manual inspection don't seem to apply for an automated process. Additionally, the difference in how the information about defect numbers is gathered is also posing a challenge in establishing the process. Before we try to 'reinvent the wheel,' it seemed most logical to enlist your help.

- **How did you establish your initial defect limits, given that you have no data of automated inspection?**
- **How do you account for defect numbers during inspection? (Do you evaluate all defects ejected from the machine? Do you account simply for quantities of defects in each eject bin? Do you leverage automated reports from the inspection machine, and if so, did you validate these reports? What are the methods that you use to establish your defect quantities?)**

I very much appreciate your thoughts and shared experiences. Thank you.

Respondent

Great questions, and I'd like to propose the following as possible methods to address the differences in trending defects from manual inspection processes and automated processes. I hope this starts some additional conversations regarding this topic.

First of all, I'd like to propose that trending and the response to these trends is an opportunity for improvement, rather than a direct quality event. The primary purpose of trending is to provides an indicator of special cause variation, to which resources can be supplied to investigate, in the hope of preventing this type of variation in the future.

How do you account for defect numbers during inspection? Do you evaluate all defects ejected from the machine? Do you account simply for quantities of defects in each eject bin?

Do you leverage automated reports from the inspection machine, and if so, did you validate these reports?

What are the methods that you use to establish your defect quantities?

For automated inspection, the reports or on-screen generated defect rate most likely do not provide a true number of defects, as false rejects may account for many of the number. For this reason, the manual inspection and classification of the rejects would provide the best indicator of true defect numbers.

Ideally, all rejects would be inspected and classified, but other hybrid approaches could be defensible. For example, if a certain reject bin has a very high proportion of true defects, all of these could be classified. Other reject bins that normally contain a large amount of false rejects, could be sampled. It is important to normalize the sample to an overall percentage in the batch.

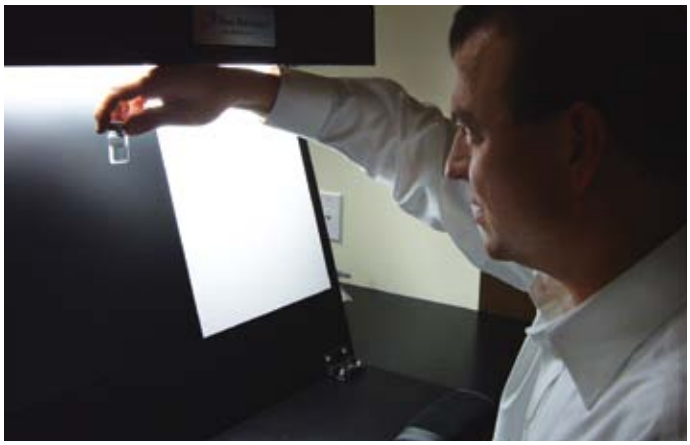
Another consideration of classification, are areas in automated inspection that have been proven to be superior to human inspection. A case in point, is the particle rejects; it may be necessary to use the automated inspection numbers to provide the ongoing rate, yet still classify some of these rejects to understand the particle types coming through the process. This situation may also apply to leak detection rates. Both of these types of automated inspection have been consistently proven superior to human inspection, so the rates of defects may use the automated numbers, but human classification should also be employed to ensure atypical and level 1 characterization can be applied.

How did you establish your initial defect limits, given that you have no data of automated inspection?

Initial defect limits could be transferred from the manual inspection process, especially if you intend to use the classification method of rejects to provide the numbers. As mentioned, if trending is primarily a continuous improvement exercise, maybe the first 10 batches could provide the initial sample for statistical limits, and then they could be refined after a more powerful sample can be collected, say 30 batches.

Another possibility, is to concentrate on critical defect limits and set the major and minor limits to some value that has either been established by the manual process, or some other logical limit. Many times minor defect limits can be exceeded, based on the wide variety of severity in these classifications, but should time be spend on minor defect investigations vs. major or critical defects?

Good Luck and any comments are appreciated. **[Editor's Note:** The Visual Inspection of Parenterals Interest Group will convene at 4 p.m., April 4 at the *2017 PDA Annual Meeting*.**]**



Could Big Data Lead to Big Industry Changes?

Aaron R. Goerke, Hoffmann-La Roche, and Tor Gråberg, AstraZeneca

2017 PDA Annual Meeting

The collection of data has become a formality within pharmaceutical manufacturing. Its real potential lies in analysis combined with the knowledge to answer complex questions. This kind of analysis is often referred to as "Big Data."

Big Data creates new possibilities for the pharmaceutical and biotechnology industry to drive operational and business performance to higher levels. A handful of pharmaceutical and biopharmaceutical companies are seeing success with Big Data, leveraging this analysis for more thorough decision making and process optimization.

But taking advantage of Big Data requires new strategies, processes, mindsets and skills. It is easy to sit back and bemoan the lack of solutions when it comes to new technologies, like Big Data, in the industry. Many others are in the same situation.

One way to get out of that bubble is to make time for the *2017 PDA Annual Meeting*. On the last day of the conference, **Michele D'Alessandro,** Vice President & Chief Information Officer, Manufacturing IT, Merck & Company, Inc., and **Adam Fermier,** PhD, Scientific Director, PDMS, Janssen Pharmaceuticals R&D, will speak about their companies' experiences with Big Data in the plenary session, "Application of Big Data for Manufacturing Process Design and Optimization."

Other sessions at the meeting will look at analytical sciences and process monitoring, delivery system design, future facility design, real-time release testing, immunotherapies, manufacturing and logistics for personalized medicines, analytical sciences and quality control strategies, development in patient-centered precision medicine, next generation manufacturing and more.

If you are new to the pharmaceutical and biotechnology industry, or an experienced professional interested in Big Data and other new ideas, the *2017 PDA Annual Meeting* is an excellent opportunity to create, improve and expand your networking among new and long-standing colleagues.

2017 PDA Annual Meeting and PDA Education Courses

Anaheim, Calif.
April 3–7
www.pda.org/2017annual

2017 PDA Upcoming Events

SAVE THE DATE for PDA's 2017 Events

MARCH

20
Particle Identification in Parenterals
Berlin, Germany
pda.org/EU/TCParticleID2017

21
Interest Group Meeting: Visual Inspection
Berlin, Germany
pda.org/EU/IGVisual2017

21
Interest Group Meeting: Freeze Drying
Berlin, Germany
pda.org/EU/IGFreezeDrying2017

21-23
Design, Operation and Qualification of Pharmaceutical Water Systems NEW COURSE
Bethesda, MD
pda.org/2017PWS

22-23
An Introduction to Visual Inspection: A Hands-on Course
Berlin, Germany
pda.org/EU/TCVisual2017

27-31
PDA #100 Aseptic Processing Option 2 Week 2: Apr. 24-28
Bethesda, MD
pda.org/2017Aseptic2

APRIL

3-5
2017 PDA Annual Meeting
Anaheim, CA
pda.org/2017Annual

3-7
Praxis der Pharmazeutischen Gefriertrocknung
COURSE IN GERMAN LANGUAGE
Osterode, Germany
pda.org/EU/Gefriertrocknung2017

5-6
2017 PDA Cell and Gene Therapy Workshop
Anaheim, CA
pda.org/2017CGT

6-7
2017 PDA Annual Meeting Course Series
Anaheim, CA
pda.org/2017AnnualCourses

11-13
Validation of Biotechnology-Related Cleaning Processes
Bethesda, MD
pda.org/2017AprBio

18-20
Airflow Visualization Techniques and Practices
Bethesda, MD
pda.org/2017AprAir

18-21
Regulatory and Compliance Course Series
Bethesda, MD
pda.org/2017RCS

26-27
Current Trends in Aseptic Fill & Finish of Pre-filled Syringes Conference
Lindau, Germany
pda.org/EU/FillFinish2017

MAY

1-4
Fundamentals of Aseptic Processing
Bethesda, MD
pda.org/2017FundAPT

3-4
Basics of Successful Auditing
Berlin, Germany
pda.org/EU/Auditing2017

8-9
2017 PDA Implementation of SUS and Delivery Systems: Material Safety and Compatibility Workshop
Washington, DC
pda.org/2017MSC

10
2017 PDA Pre-filled Syringe Interest Group Meeting
Bethesda, MD
pda.org/2017PFS

10-11
2017 PDA Annex 1 Workshop
Washington, DC
pda.org/2017Annex1

11
2017 PDA Combination Products Interest Group Meeting
Bethesda, MD
pda.org/2017Combo

12
Technical and Regulatory Challenges of Drug Delivery Combination Products – Pre-filled Syringes, Autoinjectors and Injection Pens
Bethesda, MD
pda.org/2017TRC

15-19
PDA #100 Aseptic Processing Option 3 Week 2: Jun. 12-16
Bethesda, MD
pda.org/2017Aseptic3

22-25
Lyophilization Course Series
Bethesda, MD
pda.org/2017Lyo

Denotes Laboratory Courses | Denotes Lecture Courses

PDA
Parenteral Drug Association

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

23-24
Single Use Systems for the Manufacturing of Parenteral Products
Bethesda, MD
pda.org/2017SUS

30-1
Virus & TSE Safety Forum
Dubrovnik, Croatia
pda.org/EU/Virus2017

31-2
Validation of Moist Heat Sterilization Processes
Bethesda, MD
pda.org/2017MayMH

JUNE

2
Virus Filtration
Dubrovnik, Croatia
pda.org/EU/Virus-Filtration2017

6-7
Isolator Technology
Bethesda, MD
pda.org/2017IT

12
Cleaning and Disinfection
Berlin, Germany
pda.org/EU/CD2017

12
Quality by Design for Biopharmaceuticals
Berlin, Germany
pda.org/EU/QBD2017

12
Supply Chain Strategies for API and Drug Products
Berlin, Germany
pda.org/EU/API-Drug2017

13-14
2nd PDA Europe Annual Meeting
Berlin, Germany
pda.org/EU/Annual2017

15-16
Introduction to Aseptic Processing Principles
Berlin, Germany
pda.org/EU/TCAseptic2017

19-20
2017 PDA Quality Risk Management for Manufacturing Systems Workshop
Chicago, IL
pda.org/2017QRM

19-22
Biotechnology Course Series
Bethesda, MD
pda.org/2017BCS

20-22
Environmental Monitoring Course Series
Bethesda, MD
pda.org/2017JunEM

26
Practical Application of Phase-Appropriate GMP & Quality to Clinical Development of ATMPs
Valencia, Spain
pda.org/EU/TCATMPs2017

26-27
2017 PDA Biosimilars Conference
Bethesda, MD
pda.org/2017Bio

26-30
Quality Course Series
Bethesda, MD
pda.org/2017QCS

27-28
Advanced Therapy Medicinal Products
Valencia, Spain
pda.org/EU/ATMPs2017

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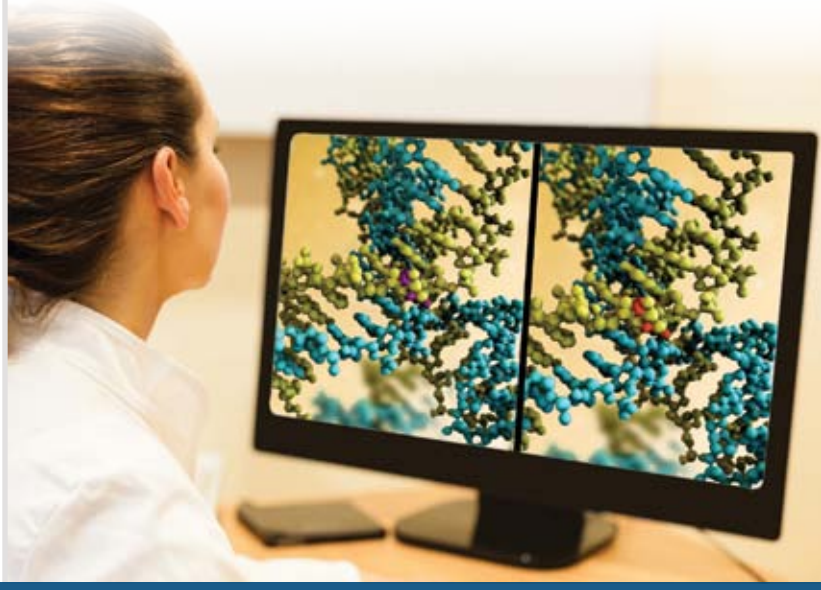
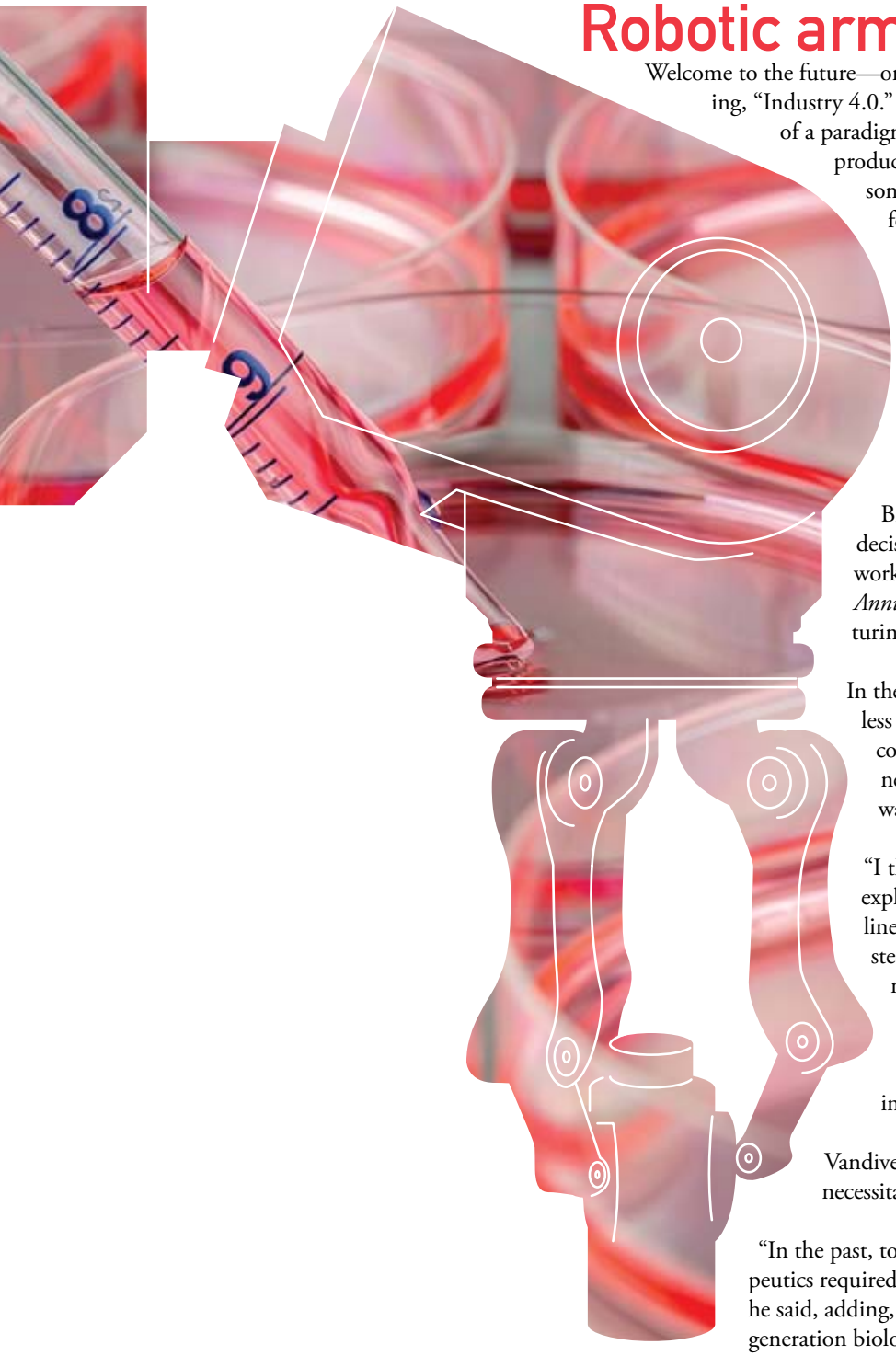


Reaching for Next Gen Biopharma Manufacturing

Rebecca Stauffer, PDA

2017 *PDA Annual Meeting*



Robotic arms. Gloveless isolators. Manufacturing pods. Process modeling. Big data. Automation. Welcome to the future—or "next generation"—of pharmaceutical manufacturing, "Industry 4.0." Pharmaceutical manufacturing is on the precipice of a paradigm change, particularly when it comes to biologic products. As biologic lots become more and more specific, some even personalized for individual patients, the need for flexible, high-tech manufacturing equipment and solutions becomes critical.

Yet when a biologics manufacturer decides to employ these next generation technologies, serious practical considerations emerge around finances, training, and implementation. **Barry Starkman,** Principal Consultant, Parenteral Manufacturing, DPS Engineering, and **Mike Vandiver,** Vice President, Manufacturing and Plant Design, Just Biotherapeutics, are both well aware of the heavy decisions involved in putting these new technologies to work. They will share their experiences at the *2017 PDA Annual Meeting* (Plenary 3: "Next Generation Manufacturing & Facilities," April 4, 8:30 a.m.).

In theory, next generation manufacturing should require less capital investment than conventional facilities. Still, cost does factor in when installing and implementing new technologies. Yet some companies have found ways to successfully manage these expenses.

"I think that the big issue is around investment," explained Starkman. "The cost for putting in a filling line, once you've made the decision to do that, is pretty steep." For this reason, he explained, some biologics manufacturers are using their clinical manufacturing facilities to launch. This enables the company to gauge how well the product performs on the market before committing to invest in flexible manufacturing technology.

Vandiver believes that the production of innovative biologics necessitates flexible manufacturing.

"In the past, to very successfully supply the world with biotherapeutics required a huge investment and substantial fixed assets," he said, adding, "in the future, the primary characteristic of next generation biologics manufacturing is flexibility. The key tenets supporting flexibility are speed and cost-effectiveness."

Starkman, who handles the conceptual design of facilities for DPS Engineering's clients, also pointed out that companies that have invested significantly in the research and development of a new biologic product may be gun-shy about taking the risk when there are major obstacles to overcome in getting the product on the market in a timely manner. Particularly when one of those hurdles is fitting next generation manufacturing technologies in with existing regulations.

"At some level, as you're moving technology [ahead], somebody has to be first, and then you run the risk of a regulator either not understanding or not agreeing," he said. "And when you have large sums of money on the line, both in terms of investment and in research and development as well as the capital equipment…it becomes quite easy to say 'you know, let's just go with what we know.'

"That's a very difficult decision for the owner to make, to go forward with something totally new. I'm not sure how to overcome that in total. Other than the fact that more work may need to be done with prototypical process design."

In addition, Vandiver noted that certain products may be produced using legacy systems for a variety of reasons. Moving existing products to new production technologies would require a large investment in clinical trials to establish comparability, something many companies may not be able to do.

"When you look at these [legacy] systems, people have invested hundreds of millions of dollars in a facility such as this. And for them, it may not necessarily make sense to invest in one of these other types of facilities," he said. "They made such a large investment; they want to make sure it's fully depreciated. And, if I were in their shoes, I would believe the same thing."

Maik Jornitz, CEO, G-Con Manufacturing, and moderator of the Annual Meeting session featuring Starkman and Vandiver, sees the key performance factors behind next generation manufacturing as flexibility, speed and cost.

"Flexibility is required to be able to act rapidly on changing environments, but also to be able to manufacture multiple products within the same facility. Speed, another key aspect, means the time-to-run frame needs to be lowered to less than a year instead of the [current] three to four years," he said. "Cost, the third element, should be [seen] as total cost of ownership and not in the legacy approach of cost per square foot."

Just Biotherapeutics is designing and building a small, efficient biologics manufacturing facility, named "J.Pod," that Vandiver believes will drive down capital investment and the cost of goods. He sees J.Pod as complementary to existing conventional production facilities.

"I want to be very clear. I am not actually advocating that these new types of flexible facilities actually replace conventional facilities," he emphasized. "I believe they complement existing conventional production facilities," explaining that, if you need multimetric tons of product, it would not make sense to invest in a J.Pod facility. But it would be suitable for moderate-scale production, up to a metric ton.

Just Biotherapeutics starts by using modeling of the process technologies under consideration in order to identify bottlenecks and prioritize technologies on which to focus attention.

"We actually use modeling first," Vandiver explained. "We start by modeling mass throughput and investigating options. We then model the economics around these options, in terms of cost of goods." This allows his company to determine the impact of volumetric productivity and its role in reducing the cost of goods.

"Let's just say that my initial market only requires two bioreactors. Based on the volumetric productivities, our cost per gram is potentially going to be something around $100–$150 a gram. As we then require more capacity, our markets increase, our demands increase. We can increase to four to six bioreactors very quickly ➤

Article at a Glance

- Flexibility necessary for new wave of biologics but investment costs a factor
- Regulators open to next gen manufacturing technology
- Training critical for new technologies on the floor

> **In the future, the primary characteristic of next generation biologics manufacturing is flexibility**

and very cost-effectively. And we actually see the potential to lower the cost per gram to the $40–$60 range, so what we're seeing, then, is about a three-fold reduction in the cost of goods."

Yet, while the regulatory concerns of migrating to new technologies remain, both Starkman and Vandiver stressed that regulatory agencies, such as the US FDA, understand the need for innovative manufacturing technologies.

"I think there's been a step change," Starkman said. "There is more of an openness."

From what he's seen with his clients, the key to receiving regulatory approval when implementing new technologies lies in truly understanding the manufacturing processes of the new equipment and effectively communicating this to regulators. Risk assessments, in particular, have proven to be an effective tool.

"Certainly, FDA has moved toward new technologies as an organization because they see the value in it. It's still in its early stages but I think it's in the right direction, for sure," Starkman said.

Vandiver agrees that the Agency is supporting new technologies, especially disposable technologies, which are becoming the standard in the industry over stainless steel.

In fact, he pointed to a recent survey from *BioPharma-Reporter* showing that "70% of the respondents actually agree that disposable technologies are becoming standard, and it shows that the regulatory agencies are supporting this as well."

New Training for New Tech

When a biologics manufacturer makes the decision to implement next generation technologies, training is just as critical, if not more so, as it is when implementing conventional equipment.

Starkman explained that training becomes particularly pertinent when working with automation, which requires a different level of understanding. A worker on the production line must understand "how it feels to control the equipment, [as] the days of just being able to turn a wrench and being able to set up a machine like that are somewhat diminished."

With these new technologies, operators are responsible not just for running it, but for setup, preventative maintenance and understanding how it operates. Vendors do a "great job" of designing the equipment and developing innovative improvements. Yet at the end of the day, "they don't stay and run the machine; they disappear after the machine is on the floor producing every day."

When building a line, DPS Engineering brings the workers who will be responsible for the line into the design process, including taking operators to specialized training at a site in Germany. This ensures the workers understand upfront how the machine works, moving up the learning curve, and fostering commitment on both sides.

"You need to have that kind of commitment in the parenteral drug business because the criticality of what we're doing is so important," Starkman explained. "Building that relationship among all the parties involved is very important, and it starts at the very beginning."

Just Biotherapeutics will also develop internal training programs to prepare the staff, mitigating risk.

"We are creating internal training programs that bring people up to speed and prepare them for these new types of operations," he said. His company approaches it more as expanding skill sets rather than replacing old ones. This makes the employees more flexible, enabling them to work in different types of facilities—a highly desirable trait.

And Vandiver has found that Just's staff is receptive to learning to work with new types of equipment. "For them, it's exciting; it's new. They're not doing the same thing that they've done for the past 10 or 15 years," he said. "They're being exposed to new ways of doing things. They have actually embraced the change."

Starkman agrees that workers have generally been receptive to learning new skills. "I think that people love the technology. They love the sophistication of it. They love the ability to learn new things."

And while operator skill sets are changing, one thing is staying the same: the human element. At least for the time being.

In his personal time, Starkman is a pilot and enjoys flying. He finds aerospace automation analogous to biotech automation.

"Flying airplanes years ago was a very 'seat-of-the-pants' type of operation. You flew an airplane by feel...today's airplanes are very automated. Everything is digital," he said. "There is a tendency for pilots to get overly reliant on the automation of the airplane—to just let it go—and they're not paying attention. There have been a number of serious situations that have occurred as a result."

To prevent overreliance on automation, Starkman recommends better understanding of the manufacturing process itself. This builds an "envelope" of understanding.

"We can build in controls with the right sensors," he said, and by "understanding the process, understanding the risks of the process very well, the machine can, in effect, monitor itself at some levels better than a human can. But I don't think you will ever get away from [a human presence] in such a critical scenario like making parenteral drugs. I think the human factor is always going to be there."

In the end, no matter what types of next-

Continued at top of page 41

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Leveraging Video to Improve Operations

If a Picture is Worth a Thousand Words, What is a Video Worth?

Colleen Walson-Billin, Amgen

According to YouTube, they have over a billion users, almost one-third of all people on the Internet, and every day people watch hundreds of millions of hours of YouTube videos, generating billions of views. It's also been reported that videos increase people's understanding by 74% ***(1).*** If a photo is worth a thousand words, a video is worth 1.8 million words per minute **(Figure 1)** ***(2).***

In early 2015, Amgen's quality leadership team identified a pressing need to improve adherence to procedures on the manufacturing floor. The quality leadership team saw this as an opportunity to look at the company's document structure and evaluate whether or not procedures were truly written for the benefit of those working on the floor. The company had already provided iPads to manufacturing staff so they could access documents in real-time. In addition, Amgen's leadership had led efforts to simplify SOPs,

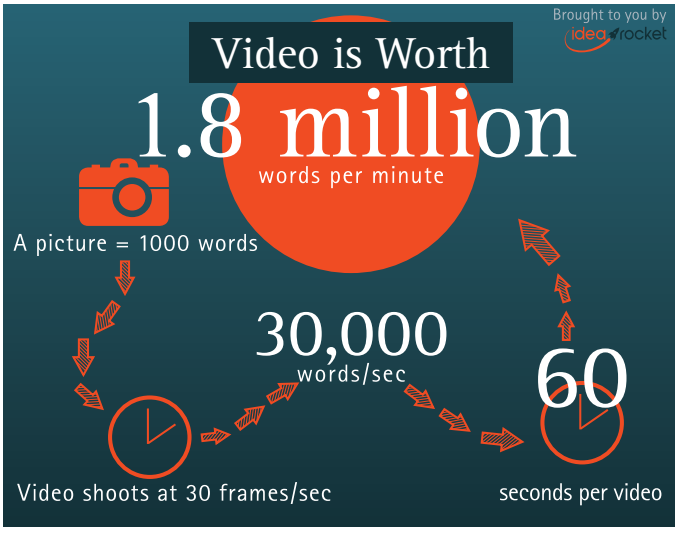

Figure 1 Videos vs. Pictures | www.idearocketanimation.com

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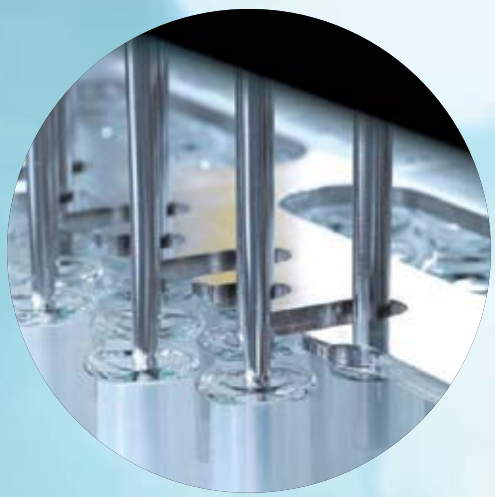

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> **Personnel are able to focus on flawless execution instead of SOP interpretation**

encouraging those maintaining and updating the documents to insert symbols and pictures. But was this enough? Amgen's then Chief Quality Officer **Martin VanTrieste** challenged the status quo and felt "it was unacceptable that we don't provide the tools necessary for frontline employees to be successful." He wanted a disruptive/transformational approach to enable frontline professionals to be successful, not frustrated, when it came to using SOPs.

Around the same time, VanTrieste realized that the taillight on his car was not working. As an avid DIYer, he went enthusiastically and confidently into his garage to replace the light, only to become frustrated after 20 minutes of trial and error. In hopes of avoiding an expensive trip to the dealer, he resorted to an Internet search which, to his surprise, immediately pulled up a link to a short video demonstrating how to properly fix a taillight. Five minutes later, the repair was complete and VanTrieste quickly realized the power video could bring beyond home projects. Not long after, he initiated a project to bring video capabilities to Amgen's SOPs.

After a successful pilot in one of its manufacturing plants, Amgen collaborated with Google to develop a YouTube-based platform, compliant with 21 CFR Part 11, that allows for the storage and linking of videos directly into controlled documents. This has enabled Amgen to improve overall quality and facilitate "right first time," as manufacturing personnel have access to short visual demonstrations of key process steps. A strong team composed of expert information systems, quality assurance, and validation leads launched the SOP video platform, known as "mySOP," in May 2016.

What Exactly is mySOP?

The mySOP platform consists of short, focused video segments that demonstrate particular steps. It complements—but does not replace—existing written SOPs.

"Video clips should be short stories for critical tasks, not two-hour Hollywood movies representing complex 100-page SOPs," VanTrieste said.

The platform leverages the existing document review and approval process. Although it initially covered only SOPs, mySOP could be used for any type of GMP document. It is a cloud-based system, using the Google Cloud Platform,

that has no restrictions on number of users or total file size, and videos are version- and access-controlled with full user activity-tracking available.

But videos are not added haphazardly to the system. If an owner or operator wants to add a video to the mySOP system, they first have to complete an assessment that addresses at least two of the following:

1. A focused deviation analysis to determine if there are steps that consistently result in error
2. Consideration of what operators feel would improve their right first time operations
3. A deep understanding of process step complexity and criticality (i.e., the higher the complexity and/or criticality, the more likely a video is warranted)
4. Assessment of usage frequency (i.e., in a high mix/low volume manufacturing line, the processes that are not used frequently would benefit from an additional video demonstration)
5. Training difficulty and duration (e.g., if a step is particularly complex or intricate, a trainer may be required to watch or "shadow" a newly trained associate multiple times before feeling confident they can complete the task on their own; videos could be added to the procedures so that the trainee could complete the required training and refer to the video instead of relying on the trainer)

Once assessments are completed, the owner finalizes details about the video, such as what, if any, narration will be included, which point of view (e.g., operator vs. observer) would be best, and when the video can be recorded.

Once the specific what, how, and when has been decided, the video can be created using any recording device, such as an iPhone, iPad or GoPro. Simple video editing is usually required to clean up the start and finish of the video, but editing is generally minimal.

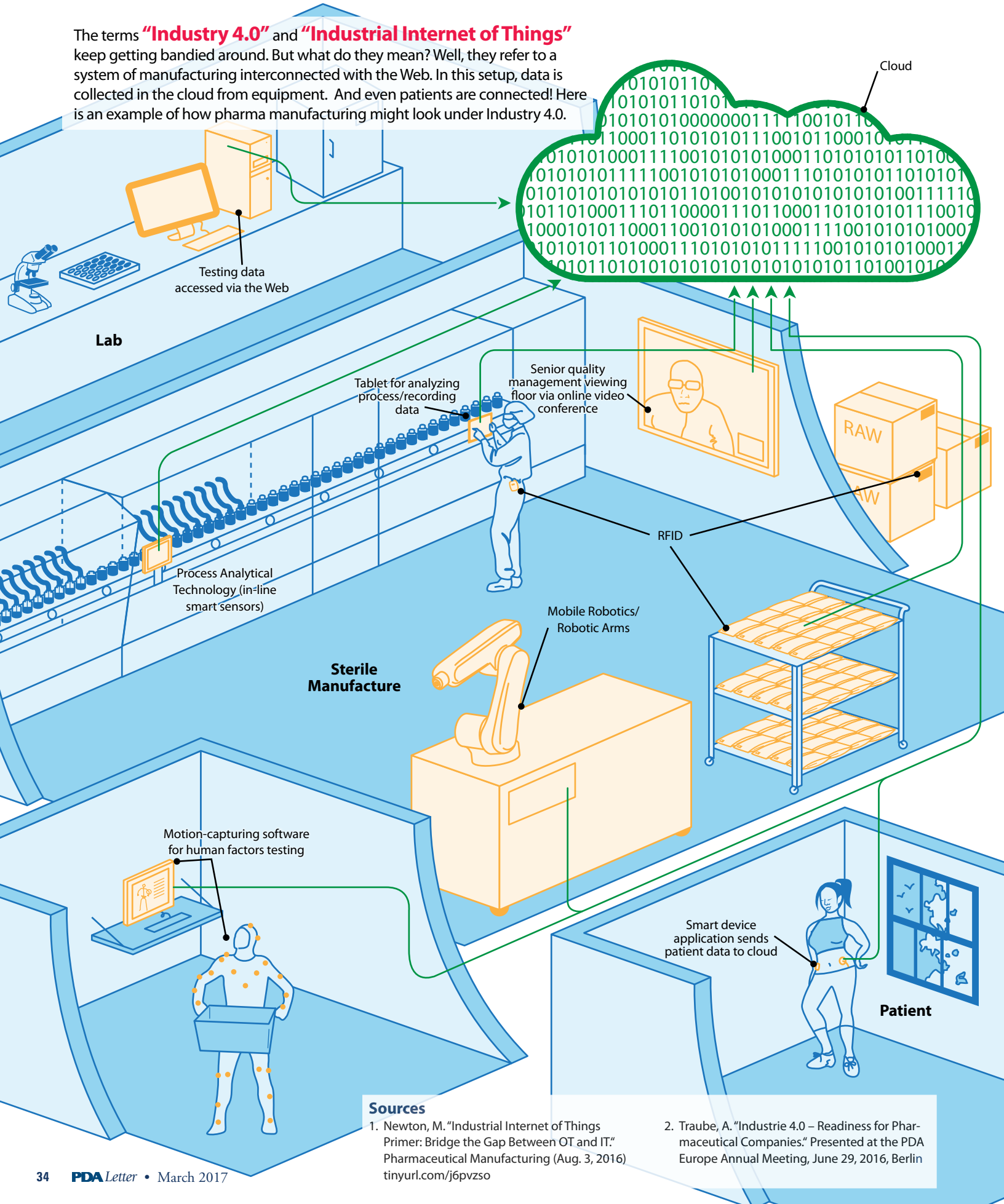
Expected Benefits of mySOP

The use of GMP videos in SOPs is expected to significantly benefit operations at Amgen. Seeing a video demonstration in real time can reduce length of training, improve the end user's understanding of steps to be performed, diminish deviations, increase adherence to procedure, allow for further simplification of documents, and increase the company's ability to consistently supply drug products to patients. Manufacturing personnel are able to focus on flawless execution instead of SOP interpretation. The quality leader-

Continued at bottom of page 41

An Inside Look at Industry 4.0

The terms **"Industry 4.0"** and **"Industrial Internet of Things"** keep getting bandied around. But what do they mean? Well, they refer to a system of manufacturing interconnected with the Web. In this setup, data is collected in the cloud from equipment. And even patients are connected! Here is an example of how pharma manufacturing might look under Industry 4.0.



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Meeting *Preview*

Interest Group Schedule

As always, interest groups falling under the Regulatory Affairs and Quality Advisory Board (RAQAB) will convene at the *2017 PDA Annual Meeting.* Below is the schedule for the RAQAB interest group meetings, which are open to all conference registrants. For interest group meetings falling under the Science and Biopharmaceutical Advisory Boards, see page 18.

Monday, April 3	Tuesday, April 4
4:15 p.m.–5:30 p.m.	4 p.m.–5:15 p.m.
Management of Outsourced Operations Interest Group	Quality Risk Management Interest Group Technology Transfer Interest Group

Translate Your Knowledge into Reliability

Chris M. Hanff, ValSource

2017 PDA Annual Meeting

Knowledge management, along with risk management, is an enabler of an effective pharmaceutical quality system (PQS) ***(1).*** We've read and heard this statement extensively for about a decade since the emergence of ICH Q10, yet knowledge management is still somewhat unclear compared to the concept of risk management. Quality system elements, such as lab controls, computer system validation (CSV), supplier management and corrective and preventive actions (CAPAs), are quite standard in practice. Comparatively, knowledge management appears less well-developed and tangible than any other quality system element. If it is true that knowledge management is abstract in concept, how can we realize knowledge management in the workplace? I would like to see an industry that relies on already abundant real-world expertise and knowledge transfer to achieve continuous improvement. This article is the first of two parts exploring knowledge management—particularly knowledge transfer. My second article will illustrate how finding a common language is key to learning from each other (i.e., knowledge transfer). I hope this first piece sets a foundational understanding of knowledge management and focuses on opportunities for meaningful, practical knowledge transfer. I also want to cover the barriers and challenges to learning from each other.

Early in my career, I had the good fortune to work the manufacturing floor where I learned from the company's facilities and engineering professionals. Later, as I reflected on what I'd learned from these colleagues, I also thought about how I learned. This also made me think about how learning happens in other trades. Outside pharma, a painter or a pipefitter learns a trade without SOPs, without specialized learning software, and without a quality function diametrically distinct from their work. An apprentice pipefitter learns hands-on directly from a master pipefitter to become a journeyman. The journeyman pipefitter learns from multiple masters who collectively expand the pipefitter's body of knowledge. The journeyman pipefitter successfully performs enough pipefitting to ultimately become a master in the trade. This learning is largely undocumented (without SOPs), yet demonstrable and reliable. If the pipefitter wants to learn carpentry, architecture, etc., that learning is pursued from others who possess the knowledge. This is a simple example of recognizing and filling knowledge gaps. Is it more complicated in pharma? Yes. But should it be?

Whatever we know individually, it's not valuable to others if it's not available to others

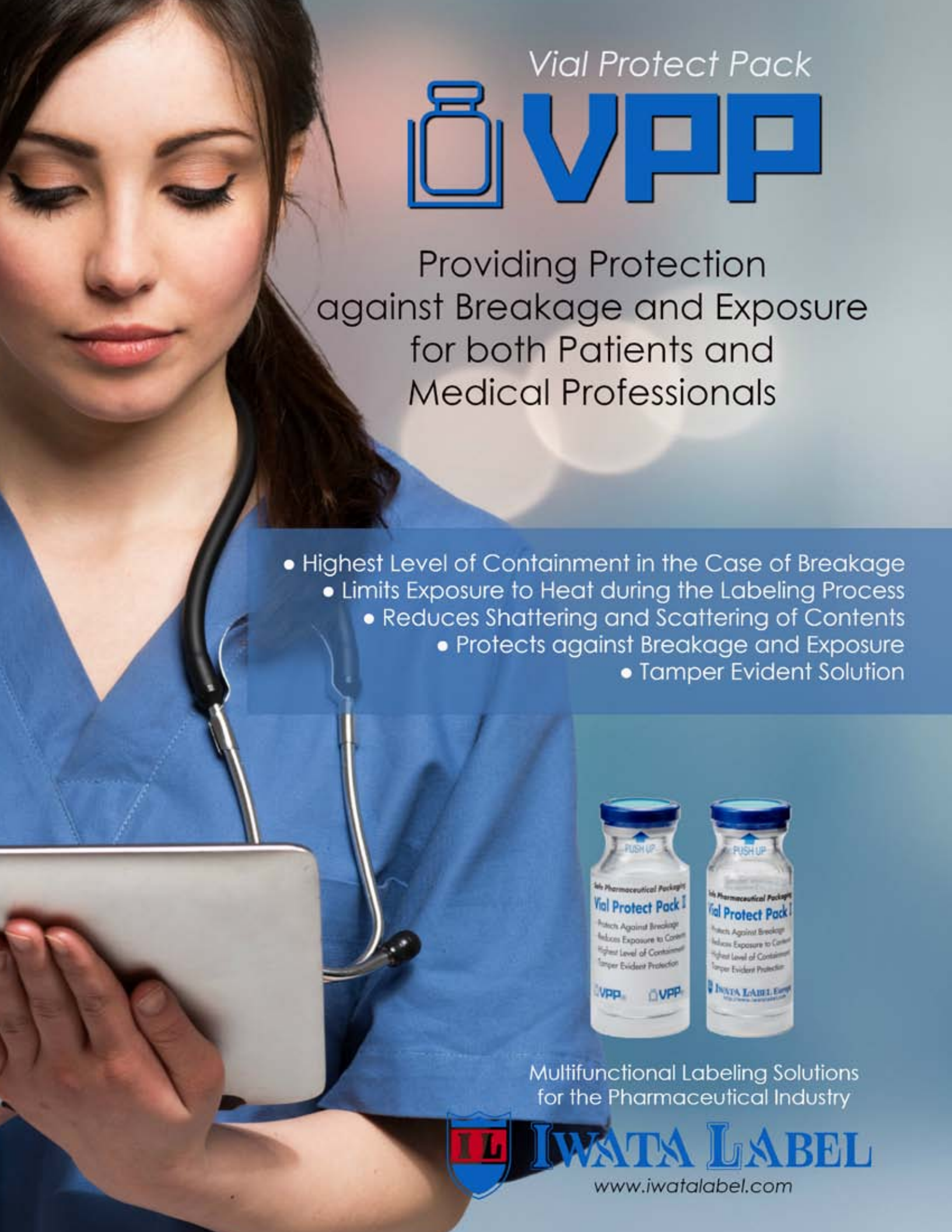
As my own career has progressed, I've found that facilities and engineering expertise too often goes untapped by decision-makers. Consider our industry's issue with aging facilities. From my perspective, we've been collectively slow to learn that bolstering quality controls (or as it sometimes feels, a "quality police state") does little to mend outmoded facilities and equipment. In our industry's aging facilities, what's outmoded will not be remediated through voluminous quality records that rationalize the continued and noncompliant use of outmoded facilities and equipment. All those quality records are a type of failure cost that does not add value. Instead, additional work is needed to chase documentation deliverables—and, that comes at the expense of complicating and delaying true remediation.

Why do aging facilities face reactive remediation instead of preventive maintenance? What don't we know until it's too late, and why (not)? Whatever we know individually, it's not *valuable* to others if it's not *available* to others. Unless our knowledge is transferred to decision-makers, how can a decision-maker be successful in deciding if or when to take a specific action and allocate enough resources to do so? Do decision-makers in pharma fully know what it takes to maintain facilities and equipment in reliable order? The prevalence of aging facilities answers this question.

So, how can we as an industry fill our knowledge gaps? Well, based on my experience, I offer two suggestions:

First, recognize that the greater the problem, the greater the deliberation needed. This is an adaptation from ICH Q9, "the level of effort, documentation, and follow through is commensurate with the level of risk" ***(2).*** Focus on reliable quality and delivery by focusing on facilities and engineering reliability. Hold an audience with your facilities and engineering professionals. Form a risk question, asking what is the impact on quality and delivery based on the issues observed and reported from facilities and engineering expertise.

Second, consider using the Bathtub Model (**Figure 1**) to manage issues that arise during the lifetime of facilities and equipment. At the installation of new equipment, for example, expect a higher incident of "issues" needing decision-makers, which in turn demands a higher rate of discussion with facilities and engineering professionals. Use predictive maintenance models/metrics to understand equipment reliability before equipment failure. As illustrated in **Figure 1,** when in the "Wearout" phase, much more discussion among decision-makers and facilities and engineering professionals is needed to prevent ever-increasing failures in aged, outmoded equipment.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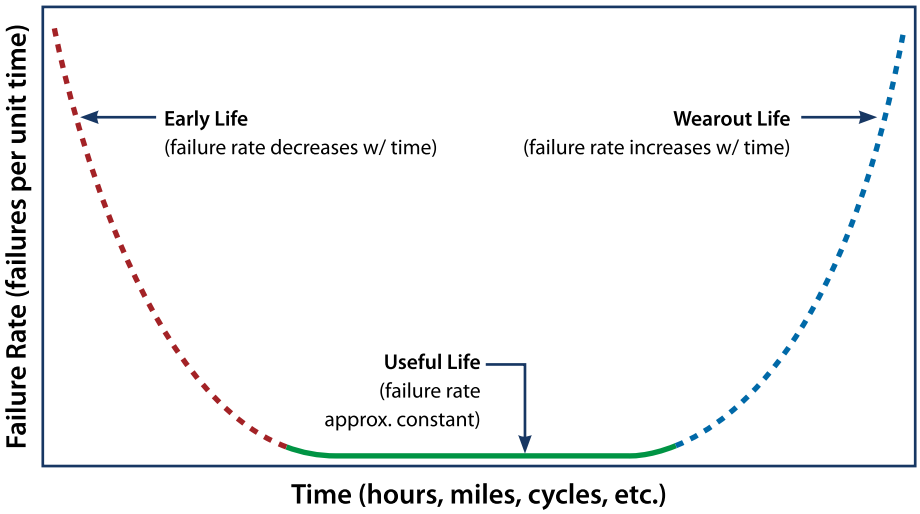
Conclusion

Knowledge management, particularly knowledge transfer, can be made tangible and can drive continuous improvement — or as I like to say, "the right information at the right time compels the right actions." Our expertise and knowledge must be made available and solicited to learn from each other so that the most well-informed decisions are reached. It takes courage to admit, "I don't know," and expose our own knowledge gaps. It takes a common language to teach what's not known to those seeking to learn and wanting to make the best decision. In my next article on this series, I will suggest that Cost of Quality is critical to that common language.

Figure 1 Bathtub Model



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2. ICH Q9: *Quality Risk Management*

About the Author

Chris Hanff is a senior consultant in the pharma industry, providing his insights and expertise as an architect of effective quality and business systems, and as an agent of transformational change. He will be teaching the PDA Education course, "Knowledge Management Applied in Facilities & Engineering to Improve Manufacturing Reliability," directly following the *2017 PDA Annual Meeting*. For more information, go to: www.pda.org/2017annualcourses.

Reaching for Next Gen Biopharma Manufacturing continued from page 28

generation manufacturing technologies are implemented, multiple factors need be taken into consideration. Such firms might consider taking into account the specific needs of the product and the market demands.

Jornitz urges companies to look into next generation manufacturing to avoid being left behind.

"The early adopters are already out front," he said. "The most radical change that has to happen is in the attitude and thought process within the industry."

About the Experts

Barry Starkman has amassed over 30 years of experience in biopharmaceutical facility design and operation.

Michael Vandiver is Vice President, Manufacturing and Plant Design at Just Biotherapeutics. He has over 29 years of biopharmaceutical process development and manufacturing experience.

Maik Jornitz is a distinguished technical expert with close to 30 years of experience in bioprocesses.

Leveraging Video to Improve Operations continued from page 33

ship team will continue to evaluate monthly deviation rates and potentially conduct an assessment of the personnel using these videos to determine their actual benefit.

Looking to the Future

While the initial rollout focused on Amgen's largest manufacturing location in Puerto Rico, mySOP provides the company's entire operations staff another tool to enable further simplification of procedures and processes. Numerous departments within the company, such as supply chain, cybersecurity, commercial marketing and R&D, have reached out in pursuit of leveraging this new, exciting capability. This video platform has the potential to make a significant impact on the business and, ultimately, the patient.

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About the Author

Colleen Walson-Billin is a Director of Quality at Amgen. In this role, she leads business-critical, large-scale projects and manages the business operations and strategic planning for the Senior Vice President of Quality.

A Case Study in Real-Time Release Testing

Juan L. Torres, PhD, Biogen

2017 PDA Annual Meeting

Now is the time to revolutionize how both manufacturers and regulators think about biotech manufacturing in order to proactively respond to the anticipated need for vastly increased productivity and efficiency. In order to continuously improve, manufacturers must work together as an industry and in collaboration with regulators to realize the intent of Quality by Design (QbD) and ICH quality guidelines. Transparency and open communication to make real-time release testing a reality is part of the larger vision of "a maximally efficient, agile, flexible manufacturing sector that reliably produces high-quality drug product without extensive regulatory oversight" ***(1).***

Real-time release testing can be defined as a set of in-process controls that may provide greater assurance of product quality than end-product testing. It leverages real-time analysis, including at-line and on-line measurements of critical quality attributes and process parameters, to ensure product quality. The availability of real-time release testing data at the time of batch manufacturing can also improve operational efficiency and inventory control, reducing the resources needed to test batches following manufacture. Increased product and process knowledge—a fundamental concept of QbD and the ICH quality guidelines—is key to effective real-time release testing.

Typical GMP operations involve performing an extensive set of tests according to approved specifications before the material is released to the market or for further processing. Recent ICH guidelines (ICH Q8, Q9, Q10 and Q11), however, suggest an alternative real-time release strategy to provide assurance of product quality prior to release. Real-time release testing uses the principles of QbD to optimize release and stability testing. A combination of manufacturing process understanding, process control, and product knowledge can be used to demonstrate that the material was made according to GMP.

Despite the potential gains that can be realized from real-time release testing, the industry continues to struggle with implementation and, therefore, has not yet realized the potential benefits. Many questions remain. When and where should tests be conducted on the manufacturing line? Which instrumentation should be used? What associated validation requirements are necessary? Where should real-time release data be recorded? How should on- or in-line analyzers be evaluated during manufacturing. And more critically, what do regulators expect?

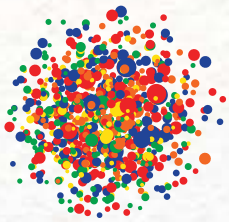
Consider the following case study of real-time release testing that leverages historical process understanding and robust quality systems to implement real-time release for a biological drug substance process using a science- and risk-based approach. The models are based on substantial historical data and number of completed manufacturing batches: 64 batches used to develop the model and 40 to validate it.

Real-Time Release in Real World

Using enhanced product and process understanding—an overall awareness of the process based on development studies and real-time data from the manufacturing floor—in combination with quality risk management, the enhanced control approach leverages additional drug substance in-process testing and manufacturing controls in order to eliminate redundant testing. This, combined with full endpoint release testing of the subsequent drug product (which has the same formulation and composition as the drug substance) ensures that the drug substance continues to be manufactured with consistent and controlled quality. **Figure 1** shows an example of how real-time release testing and predictive models could be used, not only for overall quality oversight, but for real-time adjustments to optimize process reliability.

As part of this case study, current drug substance release tests for pH, osmolality, polysorbate 80, protein concentration, purity, charge heterogeneity, aggregation and low molecular weight impurities were performed and controlled at points upstream in the drug substance manufacturing process. The testing points were selected based on the unit operations that either govern or control the generation of the respective product quality attributes. As an additional means to further enhance control of product quality, the action limit ranges for two of the chromatography step yields were narrowed to reflect manufacturing experience obtained over the past five years of production. The tighter action limit ranges further assure ➤

Figure 1 Example of Real-Time Release Testing and Advanced Process Control of Drug Substance Manufacturing



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the chromatography steps perform as expected and ensure that product quality remains consistent. Safety tests for bioburden and endotoxin, including some rapid test methods, were maintained for the final drug substance release to mitigate potential contamination risks in the drug substance. Based on manufacturing experience, which demonstrated comparability of the analytical results between source drug substance and resulting drug product, testing for appearance, purity (by reducing gel chip) and biological activity was performed only on the drug product, and removed as part of drug substance release testing.

The team overseeing this project submitted it to both US FDA and EU regulators with substantial data and justifications. Meetings were held with the both the US and EU regulators to better understand expectations prior to the submission. These meetings were productive and informative, including open dialogue on expectations. Progress was made through both regulatory bodies and approval has been obtained for EU markets. The team remains optimistic that continued dialogue will open paths to additional markets as both industry and regulators learn more about the possibilities of real-time release testing.

Overall, the development of the data package and submissions for real-time release testing led to open dialogue with both the US and EU regarding expectations and resulted in productive collaborations. This dialogue and interaction between regulators and industry will ultimately define the requirements to move forward into an era where robust process understanding and science- and risk-based approaches are routinely approved. Continued transparency and open communications will pave the way for industry to continuously improve and provide high-quality products.

[Editor's Note: The author will be presenting this case study at the *2017 PDA Annual Meeting* on Tuesday, April 4, at 10:45 a.m. in session "A2 — Advances in Analytical Sciences & Quality Control Strategies."**]**

Reference

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About the Author

Juan Torres, PhD, is Senior Vice-President of Global Quality for Biogen. In this capacity, he has worldwide responsibility over corporate quality, quality control and quality operations at all Biogen production sites.

2017 PDA/FDA Joint Regulatory Conference

PDA/FDA JRC to Explore Current FDA Thinking

David J. Cummings, US FDA, and Maria G. Jacobs, PhD, Pfizer

Each year, the *PDA/FDA Joint Regulatory Conference* provides a forum for the medical products industry to identify, discuss, and explore its unique challenges and opportunities. This conference addresses product quality, lifecycle management, innovation and regulatory developments for effectively delivering future medicines and innovative therapies.

Conference sessions engage regulators, their industry colleagues and other stakeholders in dialogue on topics of mutual interest. The meeting also explores how the US FDA regulates drugs, devices and biologics such that products can be moved to patients more quickly while also maintaining the gold standard for safety and effectiveness established by the Agency.

The 2017 conference will look at "Ensuring Product Quality in an Era of Innovative Therapies." This year, advanced therapies such as cell and gene therapies, including regulations and submission expectations, will be a topic of discussion, as will combination products. Both are timely subjects for attendees.

Modernization of regulations and advances for innovative initiatives, such as cancer research, regenerative medicine, and continuous drug manufacturing will also be examined. Likewise, efforts to encourage integration of patient perspectives into the decision-making processes for drugs and devices will also be highlighted.

Industry endeavors to monitor quality control systems and processes and drive continuous improvement in drug manufacturing will also be explored.

In addition, attendees can look forward to the usual set of updates from each of the medical product areas within FDA on program-specific initiatives. The newly launched regulatory track session, to be held on Day 2 of the conference, will allow attendees to hear presentations directly from the Agency's review staff regarding quality assurance and regulatory considerations for new drugs.

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MSOP and the Pursuit of Operational Excellence

Hal Baseman, ValSource

Operational excellence should be the goal of everyone in our industry. "Operational excellence" refers to reliable, error-free, efficient, cost-effective, productive, ever-improving, modern drug manufacturing. It is the cornerstone of quality processes and quality output. It is the essential business link between quality performance and reliable product quality. It should be inherent in the mission of every pharmaceutical company and organization. Its keys are manufacturing science, process understanding, technology implementation, risk-based thinking and decision-making, knowledge transfer, education/training and pragmatic operations.

Today's business and regulatory environment presents challenges to achieving and maintaining high levels of operational excellence. Meeting these challenges requires an understanding of where improvements can be made and the means to achieve them, communication of available new technologies and approaches, ROI models aligning with product lifecycle financial returns, and development of more streamlined processes for post-approval change approvals and a partnership between manufacturers, regulators, and suppliers. We each play an important part.

PDA has long been a leader in bringing parties together to discuss, understand and provide valuable information to meet our industry's manufacturing needs. This content includes technical reports, publications, articles, conferences, workshops, meetings and educational programs. From its first technical report on moist heat sterilization to its current slate of publications, meetings, and training courses covering a wide range of topics (e.g., process validation drug shortages, blow-fill-seal, etc.), PDA has played an essential role in developing and disseminating the information used by manufacturing professionals in the pharma industry to better understand and do their jobs effectively. In fact, it is hard to name any PDA offering that does not benefit pharmaceutical manufacturing.

In an effort to further support and communicate this most important segment of our business, PDA has initiated its new Manufacturing Science and Operations Program, or MSOP. A steering committee has been assembled to help guide its efforts to support manufacturing. The MSOP steering committee consists of senior manufacturing management and manufacturing science leaders from a broad section of our industry, including drug substance (small and large molecule), drug product, personalized medicine, cell therapy and other manufacturers.

The objective and charge of the MSOP Steering Committee is to use the group's collective knowledge to identify areas that PDA should be looking into that would help manufacturing, both in the science and the operations. The MSOP Steering Committee will recommend topics and actions to PDA's technical advisory boards, conference planning committees, and training/education instructors. This effort is designed to dynamically facilitate PDA's manufacturing and operational excellence efforts based on the demands of the industry.

We are looking for manufacturing individuals within our membership and industry to join PDA's efforts and continue to build on its legacy of advancing manufacturing excellence within the industry. MSOP Steering Committee Co-chair **Glenn Wright** and I invite you to participate and become actively involved in these efforts. If you are interested in making a difference in our industry, please contact us or contact the PDA membership and volunteer coordination teams.

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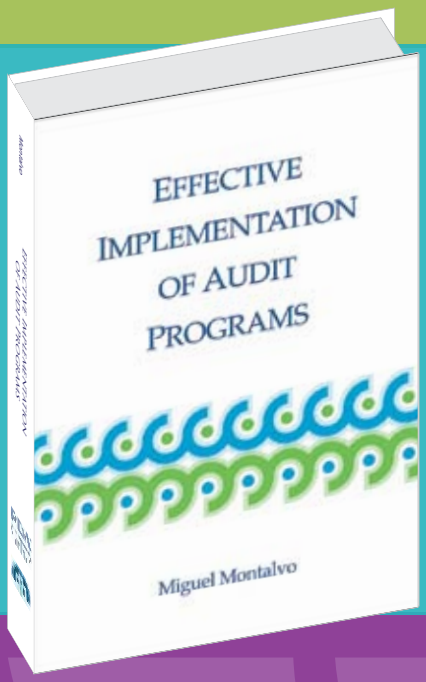

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ABOUT THE AUTHOR

Mr. Miguel Montalvo has more than 32 years of extensive experience in the areas of cGMP compliance, quality operations/systems and validation functions/responsibilities. He has been a frequent speaker/chairman/instructor at hundreds of compliance, validation and quality related conferences and courses around the world for such groups as PDA, PTi, CfPIE, IVT, Barnett International and the CTFA. Mr. Montalvo's articles and papers have been published in the *American Pharmaceutical Review* and the *Journal of Validation Technology*, and he has also authored chapters in recognized industry reference books.

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