People • Science • Regulation

PDA Letter

Volume LI • Issue 10 www.pda.org/pdaletter November/December 2015

Career Breaks

Paths to Reentry 34

PDA Bookstore New Release

Pre-order and Save 15% through November 15, 2015.
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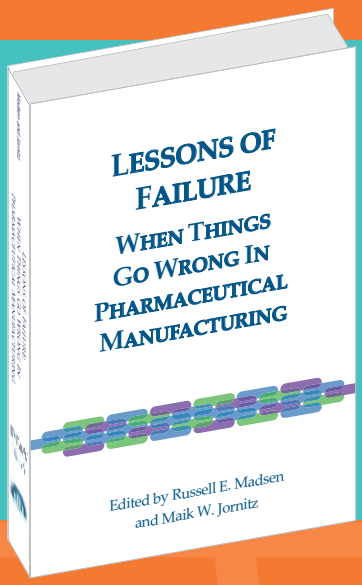

LESSONS OF FAILURE: WHEN THINGS GO WRONG IN PHARMACEUTICAL MANUFACTURING

EDITED BY: RUSSELL E. MADSEN AND MAIK W. JORNITZ
PDA MEMBER PRICE: ~~$210~~
PRE-ORDER PRICE: $178.50
ITEM NO. 17332

Robust analysis and investigation are essential tools to identifying the root cause of problems and to creating an effective corrective action for any complication in a manufacturing process. However, root cause analysis is often hindered when investigational teams wander down the wrong path or get stuck in the details. World renowned experts share their global work experiences to highlight root cause analysis and problem solving in *Lessons of Failure When Things Go Wrong in Pharmaceutical Manufacturing.* The stories are not only examples of what can go wrong, but also contain lessons learned – key points to take away and apply. For those who provide GMP and quality training, this book is a goldmine.

go.pda.org/lessons

ABOUT THE EDITORS

Russell E. Madsen, President, *The Williamsburg Group, LLC*, provides expert pharmaceutical consulting services including: CGMP compliance, quality systems, aseptic processing and sterilization, sterilizing filtration, design review, due diligence and regulatory liaison. He holds a Bachelor of Science degree from St. Lawrence University and a Master of Science degree from Rensselaer Polytechnic Institute.

Maik W. Jornitz, President, *G-Con Manufacturing, Inc.*, has close to 30 years of experience in separation and single-use technologies, related regulations and validation requirements. He supports the biopharmaceutical industry on a worldwide basis, has co-edited and -authored nine books, received five distinguished author awards and contributed to a total of 15 chapters in various technical books. Maik received his Master of Engineering in Bioengineering at the University of Applied Sciences in Hamburg, Germany and accomplished the PED program at IMD Business School in Lausanne, Switzerland.

The Parenteral Drug Association Presents...

2015 PDA/FDA Vaccines Conference

The New Vaccinology: Global Trends in Development, Manufacturing & Regulation

December 1-2, 2015 | Bethesda, MD

Bethesda North Marriott Hotel and Conference Center

Exhibition: December 1-2 | Courses: December 3-4

Focusing on Today's Challenges to Deliver Tomorrow's Vaccines

The *2015 PDA/FDA Vaccines Conference* will deliver a global perspective on the rapidly evolving vaccine industry. Come hear industry and regulatory experts address technical and regulatory challenges of development, showcase innovative manufacturing approaches and how they are being applied, and explore how to effectively deliver new vaccines to the global patient population.

NEW THIS YEAR! For the first time, PDA Europe will host the *2015 Europe Vaccines Conference* concurrently, December 1-2 in Berlin, Germany, and several presentations will be simulcast, in real time, between the two events. This brand new, unique format will give participants a truly global experience.

Hear from noted industry and regulatory speakers to include:

- **Arifa S. Khan, PhD,** Senior Investigator, CBER, *FDA*
- **Cliff Lane, MD,** Deputy Director, Clinical Research and Special Projects, NIAID, *NIH*
- **Michael T. Osterholm, PhD,** Professor, Environmental Health Sciences, CIDRAP, *University of Minnesota*
- **Edward Patten,** Associate Director, Manufacturing Science, CBER, *FDA*
- **Rino Rappuoli, PhD,** Chief Scientist, *GlaxoSmithKline Vaccines*
- **David Wood, PhD,** Coordinator, Quality Safety and Standards Team, Department of Immunization Vaccines and Biologicals, *World Health Organization*
- **Kathryn Zoon, PhD,** Chief, Cytokine Biology Section, Division of Intramural Research, NIAID, *NIH*

The worldwide demand for vaccines that prevent current and emerging infectious diseases is increasing — be part of the global discussion about emerging trends in vaccines development and manufacturing. **Learn more and register at pda.org/vaccines2015**

On December 3 and 4 at the Bethesda North Marriott Hotel and Conference Center, PDA Education will hold the *2015 Vaccines Course Series*. Learn the complexities and unique challenges of the vaccine field and effective methods for the manufacture of vaccines with the *Current Challenges in Vaccines* (Dec. 3) and *Modern Manufacturing and Trend Monitoring Techniques for Vaccines* courses (Dec. 4).

For more information and to register for the *2015 PDA Vaccines Course Series*, visit pda.org/vaccinescourses

#Vaccines2015

PDA Letter

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

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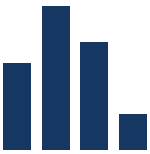


PDA Remembers Scott Sutton, Supporter for 20 Years

PDA was saddened to learn of the passing of **Dr. Scott Sutton** shortly before PDA's 10th annual microbiology conference—an event that he was heavily involved with as a member of the planning committee from 2009 to 2011 in addition to speaking on various panels.

Scott lended his expertise in industrial microbiology to PDA through his prolific writing, contributing a number of articles to the *PDA Letter,* the *PDA Journal of Pharmaceutical Science and Technology,* and books and chapters to the PDA/DHI collection of books. He served on the Technical Book Committee in 2013, and won the PDA Distinguished Editor/Author Award in 2007 for his work, *Pharmaceutical Quality Control Microbiology: A Guidebook to the Basics.*

Scott also served on the inaugural *PDA Letter* Editorial Committee in 2007, and remained an active member of that group until 2011. He also contributed to the microbial data deviations task force which is preparing a technical report and the task force for *PDA Technical Report No. 67: Exclusion of Objectionable Microorganisms from Nonsterile Pharmaceuticals, Medical Devices and Cosmetics.*

A memorial fund has been established in his name:www.gofundme.com/scott-sutton. His obituary can be found at https://shar.es/1u8jCz.

The *PDA Letter* Podcast Series

Listen to leading experts on LAL, CMOs, the future of manufacturing, new manufacturing technologies and more!

www.pda.org/pdaletter

In our Podcast Archive, you can listen to the following experts:

Dr. Jack Levin, co-discoverer of the groundbreaking LAL test

Lonza's Allen Burgenson

Vetter's Joachim del Boca

Amgen's Madhu Balachandran

Pfizer's Michael O'Brien on modular manufacturing

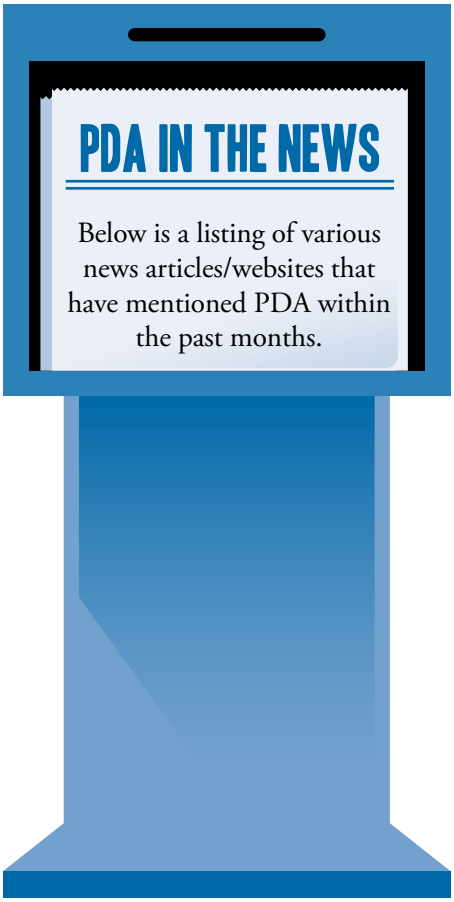
PDA Education Head Bob Dana to Retire; Craig Elliot Takes Helm

PDA's **Bob Dana,** Sr. VP, Education has announced that he will retire at the end of 2015. Bob has been a long-term contributor to PDA in many ways, starting as a member, volunteer, Board member, and, for the past ten years, as an employee—first as VP of Quality and Regulatory Affairs, and more recently as Sr. VP, Education. His commitment to PDA has been unwavering. Bob had over 30 years' experience with industry prior to joining the staff. PDA wishes Bob all the best as he transitions to this new phase of his life.

Craig Elliott, Sr. VP, Finance/CFO, will assume the Sr. Vice President, Education role at the beginning of 2016. Craig has been at PDA more than six years in the CFO capacity, and this new challenge will give Craig the opportunity to expand his contributions to our organization, and to utilize his background in pharmaceutical manufacturing in a new way. Craig has a Bachelor's degree in Microbiology and a Master's in Business Administration. Prior to his 6 years with PDA, his career also includes 5 years at Merck & Co. in the QC & QA functions and 5 years with Genentech supporting the Operations, Quality & Regulatory Affairs functions.

PDA is in the process of identifying a candidate for the Finance position

The Education activity is a key component of PDA's future strategy, and our commitment to continue to invest and expand this function is clear. Craig and Bob began working together on this transition in September. PDA looks forward to Craig's continued contributions to the organization in this new role.



American Pharmaceutical Review

July/August 2015

"A Fresh Look at USP <1223> *Validation of Alternative Microbiological Methods* and How the Revised Chapter Compares with PDA TR33 and the Proposed Revision to Ph. Eur. 5.16"

— Michael Miller

"Conducting Microbial Investigations"

— Jeanne Moldenhauer

Endotoxin Supplement

"LER Frequently Asked Questions"

— Karen Zink McCullough

"Endotoxin Detection Methods –Where are we now?"

— Kalavati Suvarna

"Bioburden Contamination Control: A Holistic Overview"

— Scott Sutton

BioPharm International

Aug. 1, 2015

"Selecting a Comprehensive Bioburden Reduction Plan"

— Randi Hernandez

tinyurl.com/nojmlj9

BioProcess International

June 16, 2015

"Challenges in Implementing Quality By Design: An Industry Perspective"

— Michael Torres

tinyurl.com/ppue3zm

Aug. 24, 2015

"New Approaches to Fill and Finish: A BPI Theater Roundtable at Interphex 2015"

— Cheryl Scott

tinyurl.com/pnjgkyy

The Economic Times

Aug. 9, 2015

"Questions on data integrity undermines framework of trust: Richard Johnson, PDA"

— Vikas Dandekar

tinyurl.com/qjec95k

European Pharmaceutical Review

September 3, 2015

"Rapid methods update: revisions to a United States Pharmacopeia chapter"

— Michael Miller

tinyurl.com/noyr5dc

GMP LOGFILE

July 23, 2015

"Risk Evaluation – more than just data and facts: An excerpt from the PDA/DHI publication *Risk Assessment and Risk Management in the Pharmaceutical Industry - Clear and Simple*"

— James L. Vesper

tinyurl.com/ok988em

The Hindu

Sept. 15, 2015

"Global Standards to be followed in drug inspections"

tinyurl.com/pt3fclw

IPQ Monthly Update

July/August 2015

"Culture and Process Capability Continue In Focus as FDA Releases Its Draft Quality Metrics Guidance"

Life Sciences Logistics

August 25, 2015

"Three primary cold chain packaging pain points and priorities"

— Kevin Lawler

tinyurl.com/p3oj8xq

Pharmaceutical Technology

August 2, 2015

"Import Testing of Pharmaceutical Products Has Limited Safety Benefits and Can Add Risk to Patients"

— Joerg H.O. Garbe, Karl Ennis, Guido M. Furer, Maria G. Jacobs and Stephan Rönninger

tinyurl.com/o8b7o5q

August 24, 2015

"Industry Responds to FDA Metrics Program"

—Jill Wechsler

tinyurl.com/p9g4abu

September 2, 2015

"Data Integrity: Getting Back to Basics"

— Richard M. Johnson

tinyurl.com/opajd68

September 15, 2015

"FDA Faces Controversy Over Quality Metrics and Biosimilars"

— Jill Wechsler

tinyurl.com/ngr6n82

The Pink Sheet Daily

September 29, 2015

"Updated: FDA Manufacturing Inspectors Could Be Further Divided Into Subspecialties"

— Derrick Gingery

September 30, 2015

"FDA Adding Managers, With Goal Of Quicker Inspection Reports"

— Derrick Gingery

Gain access to hundreds of key decision makers when you Sponsor and/or Exhibit at the *2016 PDA Annual Meeting*

Having a presence at this signature event will help you to introduce new products and services, expand your customer base and network with key decision makers. Take advantage of unopposed exhibit hours during extended refreshment breaks, lunches, and a networking reception – all held in the Exhibit Hall – allowing ample time for you to network with attendees and showcase your company's products and services.

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- Lanyards
- Final Program Advertising
- Hotel Keycards
- Fun Run/Walk
- Orientation Breakfast
- Cyber Cafe
- Refreshment Breaks
- Opening Night Reception
- And More

Stand out from the competition with unmatched visibility and branding when you exhibit and/or sponsor at the *2016 PDA Annual Meeting*. ***To learn more, please visit pda.org/2016annualmeeting or contact David Hall at + 1 (240) 688-4405 or hall@pda.org.***

The Parenteral Drug Association presents...

2016 PDA Annual Meeting

Achieving Manufacturing Excellence:
Current Trends and Future Technologies in Bioprocessing

March 14-16, 2016 | San Antonio, TX

JW Marriott San Antonio Hill Country Resort and Spa

Exhibition: March 14-15 | Post-Conference Workshop: March 16-17 | Courses: March 17-18

PDA®
Parenteral Drug Association

PDA Volunteer Spotlight

Anthony Warchut

- Vice President, Technical
- *PAREXEL Consulting*
- Member Since | 2002
- Current City | Manchester, Connecticut
- Originally From | Haverhill, Massachusetts

Nothing in our industry is static


Incorporating Data Integrity into Your Quality Management System

Anthony wrote an article for the April PDA Letter

Why did you choose to join PDA?

PDA provides me with information on the current hot topics in the pharmaceutical industry as well as opportunities to participate in task forces that work with the U.S. FDA in responding to prominent issues in the industry.

What are some of the volunteer activities you've done for PDA?

I've been a coauthor on Technical Report No. 54 as well as Annex 2 of TR-54. I have also enjoyed doing peer reviews of articles for publication by PDA.

What is something you gained from your PDA membership that you couldn't have gotten anywhere else?

Earlier this year, PDA released Part 1 of its *Points to Consider for Aseptic Processing,* which updates PDA's 2003 Points to Consider on the topic. This document is a great reference and I look forward to Part 2.

How can PDA benefit someone who is established in the pharmaceutical industry?

Both the industry and its associated regulatory expectations are constantly evolving. PDA helps keep pharmaceutical professionals knowledgeable on current topics so they don't have to learn lessons the hard way via regulatory action.

What about the industry keeps you up at night?

The fact that many companies lack a meaningful quality culture. This is evidenced by data integrity issues that are being found by regulatory agencies.

What is a trend you think more people should be talking about?

I see that companies are not adequately qualifying their vendors before contracting for services such as contract manufacturing, contract lab work, research, clinical logistics, IXRS, to name a few.

What would you tell someone who is just starting out in the industry?

Try a variety of jobs early in your career! Work in production, quality, regulatory and even at the FDA, if possible, so that later in your career you can draw from those experiences to solve the problems you will face.

Your Local PDA Connection

Are you curious about the issues unique to your region?

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

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

PDA Education in 2015: A Look Back. But Wait—There's More!

Bob Dana, PDA

It's early October as I sit down to write another year in review of PDA's Education activities. It's a beautiful fall day in my hometown of Liverpool, N.Y., just outside Syracuse, and it's been unseasonably warm so far this autumn, so the leaves haven't turned much yet. And, unfortunately, the Red Sox have managed to secure last place in the American League East for a second straight year. Still, I know that by the time you read this, unless centuries of weather patterns change, it will be cold and there will be plenty of snow on the ground—and hopefully the Giants will be in the thick of contention for the 2016 Super Bowl.

But enough of that. Let's talk about 2015. What kind of year was it for PDA Education? In a few words, it was a pretty good year (isn't that a song?). It was also a year marked by some significant changes for PDA Education.

Last year, our flagship "Aseptic Processing Training Program" experienced a first: we failed to sell out all five sessions. I was really puzzled. As I know you are aware, there is nothing we do in this industry that is more challenging than manufacturing sterile drug products using aseptic processing technology. We didn't understand why our courses weren't full. Was it an anomaly or the beginning of a trend? Well, I'm really happy to say that I misread my budget report. We, in fact, did sell out the four *scheduled* sessions. Because of the high demand, we set up an extra, or off-budget, session to accommodate students who missed out. It was that unscheduled session that came up a little short in attendance, but overall the course oversold for the year. So, here's a word to the wise—if this is a course you are interested in taking, register early before all the spots are taken. Sellouts are the norm and people wind up on a waiting list. Don't let that happen to you.

Most of our other courses were also well-attended in 2015. We trained well over 1200 students in more than 65 courses held at PDA's Training and Research Institute in Bethesda, Md. and off-site in conjunction with all of our U.S. conferences. More than 25 of these courses utilized PDA-owned material, generally derived from our technical reports. We also continued with our plan to better integrate U.S. and European training programs by working closely with European Senior Director for Training and Education **Falk Klar.**

We extended the tradition of offering training courses exclusively for U.S. FDA personnel. We conducted two programs on microbiology for FDA compliance and review staff and aseptic processing training and three courses to support FDA's API, preapproval inspection and sterile inspection training programs.

The Education Advisory Board, under the leadership of Chair **Edward Trappler** and Vice-Chair **Brent Watkins,** was instrumental in helping us chart a course intended to focus on our Education Strategic Plan. This Plan positions our education programs for the next five years. We made the transition from paper course notes to electronic notes, moving PDA into the 21st Century and saving money and trees.

To help strengthen our quality assurance program, we developed an instructor orientation program focused on instructional design, and provided it to our cadre of instructors. This program was extremely well received by both new and experienced instructors.

To provide an additional benefit to our students, the Accreditation Council for Pharmacy Education approved us for another six-year extension of our accreditation. This allows us to provide continuing education credits for pharmacists taking our courses. In addition, we received approval to provide continuing education credits for professional engineers from the states of New Jersey and North Carolina. These approvals speak to the quality of our education programs and provide a means for pharmacists and engineers to satisfy the continuing education requirements needed to maintain their professional licensure.

For the fourth consecutive year, we employed a summer intern. **Reid Nakashima**, a chemistry student at Azusa Pacific University in California, spent 13 weeks with us this summer learning about nonprofit organizations and was a great help with our "Aseptic Processing Training Program." **[Editor's Note:** Read Nakashima's account of his internship in the October issue, p.14.**]**

PDA TRI Comings and Goings in 2015

We were also excited to welcome **Stephanie Grinan** to PDA as our new receptionist and education administrative assistant. Stephanie is a fast learner, and we enjoy her excitement and enthusiasm for all things new. And, speaking of our staff, **Kim McIntire** who joined us in October 2014, took on a new role this year when she was named Assistant Manager of Laboratory Operations. She is now responsible for the labs and the maintenance and operation of all the equipment in them.

It was with mixed feelings that we said goodbye to **James Wamsley**, our Senior Manager of Laboratory Education in May. He left to take a position in the pharmaceutical industry. While we miss him, we wish him all the best. James continues to contribute as a PDA member and a volunteer on the Education Advisory Board.

So, as I inferred in the title to this article, there is more. After ten-and-a-half years

Continued at bottom of page 15

PDA ***Education*** *– Where Excellence Begins*

SAVE THE DATE for PDA's 2016 Courses

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

JANUARY 2016

GSA Schedule Contract GS-02F-113BA

Aseptic Processing Training Program – Session 1
Week 1: January 25 – 29
Week 2: February 22 – 26

FEBRUARY 2016

16-17

Fundamentals of an Environmental Monitoring Program
Bethesda, MD

18

Establishment of a Risk-Based Environmental Monitoring Program
Bethesda, MD

29 – MARCH 3

GMP Week
Bethesda, MD

- Biopharmaceutical Manufacturing under Regulatory Compliance: Process Strategies, CGMP Considerations and Facility Requirements
- Application of a Quality Systems Approach to Pharmaceutical CGMPs

MARCH 2016

17-18

2016 PDA Annual Meeting Course Series
San Antonio, TX

- Recommended Practices for Manual Aseptic Processes
- Establishment of a Risk-Based Environmental Monitoring Program
- Quality Metrics: Performance Indicators
- Process Validation and Verification: A Lifecycle Approach
- Process Simulation Testing for Aseptically Filled Products
- Clean Room Design, Contamination Control and Environmental Monitoring for Controlled Environments

29-31

GSA Schedule Contract GS-02F-113BA

Risk-Based Qualification of Sterile Drug Product Manufacturing Systems
Bethesda, MD

APRIL 2016

GSA Schedule Contract GS-02F-113BA

Aseptic Processing Training Program – Session 2
Week 1: April 4 – 8
Week 2: May 2 – 6

19-21

GSA Schedule Contract GS-02F-113BA

Validation of Biotechnology-related Cleaning Processes
Bethesda, MD

21

GMPs for Manufacturers of Sterile and/or Biotechnology Products
San Diego, CA

MAY 2016

9-12

GSA Schedule Contract GS-02F-113BA

Lyophilization Week
Bethesda, MD

- Fundamentals of Lyophilization
- Validation of Lyophilization

16-17

GSA Schedule Contract GS-02F-113BA

An Introduction to Visual Inspection
Bethesda, MD

24-26

Management of Aseptic Processing
Bethesda, MD

JUNE 2016

GSA Schedule Contract GS-02F-113BA

Aseptic Processing Training Program – Session 3
Week 1: June 6 – 10
Week 2: June 27 – July 1

15-16

GSA Schedule Contract GS-02F-113BA

Fundamentals of Cleaning and Disinfectant Programs for Aseptic Manufacturing Facilities
Bethesda, MD

22

Biosimilar CMC and Regulatory Challenges – ***New Course***
Chicago, IL

Denotes Laboratory Course

GSA Schedule Contract GS-02F-113BA Denotes GSA Schedule Contract

chapter update

Students "Meet the Professionals" at Chapter Event

Renee Morley, STERIS Corporation, President-Elect, PDA Southeast Chapter

This year, the Southeast Chapter of PDA, held its "Meet the Professionals" event with over 100 attendees Sept. 30 at North Carolina State University's Biomanufacturing Training and Education Center in Raleigh, N.C. This yearly event provides an opportunity for the chapter to introduce students interested in our industry to professionals from different companies who offer views of what the "real world" is like and discuss their experiences in the industry, along with words of wisdom. The students that attend are either in their undergraduate, graduate or certificate coursework and are involved with the chapter's student chapter.

This year's speakers represented different disciplines, however, all shared a common theme on getting involved as early as possible in groups like PDA, the importance of networking and working hard. At the end of the event, the Chapter held a networking session that allowed students ask questions and speak to the professionals one-on-one. ➤

PDA Who's Who

Chelsea Boudreau, Hospira, a Pfizer Company

Alec Butler, Hospira, a Pfizer Company

Jody Council, Novartis

Dave Dumers, Medicago

Dave Henry, Medicago

Amber Johnson, Hospira, a Pfizer Company

Jessamyn Ren, SpecLine Consulting

David Smith, Biogen

We were very lucky this year as we were able to have an abundant amount of speakers ranging from 20 years in the industry to just six months. The following people who participated should be commended for their passion for their respective companies **David Smith, Dave Henry, Dave Dumers, Jody Council, Jessamyn Ren, Chelsea Boudreau, Alec Butler** and **Amber Johnson.**

Thank you to all who attended and helped to make the event a success.

PDA Education in 2015: A Look Back. But Wait—There's More! *continued from page 12*

on the PDA staff, as Quality and Science Advisor, Vice President of Quality and Regulatory Affairs—and since 2007—Vice President and Senior Vice President of Education, I have decided to retire at the end of 2015.

In March 2005, I agreed to join PDA at the request of then PDA President **Neal Koller** for, as he put it, "a few weeks until I can find someone permanent to do the job." Somehow, a few weeks morphed into a decade; and a great one it has been. I have truly enjoyed the various roles I played at PDA and have benefited greatly from all the people I have met and the friendships I have made.

I just completed 30 years as a PDA member and I can truly say this organization and its members are the best in the industry. We accomplished a great deal together and I am proud of all of it.

Of course, none of it would have been possible without the people I have worked with. I owe them all a giant-sized thank you. It's impossible for me to single out each one by name, but I would especially like to recognize the tremendous support I have received from my current staff—**Stephanie Grinan, Stephanie Ko** and **Kim McIntire**, as well as special assistant **Bethanne Bond.** Current PDA Sr. VP/CFO **Craig Elliott** will assume the responsibility for PDA's Education programs going forward and I ask that you provide him the same support you have provided me and join me in wishing him great success in his new assignment.

I intend to remain active with PDA as a member volunteer and hope to see many of you at a future PDA event soon.

Finally, as I do every year, I want to thank all of our students and instructors who participated in PDA courses in 2015. Without you, there would be no PDA Education programs.

On behalf of my staff, I wish you all a safe, happy, healthy and prosperous 2016.

2015 PDA/FDA Joint Regulatory Conference

Plenary Sessions

P1: Innovative Manufacturing and Regulatory Solutions for Patient Care in a Crisis

(l-r) Joseph Woodring, DO; Richard Johnson, PDA; Luciana Borio, U.S. U.S. FDA; Monica Caphart, U.S. FDA; PDA Chair Harold Baseman, ValSource

P2: Regulatory Submissions Update

(l-r) William Maisel, MD, CDRH, U.S. FDA; Christopher Joneckis, PhD, CBER; Ann Marie Montemurro, ORA; Laurie Norwood; CBER; Dennis Bensley, Jr., PhD, CVM; Lawrence Yu, PhD, CDER

P3: Data Integrity

(l-r) Carmelo Rosa, U.S. FDA; Joyce Bloomfield; Rebeca Rodriguez, U.S. FDA; Douglas Stearn, U.S. FDA; Monica Cahilly, Green Mountain Quality Assurance;

P5: Program Realignment and Reorganization of ORA and CDER

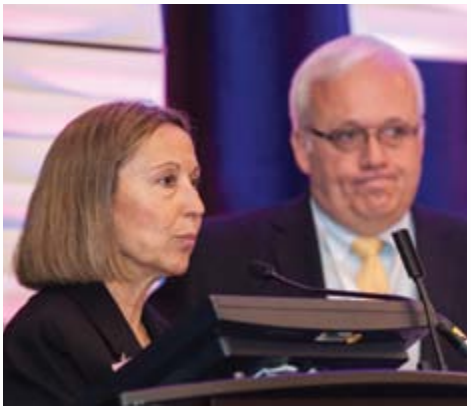
(l-r) Janet Woodcock, MD, CDER; Susan Schniepp, Regulatory Compliance Associates; Melinda Plaisier, ORA

P6: Compliance Update

(l-r) Alicia Mozzachio, CDER, U.S. FDA; Martine Hartogensis, CVM; Cynthia Schnedar, CDER; Mary Anne Malarkey, CBER; William Macfarland, CDRH; Douglas Stearn, ORA

A1: Change Management Q12 Discussion
(l-r) Chris Watts, PhD, VolPal; Rick Friedman, U.S. FDA; Ashley Boam, U.S. FDA; John Ayres, MD, Eli Lilly and Company

B1: Effective Corporate Auditing Program
(l-r) Susan Schniepp, Regulatory Compliance Associates; Shane Ernst, Hospira; Zena Kaufman, ZGK Quality Consulting; Scott Gunther, Catalent Pharma Solutions; Jessica Walker, Afton Scientific



C1: Supply Chain
(l-r) Steven Wolfgang, FDA; Maria Jacobs, PhD, Pfizer; David Schoneker, IPEC-Americas

B2: International Efforts
(l-r) Douglas Campbell, Interpro QRA; Anabela Marcal, EMA

A2: Quality Systems
(l-r) James Morris, NSF Health Sciences; Rick Friedman, U.S. FDA; David Jaworski, U.S. FDA; Robert McElwain, U.S. FDA; Mai Huynh, U.S. FDA; Scott MacIntire, U.S. FDA

2015 PDA/FDA Joint Regulatory Conference

Breakout Sessions

A3: USP

(l-r) John Ayres, MD, Eli Lilly and Company; Pallavi Nithyanandan, PhD, U.S. FDA; Desmond Hunt, PhD, USP; Donald Klein, PhD, U.S. FDA; Laura Huffman, U.S. FDA

C4: Continuous Manufacturing/PAT

(l-r) Maria Jacobs, PhD, Pfizer; Phillip Nixon, PhD, Pfizer; Celia Cruz, PhD, U.S. FDA; Tara Bizjak, U.S. FDA

B3: Environmental Issues for Regulated Biologic Products

(l-r) David Cummings, U.S. FDA; Patricia Foley, PhD, USDA; Pamela Resch, Vical; Michael Havert, PhD, U.S. FDA

C2: CMOs

(l-r) Susan Schniepp, Regulatory Compliance Associates; Rebeca Rodriguez, U.S. FDA; Milind Ganjawala, U.S. FDA; Qiao Bobo, PhD, U.S. FDA; Gil Roth, Pharma & Biopharma Outsourcing Association

C5: User Fees

(l-r) Shane Killian, J&J; Ted Sherwood, U.S. FDA; Marcie McClintic-Coates, Mylan

C3: Regulatory Trends

(l-r) Alicia Mozzachio, CDER, U.S. FDA; Debra Pagano, DLP U.S. FDA Consultants; Thomas Cosgrove, U.S. FDA; Maridalia Torres Irizarry, U.S. FDA; Uduak Inokon, PharmD, U.S. FDA

A5: U.S. FDA/EPA Compliance Environmental Impact
(l-r) Betsy Behl, EPA; Holly Zahner, PhD, U.S. FDA; Raanan Bloom, PhD, U.S. FDA

B5: Innovation
(l-r) Renee Kyro, AbbVie; Sarah Pope Miksinski, U.S. FDA; Mahesh Ramanadham, U.S. FDA; Susan Berlam, Pfizer

2015 PDA/FDA Joint Regulatory Conference

Passport Drawing

Vijaya Rangavajhula received an iPad Mini from CAI

Abasha Williams walked away with a Bluetooth speaker from Hyde

Hyde presented a Fitbit to Roya Ravanbakhsh

PDA TRI presented an Apple Watch to Audrey Jia

Aptar gave Jennifer Goodman a French wine

PDA presented Joanne Izyk with a $100 American Express gift card

Masa Layer recieved a $100 Amazon gift card from Novatek

Complya presented Alamelu Ramesh with a $100 Visa gift card


NOVATEK


Automate, Analyze
Your Quality
SmartSolve

snapshot

LER: The Challenge of Meeting Regulatory Expectations

Josh Eaton, PDA

Low endotoxin recovery (LER) has been widely observed in certain biologic drug substance and drug product matrices when samples are tested using the USP <85> *Bacterial Endotoxins Test*. The underlying mechanism of the LER phenomenon is poorly understood, however, and inconsistencies in study designs across the biopharmaceutical industry are resulting in confounding and, sometimes, contradictory data. Based on recent regulatory communications and presentations by the U.S. FDA ***(1,2),*** it is evident that LER is of significant safety concern. As a result, FDA has outlined specific expectations for the Biologics License Application (BLA) with regard to endotoxin control and testing. But an issue remains—the lack of standardized procedures for endotoxin recovery studies. This represents a significant technical challenge for meeting regulatory expectations throughout the biopharmaceutical industry.

Clearly, there is an urgent need for the entire industry to work together and develop a strategy to resolve the LER problem as quickly as possible. Because of its longstanding and close working relationship with both FDA and the biopharmaceutical industry, PDA is uniquely positioned to take the leading role in addressing the pressing concerns about LER. As a first step, a PDA task force has developed a survey for the industry regarding LER hold studies. The intent is to gather data on current hold study practices in order to gain a clearer picture of the true state of LER testing currently conducted in order to comply with FDA expectations. From the submitted responses, the team will attempt to draft a points-to-consider document containing best practices that would serve as a reference when designing and conducting LER hold studies. The rationale behind the effort is that standardizing the testing practices will aid the industry overall in presenting cohesive data that may point to further elucidation of the LER phenomenon.

Further information about the activities of the task force will appear in upcoming issues of the *PDA Letter*.

Reference

1. Guidance for Industry Pyrogen and Endoxtoxins Testing: Questions and Answers, U.S. Food and Drug Administration, June 2012 www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm310098.pdf
2. Hughes-Troost, P. "Endotoxin – A FDA Perspective." Presented at the PDA 10th Annual Global Conference on Pharmaceutical Microbiology, Bethesda, MD, October 2015.

Journal *Preview*

Leachables, Glass Delamination Filters, and More

Container issues and manufacturing component selection are the topics of three research articles in the November/December edition of the *PDA Journal of Pharmaceutical Science and Technology.* Learn about the use of vial adapters for filtering glass delamination particles. Find out how a risk evaluation matrix can be used in the process of selecting plastic production components. Take a look at a low leachable container system with a polymer-based syringe.

Letter to the Editor

Oliver Stauffer, "Letter to the Editor"

Research

Elinor H. Zarour-Shalev, et al., "Filtration of Glass Delamination Particles with West Pharmaceutical Vial Adapters"

Dennis Jenke, "Development and Justification of a Risk Evaluation Matrix To Guide Chemical Testing Necessary To Select and Qualify Plastic Components Used in Production Systems for Pharmaceutical Products"

Hideaki Kiminami, et al., "Low leachable container system consisted of a polymer-based syringe with chlorinated isoprene isobutene rubber plunger stopper"

Harry Yang, Jianchun Zhang, "A Generalized Pivotal Quantity Approach to Analytical Method Validation Based on Total Error"

Technology/Application

Marla Phillips, Vishal Kashyap, Mee-Shew Cheung, "Increasing Product Confidence—Shifting Paradigms"

Raphael Bar, "Charting and Evaluation of Environmental Microbial Monitoring Data"

Case Study

Nader Shafiei, Regis De Montardy, Edwin Rivera-Martinez, "Data Integrity—A Study of Current Regulatory Thinking and Action"

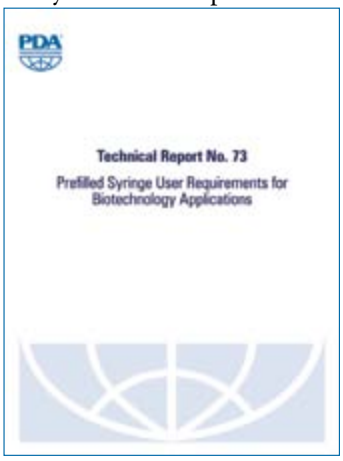
snapshot

Task Force *Corner*

TR Offers Guide for Prefilled Syringe Development

As healthcare costs increase year after year, it is more important than ever to find ways of providing that care in the most cost-effective manner. One way of lowering costs is to administer medications to the patient in a home environment rather than a clinical setting **[Editor's Note:** For more on self-care, see the story on p. 17 of the October issue**].** This has been done for many biotechnology drugs by providing them in prefilled syringes. Developing a prefilled syringe drug product, however, is not a trivial endeavor. To assist in this effort, PDA has developed a new technical report, *Technical Report No. 73: Prefilled Syringe User Requirements for Biotechnology Applications.*

The technical report was developed by a team of experts drawn from the PDA membership, and included representatives from biotechnology companies, contract manufacturers, contract testing labs, component suppliers and the U.S. FDA. The overarching goal of the task force was to provide a comprehensive discourse of user requirements for successfully developing and prefilled syringe drug product.



The task force started work in 2012, led by **Ronald Forster,** PhD, Executive Director, Device Technologies, Amgen, and kicked off with a face-to-face meeting at the PDA headquarters where subteams were formed around the topics listed in the table of contents. After that, the writing began. Subsequent meetings involved review and discussion of the draft sections, providing opportunity for robust discussions and input from the many experts on the task force.

The topics covered in the technical report include a comprehensive discussion of the information that would be required to successfully develop a prefilled syringe drug product. These requirements include: regulatory considerations, human factors studies, extractables and leachables, glass barrel geometry, elastomers, needle considerations, container closure integrity, and compatibility, to name a few.

This technical report is available for purchase through the PDA Bookstore at www.pda.org/bookstore. In addition, PDA members can download it for free for 60 days.

Case Studies in Bioburden Testing

Bioburden control remains a pressing topic for our industry. Sessions at the recent PDA 10th Annual Global Conference on Pharmaceutical Microbiology *featured presentations on it as well. For this reason, the* PDA Letter *editors reached out to three of the exhibitors at the meeting for short case studies on bioburden control utilizing data from their own solutions and products.*

A Rapid Method for Bioburden Testing of Disinfectant Samples

Shari Spector, EMD Millipore

Disinfectants can be classified for cleaning surfaces in pharmaceutical production and testing environments or for cleaning in hospital environments to prevent hospital-associated infections. Whichever the intended application, they must be tested for bioburden to ensure that they are not adding to potential surface contamination. These products are difficult to test, however, because by their very nature, disinfectants inhibit microbial growth.

The goal in this case study was to develop a rapid bioburden method for the testing of six different detergents using Milliflex® Quantum. Sample preparation is based on membrane filtration, and rapid results are achieved using a fluorescent viability stain that enables the detection of microcolonies in approximately one-third the time of traditional methods. The stain is nondestructive, so with re-incubation it is still possible to isolate colonies for microbial identification. In this study, the detergent products were evaluated first for filterability, then for recovery and

Continued at bottom of page 28

Evaluation of Amplified-ATP Bioluminescence and Compendial Plate Count Methods

Jeremy Robertson, Charles River Microbial Solutions

Rapid microbial detection methods save manufacturing companies millions by reducing production cycle times and getting product to market quickly. Amplified-ATP bioluminescence (ATP+) provides results in 24 hours while maintaining the accuracy, precision, specificity and sensitivity needed to detect organisms in the rare event of a contamination.

The equivalence of Amplified-ATP bioluminescence (ATP+) and the compendial plate count method was evaluated by comparing positive and negative results obtained from samples of a betamethasone suspension in broth inoculated with a target CFU of 0.1, 1.0 and 10.0. Accuracy, precision, specificity

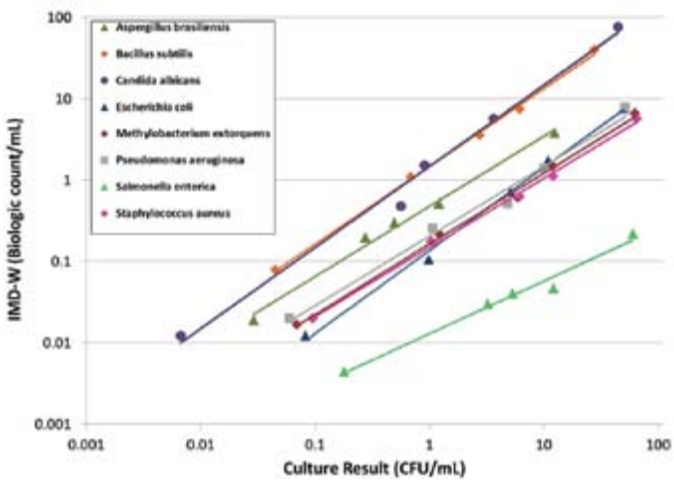
Continued at middle of page 29

Industry Need for Rapid Bioburden Detection

Aric Meares, BioVigilant –a division of Azbil North America, Inc.

Current regulations require manufacturers to monitoring bioburden levels in pharmaceutical grade waters, resulting in testing that is typically performed intermittently with retrospective results. This creates a need for tools that can rapidly and continuously analyze bioburden. An industry workgroup comprised of members from some of pharma's household names, including Amgen, Baxter, Pfizer and others ***(1),*** recongized this need, and produced a user requirements specification for instrumentation fit for that purpose. One of the cited end goals for such instrumentation is to provide an online, early warning indicator that could work alongside compendial methods to drive a greater degree of process understanding and quality assurance, while improving costs.

Figure 1 IMD-W™ Correlation to CFU Culture Counting Method



A capable technology for the instantaneous detection of bioburden in UPW and WFI water applies the principles of laser induced fluorescence. This technology utilizes light at a certain wavelength, in this case 405nm, to excite particles in water and produce a fluorescence emission when a biologic particle is encountered. When used in concert with a set of complex software algorithms, non-

Continued at bottom right of page 32

Hit the Sandbox to Achieve Product Development Success

Stephen Fournier, NNE Pharmaplan

A solid plan for any drug delivery program for a combination product helps bring together all the necessary requirements including devices, primary packaging and aseptic processing. This plan is often referred to as the Target Product Profile (TPP). The TPP should enumerate all the goals and assumptions for a drug delivery combination product, and it should be done prior to design. Since this plan contains relevant commercial considerations, it is a very important strategic alignment document.

With the TPP, you can then make more informed assessments of product options. After all, as **Figure 1** shows, significant investment in the early phases of development ("frontloading" or "front-end loading") impacts cost and quality.

Sandboxing: A Risk-Mitigated Approach

A robust drug delivery program has three parts: **1)** primary container, **2)** medical device, and **3)** aseptic processing. Making sure that these three parts converge is key. An effective way to gain agility and ensure that future drug delivery needs are addressed during the early-yet-important phases of development is to adopt a Sandboxing methodology **(Figure 2).**

Sandboxing refers to a method of comparing ideas and concepts for a product through the development of multiple designs in parallel. This innovative approach allows companies to spend more time differentiating the product in the marketplace, analyzing future trends, learning from past experiences, reviewing complaints and reports, evaluating user preferences and matching formulation changes in early phases of combination product developments. Another significant benefit from using this methodology is that prevents problems being pushed to the next development phase. But chiefly it allows time for screening multiple designs in parallel with operations and user needs to stay ahead of constant market pressures.

In many regards, this approach is akin to designing from the inside out: The drug company develops building blocks such as the primary container and then drives mechanisms for actuation. The key is to conceptualize multiple options, so that a couple of leading choices (or even an optimal choice) emerge for further development. For example, when developing a new primary container, evaluating multiple rubber compounds not only for drug compatibility, but also for friction and sealing properties provides a better product understanding for how the entire mechanism of an autoinjector or pump needs to function.

Furthermore, a major benefit of this approach is being able to prototype, test, challenge, and evolve concepts facilitating product understanding. This product understanding helps the pharma or biotech company know what is important to the functionality of a combination product. Therefore, when decisions need to be made about what to outsource or in-source, the criticality of various processes is already fairly well understood. Even if the drug company's desired plan is to outsource all production, the drug company understands what is central and can then conduct the process more effectively.

Multiple Ideas Lead to Multiple IPs

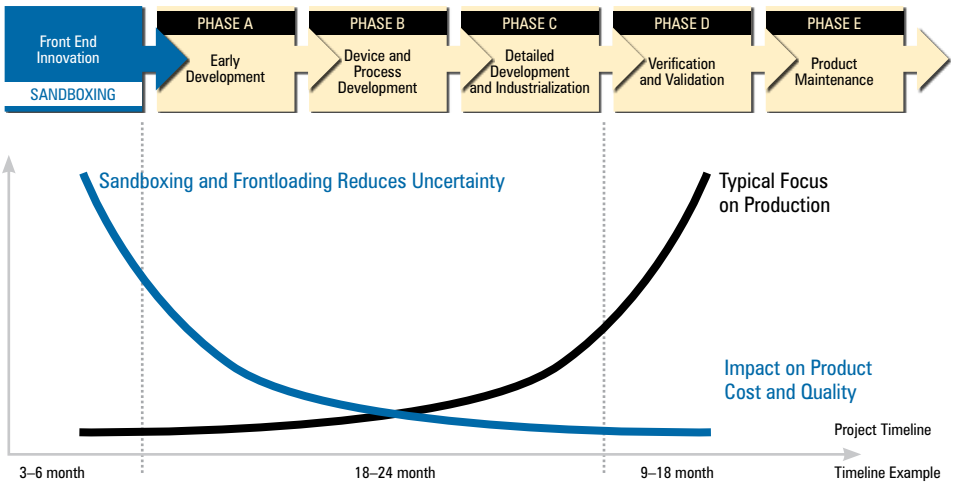
By evaluating multiple concepts during the Sandboxing phase, drug companies can also be developing potential intellectual property (IP) from multiple ideas. This IP can then be used to help secure operations in an increasingly competitive environment. Also, by having IP for various concepts, drug companies help to provide themselves with a greater IP portfolio to draw upon for future business considerations.

And if using partners, it is essential that a pharma or biotech company retain IP that results out of any contractual arrangement. Otherwise, any differentiation may be lost or undermined.

It is important that developers conduct challenge exercises via preference studies early on to determine what users want. These studies will also provide further design considerations. But developers should not limit product challenge exercises just to users; key stakeholders should also be involved because as the concepts evolve seemingly benign design changes can have drastic effects on manufactured costs. For example, will the design create issues with automated manufacturing

Continued on page 33

Figure 1 Front end loading impacts product cost, quality and reduces uncertainty



Closed System Filling Technology: A New Paradigm

James Agalloco, Agalloco & Associates, John L. Quick, Quick & Associates Inc., Leonard Mestrandrea, PhD, Mestrandrea Consulting, Inc. and David Hussong, PhD, ValSource

"Closed system filling" is a new set of processing controls appropriate for a sterile filling process that eliminates potential microbiological contamination from environmental and operator sources through the use of closed systems. This is an automated sterile connector technology by which presterilized closed containers are filled through an engineered and controlled passage enabling the filled product, the internal container and the closure system surfaces to avoid exposure to the background environment. When using this manufacturing technology, the sterile solution remains within a sterile fluid path at all times.

A Need for Rapid Technological Advancement

Aseptic processing has been used for decades to produce various sterile products. The technology has advanced greatly from its origins when an operator would add solutions to a sterile vial using a manual pipette in an unclassified environment.

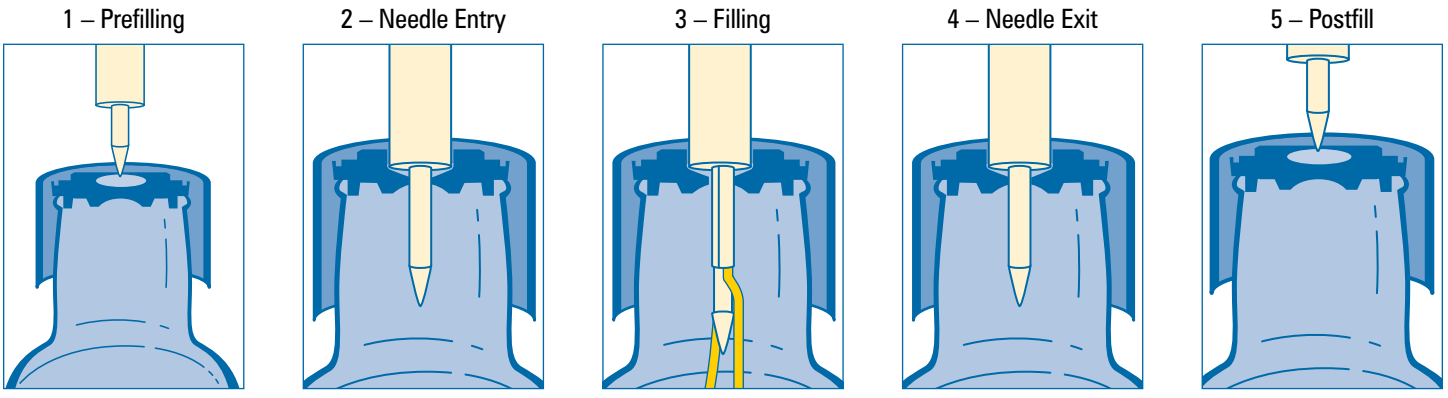
In 1973, the World Health Organization "standard" for aseptic filling included the observation that microbiological contamination rates for vaccines should not exceed 0.3% ***(1).*** This is the earliest reference to media fill capabilities. Technology certainly has enhanced our expectations since that time. Robotic filling equipment has replaced manual filling, and cleanrooms have become highly advanced to protect in-process components from environmental contamination. Self-contained filling machines, such as blow-fill-seal technology, have been developed and implemented. Environmental control technologies, e.g., isolators and restricted access barrier systems, have permitted advances in the controls used in aseptic filling, offering greater confidence in product quality, particularly in the microbiological attribute of sterility. Common to all of these technologies, however, is that sterilized components are exposed to the environment, resulting in potential risks for nonsterility.

Historically, these advances in aseptic processing technologies occurred incrementally as subsets of the processes involved achieved breakthrough discoveries. Many of these new technologies took long periods of time to be accepted.

As noted by **Russell Madsen,** advanced technologies used in aseptic processing go through lifecycles that can be described as "S-curves" where the technology is discovered, matures, gains acceptance, undergoes refinements and then may be replaced ***(2).*** Further, Madsen pointed out that standards applied to the old technology may remain in place as a legacy notwithstanding that the new technology does not benefit from the old paradigm. As an example, he cited "…the perceived need in unmanned isolators for unidirectional airflow at 90 ft/min and a minimum of 20 air changes/h." This expectation is not implied in any regulation but has been widely adopted due to over caution.

For this reason, he expressed that the industry and regulators should periodically reexamine well-established practices. We agree with his position that past practices should be revisited when new technologies make them unnecessary.

Figure 1 Closed System Filling Process Sequence



1. Closed container and needle ready to fill (both radiation sterilized)
2. Container penetrated by closed needle
3. Needle opens inside container, dispenses liquid, needle closes inside container
4. Closed needle exits container, container opening recloses
5. Closed container externally resealed, closed needle ready for next container

In the case of closed filling technology, we assert there is no benefit to the use of a classified environment for closed system filling technology.

According to a 2012 article in *Pharmaceutical Engineering* ***(3),*** controlled nonclassified (CNC) manufacturing environments are the next generation for pharmaceutical manufacturing, and CNC is well suited to closed system filling.

To describe this new technology, we have presented its attributes in the form of an appendix, analogous to those in the U.S. FDA *Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice* ***(4).***

We offer this as a potential Appendix 4 to that document.

APPENDIX 4: CLOSED SYSTEM FILLING TECHNOLOGY

Closed system filling technology is an automated sterile connector technology by which presterilized closed containers are filled through an engineered and controlled passage enabling the filled product, the internal container and the closure system surfaces to avoid exposure to the background environment. When using this manufacturing technology, the sterile solution remains within a sterile fluid path at all times.

This manufacturing technology eliminates direct human intervention with sterile surfaces and can be used for the filling and packaging of ophthalmics, respiratory care products, injectables, liquid media and other sterile products.

Closed system filling technology is also unique in that there is no human intervention with exposed product or container internal surfaces, and no opportunities to bypass the safeguards engineered into the sterile connection processes. It is also unique in that it does not need a "sterile air" shower, as there are no exposed sterile product contact surfaces, hence, a classified environment is not required. All components including filling components are assembled and closed prior to sterilization. Sterility of the filled product is dependent only upon a validated connection process.

Because the sterile transfer capabilities of closed system technology are independent of the environmental conditions and performed without personnel intervention of exposed sterile items, there is no requirement for the environmental monitoring controls typically required for any conventional or even advanced aseptic filling and sealing technologies.

This appendix discusses some of the critical control points of this technology.

Equipment Design and Container Systems

Closed system technology typically relies upon the following steps:

The closed system filling technology uses engineered connector technology by which presterilized closed containers are filled through an automated sterile connector technology in which there is no human intervention or environmental exposure to product contact surfaces. All closed system filling technology systems conform to the following:

- Sterilization of sealed containers with specifically designed closure to accept a sterile transfer connector
- Validated sterile closed connector system for all connections
- HEPA filtered air may be provided immediately above the filling area as a precautionary measure, although HEPA air is not a requirement to validate closed system filling technology
- No external air and/or gasses (sterile or nonsterile) will come in contact with the internal product contact surfaces of the sterilized container and connector system at any time during the process
- No human manipulation of the sterilized container during filling through the sterile connector system
- Following the sterile connection and filling through the sterile connector system, provision is made to ensure that no further entry through the sterile filling connection can be made
- The permanent closure process must be validated (21 CFR 211.160(b))

Container Configuration and Transfer Port

Closed System/Sterile Connector Systems will employ the following:

- Sterilization of the entire system, including container/closure and all product contact surfaces in the closed systems, must be validated
- The container closure system, including the sterile connection component and other ports, will have been validated through a standardized and/or validated microbial ingress process
- The integrity of the filled container closure system must have been validated throughout the shelf life for sterility maintenance (21 CFR 211.166)

Validation/Qualification

Closed system technology must be validated to establish the ability to effect transfers in a nonclassified environment (21 CFR 211.113(b)). Media fills, material controls, product-plastic compatibility, container resealing integrity, and unit weight variation are among the key issues to address in validation and qualification studies.

Controlled Nonclassified Environment (CNC):

With the process is performed as described above, there is no requirement for a classified environment and/or environmental monitoring due to the technology. The following would be the specifications for a CNC environment in which the filling equipment is located:

- Controlled by lock-in and lockout devices to prevent unauthorized access
- HEPA filtered air but not classified
- Pressure differential to outside rooms is specified, monitored and measured
- Gowning in accordance to a Class 8 environment although the actual environment would be CNC
- Applicable cGMP training for all operators involved in the upstream and downstream processes would be required. Specific aseptic filling training relevant for aseptic filling is no longer critical with the closed sterile transfer technology
- Full documentation applicable to cGMP and release procedures

References

1. WHO Expert Committee on Biological Standardization – Twenty-fifth Report. *World Health Organization Technical Report Series No. 530.* World Health Organization: 1973
2. Madsen, R., "The Future of Aseptic Processing", *Pharmaceutical Technology* 27 (supplement) (2003): 41-42.
3. Witcher, M.F., and Odum, J, "Biopharmaceutical Manufacturing in the Twenty-First Century – The Next Generation Manufacturing Facility", *Pharmaceutical Engineering* 32 (2012): 1-8.
4. FDA Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice, U.S. Food and Drug Administration, 2004 www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm070342.pdf

About the Authors

James Agalloco is President of Agalloco & Associates, a consulting firm to the pharmaceutical and biotechnology industry. Previously, he was employed at Bristol-Myers Squibb, Pfizer and Merck, and has also served as a past PDA President and Director.

Leonard Mestrandrea is a pharmaceutical consultant with experience in industry, government and academia. In addition to nine years of experience as Chief Microbiologist within FDA, he has more than 35 years of experience in the pharmaceutical industry.

John L. Quick is currently a consultant to the pharmaceutical industry having established Quick & Associates, Inc. in 2003. Prior to that, he spent 37 years with Baxter International. For his last few years at Baxter, Quick was the Corporate Vice President for Quality and Regulatory.

David Hussong is a Senior Consultant with ValSource, LLC. He retired from the Commissioned Corps. of the U.S. Public Health Service after 30 years with the FDA. While at FDA, he served four years in CBER, and 26 years in CDER's microbiology review program.

A Rapid Method for Bioburden Testing of Disinfectant Samples continued from page 24

time to result with *Staphylococcus aureus*, *Aspergillus brasiliensis*, *Candida albicans*, *Bacillus subtilis* and *Pseudomonas aeruginosa* recovered on tryptic soy agar (TSA) incubated at 32.5 ± 2.5 °C.

Often the best way to overcome inhibition is through the development of an appropriate rinse protocol. The three rinse fluids described in USP <71> *Sterility Tests* can also be used in bioburden testing. The simplest rinse solution, fluid A, is a neutral peptone solution. When product sticks to the membrane, however, it may be necessary to use a surface active agent such as polysorbate 80 for effective rinsing. Fluid D has the same composition as fluid A, supplemented with 0.1% (v/v) polysorbate 80. The strongest rinse solution described is fluid K, which contains beef extract and 1% (w/v) polysorbate 80. Beef extract can inhibit recovery, so when fluid K is used it should always be followed by a final rinse with fluid A, PBS or sterile saline. USP <61> *Microbial Examination of Non-Sterile Products: Microbial Enumeration Tests* also mentions the use of polysorbate 80 to improve filterability. As a result, the <71> rinse fluids are also often used as diluents to improve filterability of samples.

Various combinations of prewetting solutions, diluents and rinses were tested. Fluid D was shown to improve filterability through 0.45 µm mixed cellulose ester (MCE) membrane and to eliminate the inhibitory effects of the detergents. In the final protocol, the membrane was prewet with 50 mL of fluid D, 1 mL of product was added to 250 mL of fluid D, the membrane was rinsed with 250 mL sterile saline (0.85%). Testing 1 mL of sample is adequate given that tightest product specification in this set was ≤100 cfu/mL. An incubation time of 27 hours was sufficient for the recovery all of the organisms including *Aspergillus brasilien-*

sis, the slowest grower, which can take up to five days by traditional methods.

In the end, it was possible to test all six detergents with the same method, improving laboratory efficiency and reducing the risk of operator error. Using Milliflex® Quantum for detection, time to result was reduced from five days to 27 hours, enabling faster product release.

About the Author

Shari Spector, PhD, is a Field Marketing Manager at EMD Millipore, supporting bioburden and sterility applications.

Evaluation of Amplified-ATP Bioluminescence and Compendial Plate Count Methods continued from page 24

and sensitivity were determined using a receiver operating characteristic table. 70% was used as the acceptance criteria based on the USP 32 General Chapters <1223>. Calculations for the evaluation parameters are presented in **Table 1.**

The ATP+ method met or exceeded a 70% acceptance criterion for each of the parameters evaluated.

To further evaluate sensitivity, the limit of detection (LOD) was calculated using logistic regression where the response variable is detection of a contaminant (positive/negative growth). **Figures 1** and **2** present the inverse interpolation for the limit of detection on the log scale for each test method.

The red dashed lines represent the 95% one-sided upper confidence limit on the probability of detection. The solid curved lines represent the predicted probability of detecting an organism. The horizontal lines are at 0.1 (10%) and the vertical lines are situated at the dilution levels, at which the confidence limits reach 10%.

Table 1 Calculations for Evaluation Parameters

Inoculum Level	Accuracy	Precision	Specificity	Sensitivity
All	76.70%	77.40%	70.00%	82.00%

Figure 1 ATP+ Method

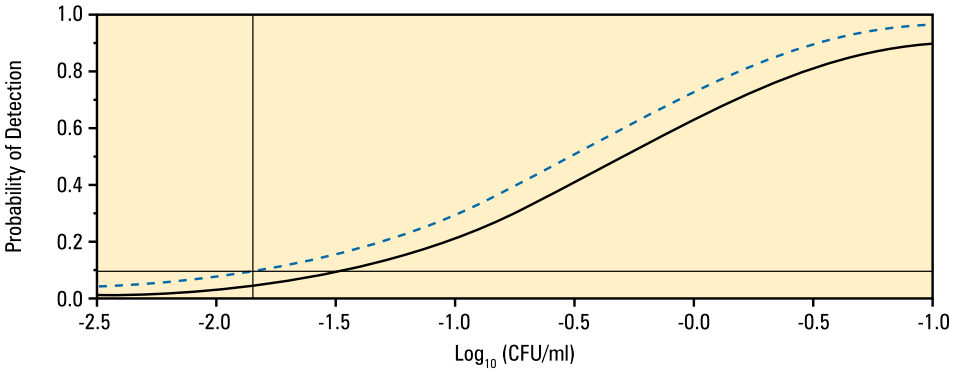
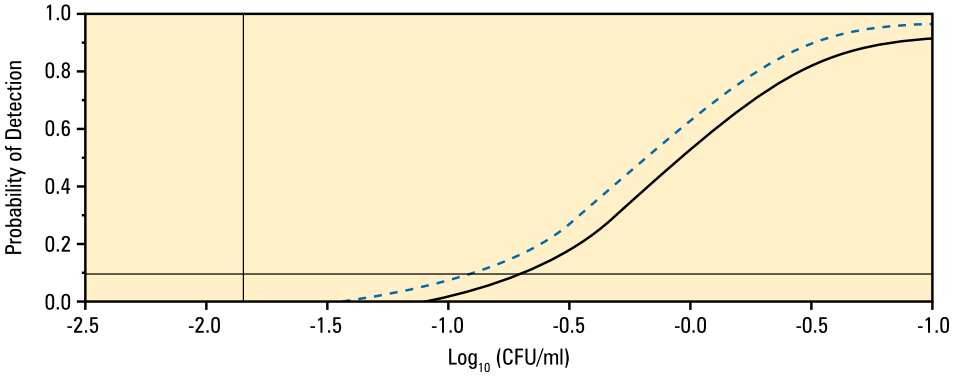


Figure 2 Plate Count Method



The smaller LOD for the ATP+ method (-1.85) indicates that it is able to detect lower levels of contamination than the plate count method.

The author believes that the data supports the notion that the method is equal to or better than the compendial method.

About the Author

Jeremy Robertson is the Senior Product Manager for Celsis products at Charles River. He has worked in the rapid microbial methods industry for over ten years in sales, marketing and technical roles.

2016 PDA Upcoming Events

SAVE THE DATE for PDA's 2016 Events

FEBRUARY

23-24
Pharmaceutical Microbiology
Berlin, Germany

MARCH

14-16
2016 PDA Annual Meeting
San Antonio, TX

16-17
Preparing for the Next Generation of Regulatory Inspections: A 2016 PDA Manufacturing Science Workshop
San Antonio, TX

APRIL

12-13
Parenteral Packaging
Venice, Italy

19-20
Annex 1 Conference
San Diego, CA

MAY

18
Visual Inspection Interest Group
Bethesda, MD

JUNE

TBD
Biosimilars Conference
TBD

7-8
Advanced Therapy Medicinal Products
Berlin, Germany

27
Annex 1 Conference
Berlin, Germany

28-29
PDA Europe Annual Meeting
Berlin, Germany

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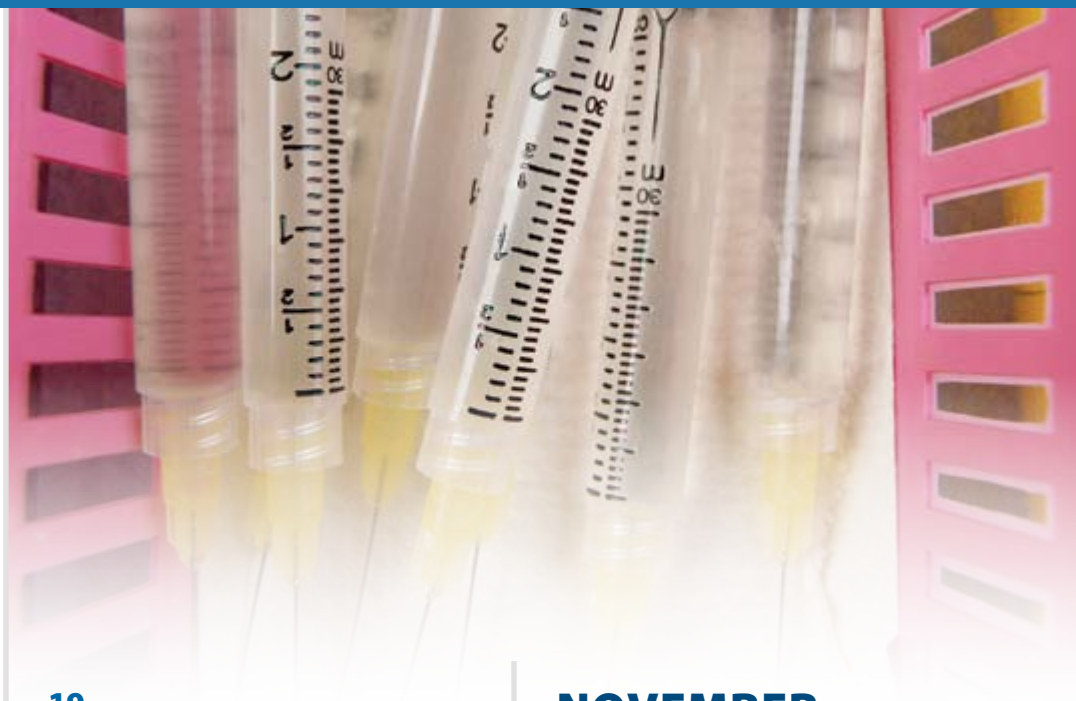
For an updated PDA calendar of events, please visit:
pda.org/calendar



SEPTEMBER

12-14
25TH ANNIVERSARY 1991-2016
PDA/FDA Joint Regulatory Conference
Washington, DC

14-15
Data Integrity Workshop
Washington, DC

20-21
9th Workshop on Monoclonal Antibodies
Rome, Italy

27-28
Pharmaceutical Freeze Drying Technology
Strasbourg, France

OCTOBER

11-12
Pharmaceutical Cold & Supply Chain Logistics
Amsterdam, The Netherlands

17-18
2016 PDA Universe of Pre-filled Syringes and Injection Devices
Huntington Beach, CA

19
Drug Delivery/Combination Products Interest Group
Huntington Beach, CA

24-26
PDA 11th Annual Global Conference on Pharmaceutical Microbiology
Arlington, VA

25-26
Visual Inspection Forum
Berlin, Germany

26-27
Annex 1 Conference
Arlington, VA

NOVEMBER

3-4
Outsourcing/CMO Conference
Washington, DC

15-16
Outsourcing & Contract Manufacturing
Copenhagen, Denmark

DECEMBER

7-8
Data Integrity Workshop
San Diego, CA

2016 Annual Meeting

New Age of Medicines Needs New Approaches

Jean Stanton, Johnson & Johnson, and William Miele, PhD, Pfizer

Rapid scientific and technological advances in stem cell biology and genetic engineering have ushered in a host of new products capable of treating a variety of diseases and injuries. These new products can come in the form of genetically engineered human or bacterial cells. For example, human autologous dendritic cells or genetically modified bacterial cells such as Salmonella or Lactococcus strains. They can also come in the form of viral vectors expressing naturally occurring human factors such as growth or expressing proteins expressed by tumor cells, such as prostate specific antigen (PSA).

Development of traditional biologics is well established, with many companies utilizing a "platform" approach for these types of products with specific and reliable quality systems and development strategies. These proven methods, however, may not be as effective for novel products or emerging technologies.

One of the challenges faced by companies entering this new field is identifying and understanding *what is* different and the steps necessary to address those differences. Differences can include: the complexity of the products themselves and the regulations that govern them, reduced possibilities to remove impurities a purification steps may impact the cells, limited pharma grade raw materials, and lack of appropriate methods to test container closure integrity for products stored in vapor phased nitrogen. Companies need to evaluate outsourcing, procurement, microbial controls, supply chain, product and process design, and other critical areas that have potentially different impact on new therapies than on traditional biological processes.

At the *2016 PDA Annual Meeting,* **Brian Urban** and **Tolga Musa** from Biogen Idec along with GlaxoSmithKline's **Michele Myers** will look at how companies can adapt to concepts of assay and batch release, sterility testing and other classic GMP systems to these new therapies. In addition, another presentation will highlight a decision matrix tool for appraising this new technology as well as a case study demonstrating this tool. All in all, these presentations will present options for companies to identify how to successfully address the differences in these products from traditional GMP product.

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Industry Need for Rapid Bioburden Detection continued from bottom of page 24

biologic matter that could also fluoresce can be discriminated.

A system based on these principles, the IMD-W™, is being tested with a select group of users. Initially, the system was challenged with eight industry relevant microorganisms at five distinct concentrations. Testing was designed such that single cells were sampled by the system to ensure sensitivity down to the level of intrinsic fluorescence emitted by planktonic microbes. The results (**Figure 1**) show a high level of correlation to conventional CFU culture results across a wide range of concentrations and organisms. Note that the lowest concentration data point is not indicative of the system's limit of detection but is instead based on the minimum concentration tested. User testing currently underway continues to provide feedback for further system refinements to further improve biologic detection performance.

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About the Author

Aric Meares is executive vice president at BioVigilant, a division of Azbil North America.

Recommended Readings

Did these mini-case studies spur additional questions for you? We recommend reading the following PDA technical reports that pertain to bioburden and microbial control strategies.

Technical Report No. 69: Bioburden and Biofilm Management in Pharmaceutical Manufacturing Operations

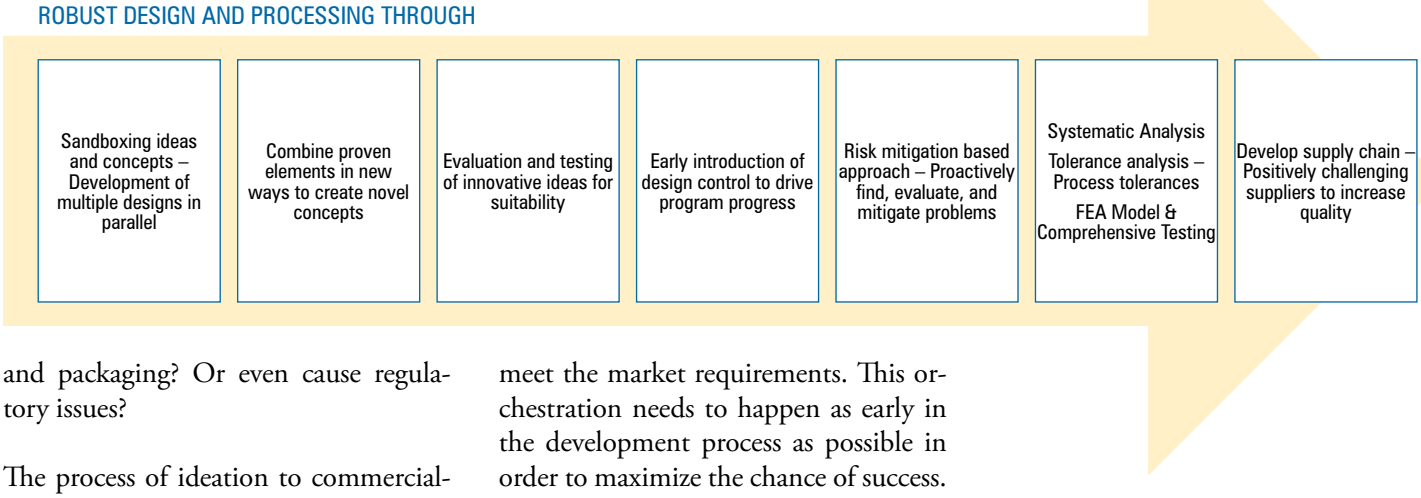
Technical Report No. 33 (Revised 2013): Evaluation, Validation and Implementation of Alternative and Rapid Microbiological Methods

Technical Report No. 70: Fundamentals of Cleaning and Disinfection Programs for Aseptic Manufacturing Facilities

PDA members can access all three of these technical reports for free using the PDA Technical Report Portal. In addition, all three are available for purchase at the PDA Bookstore.

Hit the Sandbox to Achieve Product Development Success continued from page 25

Figure 2 Sandboxing



and packaging? Or even cause regulatory issues?

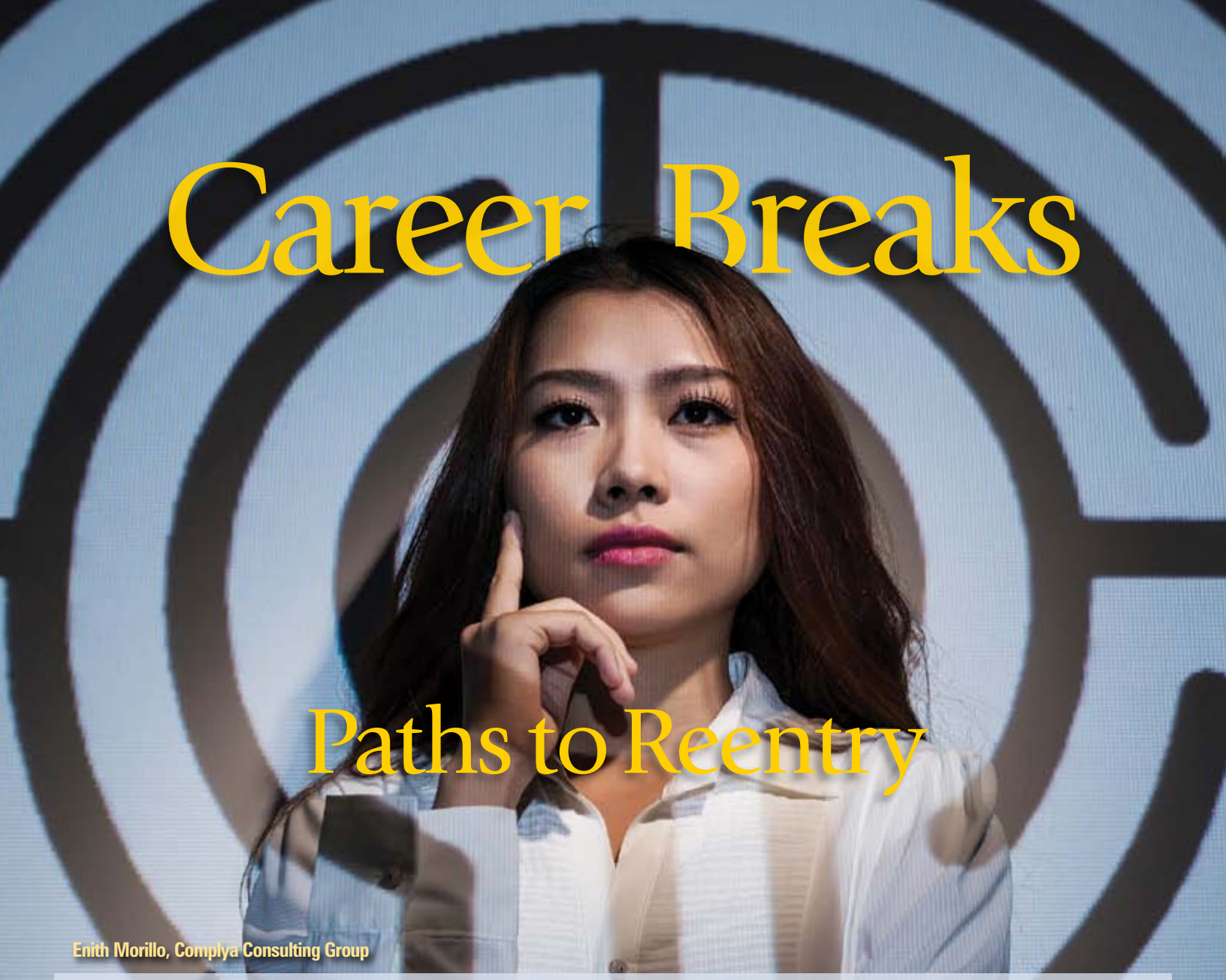
The process of ideation to commercialization is like all business processes, a management process. The process must be constantly reviewed and improved to ensure the continued growth of any business. Sandboxing enables development teams to generate, define, propose and review new product ideas efficiently to accurately identify the ones that will meet the market requirements. This orchestration needs to happen as early in the development process as possible in order to maximize the chance of success.

About the Author

Within NNE Pharmaplan, **Stephen Fournier** specializes in medical device product development, product commercialization, and in developing business partnerships.

Career Breaks

Paths to Reentry



Enith Morillo, Complya Consulting Group

Those of us in the industry who choose or are forced to take a break from a thriving career face the challenge of taking the road "less traveled," to quote poet **Robert L. Frost,** when reentering the workforce. Whether to raise a family, care for elderly parents, serve in the military or travel the world, professionals who take a break compete for employment with those who have uninterrupted career paths. A similar challenge faces "late entrants"—college graduates who, for many reasons, do not immediately enter the workforce right after finishing school.

Several factors can compound the difficulties professionals will face when reentering the workforce or entering it late, such as the state of the economy, technological advancements, and the length of the career break. Yet despite these factors, reentry professionals and late entrants can effectively control their career trajectories by leveraging the break.

Companies continue to evolve their talent acquisition strategies, many factoring in research that touts the benefits of a diverse workforce. As a result, a new recruitment trend has emerged in this environment: reentry programs. These are programs designed to help professionals who have experienced a career break to successfully transition back into the workforce.

As a late entrant, I used an amalgam of reentry strategies and resources that I would like to share. This helped me not only to get my foot in the door but also to establish a career path within the pharmaceutical industry.

Article at a Glance

- No matter the cause of a career break, a reentry strategy is key
- Networking should comprise a large component of your strategy
- Companies are beginning to develop specialized reentry programs

Mind the Gap: Success Stories

From an employer's perspective, legitimate concerns arise when considering a reentry or late entry candidate. Can they pick up where they left off? How fast can they take on new technologies? Have they kept a pulse on the industry? On a more subtle note, are they capable of putting work over all else when needed?

This is why indispensable organizations such as iRelaunch have emerged; to bridge the gap between reentry professionals and employers exploring this untapped talent pool. Cofounded by reentry guru **Carol Fishman Cohen,** iRelaunch not only offers invaluable platforms such as the annual *iRelaunch Return to Work Conference,* but also seeks to change the professional landscape that often stigmatizes career breaks by showcasing successful transitions ***(1).***

Earlier this year, my unconventional late entry career story was featured on iRelaunch ***(2).*** I shared how a nine-year hiatus forced me to reinvent myself. For almost a decade after graduating from Worcester Polytechnic Institute with a master's degree in biomedical engineering, I travelled across the globe, learned a third language and raised five children in a foreign country. Reentering the life sciences workforce meant that career options were limited. Through mentoring, volunteering, a certificate program at the local community college, a professional certification and a great deal of zest, I relentlessly worked to make up for the "missed" years.

In addition to mine, other successful reentry stories abound, such as those profiled in *Science* ***(3),*** and in *Chemical & Engineering News* ***(4),*** where engineers and scientists shared their unconventional journeys, offering inspiration and tools to those following the road less traveled.

The common factor to all these successful reentry stories? A reentry strategy.

What's Your Strategy?

It is common for professionals to downplay the transferable and marketable skills developed during a career break. Yet, you may have learned valuable skills during your time out of the workforce. This is why the first step to developing a reentry strategy is introspection, taking stock and asking yourself, "how can I leverage *all* that I have done these past years in a professional setting?"

It appears that the life science industry remains limited in outreach to the reentry talent pool

In addition to identifying transferrable skills, professionals need to assess, grow, and take advantage of their network. With the advent of social media, one can turn to platforms like LinkedIn as a tool to reconnect with former colleagues, follow employers of interest, and discover how acquaintances and friends are positioned in their industry. Along these lines, joining and volunteering for professional organizations relevant to your industry is crucial to building a network with direct access to career opportunities.

To succeed at networking requires broadcasting your plans to reenter the workforce to those in your network. This takes precedence. It's easier to learn about career opportunities when others in your network are aware of your intentions. To that end, it's crucial to go public about the intent to return and probe for opportunities where possible.

Depending on the industry, continuous education might be necessary to add a competitive edge. Whether learning a new computer software or language, pursuing a professional certification, or attending education-focused industry conferences, a reentry strategy is incomplete if it doesn't include actualization.

Professionals who experience a career break often wish they had done certain things differently in hindsight, such as staying in touch with former colleagues, not burning bridges with an employer, or staying current on industry trends ***(5).*** The good news is that if you are considering a career break, these can serve as lessons learned when planning both your exit and reentry strategy. Earlier this year, Cohen shared some of these strategies during a career break panel at Harvard Business School:

1. Make your mark: While you are still working, make sure you are a valuable employee, who is a top performer and lends a hand when needed. Former employers and colleagues who have firsthand experience with the quality of your work and work ethic are the pinnacle of your network. Do not disappoint!

2. Be strategic when volunteering: There is no doubt that volunteering opportunities abound, whether at a school, nursing home, nonprofit organization, industry conference, or professional organization, to name a few. Think about the skills you need to develop during the break that will be transferrable when returning to work. Do the research, weigh the options, and then become involved. Remember, it's all about return on investment.

3. It *is* who you know: The importance of building and nurturing a network cannot be overemphasized. Whether professionals in the field, members of the parent/teacher organization at your children's school, or just about anyone you meet: network and build meaningful connections. Over 40% of career opportunities materialize through someone who knows someone ***(6).***

Reentry Programs Jumpstart Careers

In addition to developing a strategic plan to relaunch your career, it also helps to look at companies and industries with successful reentry programs. These programs generally focus on training as a means to transition professionals back into the workforce.

The finance industry is at the forefront of reentry programs, with Wall Street giants J.P. Morgan and Morgan Stanley leading the way. Using a paid internship model, these companies' programs allow some-

one reentering the workforce to get their foot in the door and actualize their skills while reconnecting with the industry at the same time. The programs are effective in bringing top talent back into the workforce, as in the case of **Andrea Chermayeff,** a Harvard Business School MBA graduate who, after taking a 15-year career break, participated in J.P. Morgan's reentry program. She is now a full time business manager at the firm ***(7).***

In the academic world, reentry programs are also common. Colleges and universities have a long-term and vested interest in seeing alumni succeed. Fast track graduate certificate programs are on the rise, including classroom, online and hybrid programs, which are particularly beneficial to late entry professionals that don't have previous work experience to fall back on. Other programs offered by universities target specific professions, such as Drexel University's Physician Refresher/Re-entry program ***(8);*** other programs are boot camp-style, offering lectures, career counseling, and career fairs as an effective platform for reentry.

Other industries with reentry programs include law firms, IT, government and the nonprofit sector. Yet it appears that the life science industry remains limited in outreach to the reentry talent pool, with only a few companies and organizations offering reentry programs.

The National Institute of Health (NIH) is one of the few in the life sciences space actively reaching out to professionals reentering the industry. NIH utilizes a research grant and cooperative agreement model to help men and women reactivate their research careers. A laudable feature of NIH's approach is its support of a progressive transition that offers part time reentry opportunities that counteract the culture shock that professionals can experience when going back to work and allows for a measured strategy for professionals unable to fully jump back on board ***(9).***

Some pharmaceutical firms offer reentry programs specifically designed for veterans. Healthcare giant Johnson & Johnson boasts a program for service members, veterans and military spouses ***(10)*** through their support of Joining Forces, a nationwide initiative that actively seeks to connect veterans and their families with educational resources and career opportunities ***(11).***

Merck, Pfizer and Bristol-Myers Squibb, along with others such as Mylan and Fering Pharmaceuticals, also encourage veterans to seek career opportunities on their career websites by highlighting how leadership and teamwork skills acquired in the service are transferrable into the industry.

Other companies, such as Forest Laboratories and Thermo Fisher Scientific, cater to reentry professionals indirectly by offering flexible work arrangements and telecommuting, which can be appealing to those looking to join back on a part time basis.

Eli Lilly and Company is one of the few pharmaceutical companies that proactively addresses reentry by offering employees access to internal job postings when they wish to return from extended dependent care leave ***(12).*** By following this model, employers mitigate the cost of attrition and are afforded the opportunity to retain high performers.

With a growing emphasis on retaining top talent and recruiting a diverse workforce, the life sciences industry can establish reentry programs as a means to attract eager professionals with unique backgrounds that are ready to work hard, take risks, and prove themselves. Similarly, as professionals consider taking a career break, both the employer and employee can lay the groundwork to facilitate reentry down the line.

As companies strive to support work/life balance through increasingly flexible work arrangements, there is a potential for the industry to see a decline in career breaks. Yet, for those professionals that must leave a thriving career for a few years, companies can proactively lay a foundation to bring back top talent when they are ready to return. Reentry professionals bring unmatched energy and an uncanny desire to give 100% in return for the opportunity to get back in the game. Offering reentry programs to scientists, engineers, and other professionals in the life sciences industry is a means to reinforce its pipeline with untapped potential.

"…And that has made all the difference."
—Robert L. Frost

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Which Laboratory Software is the Right One For Your Lab?

Joe Liscouski, Institute for Laboratory Automation

"Why do you need this laboratory information management system (LIMS)?" "We have an enterprise resource planning (ERP) system, why do we need to purchase yet another software product?" "How will the system you're recommending improve lab operations?"

These questions are certainly familiar to those of us involved in laboratory operations any time we request software to improve laboratory workflow. While it is easy for us to understand the need for a specific software product in our day-to-day lab operations, our senior management—who controls the purse strings and often isn't involved in daily operations—requires a full understanding of exactly how a specific software will benefit the lab and the role it will play amidst the various software systems used throughout your company.

To ensure that your requests for specific software and systems receive full consideration, it pays to fully understand the types of lab management software available and how they relate to the particular requirements and needs of your specific laboratory. This way you can make a better case to your management for a software product that alleviates workflow issues.

Research vs. Testing Lab Requirements

For years, laboratories have had sophisticated technology developed to help scientists in their work, but unless you've been educated in these systems their use can be a mystery. The names of these systems—instrument data systems, laboratory information management systems, scientific data management systems, electronic laboratory notebooks, lab execution systems—aren't much help, particularly for the nonscientists who approve or deny requests for new technology. Each of these systems supports a different laboratory function. Some are more appropriate for specific types of laboratory environments than others.

Determining the appropriate software to request first requires understanding the type of laboratory you work for, and evaluating its needs. Broadly speaking there are two types of laboratories: research and testing.

There are different types of **research laboratories** but they have one thing in common: conducting experimental work to solve problems of interest to the funding organization. That can include drug discovery, product development, etc. In any case, questions are posed, experiments designed and run, data and information collected, analyzed and reported.

The paper lab notebook served as the tool of choice for recording lab work in research labs. These notebooks featured descriptions of data, charts and images drawn or pasted in place along with printouts from equipment, and ending with a signature that the work was performed. Naturally, the paper lab notebook lost its effectiveness when computer-based data analysis, spreadsheets and imaging systems arrived on the scene. This additional technology posed challenges for users of the traditional paper notebook. Data and information in easy-to-use formats had to be printed out to meet recordkeeping requirements. Collaboration meant paper records had to be copied and sent. Paper notebooks could also be damaged by water, chemicals, fire, misfiling, and loss.

The *Electronic laboratory notebook (ELN)*, as a concept with a variety of implementations, relieved the shortcomings of its predecessor and gave researchers additional capabilities. Developers built systems with increased flexibility so that the system can adapt to the user's requirements instead of the reverse with the ability to use all the electronic data and information representations noted above. Beyond that, electronic "pages" can be sent to collaborators, shared with controlled read/write access, searched electronically and backed up automatically on other systems to avoid loss and be easily retrievable in an audit. They also provided researchers with the ability to access application-specific databases and search for reaction mechanisms, organisms, chemicals, material in inventory, etc., reducing costs and increasing the efficiency of research programs.

Testing laboratories follow a different workflow than research laboratories. Unlike the flexible nature of research laboratories, these labs follow a set of procedures that depend on the samples submitted to them. Here, samples are received, logged in, assigned for testing and analyzed with results recorded and distributed as needed. This process results in two primary challenges: receiving and analyzing the data from instruments, and managing the workflow. The first issue can be addressed by using *instrument data systems*. These systems automatically collect data from the instrument, analyze it and then report it. *Laboratory information management systems (LIMS)*, on the other hand, address the issue of workflow management, allowing researchers to prioritize work, locate samples, record results, etc. In addition to greatly improving workflows, LIMS also can aid management in evaluating productivity, changing trends in work requests and reviewing/approving completed test results.

The workflow similarities between testing labs and other production environments have led some to adapt *enterprise resource planning* (ERP) systems to this kind of lab work. Yet both LIMS and ELNs provide something that ERP systems do not: the ability to connect to instrument data systems with bidirectional transfer of worklists and experimental results. This interconnection is another reason why these products can improve lab work and reduce costs. It also improves data integrity as well. ➤

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Connecting with instrument data systems occurs in one of two ways:

- The first is a direct connection between an instrument (balance, pH meter, etc.) with a LIMS or ELN, which is particularly useful when acquiring information in real time as an experiment progresses.

- A second connection method is through the use of a *scientific data management System (SDMS)*, a database system designed to collect instrument data from a variety of sources and managing it within a single system, reducing redundancy, and acting as a useful middleware component between instruments and LIMS/ELNs.

The value of the instrument-to-LIMS/ELN connection, regardless of the means, shouldn't be underestimated since it provides speed, accuracy, and an accepted means of meeting regulatory requirements.

Another useful software tool for testing lab are *laboratory execution systems (LES)*, available either as products, or increasingly, as programmable components of LIMS and ELNs. Implementation methods vary, but these systems provide a rigorously controlled execution of a laboratory procedure by a technician ensuring that the procedure is performed correctly, by qualified personnel, using calibrated equipment, and that the data is collected from instruments and transferred to LIMS, ELN, and/or SDMS.

Solutions for Hybrid Labs

The technologies used within research and testing labs continue to improve as the marketplace responds to new types of instruments and better support for workflows and collaborative environments. One trend surrounds the merging of product capabilities to maintain increasingly complex work environments. This is crucial as research labs take on testing roles and vice versa in larger numbers.

Research-in-Testing and **Testing-in-Research** situations exist, particularly in small companies and start-up organizations. For example:

- an analytical chemistry lab might be tasked with doing method development or researching an unusual problem; or,

- a research lab may need to provide for routine testing of samples for purity.

Vendors are recognizing that these situations exist and are bringing together the functionality of previously distinct technologies. A LIMS with ELN capability, or an ELN with a lab execution system facility, or other combinations that might include external database access, instrument connections and document management, are either already available or becoming available.

Each of the technologies mentioned here addresses different requirements. The first step in understanding which technology is right for your situation is ensuring that you and all those who will use the system are well educated in the technologies available. The second step is fully understanding what you need and why. Thorough planning is essential; this isn't a do-it-once-and-done effort, but a continual assessment of needs vs. solutions as your lab develops and expands. These systems take time to plan and implement. You want to ensure that you take into account future developments.

Making the case for a new software solution requires diligently researching the options available and choosing the appropriate software that meets the needs of your specific type of lab and requirements. Presenting a full picture to your senior management will ensure that your recommendation is evaluated comprehensively and with the full seriousness it deserves.

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Report From
2015 PDA/FDA Joint Regulatory Conference

Change is Coming to FDA Inspections: Are You Prepared?

Rebecca Stauffer, PDA

Organizational changes within the Office of Regulatory Affairs and CDER's new Office of Pharmaceutical Quality will impact the nature of U.S. FDA inspections in the coming years. Naturally, companies are anxious to see how these new approaches to inspections will look like as they get off the ground.

At the *2015 PDA/FDA Joint Regulatory Conference* in Washington, D.C. this September, both **Melinda Plaisier,** Associate Commissioner for Regulatory Affairs, ORA, and **Janet Woodcock,** MD, Director, CDER, highlighted the structural changes underway at their respective divisions and how these changes will impact the inspection process.

Plaisier provided an extensive update on ORA's realignment ***(1).*** In the past, Agency inspectors covered a varying range of inspections from food operations to drug manufacturing sites to tobacco manufacturers based on geographic divisions. Concerns arose that individual inspectors lacked the effective expertise to truly analyze a facility. Therefore, ORA divided its inspection operations into six areas: drugs, biologics, medical devices, bioresearch monitoring, tobacco and human and animal food products. The inspection program for drug manufacturing facilities will be based out of four offices throughout the country and is expected to begin sometime next year.

"These new frameworks and approaches to inspections will ultimately achieve greater consistency," Plaisier said. "Going to the specialized inspections is certainly going to foster increased consistency across inspections."

Yet, she explained during her talk, the specialties may be divided into additional subspecialties, including APIs, sterile products and pharmacy compounded products.

In addition, Plaisier said that new operational models at ORA require the hiring of additional supervisors.

"We are going to actually need more managers, rather than fewer, in order to have a reasonable staff-to-supervisor ratio," she indicated.

ORA is also working with CDER on FDA's New Inspection Protocol Project. Here, inspectors will focus on manufacturing quality and inspections will be team-based featuring real-time communication with the Agency.

"The new inspection protocols are for both preapproval inspections and surveillance inspections," said Woodcock during the Q&A following her and Plaisier's presentations. "We would like to, in the future, be talking to the investigators while they're in the firm…talk about the problems [and] hopefully, immediately follow up as a team on how we can remediate."

Janet Woodcock (left) and **Melinda Plaisier** discuss how recent FDA changes will impact inspection processes

OPQ Looks at Further Harmonization

Woodcock also offered an overview of the future of FDA inspections during her talk ***(2).*** First, the OPQ's surveillance office is looking at the state of quality for all facilities importing drugs into the United States. The initial step in this project is the development of a database with an inventory of all the facilities that make drugs sold in the United States. Data contained within this database will include information on how frequently these facilities are inspected as well as the inspection results. This, she said, is a "totally new concept."

The surveillance office is also looking at a more quantitative, risk-based approach to inspections.

"This office is trying to do a risk-based model every year of what facilities we should go in," Woodcock said. For example, "If there's a facility we've never visited, it's probably a good idea to go visit them."

Greater harmonization with other regulatory entities will also be a big component of the realignment effort.

"The real frontier is the international," she said. "I hear from many of the folks in industry, [and] they're visited serially by numerous inspectorates. To me this is a recipe for errors….There's also a lot of down time when you're undergoing these multiple inspections. That's why we really want to aim to harmonize standards that we can use around the world."

Woodcock also explained that CDER and ORA continue to negotiate with ➤

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the EU on a "mutual reliance initiative" for cGMP inspections. FDA hopes to move forward with this and other international standardization efforts and develop a better way of exchanging harmonized information.

Interest Group Tackles Inspections via "Speed Dating" Exercise

Not surprisingly, these changes were on the minds of many conference attendees. With this in mind, PDA's Inspection Trends Interest Group took a unique approach to these topics at the interest group session held during the first day of the meeting. Here, attendees participated in "speed dating," spending 15 minutes each on an inspection-related topic and then discussing it in small groups. The topics that participants could "speed date" included general data integrity issues, quality metrics, basic GMP observations, validation, data integrity in the QC lab, aging facilities and how to respond to observations.

According to one participant, the "approach for interactive dialogue was refreshing and a nice change…the scenarios were excellent to facilitate discussions on what firms should do. It felt like another day in the office to me."

The "speed dating" exercise has proven to be very popular and the Inspection Trends Interest Group expects to continue it at future meetings. With all the changes underway for FDA inspection processes, there will be no shortage of topics to be covered at future "speed dating" meetings. In the end, while processes for inspections may change, the need to ensure quality product will not.

References

1. Plaisier, M. "Program Alignment and ORA Reorganization Overview." Presented at the 2015 PDA/FDA Joint Regulatory Conference, Washington, DC, September 2015.

2. Woodcock, J. "OPQ Reorganization Overview." Presented at the 2015 PDA/FDA Joint Regulatory Conference, Washington, DC, September 2015.

About the Experts

Melinda Plaisier serves as the Associate Commissioner for Regulatory Affairs. She has responsibility for over 4,600 staff and operations in the Office of Regulatory Affairs (ORA), FDA's field organization.

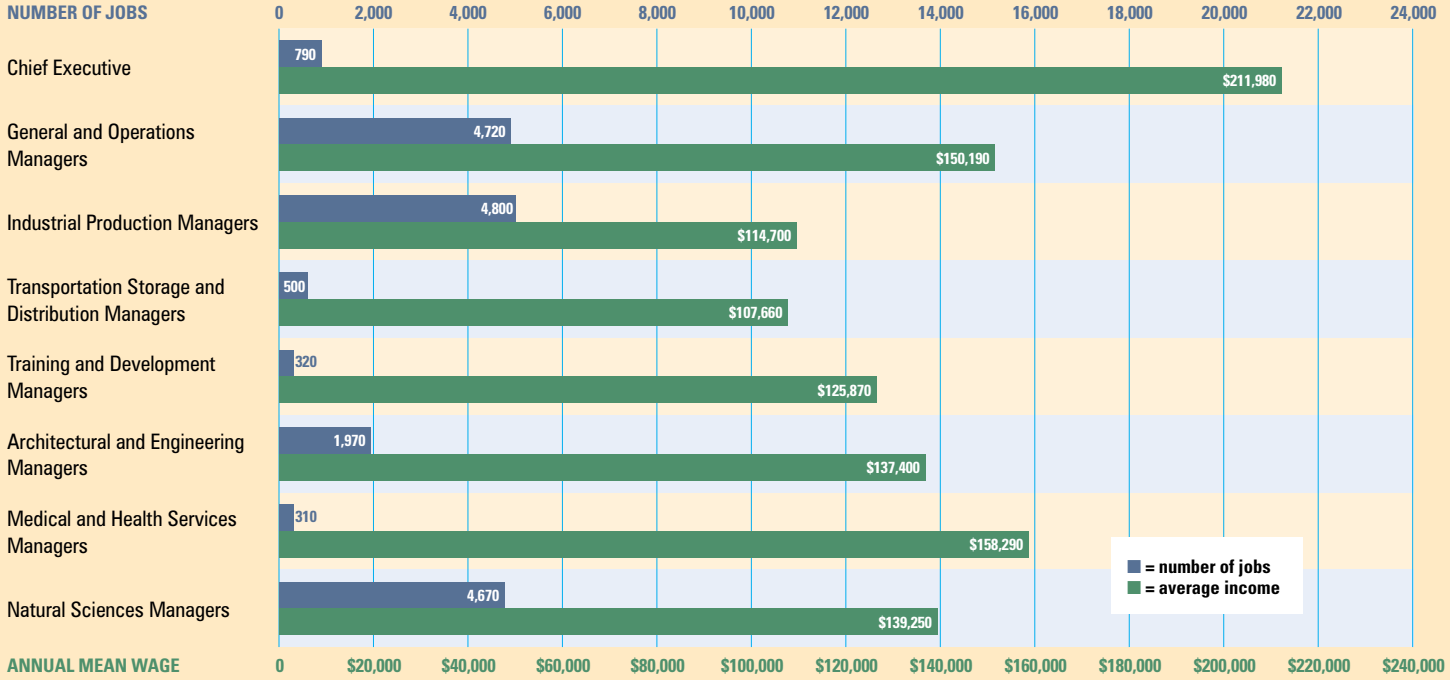
Janet Woodcock has served FDA as Deputy Commissioner and Chief Medical Officer, Deputy Commissioner for Operations and Chief Operating Officer. She previously held other positions at FDA including Director, Office of Therapeutics Research and Review and Acting Deputy Director, Center for Biologics Evaluation and Research.

The State of U.S. Pharma Manufacturing

Each year, the U.S. Bureau of Labor Statistics collects occupational data covering the next year. Below are statistics for pharma manufacturing in 2014.

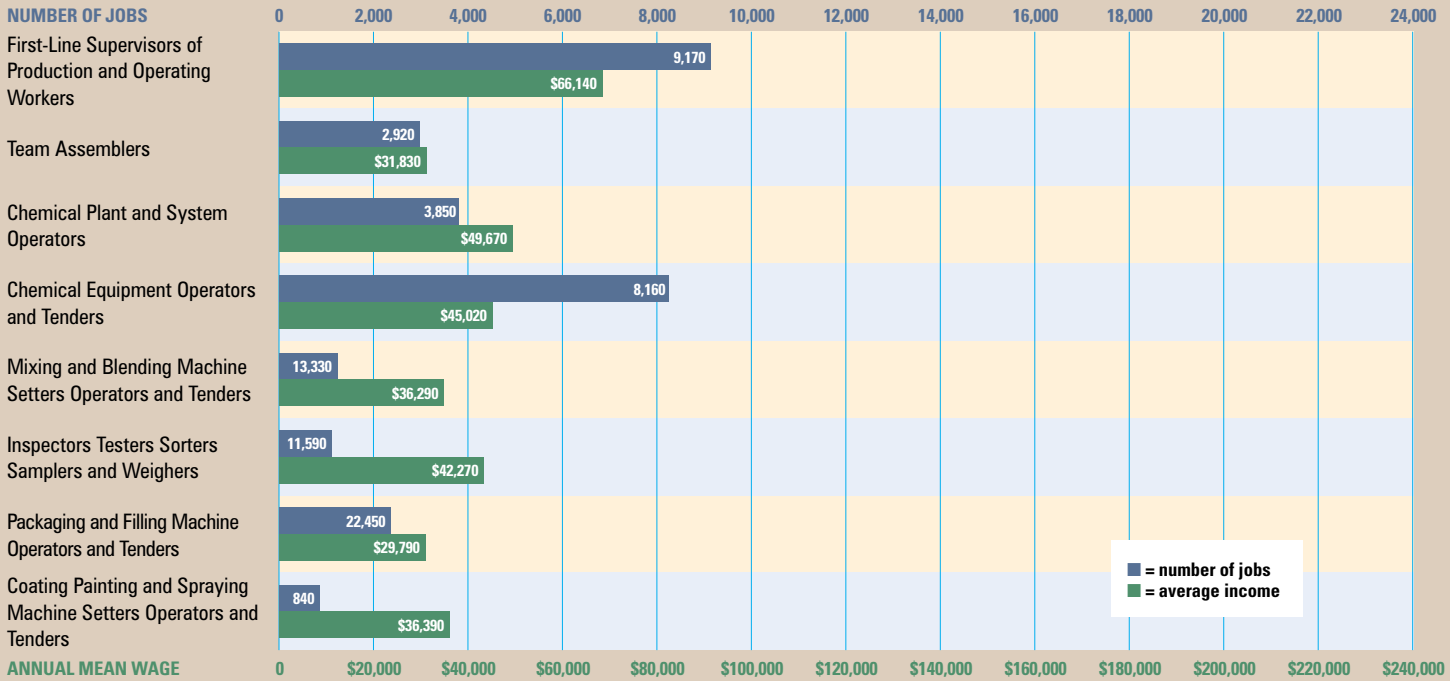
Management Jobs MAY 2014

AVERAGE INCOME: **$143,169**



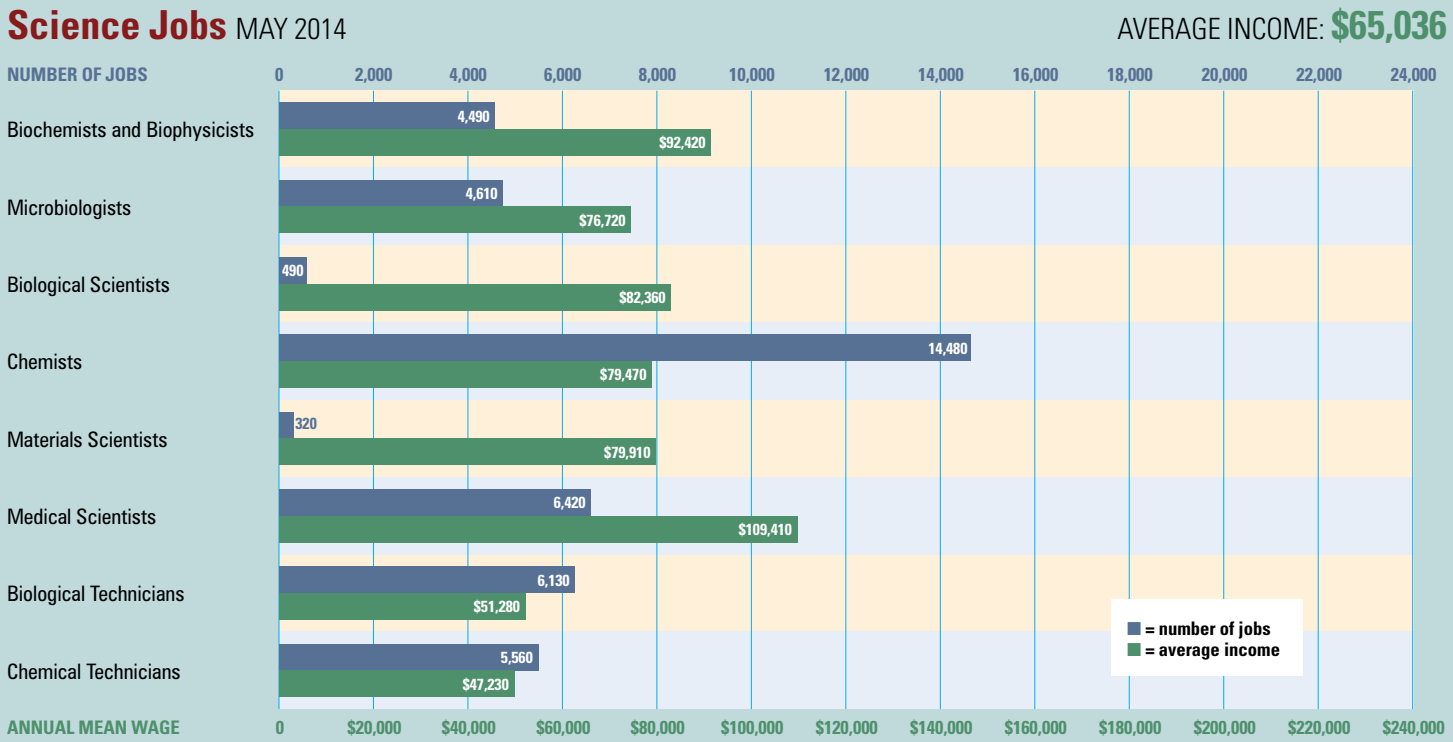
Production Jobs MAY 2014

AVERAGE INCOME: **$42,175**



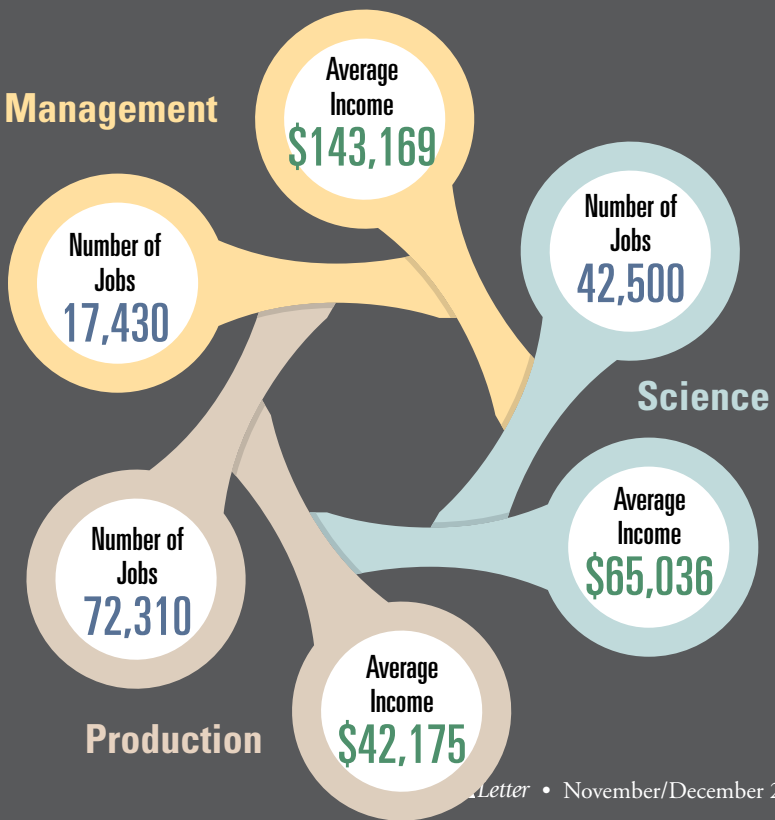
Jobs in 2014

a wide range of industries—including our own. This data is then published



By 2022, pharmaceutical and medicine manufacturing jobs will increase by almost

5%



Occupational Employment Statistics, Bureau of Labor Statistics, data.bls.gov/oes

snapshot

Light at the End of the Tunnel for PAC Complexity

Melissa Seymour, Biogen, Emma Ramnarine, Genentech/Roche, Denyse Baker, PDA, and Anders Vinther, Sanofi Pasteur

The state of regulatory postapproval change (PAC) processes worldwide can be characterized as complex and inconsistent for many reasons, such as varying classifications, different submission requirements, and implementation timelines, all of which creates unintended disincentives for manufacturers to continually improve and technically innovate or forces companies to maintain parallel inventories.

Many companies find it easier to postpone improvements to facilities, processes, and analytics or simply refrain from planning for advancements at all in order to avoid the intricate nature of implementing such changes, especially for product registered in multiple countries.

Other companies that do implement even simple changes might choose to segment their inventories over many months in order to meet regional requirements and avoid filing changes in all regions served. Attendees at the recent *2015 PDA/FDA Manufacturing Science Workshop* shared several examples of this problem. In the most extreme case, a company maintained more than 30 versions of the same product in parallel due to differences in timing of country-specific regulatory approval processes.

Both strategies—upgrade/improvement avoidance or parallel inventories—are fraught with serious consequences that can contribute to the problem of drug shortages. Technology avoidance can lead to drug shortages that could have been mitigated effectively through process or technology improvements. Segmentation of inventories, on the other hand, makes it more difficult for a manufacturer to accommodate sudden increases in product demand in one of these segments. Both strategies can result in an increasing risk of errors in releasing nonconforming product to a country, and possibly even resulting in cGMP noncompliance.

Industry and Regulators Responsibilities

At the workshop there was a general agreement by regulators and industry alike to see the fulfilment of the three objectives found in International Conference on Harmonisation (ICH) quality guideline Q10: Pharmaceutical Quality System:

- Achieve product realization
- Establish and maintain a state of control
- Facilitate continual improvement.

So how can the industry move in this direction and not let the complexity of PAC regulatory processes serve as a roadblock?

First, workshop attendees agreed that the burden of ensuring safe and compliant PACs falls on the companies themselves. As such, manufacturers must ensure that effective change management processes are in place as part of the pharmaceutical quality system (PQS) within their companies. The process of evaluating PACs must include all relevant functions/organizations in the company, leverage country-specific competences in affiliates, and bundle relevant changes as much as possible. Workshop attendees also agreed that all companies must develop lifecycle management plans and global change protocols as elements of an effective PQS.

Nevertheless, attendees believed that regulatory authorities around the world are responsible for creating a less complicated global system that allows companies to make necessary process improvements. The World Health Organization (WHO) resolution 67.20, which describes the balance between regulatory oversight and availability/access to drug products, was cited as an important guiding principal.

Attendees discussed how the regulatory burden can be reduced for both regulators and industry while encouraging PACs that aim to achieve ICH Q10 objectives. In addition, attendees cited the importance of regulatory authorities relying more on each other for science- and risk-based quality, safety and efficacy assessments of PACs rather than demanding redundant local assessments.

Workshop attendees also mentioned certain worthwhile regulatory tools, such as "expanded comparability protocols" (eCPs), as ways to facilitate postapproval changes.

Attendees pointed out that solving the quagmire of global PAC regulations is difficult at a time of a rapidly growing globalization within the industry, but increasing parochial demands of health authorities.

ICH Q12 a PAC Solution?

A unified platform for addressing the challenges and complexity of managing PACs is forthcoming from the working group for quality guideline Q12: Technical and Regulatory Considerations for Pharmaceutical Lifecycle Management.

ICH Q12 will facilitate alignment of different regions and countries on a common definition and set of established conditions. The document should define a lifecycle management strategy and harmonizing on a foundational framework for postapproval change management, including how an effective PQS can be leveraged to reduce the regulatory burden of implementing changes globally.

Moheb Nasr, Vice President, CMC Strategy, GlaxoSmithKline, who is rapporteur for the document, delivered a presentation covering ICH Q12 at the workshop. One desired objective for ICH Q12 is for it to also be adopted and used in non-ICH regions. This is important as many companies market their products globally, thus solutions to PAC complexity must take a global approach to be efficient.

PDA's PAC Solutions

PDA is taking an active role in providing input to the ICH Q12 working group to facilitate global harmonization through a science and risk-based approach, building on our 10,000+ strong membership.

In addition to discussions through workshops, surveys and discussion forums, PDA's activities are currently focused on the following key topics:

- PAC challenges awareness through promulgation of practical examples.
- Lifecycle management (LCM) plans to enable effective PAC planning and implementation
- Common technical improvements and innovation facilitated by "global change protocols" (gCPs)
- Leveraging a robust PQS to effectively manage PACs

PDA will develop reports and working papers on each of these topics and tools.

The LCM Plan will provide an opportunity for the marketing authorization holder (MAH) to prospectively provide information to the regulator regarding their plans for managing the product during its commercial life. It can serve either as a regulatory agreement between the MAH and the regulatory body, or as a mechanism for early communication and prospective planning of post approval changes.

The gCP is a detailed protocol that describes one or multiple PAC(s), including rationale for the change, risk assessment, proposed studies needed for validation and comparability, as well as acceptance criteria. The gCP will provide the possibility to standardize certain types of PACs globally based on solid scientific data and agreed upon requirements. The goal is to expedite the change through the regulatory systems of different countries.

In order for LCM Plans, gCPs and leveraged PQS to be successful, it will be important to achieve proactive planning and transparency with health authorities as early as possible. It will also be important for health authorities to further drive reliance on each other's approval processes.

A successful outcome will result in more postapproval changes implemented via a standard gCP without prior approval reporting and increased reliance on companies' robust PQS. This ability will result in faster approval or downgrading of reporting for changes that will enable or incentivize companies to incorporate new technologies, improve capability, process control, and enhance product availability.

Additionally, standard implementation and similar reporting requirements and timelines to approval globally will decrease the current complexity of varying PAC processes, ultimately reducing drug shortages and promoting ICH Q10 objectives.

The authors invite those interested in helping PDA's PAC activities to contact PDA if interested in volunteering in this space.

On Oct. 9, EMA held a drug shortage workshop with attendance by National Competent Authorities, U.S. FDA and JPMA observers, industry associations and patient and healthcare organizations. At this workshop, PDA presented its plans and highlighted the importance of addressing lifecycle management as being key to ensure supply continuity. Additionally, PDA is in the process of developing a survey to solicit input on best practices and how companies achieved successes with PACs.

About the Authors

Melissa Seymour is currently the Vice President of Corporate Quality for Biogen Idec. She is currently serving as Past-President of PDA's Southeast Chapter.

Emma Ramnarine is Senior Director, Head of Biologics QC Network at Roche Pharma and is accountable for the biologics QC network strategy.

Denyse Baker is Senior Advisor of Scientific and Regulatory Affairs at PDA.

Anders Vinther is Chief Quality Officer, Sanofi Pasteur. His experience includes QC, QA, executive and strategic management in a variety of cultures and a number of companies ranging from start-ups to large biologics companies.

GMP Oversight of Medicines Manufacturers in the EU

A System of Equivalent Member States, a Coordinating Agency and a Centralized Institution

Riccardo Luigetti, EMA, Emer Cooke, EMA, Brendan Cuddy, EMA, Sebastien Goux, European Commission, and Ian Rees, MHRA

[Editor's Note: This is Part I of an overview of the EU regulatory system for pharmaceuticals. The article in its entirety can be accessed on the *PDA Letter* website. Parts II and III will be published in the subsequent issues of the Letter.**]**

The regulatory system for supervision of pharmaceutical manufacturers and GMP inspection in the European Union is one of the most advanced in the world. Due to the globalization of pharmaceutical manufacture, it also affects industry, regulators and patients outside the European Union. This system, however, is often poorly understood beyond the EU borders.

What follows is an explanation of the EU system in order to increase awareness and facilitate cooperation on GMP between European Union regulators and those outside the European Union.

The European Union

The European Union includes 28 Member States located in Europe, which are: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and United Kingdom. The EU total population is about 500 million people.

The European Union operates through a system of supranational independent institutions and intergovernmental negotiated decisions by its Member States. It is a legal entity and can negotiate international agreements on behalf of its Member States. The European Parliament, the Council of the European Union and the European Commission are the three main EU institutions. They produce through the "Ordinary Legislative Procedure" (formerly "co-decision") the policies and laws that apply throughout the European Union.

Table 1 Marketing Authorisation procedures in the European Union

Centralized Procedure	Application to EMA
	1 scientific evaluation by EMA
	MA issued by the European Commission valid in the entire EU territory
	Mandatory for biotech products, for certain therapeutic classes and for orphan products
Decentralised Procedure	Parallel submission in n Member States
	Reference Member State (RMS) performs assessment
	Concerned Member State(s) (CMSs) have the possibility to object
	Member States (RMS + CMSs) grant national MAs
Mutual Recognition Procedure	When there is at least 1 existing National Authorization (RMS)
	Other Member States (CMSs) mutually recognize the existing national MA in the RMS
	RMS updates previous assessment
	CMSs have the possibility to object in case of serious public health concerns
	Member States (CMSs) grant national MAs
National Procedure	Application to 1 Member State only
	National MA in 1 Member State
	Not allowed if the product is already authorized in another Member State

The European Union has developed a single market through a standardized system of laws that apply in all its Member States. The same rules and harmonized procedures apply to all the 28 Member States regarding the authorization of medicines and the supervision of safety of medicines.

The EU Regulatory System for Medicines

The EU has developed a regulatory system based on a network of decentralized National Competent Authorities (NCAs) in the Member States, supported and coordinated by a centralized agency, the European Medicines Agency (EMA).

The European Commission's role is multifaceted and focuses on the following:

- Right of initiative: To propose new or amending legislation for the pharmaceutical sector
- Implementation: To adopt implementing measures as well as to ensure and monitor the correct application of EU law
- Risk management: To grant EU-wide marketing authorizations for centralized products or maximum residue limits on the basis of a scientific opinion of the EMA
- Supervisory authority: To oversee the activities of the EMA in compliance with the mandate of the EMA, EU law and the EU policy objectives
- Global outreach: To ensure appropriate collaboration with relevant international partners and to promote the EU system globally

The EMA was created in 1995 to coordinate the existing scientific resources in the EU Member States and is an interface for cooperation and coordination of Member States' activities with respect to medicinal products. EMA scientific decisions are made through its scientific committees, whose members are chosen on the bases of their scientific expertise and are appointed by the Member ➤

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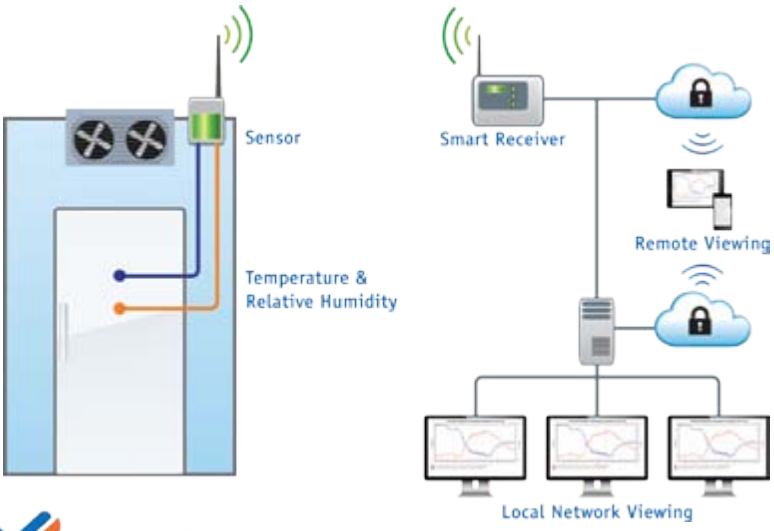

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States. One of the main roles of EMA is to mobilize scientific resources in the Member States, so that many of its scientific activities are carried out through a large network of scientific experts made available by the Member States.

The system for Marketing Authorisation (MA) of medicines, including the referral procedure, is an example of how the European Commission, the EMA and the Member States cooperate. The EU national, decentralized and mutual recognition MA procedures coexist with the centralized procedure **(Table 1).**

The referral procedure is an EU binding mechanism that ensures that the same measures are applied to products subject to national, decentralized and mutual recognition MA procedures. This procedure may be notably invoked when the conditions of authorizations need to be reviewed in the light of quality, safety and efficacy data (Union Interest Referral), when Member States have adopted different decisions regarding products that are authorized in at least two Member States (Divergent Decision Referral) or in the absence of agreement among Member States in the course of the mutual recognition or decentralized authorization procedures (Mutual Recognition and Decentralised Referral). This mechanism involves an opinion from the appropriate EMA committee and results in a decision of the European Commission that is binding for all Member States.

In order to provide for the same level of access to critical medicines to all the patients in the Union, the centralized procedure is mandatory for orphan products, biotechnological products, advanced-therapy products (gene therapy, somatic cell therapy and tissue engineering) and products intended for the treatment of critical therapeutic classes (HIV or AIDS, cancer, diabetes neurodegenerative diseases, auto-immune and other immune dysfunctions, and viral diseases). Veterinary medicines for use as growth or yield enhancers are also in the mandatory scope of the centralized procedure.

A fundamental aspect is that the legislation applicable to pharmaceuticals in the European Union is the same irrespective of the Member State or authorization route of the product, as it is developed at Union level. The same applies to the guidelines in use by assessors and inspectors for the assessment of MA applications and inspections, which are developed by EMA, in cooperation with Member States, through its scientific committees and working groups.

Clinical trials of Investigational Medicinal Products (IMPs) require authorization by each NCA and a favorable opinion by an ethics committee in which the clinical trial takes place and is granted in the form of a Clinical Trial Authorisation (CTA). The assessment for a CTA takes into account the holding of an appropriate authorization for each EU site of manufacture or importation.

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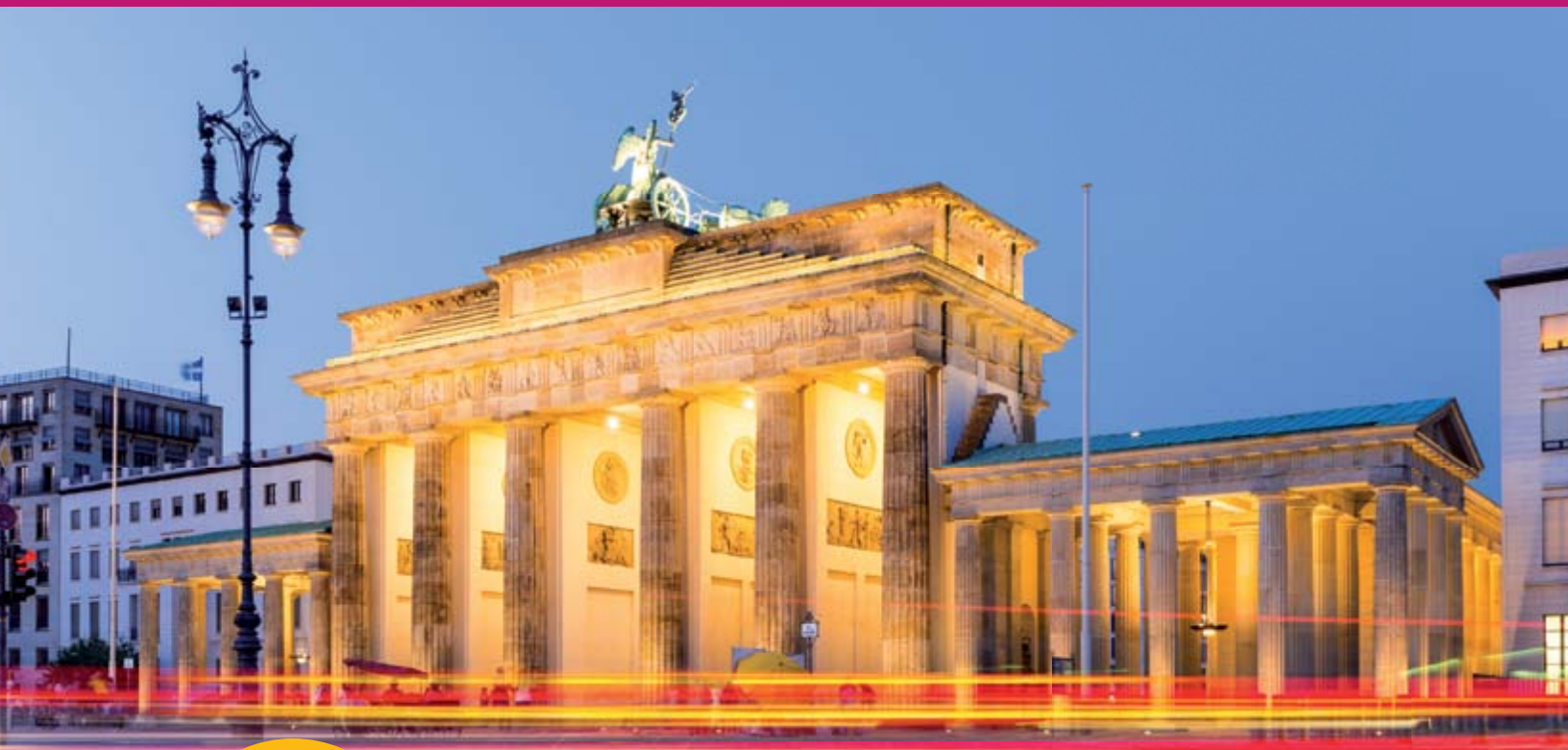

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Harold Baseman, ValSource

A Note of Appreciation

This is a thank you note. It has been a while since I wrote a thank you note, so please bear with me. My wife wrote our wedding thank you notes 38 years ago, and since then, I am pretty sure she has written every other one we've sent. In fact, the last one I wrote was probably 47 years ago.

Here is today's note: *Thank you for the great gift and for helping me celebrate this happy time in my life.* By the way, this is pretty much the same as the notes I sent when I was 13 years old.

What is the *gift*, you ask? It is the gift of providing a place to learn and exchange ideas, to advance our careers, to give back, to improve our industry, and to realize that what we do is important. That what we do helps people, that what we do can be better, and that we can make it better, that we can make a difference, and that we are making a difference.

Our business is the business of providing life-improving drugs to people in need. Our industry is good. But our industry can be better. Just about everything in life can, and therefore, needs to be better. But changing a big industry like ours is a pretty daunting task. As a colleague said at a workshop the other day, "It is easy to say it is hard."

It reminds me of the story of the man walking on the beach. He sees that thousands and thousands of starfish washed up on the beach. In the middle of the pile of starfish a second man is picking up one starfish at a time and throwing it back into the surf. The first man asks the second, "What are you doing?" The second man says, "I am saving the starfish." The first man then says, "You are wasting your time. You'll never be able to save them. There are too many." Upon which the second man picked up a starfish, threw it into the sea, and said, "I saved that one."

The message of the story is that what may seem like an inconsequential effort can make a difference. Collaborating on a task force, participating on a planning committee, serving on an advisory board, giving a presentation, teaching a course, etc., not just helps you and your career but it also helps to improve your industry, your community and the patients you serve.

Here is what I learned from being an active member of PDA for all of these years. This is a big industry that changes very slowly. But it changes. And individuals make a difference. PDA gives you an opportunity to be a person that improves this industry. And improving an industry that improves people's lives is a good thing.

So the real gift is the gift of making us aware that we can make a difference. But with that awareness, we should feel the responsibility to do just that. So, PDA also gives you the opportunity to fulfill that responsibility.

That is the *gift*. But what *happy time*, you ask? Of course, it is the more than 30 really good years being a member of this grand association.

And so to the PDA staff, volunteers, Board members, friends and colleagues who make this association so good and so valuable—keep making a difference.

And thank you once again.

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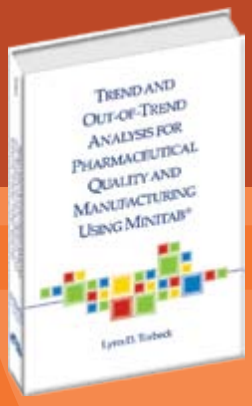

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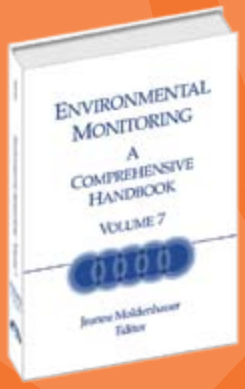

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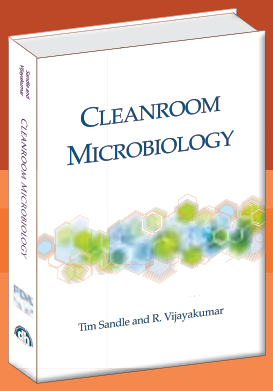

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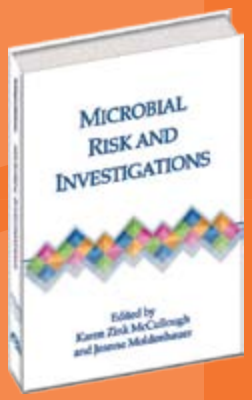

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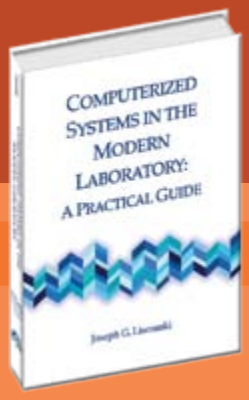

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Stephan Rönninger, PhD, Amgen

Ten Years of ICH Q9 Activities at PDA

We have come a long way in our thinking on ICH Q9: *Quality Risk Management* (QRM) since 2005. At that time, many of us were convinced that ICH Q9 was "just a toolbox." Shortly after its release, PDA developed meetings and training courses on ICH Q9, which helped advance the industry's understanding of the central role QRM plays in everything we do. These gatherings crystallized two critical concepts:

1) The importance of *risk-based* decisionmaking, and
2) QRM should never be used to justify obvious noncompliance or bad behavior

Since those early days, PDA has delved into a number of QRM-related activities resulting in a remarkable list of accomplishment. I want to use this topic as an example to show how you, as a volunteer, can be involved in PDA and make a difference in our industry through collaboration with other industry experts and regulators. Participating in one of these activities will enhance your knowledge and establish new contacts with peers, companies and regulators that you can leverage throughout the rest of your professional career.

First, teams of PDA volunteers developed technical reports supporting the practical implementation of QRM, starting with *Technical Report No. 44: Quality Risk Management for Aseptic Processes.* Then, a series of practical examples were developed under the Paradigm Change in Manufacturing Operations (PCMO®) umbrella for *Technical Report No. 54: Implementation of Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations* and its annexes. Other PDA technical reports addressed QRM and how it relates to technology transfer, temperature-controlled distribution, process validation, and statistical methods. And as a collaborative effort with six industry associations and the EMA, a team of PDA volunteers contributed *Technical Report No. 68: Risk-Based Approach for Prevention and Management of Drug Shortages,* which offers a complimentary resource for the industry. Future technical reports will take QRM principles into account as well.

All of these technical reports were used to develop specialized courses, which can be found in PDA's course catalog.

Outside of PDA's technical reports, many articles in the *PDA Journal of Pharmaceutical Science and Technology* cover risk-based auditing, evaluation of GxP requirements during the product lifecycle and the auditing process itself. Another invaluable publication is the electronic *Risk-Based Compliance Handbook,* available at the PDA Bookstore (www.pda.org/bookstore).

To help you, your companies, and regulators continuously improve on implementing QRM principles, PDA established the QRM Interest Group. The focus of this interest is to implement QRM principles into established quality and manufacturing processes, and support robust and flexible quality system implementation. In addition, the Inspection Trends Interest Group discusses implementation issues identified in inspections with examples of good and bad practices presented by inspectors. I encourage you to join both interest groups and start your own QRM discussions on the PDA Connect® website.

Most PDA signature conferences and workshops continue to offer sessions on QRM ten years later, as do events hosted by PDA's global chapters, notably the Japan and India chapters. I recommend attending any of these to keep up to date on QRM.

The pharma industry faces many challenges with the implementation of QRM principles. QRM is definitely more than just a toolbox; it is an enabler of the Quality System as described in ICH Q10. PDA offers a unique opportunity for members of industry, suppliers, contractors and regulators to informally connect on this important topic and share best practices and sound science.

The author wants to thank PDA staff and volunteers for support, and ***Emma Ramnarine*** *and* ***Jeff Hartman,*** *for their leadership on QRM implementation.*

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If you have any questions, or have any trouble logging in, please contact PDA at connect@pda.org or call 1-301-656-5900.

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Comings and Goings

It is the time of year when often we recognize those who will be moving on and welcome those who will be coming in. In this issue, we highlight a few examples of both here at PDA.

To start, **Hal Baseman** provides a final message to PDA as the volunteer Chair. As Hal points out, he has been a member for 30+ years and knows how important the contributions of the Association's various members are in improving our industry. Hal's tenure as Chair went by remarkably fast, which means it was a great two years. PDA's membership grew, as did the number of attendees and students served and the number of technical documents published. The PDA staff will hardly have time to miss Hal though, before he shows up again at our Training and Research Institute as an instructor for the Aseptic Processing training program. Hal is here so much during the year that I often forget he is not paid staff.

Speaking of PDA Education, **Bob Dana's** "few weeks of service" as a paid staff member is ending almost 11 years later (see Eye on TRI, page 12). He claimed recently that he is going to attempt retirement for the third time, but we shall see. Bob has a been a great colleague. In is first iteration as staff, Bob helped with the technical reports. He and I began the first baby steps to a formalized process of editing and publishing the TRs, which was significantly expanded under Rich Levy in recent years. Bob always had time though to share photos of the snow he was getting in Syracuse or his favorite fishing holes. He also ran our NCAA March Madness pool for a few years, and I signed up just to get his wonderfully written round-by-round updates. Like Hal, I am sure PDA members can expect to see Bob around at our conferences and events, as he is certainly bound to fail once again at retirement. And Bob, if you read this, I'm really sorry for breaking things in your office back in the day!

Not all the "goings" are happy. We were saddened to learn of the passing of **Scott Sutton,** a very strong contributor to the *PDA Letter* as a member of the inaugural Editorial Committee. He will be missed by his colleagues and his family very much. See the tribute to Scott on page 6.

The "comings" include someone who is not a new personality to the staff, but one taking on a new role. **Craig Elliott,** who has been PDA's VP of Finance and CFO, assumes Bob's position as the head of PDA Education (see p. 7 for announcement). It will be an exciting time for Craig and PDA as he strives to take our educational offerings to even new heights.

Martin VanTrieste will be PDA's volunteer chair starting in January. I first got to know Martin about a decade ago at a PDA training on aseptic processing in Las Vegas. And while "what happens in Vegas should stay in Vegas," I can say that whatever Martin tells you about that trip with respect to me is completely untrue. Nevertheless, Martin stood out to me as a highly active and effective PDA member, and he is sure to continue the success of his equally active and effective predecessors.

I also want to highlight a different sort of new arrival: the PDA Letter's first editorial video was released at the end of October and is available under the "multimedia" link on the new PDA Letter online. We leaped right into our first video production, and thanks to extremely user friendly software and equipment, I think we did a pretty good job. Of course, the three members of the PDA Data Integrity Task Force who participated in the video deserve a ton of credit too. I hope everyone gets a chance to watch the video and the second part, which will post in late November. More will definitely follow.

PDA Letter

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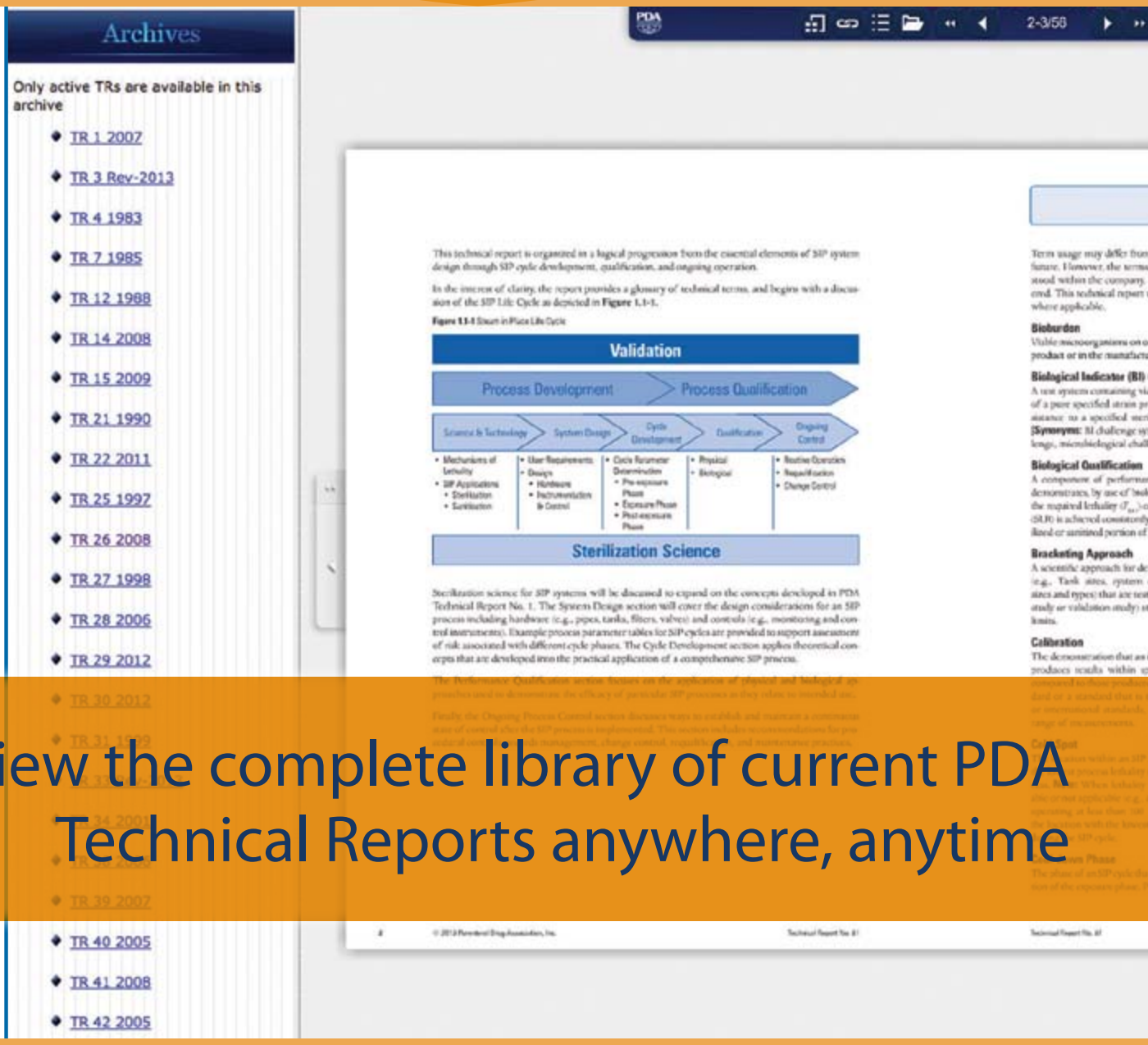

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